

# Psychological Medicine

## Prevalence and risk factors of psychiatric symptoms and diagnoses before and during the COVID-19 pandemic: findings from the ELSA-Brasil COVID-19 Mental Health Cohort.

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<b>Abstract:</b>	<p>Background: There is mixed evidence on increasing rates of psychiatric disorders and symptoms during the COVID-19 pandemic in 2020. We evaluated pandemic-related psychopathology and psychiatry diagnoses and their determinants in the Brazilian Longitudinal Study of Health (ELSA-Brasil) São Paulo Research Center.</p> <p>Methods: Between pre-pandemic ELSA-Brasil assessments in 2008-10 (Wave-1), 2012-2014 (Wave-2), 2016-2018 (Wave-3) and 3 pandemic assessments in 2020 (COVID-19 waves in May-July, July-September, October-December), rates of common psychiatric symptoms, and depressive, anxiety, and common mental disorders were compared using the Clinical Interview Scheduled-Revised (CIS-R) and the Depression Anxiety Stress Scale-21 (DASS-21). Multivariable generalized linear models, adjusted by age, gender, educational level, and ethnicity, identified variables associated with an elevated risk for mental disorders.</p> <p>Results: In 2117 participants (mean age 62.3 years, 58.2% females), rates of common mental disorders and depressive disorders did not significantly change over time, oscillating from 23.5%-21.1%, and 3.3%-2.8%, respectively; while anxiety disorders' rate significantly decreased (2008-10: 13.8%; 2016-18: 9.8%; 2020: 8%). There was a decrease along 3 Wave-Covid assessments for depression (<math>\beta=-0.37</math>, 99.5%CI [-0.50,-0.23]), anxiety (<math>\beta=-0.37</math>, 99.5%CI [-0.48,-0.26]), and stress (<math>\beta=-0.48</math>, 99.5%CI [-0.64,-0.33]) symptoms (all <math>p&lt;0.001</math>). Younger age, female sex, lower educational level, non-white ethnicity, and previous psychiatric disorders were associated with increased odds for psychiatric disorders, whereas self-evaluated good health and good quality of relationships with decreased risk.</p> <p>Conclusion: No consistent evidence of pandemic-related worsening psychopathology in our cohort was found. Indeed, psychiatric symptoms slightly decreased along 2020. Risk factors representing socioeconomic disadvantages were associated with increased odds of psychiatric disorders.</p>

## **Prevalence and risk factors of psychiatric symptoms and diagnoses before and during the COVID-19 pandemic: findings from the ELSA-Brasil COVID-19 Mental Health Cohort.**

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## Abstract

**Background:** There is mixed evidence on increasing rates of psychiatric disorders and symptoms during the COVID-19 pandemic in 2020. We evaluated pandemic-related psychopathology and psychiatry diagnoses and their determinants in the Brazilian Longitudinal Study of Health (ELSA-Brasil) São Paulo Research Center.

**Methods:** Between pre-pandemic ELSA-Brasil assessments in 2008-10 (Wave-1), 2012-2014 (Wave-2), 2016-2018 (Wave-3) and 3 pandemic assessments in 2020 (COVID-19 waves in May-July, July-September, October-December), rates of common psychiatric symptoms, and depressive, anxiety, and common mental disorders were compared using the Clinical Interview Scheduled-Revised (CIS-R) and the Depression Anxiety Stress Scale-21 (DASS-21). Multivariable generalized linear models, adjusted by age, gender, educational level, and ethnicity identified variables associated with an elevated risk for mental disorders.

**Results:** In 2117 participants (mean age 62.3 years, 58.2% females), rates of common mental disorders and depressive disorders did not significantly change over time, oscillating from 23.5%-21.1%, and 3.3%-2.8%, respectively; while anxiety disorders' rate significantly decreased (2008-10: 13.8%; 2016-18: 9.8%; 2020: 8%). There was a decrease along 3 Wave-Covid assessments for depression ( $\beta=-0.37$ , 99.5%CI [-0.50,-0.23]), anxiety ( $\beta=-0.37$ , 99.5%CI [-0.48,-0.26]), and stress ( $\beta=-0.48$ , 99.5%CI [-0.64,-0.33]) symptoms (all  $ps<0.001$ ). Younger age, female sex, lower educational level, non-white ethnicity, and previous psychiatric disorders were associated with increased odds for psychiatric disorders, whereas self-evaluated good health and good quality of relationships with decreased risk.

**Conclusion:** No consistent evidence of pandemic-related worsening psychopathology in our cohort was found. Indeed, psychiatric symptoms slightly decreased along 2020. Risk factors representing socioeconomic disadvantages were associated with increased odds of psychiatric disorders.

## Keywords

COVID-19; pandemic; mental health; depression; anxiety; cohort study.

## Introduction

The pandemic of the Coronavirus Disease 2019 (COVID-19, caused by SARS-CoV-2) may impact worldwide mental health (Xiong *et al.*, 2020). Initial studies from China, where the epidemic started in late-2019, reported high rates of depression, anxiety, and stress symptoms in quarantined communities. These findings were reported not only in COVID-19 patients (Zhang *et al.*, 2020) but also in psychiatric samples (Zhou *et al.*, 2020), health care workers (Huang and Zhao, 2020), and the general population (Gao *et al.*, 2020). A recent systematic review (Xiong *et al.*, 2020) showed high rates of symptoms of depression (14.6% to 48.3%), and anxiety (6.33% to 50.9%) in populations during the pandemic.

However, although these studies raised important concerns on the surge of, possibly, the “next global pandemic” (Mari and Oquendo, 2020), assessments conducted worldwide were mostly focused on symptoms, and not on diagnoses. Moreover, the studies employed convenience, online samples with no prior information of participants’ mental status (Vindegaard and Benros, 2020; Xiong *et al.*, 2020). Thus, due to the absence of longitudinal data, changes compared to pre-pandemic levels were not assessed.

Another issue is that the mental impact of the pandemic in communities from low- and middle-income countries has not been addressed. For instance, female sex, income, educational level, psychiatric comorbidities, and worse physical health have been associated with unfavourable mental health outcomes in these countries (Musliner *et al.*, 2016; Alonso *et al.*, 2018) and might be risk factors in the pandemic. Also, studies in China and developed countries explored whether age, severity of lockdown and disruption of daily activities, physical distancing, chronic diseases, and worries associated with contracting or having severe presentations of COVID-19 were associated with mental outcomes, with mixed findings (Pierce *et al.*, 2020; Prati and Mancini, 2021).

Therefore, there is mixed evidence of worsening psychopathology during the pandemic. Thus, we further examined pandemic-related changes in mental symptoms and diagnoses, and their determinants, in the Brazilian Longitudinal Study of Health (ELSA-Brasil), a well-characterized Latin American cohort. Our aims were threefold:

(1) to compare the rates of psychiatric disorders and changes in symptomatology between pre-pandemic and pandemic assessments. We hypothesized that an increase in psychiatric diagnoses and symptoms would be observed, as previously reported (Vindegard and Benros, 2020);

(2) to assess the overall changes of psychiatric symptomatology during intra-pandemic assessments; likewise, we hypothesized that psychiatric symptoms would increase, according to the literature (Salari and Hosseini-Far, 2020);

(3) to assess whether variables such as age, sex, ethnicity, educational level, clinical and psychiatric comorbidities, exposure to COVID-19, adherence and agreement to physical distancing and other quarantine measures, leisure activities, employment status, and financial impact, would be associated with mental disorders. We hypothesized that female sex, lower educational level, non-white ethnicity and psychiatric comorbidities would be risk factors for mental disorders, as observed in earlier ELSA-Brasil studies (Brunoni *et al.*, 2019; Librenza-Garcia *et al.*, 2020). We also hypothesized that the elderly, people with low physical health, and those with risk factors for severe forms of COVID-19 would be more stressed and thus being at greater risk for developing mental disorders. Moreover, we expected that variables associated with loneliness and stress would be associated with greater mental disorder risk (Killgore *et al.*, 2020), and those associated with leisure and stress-alleviating practices, with decreased risk for mental disorders. Finally, we hypothesized that a greater understanding of the COVID-19 (including hygiene and physical distance behaviors and agreement with the quarantine) would protect from mental illness, as this could decrease the fear of the pandemic (Brooks *et al.*, 2020) and enhance general cooperativeness (i.e., “collective effervescence”, as characterized by Durkheim) (Zumeta *et al.*, 2020).

## Methods

### *Study design*

ELSA-Brasil is a prospective, longitudinal cohort of 15,105 participants from six universities in major Brazilian cities (São Paulo, Rio de Janeiro, Salvador, Belo Horizonte, Vitoria, and Porto Alegre). At its inception, it was the first, largest cohort in Latin America. Its aims were to identify the

clinical and sociodemographic determinants of mortality and of the development of chronic diseases within a population of a low-/middle- income country. It initially aimed to recruit 15,000 out of 52,137 potential participants, stratified by sex, age and occupational category. Recruitment goals were defined by sex (50% each), age (15% aged 35–44, 30% aged 45–54, 40% aged 55–64 and 15% aged 65–74 years) and occupational category (35% of support level, with incomplete elementary school; 35% with high school and 30% with higher education/teaching level). From 16,43 interested participants, 15,821 were pre-enrolled, and gave written consent, responding to an initial pre-interview. Only 716 (4.5%) of them did not complete the baseline examination, achieving a final sample of 15,105 participants. The recruitment goals were fully achieved in all centers (Schmidt *et al.*, 2014).

The cohort began in August 2008, when eligible participants were all active or retired employees of these universities, who were between 35 and 74 years-old, and free of major neurocognitive disorders at enrollment (Aquino *et al.*, 2012; Schmidt *et al.*, 2014). Posterior waves did not recruit new participants. The 1st, 2nd, and 3rd waves occurred in 2008-10, 2012-14, and 2016-18, respectively. During each wave, onsite assessments comprised clinical interviews and examinations, collecting information on sociodemographic variables, clinical history, family history of diseases, lifestyle factors, and anthropometric measurements. Laboratory tests were also collected during the visits (M. I. Schmidt *et al.*, 2014; Aquino *et al.*, 2012).

In 2020, “COVID-19 wave” assessments were carried out only by the São Paulo research center. Data collected during 2020 consisted of 3 online assessments (c1, c2, and c3 waves, respectively, performed between May 18th to July 18th; July 20th to September 30rd; and October 1st to December 22nd). The most severe lockdown measures in São Paulo started on March 22nd, 2020 and continued through July 10th, 2020 (Quarentena, n.d.); therefore, the c1 wave corresponds to the 8th to 16th quarantine weeks; the c2 wave corresponds to an exponential increase of deaths and cases in Brazil, with some flexibility on quarantine measures adopted by the end of September. and the c3 wave corresponds to a moderate decrease in the rate of daily deaths and cases and greater quarantine relaxation measures in Brazil.

This study was approved by the Local Ethics Committee at the University Hospital, University of São Paulo and is reported according to the STROBE guidelines (von Elm *et al.*, 2007). All patients provided electronic informed consent for participation in the study.

### *Participants*

Participants in the São Paulo center are active or retired public servants from the University of São Paulo, which remained physically closed from March 20th, 2020 until the end of that year, with most activities being performed virtually, except for essential healthcare and research.

The study was advertised in the university newspapers and social media. All participants enrolled at the São Paulo research center who completed the 3rd wave and could answer online surveys (i.e., internet availability and having a smartphone, tablet, or personal computer) were eligible and initially contacted via their personal or work emails using the RedCap platform (Harris *et al.*, 2009). If they did not reply to three emails sent at weekly intervals, we additionally tried to contact them via three text messages (or via telephone calls if mobile phone numbers were not available) also sent at weekly intervals. Telephonic interviews were done if participants explicitly requested them due to difficulties in understanding or completing online questionnaires.

### *Variables*

#### Outcome variables

Psychiatric diagnoses were assessed using the validated Brazilian version of the Clinical Interview Schedule-Revised, CIS-R (Lewis *et al.*, 1992; Nunes *et al.*, 2011), a structured interview for measurement and diagnosis of current non-psychotic psychiatric morbidity in the community. CIS-R has poor sensitivity for diagnosing mental disorders, which might slightly underestimate the rates of psychiatric disorders, although its specificity is high (Brugha *et al.*, 1999). Due to its length, it was applied only during the first COVID-19 wave assessment.



The CIS-R includes the assessment of 14 symptoms and 13 psychiatric disorders based on the International Classification of Disease, 10th edition (ICD-10). The CIS-R domains are somatic complaints, fatigue, concentration and forgetfulness, sleep disturbance, irritability, worry about physical health, depression, depression ideas, worry, anxiety, phobias, panic attacks, compulsions, and obsessions. Scores for each section range from 0 to 4 (except the score for depressive ideas that range from 0 to 5), therefore the total score ranges from 0 to 57. A symptom is present if the corresponding section score is  $\geq 2$ .

The relevant symptoms are grouped to form, with accessory questions and based on an algorithm following ICD-10 diagnostic criteria, the following diagnoses: mild depressive episode without (F32.00) and with somatic syndrome (F32.01); moderate depressive episode without (F32.10) and with somatic syndrome (F32.11); severe depressive episode (F32.2); agoraphobia without (F40.00) and with panic disorder (F40.01); social anxiety disorder (SAD, F40.1); specific (isolated) phobias (F40.2); panic disorder (PD, F41.0); general anxiety disorder (GAD, F41.1); and obsessive-compulsive disorder (OCD, F42.9). Finally, F32.xx diagnoses were collapsed in “depressive disorders”, and F40.xx and F41.xx diagnoses were collapsed in “anxiety disorders”.

Moreover, the total CIS- R score is obtained by adding the scores of all 14 (non-binarized) symptoms. Based on this score, a diagnosis of common mental disorder (CMD) (CIS-R>11) is operationally defined (Lewis *et al.*, 1992). Finally, the CIS-R score of depressive symptoms was calculated by summing up symptom scores of depression, depression ideas, fatigue, concentration/forgetfulness and sleep disturbance as used previously (Khandaker *et al.*, 2018; Brunoni *et al.*, 2020).

Due to the quarantine measures, it was impossible to collect CIS-R data onsite, as done in previous waves. Therefore, we used an electronic, self-applied CIS-R format that was identical to the one used in clinical interviews. Importantly, the online version was self-applied, whereas the onsite version was read by trained personnel. Thus, uncontrolled differences in answering engagement could have occurred. However, previous studies have already validated and compared an electronic, self-

applied CIS-R version with its standard format, showing that the electronic version presents valid and reliable performance (Lewis *et al.*, 1988) (Lewis, 1994). In fact, a validation study showed that the performance of both versions was similar (Head *et al.*, 2013). In that study, no differences between mean scores in 12 of the 14 symptom scores were observed. Moreover, both versions presented similar accuracy in diagnosing psychiatric disorders (Head *et al.*, 2013).

During the COVID-19 wave assessments (but not previously), we applied the Depression, Anxiety, and Stress Scales-21 (DASS-21) (Henry and Crawford, 2005), which is a self-reported set of three scales that measure symptoms of depression, anxiety and stress. The scores of DASS-21 range from 0 to 63 and the symptoms' subscores range from 0 to 21. Higher scores indicate greater severity.

#### Exposure variables

Sociodemographic data from the 1st wave of the ELSA-Brasil, such as birth year, sex, educational level (presence or absence of university degree), and self-reported ethnicity (White, Brown, Black, Indigenous, Yellow) were used. Height (in cm) was collected onsite during the 3rd wave; therefore, we used this information that we judged less prone to bias than self-reported height, even considering eventual height changes occurring between 2016-18 and 2020. Current participant weight (in kg) was assessed in the c1 wave survey. Body mass index (BMI) was obtained dividing weight by squared height (kg/m<sup>2</sup>). Obesity was defined as BMI  $\geq 30$ .

Using additional information collected in the c1 wave survey, we codified another 24 exposure variables assessing participant home situation (which we labeled loneliness related variables), comorbidities, distress caused by the pandemic, behaviors related to it, and factors related to being exposed to the virus (Table 1) (for more details, see Supplementary Material).

(Table 1)

#### *Analysis*

At the inception of our study, there was no good-quality data available on the rate of psychiatric disorders during the COVID-19 pandemic. Therefore, we did not formally estimate a sample size based on *a priori* rates, but invited all eligible participants from the last onsite (3rd) wave. Statistical significance was set under an alpha threshold of 0.005. Accordingly, confidence intervals are reported in the 99.5% threshold (99.5% CI). Missing data were imputed as described in the Supplementary Material. For our first aim, we compared the rate of collapsed depressive disorders, anxiety disorders, OCD, and CMD between the pre-pandemic and pandemic assessments. We did not use information from Wave 2, which did not assess the complete CIS-R. A Cochran's Q test for paired data was used to compare rates between waves, and post-hoc analyses were conducted applying pairwise McNemar tests. Also related to our first aim, we used the continuous scores of CIS-R to assess changes in depressive and total symptomatology during these assessments. For wave 2, we used only data from CIS-R depressive scores.

For our second aim, we used the DASS to assess symptoms of depression, anxiety, and stress, and overall symptoms during the 3 assessments performed in 2020. Symptom changes over assessments were evaluated using linear models, with time as the independent variable and DASS scores as the dependent variables.

For our third aim, we performed generalized linear models (GLMs, binomial family, logit link) using the iteratively reweighted least squares (IRLS) method. One model was run for each exposure and outcome variables separately, and all models were adjusted by the covariates sex, age, educational level, and ethnicity. We also analyzed the influence of these covariates separately. The outcome variables were the collapsed depressive disorders, anxiety disorders, and CMD.

## **Results**

### *Participants*

Out of 4191 eligible participants from the 2016-2018 wave, data of 2117 participants (51.7%) could be included in our analyses. Reasons for non-inclusion were unwillingness to participate, impossibility of making contact, and deaths (Figure 1). The included vs. non-included sample had a

significantly higher percentage of women, were younger, with a higher educational level and lower rates of psychiatric symptoms and diagnoses (Table S1). In the included sample, 450 (21.3%) presented CMD, 169 (8%) presented anxiety disorders, and 60 (2.8%) presented depressive disorders (Table 2).

(Figure 1)

(Table 2)

*Aim 1: Prevalence of diagnoses and symptomatology between pre-pandemic and pandemic assessments*

We found no significant differences within the same sample in rates of CMD, and ICD-10 based diagnoses of depressive disorders and OCD between the 1st (2008-2010), 3rd (2016-2018), and the COVID (May-July 2020) waves (Figure 2). Anxiety rates decreased over time (1st wave: 13.8%, 3rd wave: 9.8%, COVID wave: 8.0%;  $Q=50.58$ ,  $p<0.001$ ), with significant differences between the 1st and the 3rd waves ( $\chi^2=19.7$ ,  $p_{adj}<0.001$ ), and the 1st and the COVID waves ( $\chi^2=45.8$ ,  $p_{adj}<0.001$ ) (Figure 2A).

CIS-R measurements of total symptom scores and depression scores did not significantly change over the assessments of the 1st (2008-2010), 3rd (2016-2018), and COVID (May-July 2020) waves (Figure 2B, Table S2).

(Figure 2)

*Aim 2: Changes in symptomatology during the pandemic in 2020*

Significant decreases in DASS-21 scores were observed for total symptom (c3 vs. c1:  $\beta=-1.22$ , 99.5%CI [-1.58,-0.86],  $p<0.001$ ), depression (c3 vs. c1:  $\beta=-0.37$ , 99.5%CI [-0.50,-0.23],  $p<0.001$ ), anxiety (c3 vs. c1:  $\beta=-0.37$ , 99.5%CI [-0.48,-0.26],  $p<0.001$ ) and stress scores (c3 vs c1:

$\beta=-0.48$ , 99.5% CI [-0.64,-0.33],  $p<0.001$ ) over time, although no significant changes between the 2nd and 3rd covid wave assessments were observed (Figure 2B, Table S2).

*Aim 3: Association between exposure variables and mental disorders*

Regarding age, sex, ethnicity and college degree; for CMD, being older and having completed college were associated with decreased risk, whereas non-white ethnic groups and women had increased risk (Figure 3, Table S3). For depressive disorders, having a college degree was a protective factor (Figure S1, Table S3). For anxiety disorders, older age, and having a college degree were protective factors (Figure S2, Table S3).

Multivariable models adjusted by the abovementioned covariates showed, for CMD, a protective association for describing good physical health, describing maintained or improved quality of close relationships, and for alignment with institutional, municipal and state measures. Conversely, associations that presented increased risk were having more than one chronic disease, being concerned about one's income during the pandemic, having had COVID-19 symptoms, describing elevated distress levels during the quarantine, and presenting mental disorders (Figure 3, Table S3).

(Figure 3)

Multivariable analyses for depressive disorders showed that having had COVID-19 symptoms, and presenting mental disorders were associated with increased risk, whereas no factors were associated with decreased risk (Figure S1, Table S3).

Multivariable analyses for anxiety disorders showed that having had COVID-19 symptoms, describing elevated distress levels during the quarantine, presenting mental disorders, being concerned about one's income during the pandemic, and having more than one chronic disease were associated with increased risk; whereas describing good physical health was associated with decreased risk (Figure S2, Table S3).

## Discussion

Our first aim was to compare the prevalence of mental disorders in 2117 participants in the ELSA-Brasil São Paulo study center between two pre-pandemic assessments (2008-2010 and 2016-2018) and the initial phases of the COVID-19 pandemic (May-July 2020). Contrary to our initial hypothesis, the rates of observed psychiatric disorders were not significantly different from previous assessments. Likewise, overall mental symptoms and depressive symptoms did not significantly change over time. In fact, a slight decrease in anxiety disorders was found. We believe that a lower rate in the COVID-19 assessment was partially observed due to a decrease in the rate of generalized anxiety disorder (GAD), which has a time criterion duration of 6 months or more. As the assessment was performed in May-June and the pandemic started in March 2020, possibly some participants considered that anxiety symptoms only started after the pandemic, even if they were present before (recall bias). In fact, additional analyses changing the time criterion for 2 weeks or more (for all waves) revealed similar rates of anxiety disorders among all waves (data not shown).

As for our second aim, we performed 3 longitudinal assessments from May to December 2020 to evaluate changes in depression, anxiety, and stress scores. Also contrary to our hypothesis, these symptoms were either maintained or slightly decreased during the pandemic. Notwithstanding, our findings are in line with other studies. In a prospective study in the UK with more than 70,000 people examined during the lockdown period in the first semester of 2020, depressive and anxiety symptoms were moderately high at the beginning of lockdown measures but decreased rapidly during the next 20 weeks (Fancourt *et al.*, 2020). A longitudinal study of three Dutch case-control cohorts, with well-characterized psychiatric disorders, employed data from approximately 1,500 subjects and assessed depressive symptoms, anxiety, worry, and loneliness. People without psychiatric disorders showed a slight increase in symptoms during the pandemic, whereas those with the greatest previous mental health burden tended to exhibit a slight symptom decrease (Pan *et al.*, 2020). In a longitudinal assessment in Ireland with over 1000 participants (Hyland *et al.*, 2020), rates of GAD were actually higher in 2019 compared to 2020, and further decreased during the pandemic. In contrast, other studies showed an increase in mental health symptomatology. In a US study comparing matched (but

different) adult samples before and during the pandemic, the prevalence of probable depression rose from 8.5% to 27.8% (Ettman *et al.*, 2020). In a UK study with 48,486 respondents, the prevalence of mental health symptoms rose from 24.3% in 2016-2018 to 37.8% in April 2020, further decreasing to 31.9% in June 2020. Interestingly, those with a pre-existing depressive disorder did not experience an increase in mental symptoms (Daly *et al.*, 2020).

Regarding the third aim, we confirmed, in agreement with our hypothesis, that female sex, non-white ethnicity and lower educational level were risk factors for CMD. These characteristics reflect socio-economic disadvantages and have been observed as risk factors for incident and persistent depression in a previous ELSA-Brasil study (Brunoni *et al.*, 2019)(Xiong *et al.*, 2020). People with lower educational levels also experienced more psychiatric symptoms (Xiong *et al.*, 2020), possibly due to accumulating workload and the impossibility of stopping working and/or working from home, generating distress. In a UK study, non-white ethnicities (Proto and Quintana-Domeque, 2021) also experienced higher mental distress, in line with our findings. Interestingly, meta-analyses did not find an association between these factors and psychiatric symptoms (Prati and Mancini, 2021; Wu *et al.*, 2021), although meta-analyses are usually underpowered for such analyses. Although we expected that increased age - due to stress of presenting a severe form of COVID-19 - would be associated with psychiatric disorders, what was found was that people younger than 60 years-old presented increased risk. Interestingly, this was also observed in a systematic review (Xiong *et al.*, 2020) and could be explained by factors such as the impossibility of staying at home due to employment, lower financial support and more domestic activities (e.g., taking care of children).

We also analysed several other variables corrected for age, sex, ethnicity, and educational level. Psychiatric comorbidity was a risk factor for presenting CMD, reflecting the greatest mental burden associated with these patients, as demonstrated previously (Pan *et al.*, 2020), and emphasizing the need of maintaining psychiatric care during the pandemic. Regarding clinical comorbidities, exposure variables associated with increased rates of CMD include having had COVID-19 symptoms (tests were not widely available and there were stay-at-home instructions for mild cases when data were collected, so no confirmatory assessment was done), and presenting one or more chronic diseases, while self-reported good physical health was associated with decreased risk. This suggests

that participants with greater susceptibility of presenting a severe case of COVID-19 were those more likely to develop psychiatric disorders. Conversely, obesity, being a smoker, and alcohol abuse were not associated with significant increased risk, which could be explained by inadequate perception or awareness of these variables as risk factors for severe COVID-19.

High or very high self-reported distress levels (evaluated by questions such as the distress associated with staying at home, avoiding contact with people, refraining from meeting friends and relatives, and others) and concerns about income were associated with increased odds of presenting mental disorders. However, stress alleviating practices were not associated with decreased risk, or increased domestic chores with increased risk. This possibly reveals that activities at home during the quarantine are less important for modifying mental health than initially hypothesized by researchers (Pfefferbaum and North, 2020). Notwithstanding, maintaining or improving relationship quality (e.g., using social apps) were associated with decreased risk. In fact, feelings of loneliness might have been attenuated via social media and electronic apps of mental health support; also, activities that could be done at home were not stopped (Williams *et al.*, 2021).

Interestingly, agreement with federal measures (which almost reached statistical significance) or institutional/municipal/state measures were independently associated with lower odds of having mental disorders. This is surprising as the Brazilian president adopted a radical anti-quarantine attitude, promoting mass rallies and systematically undermining the severity of the pandemic (The Lancet, 2020a), whereas the institutional/municipal/state instances adopted a pro-quarantine/pro-science perspective. Possibly, political identity and ideology are protective factors since they are cognitive shortcuts to support shared beliefs and similar choices (Pereira *et al.*, 2020), decreasing the mental burden in choosing between difficult options.

Finally, healthcare workers presented no increased odds for psychiatric disorders. Importantly, healthcare professionals from our sample work at the University Hospital, which only treated cases of moderate severity, while severe cases of COVID-19 were transferred to a tertiary university hospital. This might have reduced the stress overload of our sample of healthcare workers who worked in relatively less stressful conditions. Also, those with higher risk of COVID-19 morbimortality were kept away from work. Interestingly, a recent systematic review showed that their



rates of depression and anxiety during the pandemic are neither necessarily higher than the general population, nor increased compared to pre-pandemic levels (Liu *et al.*, 2020).

### *Limitations*

First, the mean age of our sample was around 60 years-old; therefore our results might not be applicable to younger populations. Second, approximately only half of the eligible sample answered our survey. This is in line with cohorts in the UK and the Netherlands that presented response rates in online assessments during the pandemic of 25-55% (Pan *et al.*, 2020; Pierce *et al.*, 2020; Evandrou *et al.*, 2021). These modest rates probably occurred due to the need of rapid organization for collecting timely data during the pandemic. In fact, initial response survey rates are typically around 30% and increase only after many contacts, which usually take several months (Fincham, 2008). As we aimed to capture the mental health of the sample in a short period, we only extended our recruitment for two months. Third, although the differences between responders and non-responders were mostly small, a higher educational level was observed in responders, which probably reflects the spectrum of digital literacy within the sample. Notwithstanding, inherent issues of our sample are its relatively old age and low digital literacy.

### *Generalizability*

We used a well-defined cohort, which decreased the risk of selection bias, enhancing the external validity and generalizability of the findings, in contrast with snowball sampling. However, our sample is occupational and not population-based, being composed of public servants of the University of São Paulo. Their income, which is on average higher than the national income, was essentially unaffected during the pandemic. Thus, the rates of psychiatric disorders and symptoms should not be considered as nationally representative, but rather interpreted in the context of longitudinal changes within the same sample and associated risk factors. Nonetheless, even representing a fraction of the Brazilian population, our findings are interesting for similar samples

from other developing countries that continually struggle with huge socio-economic inequalities, with vulnerable safety nets, and which have some of the highest COVID-19 excess mortality rates (The Lancet, 2020b), and for mega-cohort analyses exploring whether the observed exposure variables are of worldwide importance or country-dependent, which is important to develop comprehensive early intervention strategies in different contexts.

## **Conclusion**

During a strict lockdown period in São Paulo in May-July 2020, no major changes in psychiatric disorders and symptoms have been detected compared to earlier assessments in 2008-2010 and 2016-2018. Moreover, symptoms of depression, anxiety, and stress decreased along 3 assessments performed from May to December in 2020. Risk factors representing socioeconomic disadvantages and predictors associated with distress and loneliness were associated with increased odds of psychiatric disorders. As further quarantine periods may extend into the future, our findings are important to identify subgroups at elevated risk. Finally, follow-up surveys are necessary to identify trajectories of these disorders during the pandemic and post-pandemic phases.

(Please also check the **Supplementary Material** for further information)

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Academy of Medical Sciences (Newton Advanced Fellowship), and the International Health Cohort Consortium (IHCC).

## Conflicts of Interest

None to disclose.

## Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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**Table 1. Exposure variables**

Exposure Variables	Observations
<i>Sociodemographic variables</i>	Data from 2008-2010 - 1st ELSA-Brasil wave
Older than 60-years old	Based on Date of Birth
Non-white ethnicity	Based on self-reported ethnicity
College degree	--
Female sex	--
<i>Loneliness related variables</i>	Data from 2020 - COVID-19 wave
Relationship quality	Classified into worsened, improved or maintained according to changes in relationship quality with family and friends, in a Likert scale
Living alone	--
Married	--
Living with people > 60 years-old	--
Living with children in school age	--
<i>Comorbidities</i>	Data from 2020 - COVID-19 wave
Alcohol Abuse	Present if women reported taking >1 dose/day and men >2 doses/day during a given week
Active smoker	--
Chronic Diseases	Self-reported presence of one or more of Diabetes, High blood pressure, heart attack, stroke, asthma, chronic bronchitis, or other chronic conditions (*)
Obesity	Body Mass Index > 30, based on self-reported height (2016-2018 3rd wave) and self-reported weight (2020 COVID-19 wave)
Physical Health	Self evaluation of physical health in comparison to others of the same age, in a Likert Scale. Classified into not very good physical health or good physical health.
Previous Mental Disorders	Self-reported presence of one or more mental disorders
<i>Behaviours related to COVID-19</i>	Data from 2020 - COVID-19 wave
In agreement with institutional, municipal and state measures	Participants filled out how much they agreed with measures against COVID-19 adopted by each government instance, in a Likert Scale. "In agreement" was established when the participant completely agreed to measures.
In agreement with federal measures	
Adequately informed about COVID-19	Present when participant reported having high level information about COVID-19 symptomatology, transmissibility and preventive hygiene methods
Adopting adequate preventive measures	Present if participant adhered to recommendations to reduce risk of COVID-19 transmission (**).
Obedience to quarantine	Present if participant adhered to "stay-at-home" recommendations during the quarantine, such as leaving their home only when extremely necessary
<i>COVID-19 exposure</i>	Data from 2020 - COVID-19 wave
Being a healthcare worker	--

<b>Being retired</b>	--
<b>Working from home</b>	--
<b>Working at the office</b>	--
<b>Presented COVID-19 symptoms</b>	Present when at least one COVID-19 symptom was reported (***)
<b><i>Distress related variables</i></b>	
Data from 2020 - COVID-19 wave	
<b>Concerns about income</b>	Classified as concerned or not concerned according to the score of three questions evaluating concerns about income changes during the pandemic
<b>Stress relieving practices</b>	Classified in frequent, sporadic and no stress relieving practices based on number and frequency of stress-relieving activities performed per week, in a Likert scale
<b>Self-reported distress</b>	Classified from 1st to 4th quartiles of Self-reported distress according to how much distress they felt about determined situations, in a Likert scale (****)
<b>Increased domestic chores</b>	Present when participant reported doing more chores at home during the pandemic period than they did before

(\*) If a chronic disorder was described, we assessed whether it could be considered as one.

(\*\*) Recommendations were: washing hands frequently, removing shoes before entering their homes, wearing masks, covering mouth and nose when sneezing, refraining from shaking hands or kissing when greeting somebody, washing store bought packages before use, and using alcohol gel.

(\*\*\*) COVID-19 symptoms were: fever, cough shortness of breath, sore throat, fatigue (Physical), loss/decreased sense of smell, loss/decreased sense of taste.

(\*\*\*\*) Situations were: staying home, avoiding close contact with other people or crowds, refraining from meeting friends, refraining from meeting other family members, having postponed or canceled important events, having postponed or canceled trips, and hearing news of the COVID-19 pandemic.



**Table 2. Characteristics of the study sample.**

	Common Mental Disorder			
	Total	Absent	Present	P
	2117	1667	450	
<b>Sociodemographic variables</b>				
Age, mean (SD)	62.32 (8.41)	63.08 (8.57)	59.54 (7.17)	<b>&lt;0.001</b>
> 60 years-old, n (%)	1210 (57.2)	1011 (60.6)	199 (44.2)	<b>&lt;0.001</b>
Educational level, n (%)				<b>&lt;0.001</b>
Below High School	23 (1.1)	16 (1.0)	7 (1.6)	
High School	49 (2.3)	36 (2.2)	13 (2.9)	
Incomplete College	788 (37.2)	578 (34.7)	210 (46.7)	
College degree	1257 (59.4)	1037 (62.2)	220 (48.9)	
Self-reported ethnicity, n (%)				<b>&lt;0.001</b>
Black	224 (10.7)	153 (9.3)	71 (16.0)	
Mixed (brown)	361 (17.3)	260 (15.8)	101 (22.7)	
White	1394 (66.7)	1137 (69.1)	257 (57.8)	
Yellow	102 (4.9)	89 (5.4)	13 (2.9)	
Indigenous	9 (0.4)	6 (0.4)	3 (0.7)	
Non-white ethnicity, n (%)	696 (33.3)	508 (30.9)	188 (42.2)	<b>&lt;0.001</b>
Female gender, n (%)	1233 (58.2)	916 (54.9)	317 (70.4)	<b>&lt;0.001</b>
<b>Distress related variables</b>				
Self-reported distress level, n (%)				<b>&lt;0.001</b>
Low (1st quartile)	514 (26.5)	463 (30.2)	51 (12.5)	
Medium (2nd quartile)	534 (27.5)	443 (28.9)	91 (22.3)	
High (3rd quartile)	416 (21.5)	325 (21.2)	91 (22.3)	
Very high (4th quartile)	475 (24.5)	300 (19.6)	175 (42.9)	
Stress relieving practices, n (%)				0.403
None	163 (7.7)	123 (7.4)	40 (8.9)	
Sporadic	1131 (53.5)	886 (53.2)	245 (54.4)	
Frequent	821 (38.8)	656 (39.4)	165 (36.7)	
Concerns about income, n (%)	1210 (62.1)	894 (58.1)	316 (77.6)	<b>&lt;0.001</b>
Increased domestic chores, n (%)	1145 (58.3)	897 (57.7)	248 (60.3)	0.368
<b>Loneliness related variables</b>				
Living with child in school age, n (%)	371 (19.1)	276 (17.9)	95 (23.4)	0.016

Living with > 60 year-old, n (%)	704 (33.3)	570 (34.2)	134 (29.8)	0.088
Married, n (%)	1270 (63.9)	1034 (65.8)	236 (57.0)	<b>0.001</b>
Relationship quality, n (%)				<b>&lt;0.001</b>
Worsened	458 (23.4)	325 (21.0)	133 (32.4)	
Maintained	964 (49.2)	794 (51.3)	170 (41.4)	
Improved	537 (27.4)	429 (27.7)	108 (26.3)	
Living alone, n (%)	334 (16.8)	266 (16.9)	68 (16.4)	0.868
<i>Comorbidities</i>				
Previous mental disorders, n (%)	551 (26.0)	330 (19.8)	221 (49.1)	<b>&lt;0.001</b>
Good physical health, n (%)	677 (34.2)	600 (38.3)	77 (18.6)	<b>&lt;0.001</b>
Obesity, n (%)	582 (27.5)	430 (25.8)	152 (33.8)	<b>0.001</b>
Chronic diseases, n (%)				<b>0.002</b>
None	1102 (52.1)	897 (53.8)	205 (45.6)	
One	672 (31.7)	521 (31.3)	151 (33.6)	
More than one	343 (16.2)	249 (14.9)	94 (20.9)	
Active tobacco smoker, n (%)	176 (8.9)	123 (7.9)	53 (12.8)	<b>0.002</b>
Alcohol abuse, n (%)	251 (11.9)	206 (12.4)	45 (10.0)	0.197
<i>Behaviors related to COVID-19</i>				
Obedience to quarantine, n (%)	1595 (81.3)	1249 (80.5)	346 (84.2)	0.105
Adopting adequate preventive measures, n (%)	981 (49.5)	770 (49.1)	211 (51.1)	0.516
Adequately informed about COVID-19, n (%)	1094 (55.2)	888 (56.6)	206 (49.9)	0.016
In agreement with federal measures, n (%)	943 (48.1)	761 (49.1)	182 (44.3)	0.093
In agreement with municipal and state measures, n (%)	1069 (54.5)	866 (55.9)	203 (49.4)	0.022
<i>COVID-19 exposure</i>				
Presented COVID-19 symptoms	620 (29.3)	397 (23.8)	223 (49.6)	<b>&lt;0.001</b>
Working at the office, n (%)	343 (16.2)	271 (16.3)	72 (16.0)	0.953
Working from home, n (%)	798 (37.7)	622 (37.3)	176 (39.1)	0.52
Being retired, n (%)	491 (23.2)	403 (24.2)	88 (19.6)	0.046
Working on healthcare, n (%)	108 (5.1)	81 (4.9)	27 (6.0)	0.392
<i>Other CIS-R diagnoses</i>				
Anxiety disorders, n (%)	169 (8.0)	29 (1.7)	140 (31.1)	<b>&lt;0.001</b>
Depressive disorders, n (%)	60 (2.8)	0 (0.0)	60 (13.3)	<b>&lt;0.001</b>

P values are highlighted in bold when a significance of 0.005 was achieved in t-tests or Chi-squared tests for continuous and categorical variables, respectively. Exposure variables are described in Table 1 and in the supplementary materials.

**Figure 1. ELSA-BRASIL São Paulo center flow chart.**

CIS-R; Clinical Interview Schedule-Revised. DASS; Depression, Anxiety, and Stress Scale. The full version of the CIS-R was applied in all waves, except for Wave 2, when only questions regarding depressive symptoms were applied.

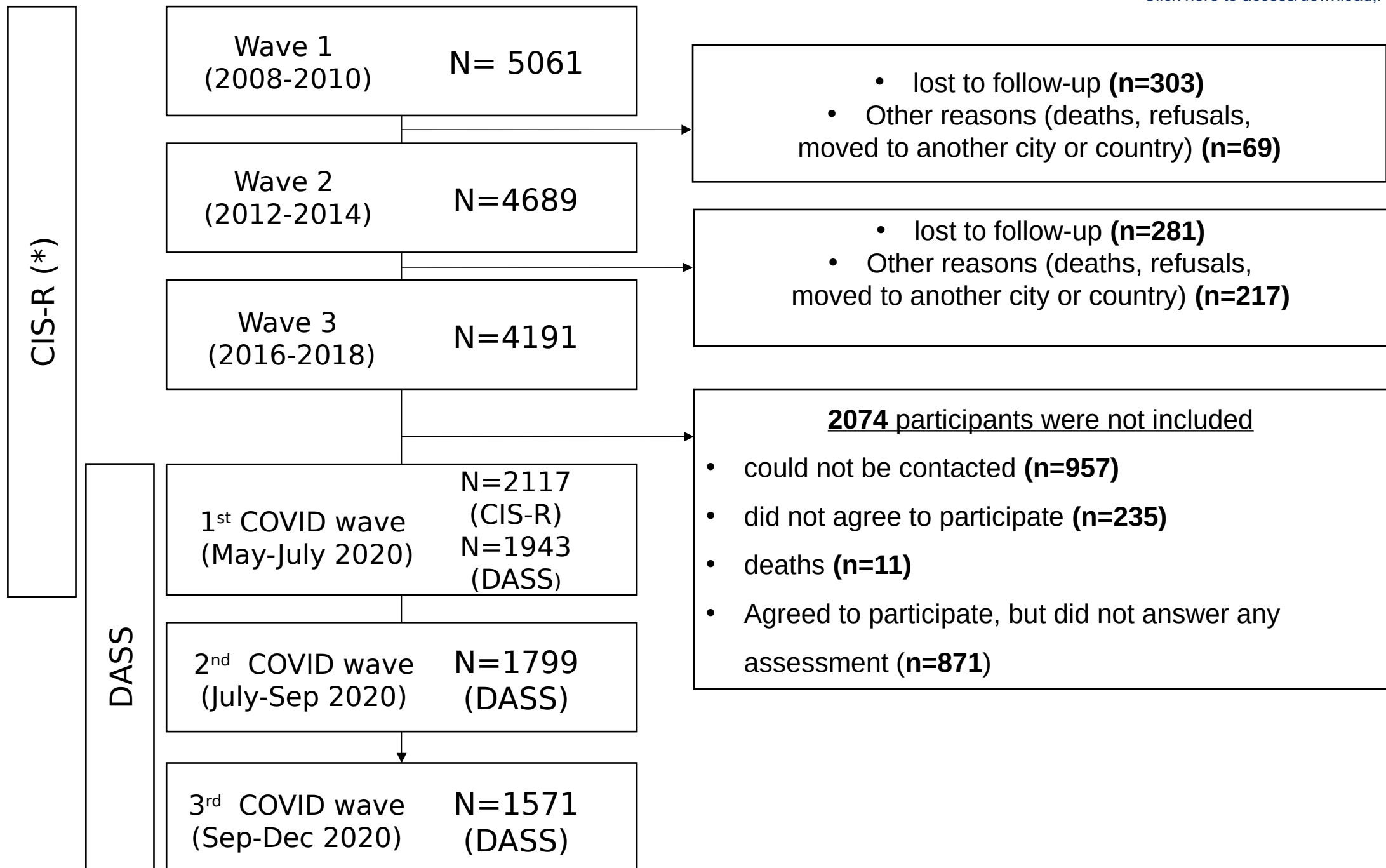
**Figure 2. Rates of psychiatric disorders and CIS-R total symptom scores at Wave 1 (2008-2010), Wave 2 (2012-2014), Wave 3 (2016-2018) and 1st COVID wave (May-July 2020), and DASS depression, anxiety, stress and overall total mental scores at 1st (May-July 2020), 2nd (July-September 2020) and 3rd (October-December 2020) COVID waves.**

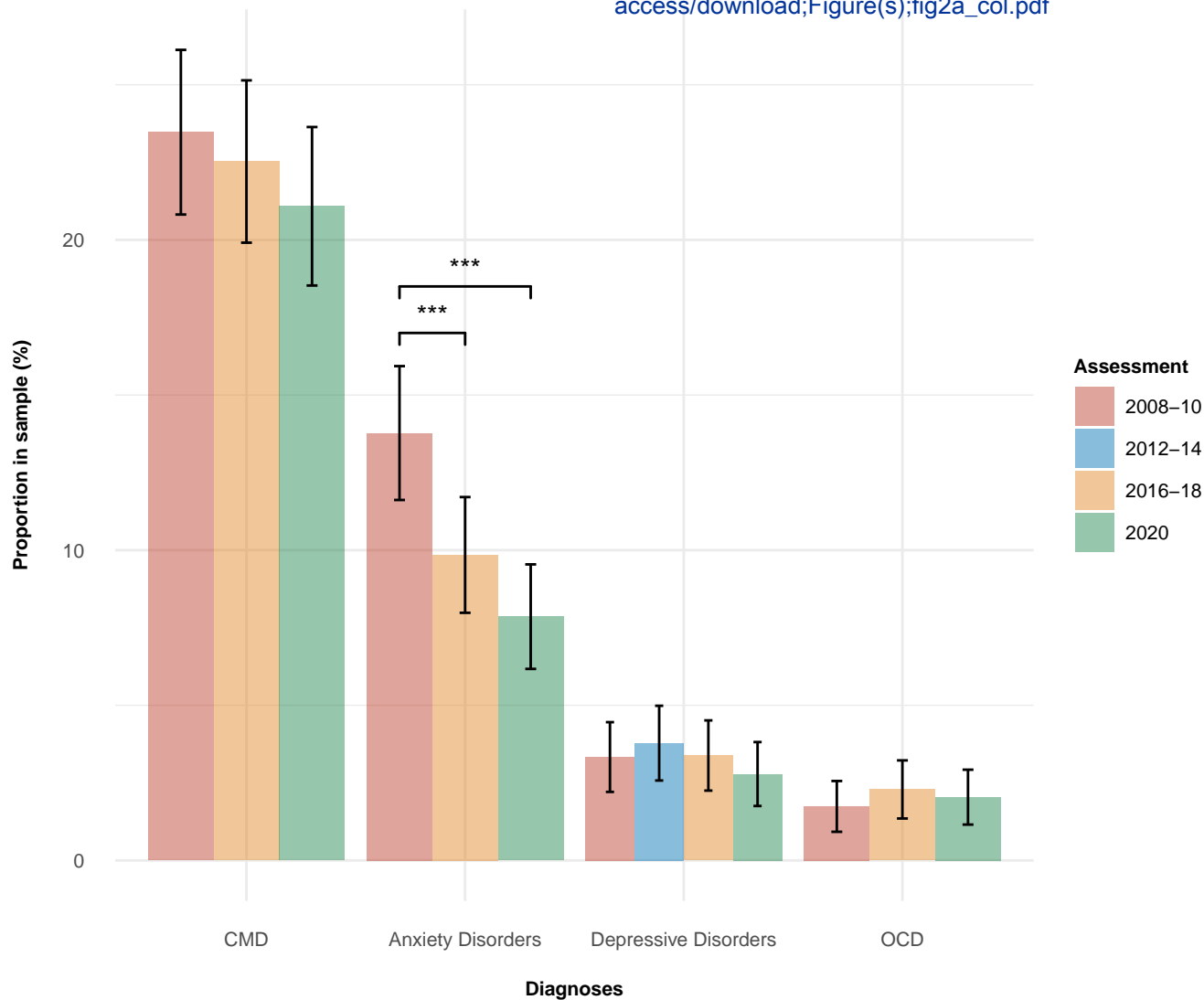
(A) For psychiatric disorders, significant changes were only observed for anxiety disorders. (B) For symptoms, DASS scores decreased along COVID waves. Diagnoses were evaluated using the Clinical Interview Scheduled - Revised and are based on the International Classification of Diseases, 10th version (ICD-10). F32.xx diagnoses were collapsed in “depressive disorders”, and F40.xx and F41.xx diagnoses were collapsed in “anxiety disorders”. Common Mental Disorders is a CIS-R based classification that describes people with relevant mental symptoms (CIS-R score >11). CIS-R (Clinical Interview Schedule-Revised). DASS; Depression, Anxiety, and Stress Scale. Error bars represent 99.5% Confidence Intervals.

**Figure 3. Association of several exposure variables with common mental disorders.**

Association was measured using Odds Ratios (ORs) and 99.5% Confidence Intervals. ORs > 1 and <1 indicate variables associated with increased and decreased risk, respectively. Models were adjusted by age, sex, ethnicity and educational level.

Figure1





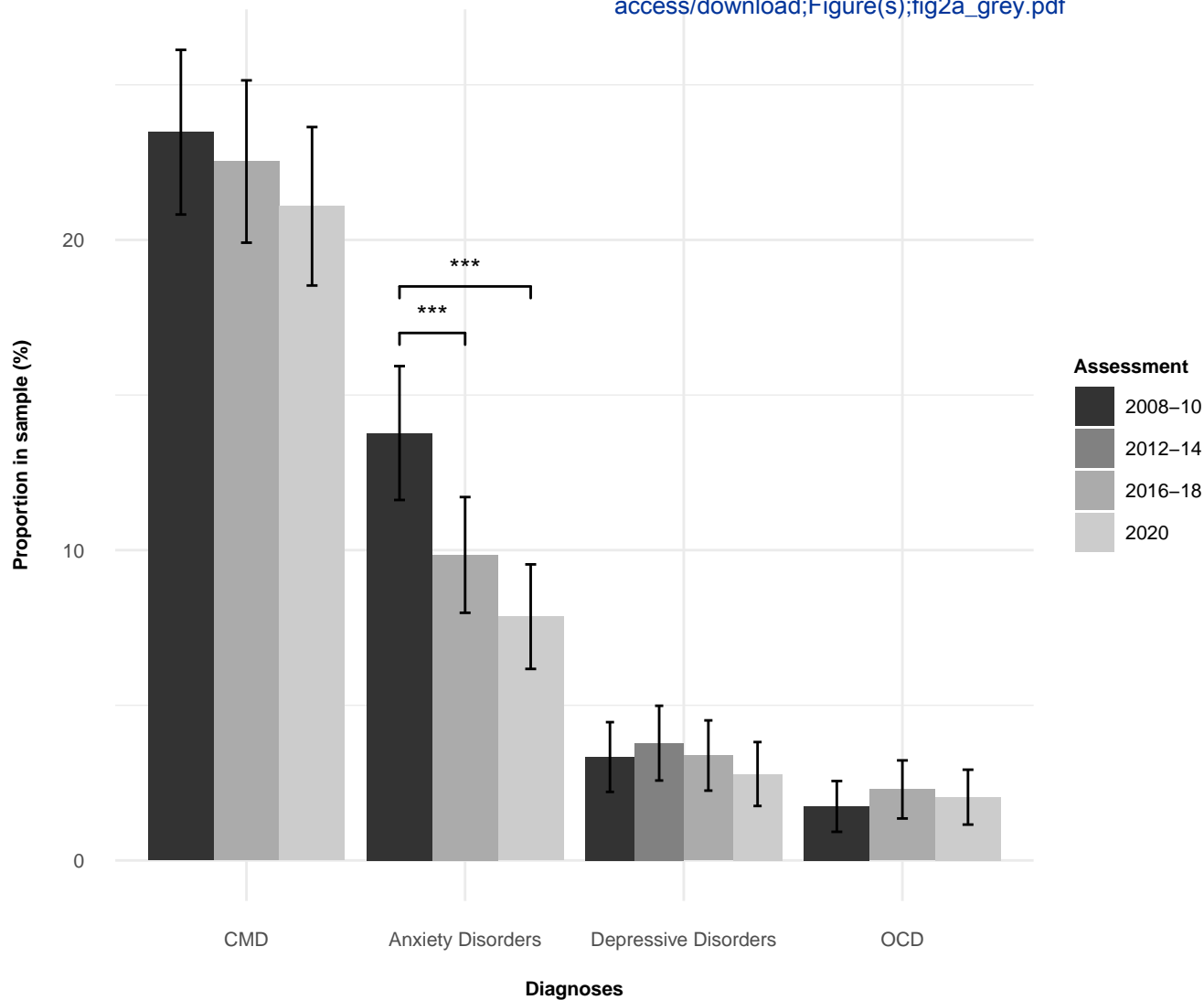


Figure2B with color

Mean scores over time for CIS-R and DASS

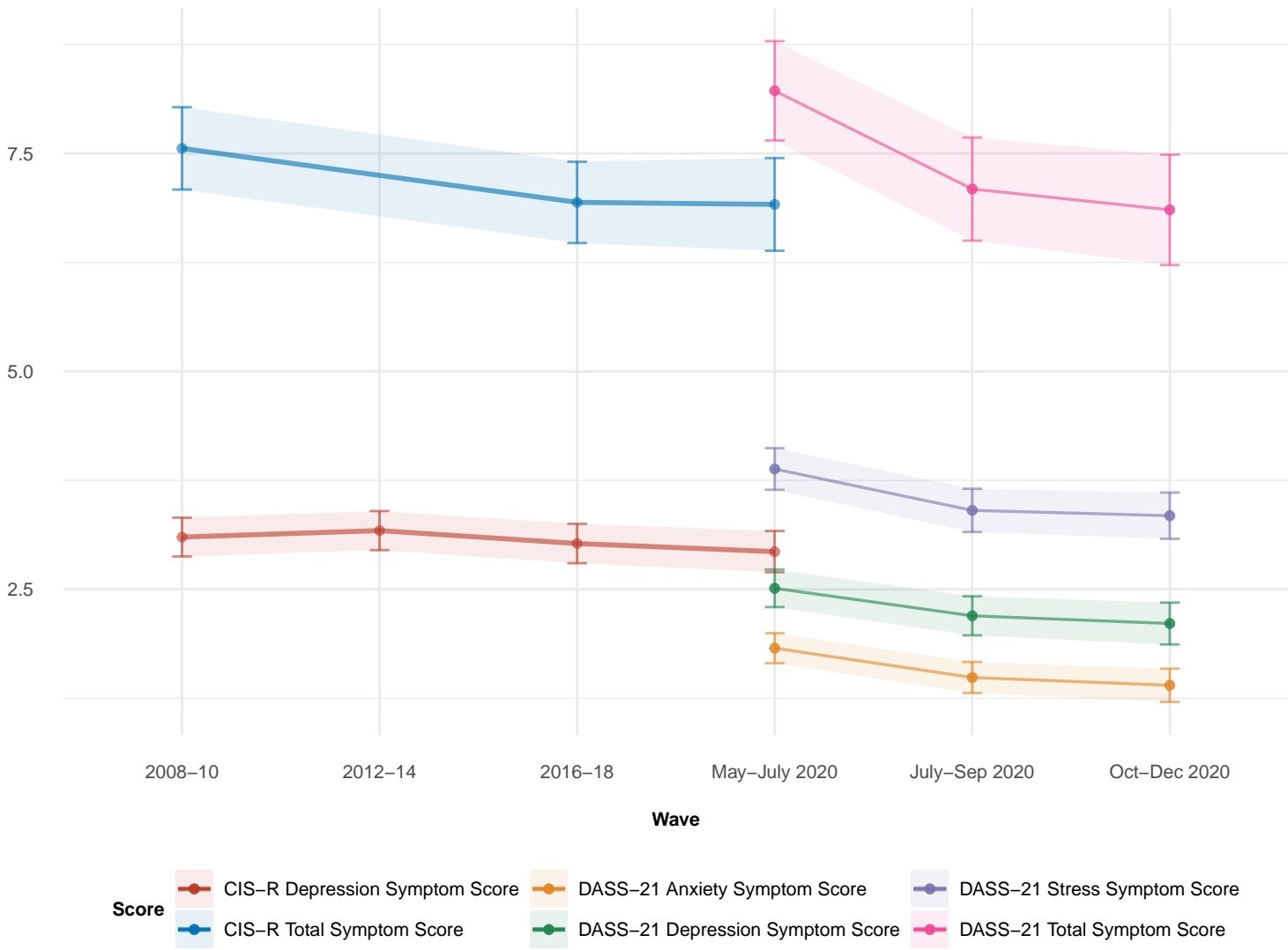
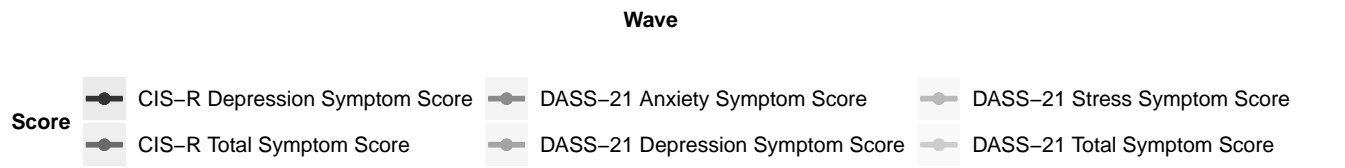
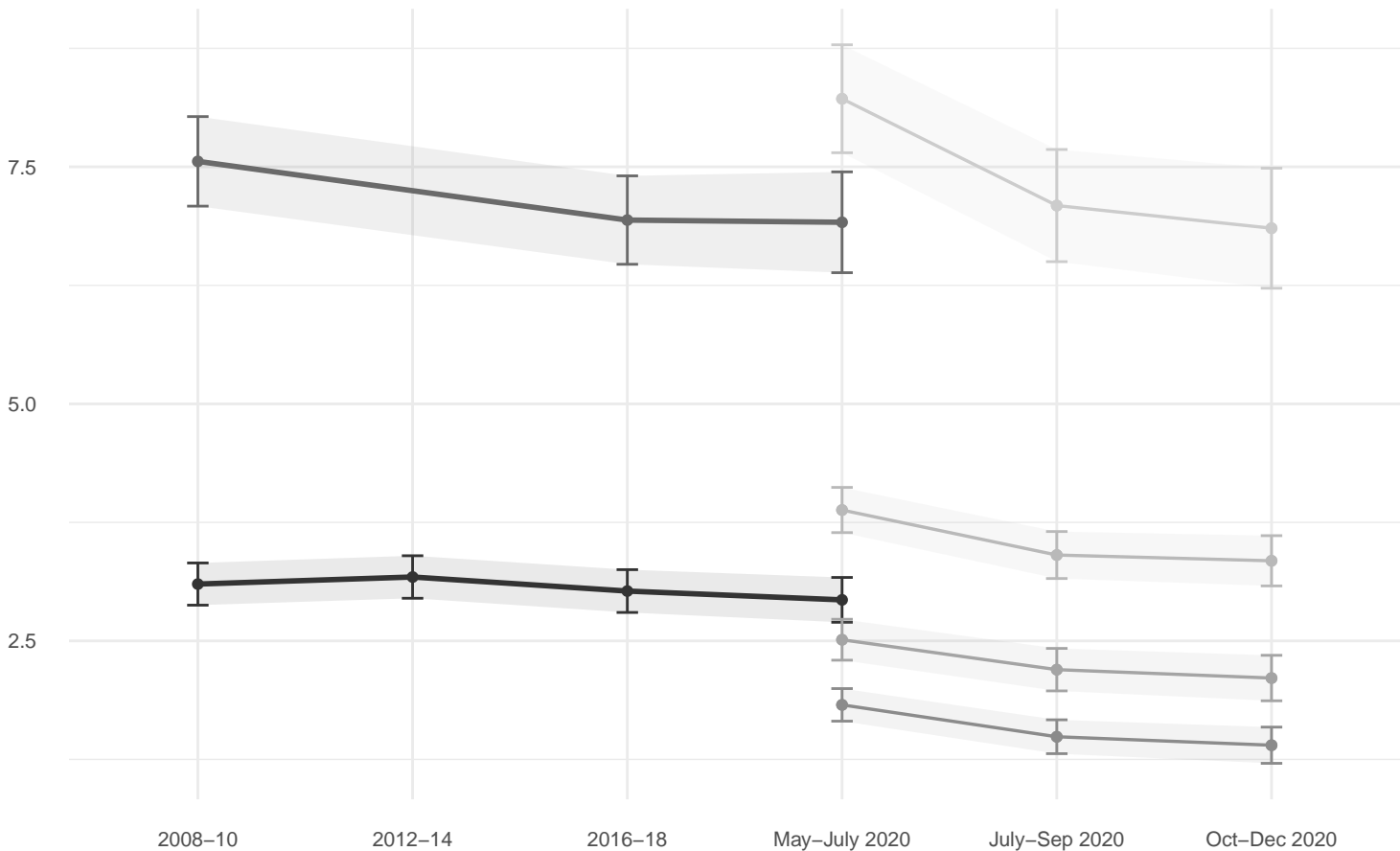
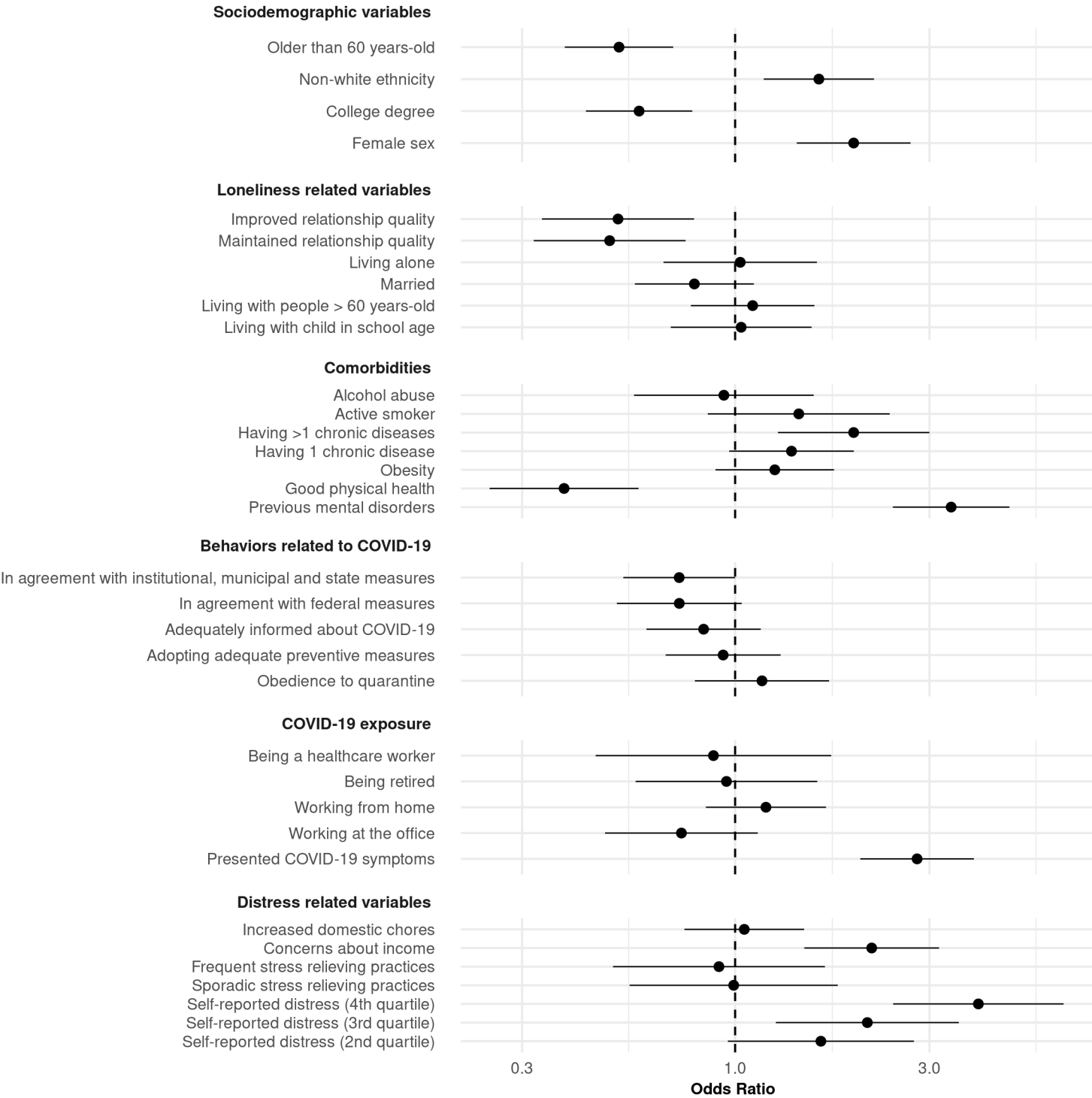




Figure2B grey





## Supplementary Material

### Supplementary methods

#### Composite variables

Variables used in the multivariate analyses were devised from the applied questionnaire in the c1 wave (performed between May and July, 2020). These variables are explained below:

#### **SOCIODEMOGRAPHIC VARIABLES**

1. *Older than 60 years-old*
2. *Non-white ethnicity*
3. *College degree*
4. *Female sex*

#### **LONELINESS RELATED VARIABLES**

1. Relationship quality:
  - *Worsened relationship quality* (reference for comparison)
  - *Improved relationship quality*
  - *Maintained relationship quality*

For relationship quality, the following variables were assessed:

- How did your relationship with your family change during the pandemic?
- How did your relationship with your friends change during the pandemic?

Each variable ranges from: *Considerably Worsened* (1) to *Considerably Improved* (5). We summed these variables and then dichotomized in tertiles. The upper tertile was *Improved*, the middle tertile was *Maintained*, the lower tertile was *Worsened*.

2. *Living alone*
3. *Married*
4. *Living with people > 60 years-old*
5. *Living with child in school age*

#### **COMORBIDITIES**

1. *Alcohol abuse*

Alcohol abuse was defined as >1 dose/day for women and >2 doses/day for men during a given week.

2. *Active smoker*

3. *Presence of chronic diseases*

- *No chronic disease* (reference for comparison)
- *Having 1 chronic disease*
- *Having >1 chronic disease*

For chronic diseases, participants were asked whether they had ever been diagnosed with one of the following:

- Diabetes
- Arterial Hypertension
- Myocardial Infarction
- Stroke
- Asthma
- Chronic Bronchitis
- Autoimmune Disease
- Other chronic diseases
- None

4. *Obesity*

We assessed current participant weight, and used baseline height data. Body Mass Index (BMI) was calculated as weight divided by the square of height. Obesity was defined as  $BMI \geq 30$ .

5. *Good physical health*

Participants were asked how they considered their physical health compared to people their own age, the answer ranged from *very bad* (1) to *very good* (5) in a likert scale. The score was then binarized in *Good physical health* (5) and *Not very good physical health* (1-4).

6. *Previous mental disorders*

Participants were asked if they have previously received one of the following diagnoses:

- Schizophrenia
- Depression
- Generalized Anxiety Disorder
- Obsessive Compulsive Disorder
- Personality Disorder
- Bipolar Disorder
- Substance Use Disorder
- Eating Disorder
- Other Psychiatric diagnosis

- None

## BEHAVIOURS RELATED TO COVID-19

1. *In agreement with federal measures*
2. *In agreement with institutional, municipal and state measures*

Participants were assessed with 4 questions asking if they agree with measures against COVID-19 from the institution they work in, from their municipality, from their state and from the federal government. Variables ranged from *Totally disagree (1)* to *Totally agree (5)*.

We observed positive correlation between the three first aforementioned variables. They were summed up and binarized, the upper part was *In agreement with institutional, municipal and state measures*.

Federal government answers had negative correlation with all the others. This variable was binarized, and the upper part was *In agreement with federal measures*.

3. *Adequately informed about COVID-19*

Three questions were elaborated regarding participants' knowledge about COVID-19. The questions were related to three main aspects:

- Symptomatology
- Transmissibility
- Prevention hygiene

All questions were measured through a scale ranging from 0 to 2 ('*not informed*' to '*well informed*', respectively). The scores of the three variables were summed up. Finally participants were classified as being *Inadequately informed* (0- 5) or *Adequately informed* (6) about COVID-19.

4. *Adopting adequate preventive measures*

Participants were assessed regarding the frequency they adopted the following recommendations to reduce risk of COVID-19 transmission:

- Washing hands frequently
- Removing shoes before entering home
- Wearing masks
- Covering mouth and nose when sneezing
- Refraining from shaking hands or kissing when greeting somebody
- Washing store bought packages before use
- Using alcohol gel

Answers ranged from never (0) to always (4), they were summed up and dichotomised into *Not adopting adequate preventive measures* (0-26) and *Adopting adequate preventive measures* (27-28).

5. *Obedience to quarantine*

*Obedience to quarantine* was considered when participants answered to be following recommendations to stay at home during the quarantine period. This was assessed through a binary variable: *staying at home vs. not staying at home*.

## COVID-19 EXPOSURE

### 1. *Being a healthcare worker*

Participants who reported to be working during the pandemic period answered in which sector they were working in. The participant was allowed to chose one or more options among 9 activities: 1) Medical and hospital area (Direct patient care); 2) Medical and hospital area (Supporting activities); 3) Public security; 4) Cleaning; 5) Supply jobs; 6) Food jobs; 7) Journalism; 8) Research; 9) Other(s).

Options 1 and 2 were considered '*Being a healthcare worker*'.

### 2. *Being retired*

### 3. *Working from home*

### 4. *Working at the office*

Participants who were not retired were assessed concerning where they were working. If they reported working exclusively from home, they were considered *Working from home*, otherwise *Working at the office*.

### 5. *Presented COVID-19 symptoms*

Participants were asked whether they presented symptoms related to the COVID-19 disease since the beginning of the pandemic crisis in Brazil. Following symptoms were assessed:

- Fever
- Cough
- Shortness of breath
- Sore throat
- Fatigue (Physical)
- Loss of smell
- Decreased sense of smell
- Loss of taste
- Decreased sense of taste

## DISTRESS RELATED VARIABLES

### 1. *Increased domestic chores*

Domestic chores were assessed by the following question: "In the last 30 days, your domestic chores were: More than usual (3); Same as usual (2); Less than usual (1); I don't know or does not apply (0). The score was binarized and participants who answered More than usual (3) were categorized as having *Increased domestic chores*.

### 2. *Concerns about income*

Concerns on income were assessed by 3 questions:

- Are you concerned about your family's financial situation in the next few months?

- Are you concerned about your family's food security in the next few months?
- Are you concerned about an income decrease in the next few months?.

Participant's answers ranged from Very concerned (3) to Mildly concerned (1).

The variables were summed up and then dichotomized; the higher scores ( $\geq 8$ ) were defined as having *Concerns about income*.

### 3. *Stress relieving practices*

- *No Stress relieving practices* (reference for comparison)
- *Sporadic stress relieving practices*
- *Frequent stress relieving practices*

Stress alleviating practices during the quarantine period was assessed through 16 options ranging from 1 to 4 ('I did not practice'; '1/2x per week'; '3/4x per week'; '5/7x per week') and the option 'does not apply'. The following practices were evaluated:

- Meditation/mindfulness
- Deep breathing techniques
- Pray or join prayer groups
- Gardening activities
- Physical activities indoor
- Arts and/or crafts
- Read books/magazines
- Writing texts, poetry, chronicles, on notebooks etc
- Watch movies, TV series, youtube videos
- Play video game
- Play musical instruments or singing
- Listen to music
- Taking care of pets
- Online psychotherapy (Skype or other platforms)

The average of the applicable variables was then calculated and the final score was dichotomized in the following tertiles: *frequent, sporadic or no stress relieving practices*

### 4. *Self-reported distress*

- *Self-reported distress (1st quartile)* (reference for comparison)
- *Self-reported distress (2nd quartile)*
- *Self-reported distress (3rd quartile)*
- *Self-reported distress (4th quartile)*

Stress under quarantine was assessed through 7 questions with answers ranging from 1 to 5, concerning how stressful it has been to:

- Stay at home
- Avoid contact
- Stop meeting friends
- Stop meeting relatives
- Cancel important events
- Cancel vacations or travel
- Follow news about the pandemic

The sum was then divided in quartiles defined in *first* (7-15), *second* (16-21), *third* (22-26) and *fourth* (27-35).

### Missing data

Missing scores for participants were imputed using multiple imputation by chained equations (MICE) (Buuren, 2010), a method which estimates missing values by using a series of regressions of non-missing values. A model is fit for each of the datasets created using MICE, and the final performance is reported as an average of all models. This method is commonly used for longitudinal, outcome variables (Liao *et al.*, 2014). Data from 1943, 1799 and 1571 participants were available at c1 (May-July, 2020), c2 (July-September, 2020) and c3 (October-December, 2020). Missing scores were imputed using the same variables from our questionnaire which were used to create the composite exposure variables. DASS models used to assess longitudinal variation of symptom scores were then evaluated in the data frames created by MICE and reported results are the pooled effects of the models (Figure 3, Table S3).

At c1, data from 2117 participants who had completed CIS-R were available. Out of these, 174 participants (8.2% of sample) did not complete the questionnaire that was sent in parallel with CIS-R to evaluate exposure variables. This data was considered to be missing at random and imputed using MICE. Results from multivariate models were obtained by pooling results from models for each generated data frame, and are reported in Figures 4, S1 and S2, and Table S2.



## Supplementary results

### Differences between responders and non-responders

**Table S1.** Comparison of responders and non-responders of Wave-Covid.

	N	Overall	Non-Responders	Responders	P-Value
<b>Socio-economic</b>					
Age		63.2 ± 8.8	64.1 ± 8.9	62.3 ± 8.4	<0.001
Educational Level					<0.001
	Bellow High School	275 (6.4)	252 (11.6)	23 (1.1)	
	High School	309 (7.2)	260 (11.9)	49 (2.3)	
	Incomplete College	1719 (40.0)	931 (42.7)	788 (37.2)	
	University Degree	1994 (46.4)	737 (33.8)	1257 (59.4)	
Gender					<0.001
	Male	1914 (44.5)	1030 (47.2)	884 (41.8)	
	Female	2383 (55.5)	1150 (52.8)	1233 (58.2)	
Self-reported Ethnicity					<0.001
	Black	580 (13.7)	356 (16.6)	224 (10.7)	
	Mixed (Brown)	889 (21.0)	528 (24.6)	361 (17.3)	
	White	2538 (59.9)	1144 (53.2)	1394 (66.7)	
	Yellow	191 (4.5)	89 (4.1)	102 (4.9)	
	Indigenous	41 (1.0)	32 (1.5)	9 (0.4)	
<b>CIS-R Diagnoses</b>					
Depressive Disorders					0.093
	0	4126 (96.0)	2082 (95.5)	2044 (96.6)	
	1	171 (4.0)	98 (4.5)	73 (3.4)	
Anxious Disorders					0.002
	0	3637 (84.7)	1809 (83.0)	1828 (86.5)	
	1	657 (15.3)	371 (17.0)	286 (13.5)	
Obsessive Compulsive Disorder					0.803
	0	4197 (97.7)	2131 (97.8)	2066 (97.6)	
	1	100 (2.3)	49 (2.2)	51 (2.4)	
Common Mental Disorder					0.012
	0	3262 (75.9)	1619 (74.3)	1643 (77.6)	
	1	1035 (24.1)	561 (25.7)	474 (22.4)	

Comparison between responders and non-responders using t-test for continuous variables and  $\chi^2$ -tests for categorical variables. Socioeconomic data reported from wave 1 (age based on date of birth), and CIS-R scores from wave 3 (collected between 2016-2018) was used for comparisons.

**Table S2.** Models for CIS-R symptom and DASS-21 scores over the course of the pandemic

	$\beta$	99.5%CI	P
<b>CIS-R Total Symptom</b>			
3rd vs. 1st	-0.62	(-1.34, 0.05)	0.012
c1 vs. 1st	-0.64	(-1.31, 0.08)	0.009
<b>CIS-R Depression</b>			
2nd vs. 1st	0.07	(-0.25, 0.39)	0.513
3rd vs. 1st	-0.07	(-0.39, 0.24)	0.516
c1 vs. 1st	-0.17	(-0.48, 0.15)	0.142
<b>DASS-21 Total Symptom</b>			
c2 vs. c1	<b>-1.08</b>	<b>(-1.44, -0.71)</b>	<b>&lt;0.001</b>
c3 vs. c1	<b>-1.22</b>	<b>(-1.58, -0.86)</b>	<b>&lt;0.001</b>
c3 vs. c2	-0.14	(-0.50, 0.22)	0.275
<b>DASS-21 Stress</b>			
c2 vs. c1	<b>-0.46</b>	<b>(-0.61, -0.30)</b>	<b>&lt;0.001</b>
c3 vs. c1	<b>-0.48</b>	<b>(-0.64, -0.33)</b>	<b>&lt;0.001</b>
c3 vs. c2	-0.03	(-0.18, 0.12)	0.614
<b>DASS-21 Depression</b>			
c2 vs. c1	<b>-0.29</b>	<b>(-0.43, -0.15)</b>	<b>&lt;0.001</b>
c3 vs. c1	<b>-0.37</b>	<b>(-0.50, -0.23)</b>	<b>&lt;0.001</b>
c3 vs. c2	-0.08	(-0.21, 0.06)	0.115
<b>DASS-21 Anxiety</b>			
c2 vs. c1	<b>-0.33</b>	<b>(-0.44, -0.22)</b>	<b>&lt;0.001</b>
c3 vs. c1	<b>-0.37</b>	<b>(-0.48, -0.26)</b>	<b>&lt;0.001</b>
c3 vs. c2	-0.04	(-0.15, 0.07)	0.270

c1 = first assessment of wave-covid, performed between May-July, 2020 . c2 = wave-covid second contact, performed between July-September, 2020. c3 = wave-covid third contact, performed between October-December, 2020. Significant comparisons with  $p < 0.005$  are highlighted in bold.

**Table S3.** Association between exposure variables and diagnoses from CIS-R.

Exposure Variables	Common Mental Disorder			Anxiety Disorders			Depressive Disorders		
	OR	99.5% CI	P	OR	99.5% CI	P	OR	99.5% CI	P
<b>Sociodemographic variables</b>									
Female sex	<b>1.95</b>	<b>(1.42-2.7)</b>	<b>&lt;0.001</b>	1.41	(0.88-2.26)	0.042	1.84	(0.82-4.16)	0.035
College degree	<b>0.58</b>	<b>(0.43-0.78)</b>	<b>&lt;0.001</b>	<b>0.52</b>	<b>(0.33-0.81)</b>	<b>&lt;0.001</b>	<b>0.41</b>	<b>(0.19-0.88)</b>	<b>0.001</b>
Non-white ethnicity	<b>1.61</b>	<b>(1.18-2.19)</b>	<b>&lt;0.001</b>	1.28	(0.8-2.04)	0.135	1.94	(0.92-4.09)	0.013

Older than 60 years-old	<b>0.52</b>	<b>(0.38-0.7)</b>	<b>&lt;0.001</b>	<b>0.48</b>	<b>(0.3-0.76)</b>	<b>&lt;0.001</b>	0.61	(0.28-1.29)	0.064
Distress related variables									
Self-reported distress (1st quartile)	ref								
Self-reported distress (2nd quartile)	1.62	(0.96-2.75)	0.01	1.5	(0.66-3.41)	0.168	0.89	(0.22-3.56)	0.803
Self-reported distress (3rd quartile)	<b>2.11</b>	<b>(1.26-3.54)</b>	<b>&lt;0.001</b>	<b>2.61</b>	<b>(1.23-5.52)</b>	<b>&lt;0.001</b>	1.66	(0.43-6.45)	0.284
Self-reported distress (4th quartile)	<b>3.95</b>	<b>(2.44-6.4)</b>	<b>&lt;0.001</b>	<b>2.93</b>	<b>(1.36-6.27)</b>	<b>&lt;0.001</b>	2.42	(0.7-8.43)	0.044
No stress relieving practices	ref								
Sporadic stress relieving practices	0.99	(0.55-1.79)	0.969	1.05	(0.44-2.54)	0.873	1.29	(0.31-5.36)	0.613
Frequent stress relieving practices	0.91	(0.5-1.66)	0.668	1.1	(0.45-2.68)	0.768	1.29	(0.3-5.48)	0.62
Concerns about income	<b>2.16</b>	<b>(1.48-3.17)</b>	<b>&lt;0.001</b>	<b>2.03</b>	<b>(1.11-3.72)</b>	<b>0.001</b>	2.64	(0.9-7.76)	0.012
Loneliness related variables									
Increased domestic chores	1.05	(0.75-1.48)	0.667	1.03	(0.62-1.72)	0.858	1.43	(0.63-3.23)	0.214
Living with child in school age	1.03	(0.7-1.54)	0.809	0.96	(0.49-1.88)	0.855	0.75	(0.27-2.1)	0.434
Living with people > 60 years-old	1.1	(0.78-1.57)	0.425	0.99	(0.58-1.69)	0.967	0.72	(0.29-1.8)	0.308
Married	0.79	(0.57-1.11)	0.054	1.34	(0.79-2.25)	0.118	0.71	(0.32-1.56)	0.22
Worsened relationship quality	ref								
Maintained relationship quality	<b>0.49</b>	<b>(0.32-0.76)</b>	<b>&lt;0.001</b>	0.59	(0.33-1.04)	0.009	0.42	(0.17-1.06)	0.009
Improved relationship quality	<b>0.52</b>	<b>(0.34-0.79)</b>	<b>&lt;0.001</b>	0.62	(0.33-1.15)	0.03	0.42	(0.15-1.16)	0.017
Living alone	1.03	(0.67-1.59)	0.85	0.66	(0.31-1.39)	0.11	1.84	(0.75-4.55)	0.057
Comorbidities									
Previous mental disorders	<b>3.39</b>	<b>(2.44-4.71)</b>	<b>&lt;0.001</b>	<b>3.93</b>	<b>(2.44-6.33)</b>	<b>&lt;0.001</b>	<b>6.15</b>	<b>(2.66-14.2)</b>	<b>&lt;0.001</b>
Good physical health	<b>0.38</b>	<b>(0.25-0.58)</b>	<b>&lt;0.001</b>	<b>0.43</b>	<b>(0.23-0.8)</b>	<b>&lt;0.001</b>	0.41	(0.15-1.11)	0.012
Obesity	1.25	(0.9-1.75)	0.06	1.21	(0.75-1.98)	0.262	1.12	(0.5-2.48)	0.701
Not having any chronic disease	ref								
Having 1 chronic disease	1.38	(0.97-1.96)	0.011	1.34	(0.79-2.3)	0.12	1.4	(0.61-3.25)	0.258
Having >1 chronic diseases	<b>1.95</b>	<b>(1.27-3)</b>	<b>&lt;0.001</b>	<b>2.36</b>	<b>(1.31-4.28)</b>	<b>&lt;0.001</b>	1.55	(0.56-4.27)	0.225
Active smoker	1.43	(0.86-2.4)	0.048	1.82	(0.96-3.43)	0.008	2.03	(0.67-6.15)	0.067
Alcohol abuse	0.94	(0.56-1.56)	0.725	0.83	(0.37-1.85)	0.516	0.47	(0.09-2.56)	0.212
Behaviors related to COVID-19									
Obedience to quarantine	1.16	(0.8-1.7)	0.261	1.04	(0.6-1.81)	0.845	1.2	(0.46-3.14)	0.594
Adopting adequate preventive measures	0.93	(0.68-1.29)	0.557	1	(0.63-1.6)	0.993	0.52	(0.23-1.19)	0.027
Adequately informed about COVID-19	0.84	(0.61-1.16)	0.121	0.84	(0.52-1.35)	0.295	0.87	(0.38-1.97)	0.62
In agreement with federal measures	0.73	(0.51-1.04)	0.012	0.9	(0.55-1.47)	0.547	0.71	(0.32-1.56)	0.224

In agreement with institutional, municipal and state measures	0.73	(0.53-1)	0.005	0.67	(0.42-1.07)	0.016	0.67	(0.31-1.43)	0.135
COVID-19 exposure									
Presented COVID-19 symptoms	<b>2.8</b>	<b>(2.03-3.86)</b>	<b>&lt;0.001</b>	<b>1.94</b>	<b>(1.22-3.1)</b>	<b>&lt;0.001</b>	<b>3.19</b>	<b>(1.48-6.86)</b>	<b>&lt;0.001</b>
Working at the office	0.74	(0.48-1.14)	0.048	0.82	(0.44-1.52)	0.358	0.83	(0.3-2.33)	0.62
Working from home	1.19	(0.85-1.67)	0.15	0.8	(0.48-1.35)	0.234	1.13	(0.5-2.57)	0.68
Being retired	0.95	(0.57-1.59)	0.767	1.64	(0.75-3.59)	0.06	0.52	(0.16-1.67)	0.101
Being a healthcare worker	0.88	(0.45-1.72)	0.605	1.01	(0.39-2.6)	0.969	1.68	(0.47-6.01)	0.255

### Figure S1. Association of several exposure variables with depressive disorders.

Association was measured using Odds Ratios (ORs) and 99.5% Confidence Intervals. ORs > 1 and <1 indicate variables associated with increased and decreased risk, respectively. Models were adjusted by age, sex, ethnicity and educational level.

### Figure S2. Association of several exposure variables with anxiety disorders.

Association was measured using Odds Ratios (ORs) and 99.5% Confidence Intervals. ORs > 1 and <1 indicate variables associated with increased and decreased risk, respectively. Models were adjusted by age, sex, ethnicity and educational level.

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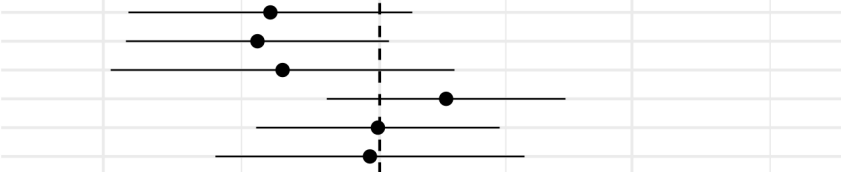
**Sociodemographic variables**

- Older than 60 years-old
- Non-white ethnicity
- College degree
- Female sex



**Loneliness related variables**

- Improved relationship quality
- Maintained relationship quality
- Living alone
- Married
- Living with people > 60 years-old
- Living with child in school age



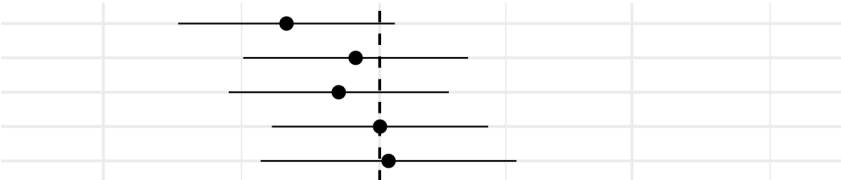
**Comorbidities**

- Alcohol abuse
- Active smoker
- Having >1 chronic diseases
- Having 1 chronic disease
- Obesity
- Good physical health
- Previous mental disorders



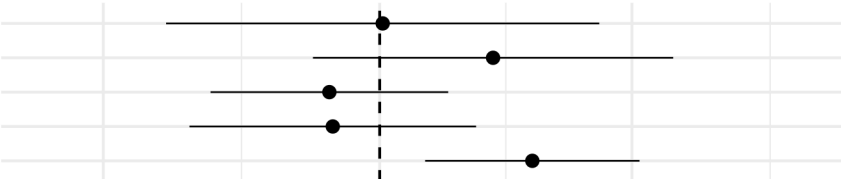
**Behaviors related to COVID-19**

- In agreement with institutional, municipal and state measures
- In agreement with federal measures
- Adequately informed about COVID-19
- Adopting adequate preventive measures
- Obedience to quarantine



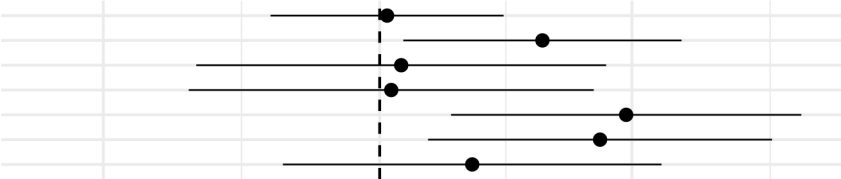
**COVID-19 exposure**

- Being a healthcare worker
- Being retired
- Working from home
- Working at the office
- Presented COVID-19 symptoms



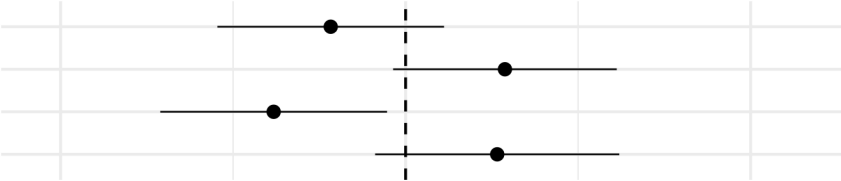
**Distress related variables**

- Increased domestic chores
- Concerns about income
- Frequent stress relieving practices
- Sporadic stress relieving practices
- Self-reported distress (4th quartile)
- Self-reported distress (3rd quartile)
- Self-reported distress (2nd quartile)



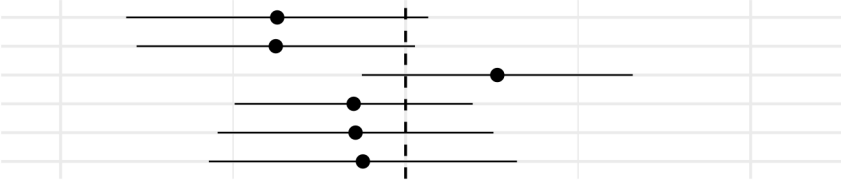
**Sociodemographic variables**

- Older than 60 years-old
- Non-white ethnicity
- College degree
- Female sex



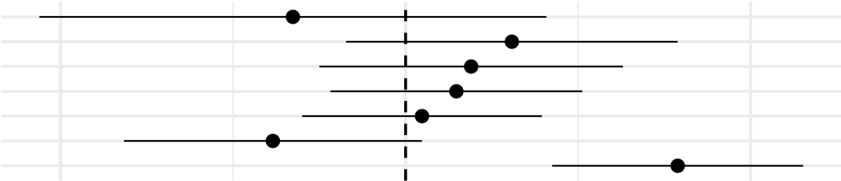
**Loneliness related variables**

- Improved relationship quality
- Maintained relationship quality
- Living alone
- Married
- Living with people > 60 years-old
- Living with child in school age



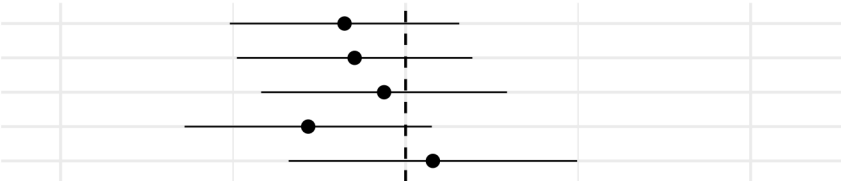
**Comorbidities**

- Alcohol abuse
- Active smoker
- Having >1 chronic diseases
- Having 1 chronic disease
- Obesity
- Good physical health
- Previous mental disorders



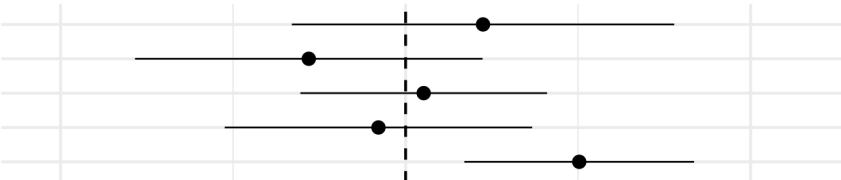
**Behaviors related to COVID-19**

- In agreement with institutional, municipal and state measures
- In agreement with federal measures
- Adequately informed about COVID-19
- Adopting adequate preventive measures
- Obedience to quarantine



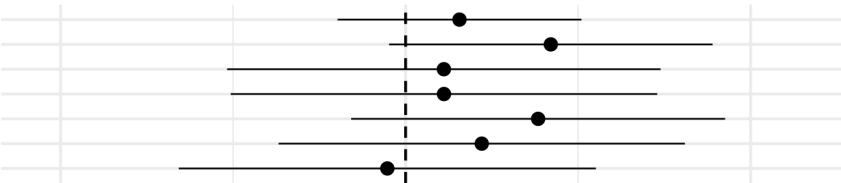
**COVID-19 exposure**

- Being a healthcare worker
- Being retired
- Working from home
- Working at the office
- Presented COVID-19 symptoms



**Distress related variables**

- Increased domestic chores
- Concerns about income
- Frequent stress relieving practices
- Sporadic stress relieving practices
- Self-reported distress (4th quartile)
- Self-reported distress (3rd quartile)
- Self-reported distress (2nd quartile)



**Prevalence and risk factors of psychiatric symptoms and diagnoses before and during the  
COVID-19 pandemic: findings from the ELSA-Brasil COVID-19 Mental Health Cohort.**

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## Abstract

**Background:** There is mixed evidence on increasing rates of psychiatric disorders and symptoms during the COVID-19 pandemic in 2020. We evaluated pandemic-related psychopathology and psychiatry diagnoses and their determinants in the Brazilian Longitudinal Study of Health (ELSA-Brasil) São Paulo Research Center.

**Methods:** Between a pre-pandemic ELSA-Brasil assessments in 2008-10 (Wave-1), 2012-2014 (Wave-2), 2016-2018 (Wave-3) and 3 pandemic assessments in 2020 (COVID-19 waves in May-July, July-September, October-December), rates of common psychiatric symptoms, and depressive, anxiety, and common mental disorders were compared using the Clinical Interview Scheduled-Revised (CIS-R) and the Depression Anxiety Stress Scale-21 (DASS-21). Multivariable generalized linear models, adjusted by age, gender, educational level, and ethnicity, identified variables associated with an elevated risk for mental disorders.

**Results:** In 2117 participants (mean age 60.79 years, 58.24% females), rates of common mental disorders and depressive disorders did not significantly changed over time, oscillating from between 23.5%-21.1%, ~~XX~~ and 3.3%-2.8% ~~XXX~~, respectively; while the rate of anxiety disorders significantly decreased (2008-10: 13.8%; ~~X~~, 2016-19: 9.8%; ~~X~~, 2020: 7.9% ~~X~~, respectively) (Wave 3: 22.53%, Wave Covid: 21.08%,  $p=0.35$ ), anxiety disorders (13.28% vs. 14.37%,  $p=0.35$ ), and depressive disorders (3.38% vs. 2.78%,  $p=0.23$ ) were not different between 2016-2018 and May-July 2020. ~~T~~Moreover, there was a decrease along 3 Wave-Covid assessments performed during 2020 for depression ( $\beta=-0.3750$ , 99.5% CI [-0.5078, -0.23]), anxiety ( $\beta=-0.3743$ , 99.5% CI [-0.4866, -0.2649]), and stress ( $\beta=-0.4854$ , 99.5% CI [-0.6486, -0.3324]) symptoms, and total scores ( $\beta=-1.12$ , 99% CI [-1.84, 0.39]) (all  $p<0.001$ ). Younger age, female sex, lower educational level, non-white ethnicity, and previous psychiatric disorders were associated with increased odds for psychiatric disorders, whereas self-evaluated good health and good quality of relationships with decreased risk.

**Conclusion:** No consistent evidence of pandemic-related worsening psychopathology in our cohort was found. Indeed, psychiatric symptoms slightly decreased along 2020. Risk factors representing socioeconomic disadvantages were associated with increased odds of psychiatric disorders.

## Keywords

COVID-19; pandemic; mental health; depression; anxiety; cohort study.



## Introduction

The pandemic of the Coronavirus Disease 2019 (COVID-19, caused by SARS-CoV-2) ~~has brought several challenges that~~ may impact ~~worldwide mental~~ worldwide the mental health of populations (Xiong et al., 2020). ~~Uncertainties on economic development have led to unemployment, economic downturns, and food and housing insecurity worldwide, aggravating social determinants of health, and straining resources for mental healthcare~~ (Nicola et al., 2020). Initial studies from China, where the epidemic started in late-2019, reported high rates of ~~mental symptoms such as~~ depression, anxiety, and stress symptoms in quarantined communities. ~~These findings were reported,~~ not only in COVID-19 patients with COVID-19 (Zhang et al., 2020); but also in psychiatric samples (Zhou et al., 2020), health care workers (Huang & Zhao, 2020), and the general population (Gao et al., 2020). A recent systematic review, ~~including only cross-sectional studies using convenience, online samples~~ (Xiong et al., 2020); showed high rates of symptoms of depression (14.6% to 48.3%), and anxiety (6.33% to 50.9%) in populations during the pandemic.

However, although these studies raised important concerns on the surge ~~about the emergence~~ of, possibly, the “next global pandemic” (Mari & Oquendo, 2020) ~~available,~~ assessments conducted worldwide were mostly ~~have often evaluated mental disorders using~~ focused on symptoms, and not on diagnoses ~~limited assessments~~. Moreover, the studies ~~employed~~ convenience, online samples with no prior information ~~knowledge~~ of the participants’ mental status (Vindegard & Benros, 2020; Xiong et al., 2020). ~~Thus, due to the absence of longitudinal data in these studies,~~ changes compared to pre-pandemic levels were not assessed.

Another issue is that ~~In addition,~~ the mental impact of the pandemic in communities from low- and middle-income countries ~~has~~ not been addressed. For instance, female sex, income, educational level, psychiatric comorbidities, and worse physical health have been associated with unfavourable mental health outcomes in these countries (Alonso et al. 2018; Musliner et al. 2016) and might be risk factors in the pandemic. Also, studies in China and developed countries explored whether age, severity of lockdown and disruption of daily activities, physical distancing, chronic diseases, and worries

associated with contracting or having severe presentations of COVID-19 were associated with mental outcomes, with mixed findings (Pierce et al. 2020; Prati and Mancini 2021).

Therefore, ~~there is the scenario of the pandemic impact on mental health scenario seems is more complex, with mixed evidence of and no consistent evidence of~~ worsening psychopathology during the pandemic was observed. Interestingly, preliminary evidence on suicide, the most severe outcome for psychiatric disorders, also showed no clear evidence for rising rates (John, Pirkis, et al., 2020), despite of previous simulations predicting an increase of up to 145% (John, Eyles, et al., 2020). Thus,

~~there is a need for we further further examineding~~ pandemic-related changes in mental symptoms and diagnoses, and their determinants, in the Brazilian Longitudinal Study of Health (ELSA-Brasil), a well-characterized ~~in longitudinal studies conducted in well-characterized Latin American and defined cohorts using appropriate instruments. We examined these issues in the Brazilian Longitudinal Study of Health (ELSA-Brasil). Based on literature findings, Our aims were hypotheses were threefoldthat:~~

(1) ~~to compare the rates of psychiatric disorders and changes in symptomatology between pre-pandemic and pandemic assessments. We hypothesized that an increase in psychiatric diagnoses and symptoms would be observed, as previously reported (Vindegaard and Benros 2020) during the pandemic compared to pre-pandemic rates;~~

(2) ~~to assess the overall changes of psychiatric symptomatology during intra-pandemic assessments; likewise, we hypothesized that an increase in psychiatric symptoms would increase, be observed according to the literature (Salari & Hosseini-Far, 2020);~~

(3) ~~to assess whether variables such as age, sex, ethnicity, educational level, associated with socioeconomic disadvantagestatus, clinical and psychiatric comorbidities, exposure to COVID-19 exposition, and adherence and agreement to social and physical distancing and other quarantine measures, leisure activities, employment status, and financial impact, would be associated with mental disordersoutcomes. We hypothesized that female sex, lower educational level, non-white ethnicity and psychiatric comorbidities would be risk factors for mental disorders, as observed in earlier ELSA-Brasil studies (Librenza-Garcia et al. 2020; Brunoni et al. 2019). We also hypothesized that the elderly, people with low physical health, and those with risk factors for severe forms of COVID-19 would be more~~

stressed and thus being at greater risk for developing mental disorders. Moreover, we expected that variables associated with loneliness and stress would be associated with greater mental disorder risk (Killgore et al., 2020), and those associated with leisure and stress-alleviating practices, with decreased risk for mental disorders. Finally, we hypothesized that a greater understanding of the COVID-19 (including hygiene and physical distance behaviors and agreement with the quarantine) would protect from mental illness, as this could decrease the fear of the pandemic (Brooks et al., 2020) and enhance general cooperativeness (i.e., “collective effervescence”, as characterized by Durkheim) (Zumeta et al., 2020).

According to these goals/hypotheses, we characterized the prevalence of psychiatric symptoms and mental disorders in ELSA-Brasil participants in São Paulo in May-July 2020 (corresponding to a severe social quarantine phase adopted in the city) compared to the most recent prior assessment in the cohort (2017-2019). Afterwards, we evaluated the rates of psychiatric symptoms in 3 online assessments performed along 2020. Finally, we aimed to identify exposure variables, including features specifically related to the COVID-19 pandemic period, collected using our online questionnaire.

## Methods

### Study design

The ELSA-Brasil is a prospective, longitudinal cohort of 15,105 participants from six universities in major Brazilian cities (São Paulo, Rio de Janeiro, Salvador, Belo Horizonte, Vitória, and Porto Alegre). At its inception, it was the first, largest cohort in Latin America. Its aims were to identify the clinical and sociodemographic determinants of mortality and of the development of chronic diseases within a population of a low-/middle-income country. It initially aimed to recruit 15,000 out of 52,137 potential participants, stratified by sex, age and occupational category. Recruitment goals were defined by sex (50% each), age (15% aged 35–44, 30% aged 45–54, 40% aged 55–64 and 15% aged 65–74 years) and occupational category (35% of support level, with incomplete elementary school; 35% with high school and 30% with higher education/teaching level). From 16,43 interested participants, 15,821 were pre-enrolled, and gave written consent, responding to an initial pre-interview. Only 716 (4.5%) of

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them did not complete the baseline examination, achieving a final sample of 15,105 participants. The recruitment goals were fully achieved in all centers (Aquino et al., 2013).

The ~~ELSA-Brasil~~ cohort began in August 2008, when eligible participants were all active or retired employees of these universities, who were between 35 and 74 years-old, and free of major neurocognitive disorders at enrollment (Aquino et al., 2012; Schmidt et al., 2014). ~~Posterior waves did not recruit new participants. The 1st, 2nd, and 3rd waves occurred in 2008-10, 2012-14, and 2016-18, respectively. During each wave, onsite assessments comprised clinical interviews and examinations, collecting information on sociodemographic variables, clinical history, family history of diseases, lifestyle factors, and anthropometric measurements. Laboratory tests were also collected during the visits (M. I. Schmidt et al., 2014; Aquino et al., 2012).~~

~~The 2nd wave (2012-2014) xxxxx. The 3rd wave — the most recent one — Wave 3 occurred between in 20176 — and 20198 — and is the most recent wave performed onsite.~~

In 2020, ~~additional “COVID-19 wave”s (WCs)~~ assessments were carried out only by the São Paulo research center. ~~We using used the REDCap platform (Harris et al., 2009) for sending out electronic questionnaires sent out by email, text message, or telephonic contacts administered on the REDCap platform (Harris et al., 2009). We hereby report on d~~Data collected during 2020 ~~consisted of~~ 3 online assessments (c1, c2, and c3 waves, WC-1, WC-2, WC-3, respectively, performed between May 18th to July 18th ; July 20th to September 30rd; and October 1st to December 22nd) (~~Figure 1~~).

(Figure 1)

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The most severe lockdown measures in São Paulo started on March 22nd, 2020 and continued through July 10th, 2020 (*Quarentena*, n.d.); therefore, ~~the c1 wave~~WC-1 corresponds to the 8th to 16th quarantine weeks; ~~the c2 wave~~WC-2 corresponds to an exponential increase of deaths and cases ~~in~~ Brazil-wide, with some flexibility on quarantine measures adopted by the end of September. Finally, ~~the c3 wave~~WC-3 corresponds to a moderate decrease in the rate of daily deaths and cases and greater quarantine relaxation measures in Brazil.

This study was approved by the Local Ethics Committee at the University Hospital, University of São Paulo and is reported according to the STROBE guidelines (von Elm et al., 2007). All patients provided electronic informed consent for participation in the study.

### *Participants*

*Participants in the São Paulo center are active or retired public servants from the University of São Paulo, which remained physically closed from March 20th, 2020 until the end of that year, with most activities being performed virtually, except for essential healthcare and research.*

*The study was advertised in the university newspapers and social media.* All participants enrolled at the São Paulo research center who completed the 3rd wave and could answer ~~the~~ online surveys (i.e., internet availability and having a smartphone, tablet, or personal computer) were eligible and initially contacted via their personal or work emails [using the RedCap platform \(Harris et al., 2009\)](#). If they did not reply to three emails sent at weekly intervals, we additionally tried to contact them via three text messages [\(or via telephone calls if mobile phone numbers were not available\)](#) also sent at weekly intervals. ~~If text messages were not possible (e.g., fixed telephone lines), we tried to reach them via telephone calls. Nonetheless, although~~ Telephone interviews were done if participants explicitly requested them due to difficulties in understanding or completing online questionnaires.

### *Variables*

#### Outcome variables

Psychiatric diagnoses were assessed using the validated Brazilian version of the Clinical Interview Schedule-Revised, CIS-R (Lewis et al., 1992; Nunes et al., 2011), a structured interview for measurement and diagnosis of current non-psychotic psychiatric morbidity in the community. [CIS-R has poor sensitivity for diagnosing mental disorders, which might slightly underestimate the rates of psychiatric disorders, although its specificity is high \(Brugha et al., 1999\). Due to its length, it was applied only during the first COVID-19 wave assessment.](#)

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The CIS-R includes the assessment of 14 symptoms and 13 psychiatric disorders based on the International Classification of Disease, 10th edition (ICD-10) psychiatric disorders (see Supplementary Material). The CIS-R domains are somatic complaints, fatigue, concentration and forgetfulness, sleep disturbance, irritability, worry about physical health, depression, depression ideas, worry, anxiety, phobias, panic attacks, compulsions, and obsessions. Scores for each section range from 0 to 4 (except the score for depressive ideas that range from 0 to 5), therefore the total score ranges from 0 to 57. A symptom is present if the corresponding section score is  $\geq 2$ .

The relevant symptoms are grouped to form, with accessory questions and based on an algorithm following ICD-10 diagnostic criteria, the following diagnoses: mild depressive episode without (F32.00) and with somatic syndrome (F32.01); moderate depressive episode without (F32.10) and with somatic syndrome (F32.11); severe depressive episode (F32.2); agoraphobia without (F40.00) and with panic disorder (F40.01); social anxiety disorder (SAD, F40.1); specific (isolated) phobias (F40.2); panic disorder (PD, F41.0); general anxiety disorder (GAD, F41.1); and obsessive-compulsive disorder (OCD, F42.9). Finally, F32.xx diagnoses were collapsed in “depressive disorders”, and F40.xx and F41.xx diagnoses were collapsed in “anxiety disorders”.

Moreover, the total CIS-R total score was also obtained by adding the scores of all 14 (non-binarized) symptoms dimensions. Based on this score, a diagnosis of to characterize the common mental disorder (CMD) diagnosis (CIS-R $>11$ ) is operationally defined (Lewis et al. 1992) and was used in our present study and to assess psychopathology dimensionally (A. R. Brunoni et al., 2019). Finally, the CIS-R score of depressive symptoms was calculated by summing symptom scores of depression, depression ideas, fatigue, concentration/forgetfulness and sleep disturbance as used previously (Khandaker et al. 2018; Brunoni et al. 2020). CIS-R was only applied at WC 1 due to its length.

Due to the quarantine measures, it was impossible to collect CIS-R data onsite, as done in previous waves. Two main deviations exist in the present CIS-R compared to previous ELSA-Brasil studies. Therefore, we first one is that we used an electronic, self-applied CIS-R format that was

identical to the one used in clinical interviews. ~~as onsite interviews were not possible due to the pandemic.~~ Importantly, the online version was self-applied, whereas the onsite version was read by trained personnel. Thus, uncontrolled differences in answering engagement could have occurred. However, previous studies have already validated and compared an electronic, self-applied CIS-R version with its standard format, showing that the electronic version presents valid and reliable performance (Lewis et al., 1988) (Lewis, 1994). In fact, a validation study showed that the performance of both versions was similar in 277 participants from a UK cohort (with similar characteristics to ours regarding age and rate of psychiatric disorders) that responded to both versions. In that study, no differences between mean scores and 12 of the 14 symptom scores were observed. Moreover, both versions presented similar accuracy in diagnosing psychiatric disorders (Head et al., 2013).

~~Second, we changed the criterion for symptom duration for generalized anxiety disorder (GAD). Traditionally, symptoms need to be present for at least 6 months. However, we considered that this could have led to a recall bias, as such period would include symptoms starting before the pandemic. Therefore, we changed the duration criterion for GAD (for both W3 and CW) to more than 2 weeks. The rates of both modified and unmodified GAD criteria (and, correspondingly, the overall rate of anxiety disorders) are presented in the results section and further discussed.~~

During the COVID-19 wave assessments (but not previously) ~~all~~, we applied the Depression, Anxiety, and Stress Scales-21 (DASS-21) (Henry & Crawford, 2005), ~~which is~~ a self-reported set of three scales that measures symptoms of depression, anxiety and stress. ~~The scores of the DASS-21 scores range from 0 to 63 and the symptoms' subscores range from 0 to 21. Higher scores indicate greater severity.~~

#### Exposure variables

Sociodemographic data from ~~the 1st previous wave~~ ~~s~~ of the ELSA-Brasil, such as ~~birth~~ year ~~of birth~~, ~~(age in years)~~, ~~height (in cm)~~, sex, educational level (presence or absence of university degree), and self-reported ethnicity (White, Brown, Black, Indigenous, Yellow); were used. Height (in cm) was

collected onsite during the 3rd wave; therefore, we used this information that we judged less prone to bias than self-reported height, even considering also obtained from the 3rd wave, since we considered that eventual height changes occurring between 2016-18 and 2020 would still produce less bias be more accurate than self-reported height, as the earlier assessment was performed by trained staff. Current participant weight (in kg) was assessed in the survey-. Body mass index (BMI) was obtained dividing weight by the square of the height (kg/m<sup>2</sup>). Obesity was defined as BMI  $\geq$  30.

The questions of our questionnaire were further codified in 25 composite exposure variables assessing behaviors, habits and lifestyle changes during the pandemic, as well as health perception, economic and home conditions, and questions related with COVID-19 disease (risk factors, presence of disease and/or symptoms, among others). (See [Supplementary Material](#))

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### Analysis

At the inception of our study, there was no good-quality data available on the rate of psychiatric disorders during the COVID-19 pandemic. Therefore, we did not formally estimate a sample size based on *a priori* rates, but invited all eligible participants from the last onsite (3rd) wave. Statistical significance was set under an alpha threshold of 0.005. This lower threshold (compared to the "standard" 0.05) has been proposed as a straightforward method to reduce the rate of false positive findings (Ioannidis, 2018) and was already used in previous studies from our group (Andre R. Brunoni et al., 2019). Accordingly, confidence intervals are reported in the 99.5% threshold (99.5% CI), which corresponds to a p-level of 0.005. Missing data were imputed as described in the [Supplementary Material](#). The study was performed in the "intention to treat" sample (for a description of the imputation procedures used to handle missing data, see [Supplementary Material](#)).

For our first study aim, we compared the rate of collapsed depressive disorders, anxiety disorders, OCD, and CMDs between the pre-pandemic and pandemic assessments. We did not use information from Wave 2, which did not assess the complete CIS-R. A Cochran's Q test for paired data was used to compare rates between waves, and post-hoc analyses were conducted applying pairwise McNemar tests.



each psychiatric symptom and disorder between the 1st and 3rd pandemic waves W3 and WC using the McNemar's test. Also related to our first aim, we used the continuous scores of CIS-R to assess changes in depressive and total symptomatology during these assessments. For wave 2, we used only data from CIS-R depressive scores.

For our second aim, we used the DASS to assess symptoms of depression, anxiety, and stress, and overall symptoms during the 3 assessments performed in 2020. Symptom changes over assessments were evaluated using linear models, using time as the independent and scores as the dependent variables. For our second aim, to analyse the mental health symptoms of depression, anxiety and stress measured by the DASS 21 over the course of the pandemic, General linear models were then fit for each outcome, using time as the independent variable, between dass scores and time. Individual symptom scores of depression, anxiety and stress, and the total DASS score were modelled. Moreover, since DASS 21 was not applied during W3, the depression symptoms and total DASS 21 scores were estimated using equipercentile linking (Albano, 2016) with CIS-R scores, using values from DASS 21 and CIS-R measurements in WC 1 when they were both collected.

For our third aim, we performed generalized linear models (GLMs, binomial family, logit link) using the iteratively reweighted least squares (IRLS) method. One model was run for each exposure and outcome variables separately, and all models were adjusted by the covariates sex, age, educational level, and ethnicity. We also analyzed the influence of these covariates separately. The outcome variables were the collapsed depressive disorders, anxiety disorders, and CMDs.  $\pm$  CMD, and the collapsed depressive disorders (F32.xx), and anxiety disorders (F40.xx, F41.xx, except for obsessive compulsive disorder). Multivariable models were also built for each covariate to analyse their influence on the main predictors, adjusting by age, sex, educational level, and ethnicity (Supplementary Material).

## Results

### Participants

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Out of 4191 eligible participants from the 2016-2018 wave W3, data of 2117 participants (51.7% of the eligible sample) could be included in our analyses. Reasons for non-inclusion were unwillingness to participate, impossibility of making contact, and deaths this study (Figure 1).

The included vs. non-included sample had a significantly higher percentage of women, were younger, with a higher educational level and lower rates of psychiatric symptoms and diagnoses (Table S1). In the included sample, 450 (21.3%) presented CMD, 169 (8%) presented anxiety disorders, and 60 (2.8%) presented depressive disorders (Table 2).

517 (24.4%) presented at least one psychiatric disorder, the most common being anxiety disorders (n= 320, 15.1%), mixed anxiety and depressive disorder (n=181, 8.5%) and depressive disorders (n= 60, 2.8%). Compared to those with no psychiatric disorders, CIS-R cases were mostly women, younger, of black or brown ethnicity and less educated (Table 1). We compared subjects participating in WC with those who did not (Table S1). The sample enrolled at WC had a significantly higher percentage of women, were younger, with a higher educational level and lower rates of psychiatric symptoms and diagnoses (Table S1).

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(Figure 1)

(Table 1)

*Aim 1: Prevalence of mental symptoms and diagnoses and symptomatology between pre-pandemic and pandemic assessments in 2017-2018 (W3) and May-July 2020 (WC)*

We found no significant differences within the same sample in rates of CMDs, and ICD-10 based diagnoses of depressive disorders and OCD between the 1st (2008-2010), 3rd (2016-2018), and the COVID (May-July 2020) waves (Figure 2) (Table S2). Anxiety rates decreased over time (1st wave: 13.8%, 3rd wave: 9.8%, COVID wave: 7.9%;  $Q=50.58$ ,  $p<0.001$ ), with significant differences between the 1st and the 3rd waves ( $\chi^2=19.7$ ,  $padj<0.001$ ), and the 1st and the COVID waves ( $\chi^2=45.8$ ,  $padj<0.001$ ) (Figure 2A).

(Figure 1)

CIS-R measurements of total symptom scores and depression scores did not significantly change over the assessments of the 1st (2008-2010), 3rd (2016-2018), and COVID (May-July 2020) waves ~~from W3 to WC-1~~ (Figure 2B32B, Table S25).

(Figure 3)

Using the CIS-R questionnaire, no significant changes in psychiatric diagnoses' rates were found between W3 (20176-20198) and WC (May-July 2020) (Table S2). Regarding symptomatology, increases in the rate of depressive ideas (9.7% vs. 12.33%,  $p=0.001$ ) and phobic symptoms (9.85% vs. 12.73%,  $p=0.001$ ) were observed between W3 and WC; conversely, the rates of fatigue (31.53% vs. 25.21%,  $p<0.001$ ), obsessive symptoms (11.69% vs. 8.11%,  $p<0.001$ ) and compulsive symptoms (9.4% vs. 7.21%,  $p=0.003$ ) decreased. (Table S2) (Figure 32).

(Figure 32)

Aim 2: Changes in symptomatology during the pandemic in 2020 *Depression, anxiety and stress symptoms during the COVID-19 pandemic in May-December 2020*

Here, data from 1943 participants who answered the DASS-21 at WC1 were analyzed. CIS-R measurements of total symptom scores (W3 vs. WC-1:  $\beta=0.02$ , 99CI [-0.69,0.65],  $p=0.933$ ) and depression scores (W3 vs. WC-1:  $\beta=0.06$ , 99CI [-0.25,0.36],  $p=0.632$ ) did not significantly change over the assessments of the 1st (2008-2010), 3rd (2017-2019), and covid (May-July 2020) waves ~~from W3 to WC-1~~ (Figure 2B, Table S5) ~~incluindo a W1 e escrever um beta unico. The same was observed for the estimated DASS-21 depression (W3 vs. WC-1:  $\beta=0.16$ , 99CI [-0.89,0.56],  $p=0.559$ ) and total symptom (W3 vs. WC-1:  $\beta=0.05$ , 99CI [-0.33,0.23],  $p=0.624$ ) scores in the same period (Figure 43, Table S5).~~ (Figure 3B)

A ~~S~~significant decreases in DASS-21 scores ~~were was~~ observed ~~for both between WC-2 and WC-1, and WC-3 and WC-1, with a reduction of~~ total symptom scores (~~c3WC-2 vs. c1WC-1:  $\beta=-1.2243$ , 99.5%CI [-1.5885,-0.8641],  $p<0.001$ ; WC-3 vs. WC-1:  $\beta=-1.12$ , 99CI [-1.84, 0.39],  $p<0.001$ ),~~

depression scores ( $c3WC-2$  vs.  $c1WC-1$ :  $\beta = -0.37$ , 99.5% CI [-0.5065, -0.2340],  $p \leq 0.001$ ;  $WC-3$  vs.  $WC-1$ :  $\beta = -0.50$ , 99CI [-0.78, -0.23],  $p < 0.001$ ), anxiety scores ( $c3WC-2$  vs.  $c1WC-1$ :  $\beta = -0.374$ , 99.5% CI [-0.4856, -0.2614],  $p < 0.001$ ;  $WC-3$  vs.  $WC-1$ :  $\beta = -0.43$ , 99CI [-0.66, -0.19],  $p < 0.001$ ) and stress scores ( $c3WC-2$  vs.  $c1WC-1$ :  $\beta = -0.487$ , 99.5% CI [-0.6479, -0.3346],  $p < 0.001$ ) over time, although no significant changes between the 2nd and 3rd covid wave assessments were observed. and no significant change in scores between WC 2 and WC 3 (Figure 2B3, Table S25).

(Figure 3)

We also analysed general linear models without including the linked values of DASS 21 total and depression scores in W3, with no significant differences compared to models which included these values (Figure 43, Table S5).

(Figure 43)

### Aim 3: Association between with exposure variables and mental disorders

Regarding age, sex, ethnicity and college degree: At WC 1, for CMD, a protective association was observed for being older and (OR 0.95, 99CI [0.93, 0.96],  $p < 0.001$ ), having completed college university (OR 0.58, 99CI [0.43, 0.78],  $p < 0.001$ ) and being of either white (OR 0.48, 99CI [0.08, 0.75],  $p < 0.001$ ) or yellow (OR 0.31, 99CI [0.12, 0.78],  $p < 0.001$ ) ethnicities. were associated with decreased risk, whereas non-white ethnic groups and women had increased a two-fold risk (OR 1.95, 99CI [1.42, 2.69],  $p < 0.001$ ) for current CMD. For depressive disorders, older age (OR 0.95, 99CI [0.903, 0.997],  $p = 0.003$ ) and having a complete college degree university degree (OR 0.41, 99CI [0.19, 0.88],  $p = 0.001$ ) was are found to be protective factors. For anxiety disorders, older age (OR 0.95, 99CI [0.93, 0.97],  $p < 0.001$ ), and having a complete university college degree (OR 0.56, 99CI [0.40, 0.80],  $p < 0.001$ ) and white ethnicity (OR 0.57, 99CI [0.34, 0.96],  $p = 0.002$ ) were protective factors.

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while being a woman was associated with increased risk (OR 1.98, 99CI [1.35, 2.88],  $p < 0.001$ ) (Figure S2, Table S3). (Table S3) (Figure 4).

Multivariable models adjusted by the abovementioned covariates showed ~~xxxx~~

#### *Association with exposure variables*

At WC, F, for CMD, general linear model analyses adjusted by age, gender, ethnicity, and educational level (Table 3) a protective association for was found with describing self-reported good physical health (OR 0.3, 99CI [0.20, 0.44]), describing maintained or improved quality of close relationships ("maintained" OR 0.48, 99CI [0.33, 0.71]; "improved" OR 0.56, 99CI [0.37, 0.85]), being married (OR 0.6, 99CI [0.43, 0.83]), and for alignment with institutional, municipal and state measures (OR 0.73, 99CI [0.54, 0.999]), and alignment with federal measures (OR 0.71, 99CI [0.52, 0.97]).

Conversely, associations that presented increased risk for CMD were having more than one chronic disease risk factor for COVID-19 (OR 2.04, 99CI [1.30, 3.21]), being feeling concerned about one's income during the pandemic worried about the pandemic (OR 2.19, 99CI [1.51, 3.17]), feeling isolated ion feelings (OR 2.72, 99CI [1.88, 3.93]), having had COVID-19 symptoms (OR 2.80, 99CI [2.03, 3.86]), describing elevated distress levels during the quarantine ("high" OR 2.2, 99CI [1.32, 3.68]; "very high", OR 4.4 99CI [2.66, 7.28]), and presenting previous mental disorders (OR 3.39, 99CI [2.44, 4.72])

(Figure 3, Table S3 Table S4, Figure 44).

(Figure 3)

Multivariable analyses for For depressive disorders showed that, we found that having had COVID-19 symptoms (OR 3.18, 99CI [1.48, 6.83]), feelings of isolated ion (OR 5.03, 99CI [1.48, 17.15]), and presenting previous mental disorders (OR 6.13, 99CI [2.66, 14.16]) were associated with increased risk, whereas no factors were associated with decreased risk describing maintained or improved quality of close relationships maintaining good ed quality of close relationships (OR 0.40, 99CI [0.16, 0.97]), and describing self-reported describing good self-reported health (OR 0.32, 99CI [0.11, 0.90]) were protective factors (Figure S1, Table S3 Table S14, Figure 4).

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For Multivariable analyses for anxiety disorders showed that having had COVID-19 symptoms (OR 2.13, 99CI [1.48, 3.07]), ~~being a current smoker~~ (OR 1.86, 99CI [1.09, 3.17]), describing elevated distress levels during the quarantine (“high” OR 2.39, 99CI [1.30, 4.39]; “very high”, OR 4.12, 99CI [2.27, 7.47]), ~~feelings of isolation~~ feelings (OR 2.46, 99CI [1.60, 3.76]), presenting previous mental disorders (~~OR 3.07, 99CI [2.12, 4.45]~~), being concerned about one’s income during the pandemic (~~worried about the pandemic~~ (OR 1.96, 99CI [1.28, 3.00]), and having more than one chronic disease (~~risk factor for COVID-19~~ (OR 1.85, 99CI [1.11, 3.07]) were associated with increased risk; whereas describing good physical/self-reported health (OR 0.37, 99CI [0.24, 0.58]) and ~~maintained or improved quality of close relationships~~ quality of close relationships (“maintained” OR 0.55, 99CI [0.36, 0.85]; “improved” OR 0.58, 99CI [0.37, 0.93]), ~~was/were associated~~ with decreased risk (Figure S2, Table S3). (Table S4, Figure S4).

(Figure 4)

## Discussion

### Main results

In this longitudinal study of the ELSA-Brasil cohort, Our first aim was to compare we evaluated the prevalence of mental disorders and symptoms in 2117 participants in the ELSA-Brasil São Paulo study center between two pre-pandemic assessments (2008-2010 and 2016-2018) and from the initial phases of the COVID-19 pandemic (May to July 2020). ~~corresponding to 8 to 16 weeks after quarantine onset, when strict measures such as suspension of all non-essential services, closure of schools and universities, confinement recommendations, and mobility restrictions took place. This was accompanied by an exponential increase of COVID-19 cases and deaths in the city. However,~~ Contrary to our initial hypothesis, the rates of observed psychiatric disorders ~~of were not significantly different between the assessments, since the prevalences of compared to our previous cohort assessment performed between 20176 and 20198. Moreover, although we found high rates of some~~

mental symptoms during the pandemic, most were already high in our previous cohort assessment and no evident pattern of worsening was identified.

We found that 21.08%, 17.16% and 2.78% of participants presented a current diagnosis of common mental disorder, anxiety disorders, and depressive disorders, respectively, were not significantly different from previous assessments. Likewise, overall mental symptoms and depressive symptoms did not significantly change over time. In fact, a slight decrease in anxiety disorders was found. We believe that a lower rate in the COVID-19 assessment was partially observed due to a decrease in the rate of generalized anxiety disorders, which has a time criterion duration of 6 months or more. As the assessment was performed in May-June and the pandemic started in March 2020, possibly some participants considered that anxiety symptoms only started after the pandemic, even if they were present before (recall bias). In fact, additional analyses changing the time criterion for 2 weeks or more (for all waves) revealed similar rates of anxiety disorders among all waves (data not shown). In addition, the rates of symptoms of depression, depressive ideas, and anxiety were 8.55%, 12.33%, and 18.15%, respectively, whereas the highest rates of symptoms observed during the pandemic were for sleep disturbances (35.11%), worries (33.22%), and fatigue (25.21%). Although high, these rates did not capture changes in mental symptoms, as no previous data were available. For our second aim, in addition, we performed 3 longitudinal assessments from May to December 2020 during 2020, from May to December 2020, to evaluate possible changes in depression, anxiety, and stress scores. Also contrary to our hypothesis, these symptoms were either maintained or slightly decreased during the pandemic.

Notwithstanding, our findings are in line with other studies evaluating the longitudinal prevalence of mental disorders before and during the pandemic in the general population. In a prospective study in the UK with data from more than over 70,000 people examined during the lockdown period in the first semester of 2020, depressive and anxiety symptoms were moderately high at the beginning of lockdown measures but decreased rapidly during the next 20 weeks (Fancourt et al., 2020). A longitudinal study of three Dutch case-control cohorts, with well-characterized psychiatric disorders, employed data from approximately 1,500 subjects and assessed depressive symptoms, anxiety, worry, and loneliness. They demonstrated that p People without psychiatric disorders showed

a slight increase in symptoms during the pandemic, whereas those with the greatest previous mental health burden tended to exhibit a slight symptom decrease (Pan et al., 2020). In a longitudinal assessment in Ireland with over 1000 participants (Hyland et al., 2020), rates of GAD were actually higher in 2019 compared to 2020, and further decreased during the pandemic. In contrast, other studies showed an increase in mental health symptomatology. In a US study comparing matched but different adult samples before and during the pandemic, the prevalence of probable depression (Patient Health Questionnaire-9 >9) rose from 8.5% to 27.8% (Ettman et al., 2020). In a UK study using the General Health Questionnaire (GHQ-12) in 48,486 respondents, the prevalence of mental health symptoms rose from 24.3% in 2016-2018 to 37.8% in April 2020, further decreasing to 31.9% in June 2020. Interestingly, those with a pre-existing depressive disorder did not experience an increase in mental symptoms (Daly et al., 2020). ~~In addition, GHQ-12 is a screening assessment with high sensitivity and poor specificity (Goldberg & Blackwell, 1970).~~

Regarding the third aim, we confirmed, in agreement with our hypothesis, that female sex, non-white ethnicity and lower educational level were risk factors for CMDs. These characteristics reflect socio-economic disadvantages and have been observed as risk factors for incident and persistent depression in a previous ELSA-Brasil study (Andre R. Brunoni et al., 2019)(Xiong et al., 2020). People with lower educational levels also experienced more psychiatric symptoms (Xiong et al., 2020), possibly due to accumulating workload and the impossibility of stopping working and/or working from home, generating distress. In a UK study, non-white ethnicities (Proto & Quintana-Domeque, 2021) also experienced higher mental distress, in line with our findings. Interestingly, meta-analyses did not find an association between these factors and psychiatric symptoms (Prati & Mancini, 2021; Wu et al., 2021), although meta-analyses are usually underpowered for such analyses. Although we expected that increased age - due to stress of presenting a severe form of COVID- would be associated with psychiatric disorder; actually people younger than 60 years-old presented increased risk. Interestingly, this was also observed in a systematic review (Xiong et al., 2020) and could be explained by factors such as the impossibility of staying at home due to employment, lower financial support and more domestic activities (e.g., taking care of children).



~~Younger age, female sex, lower educational level, non-white ethnicity, and previous psychiatric disorders were socio-demographic and clinical variables associated with increased odds of presenting psychiatric disorders.~~

~~We also analysed several other variables corrected for age, sex, ethnicity, and educational level. Psychiatric comorbidity was a risk factor for presenting CMDs, reflecting the greatest mental associated with these patients, as demonstrated previously (Pan et al. 2020), and emphasizing the need of maintaining psychiatric care during the pandemic. Regarding clinical comorbidities, exposure variables associated with increased rates of CMDs include having had COVID-19 symptoms (tests were not widely available and there were stay-at-home instructions for mild cases when data were collected, so no confirmatory assessment was done), and presenting one or more chronic diseases, while self-reported good physical health was associated with decreased risk. This suggests that participants with greater susceptibility of presenting a severe COVID-19 disease were those more likely to develop psychiatric disorders. Notably, obesity, being a smoker, and alcohol abuse were not associated with significant increased risk, which could be explained by inadequate perception or awareness of these variables as risk factors for severe COVID-19 disease.~~

High or very high self-reported distress variables (which included questions such as the distress presented when staying at home, avoiding contact with people, stopping meeting friends and relatives, and others) and concerns on income were associated with increased odds of presenting mental disorders<sup>5.6</sup>. However, stress alleviating practices were not associated with decreased risk, or increased domestic chores with increased risk. This possibly reveals that activities at home during the quarantine are less important for modifying mental health than initially hypothesized by researchers (Pfefferbaum & North, 2020). Notwithstanding, maintaining or improving relationship quality (e.g., using social apps) were associated with decreased risk. In fact, feelings of loneliness might have been attenuated via social media and electronic apps of mental health support, which were not present in previous pandemic; also, activities that could be done at home were not stopped (Williams et al., 2021).

Interestingly, compliance and agreement with federal measures or institutional/municipal/state measures were independently associated with lower odds of having mental disorders. This is surprising as the Brazilian president of the republic adopted a radical anti-quarantine attitude, promoting mass

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rallies and systematically undermining the severity of the pandemic (The Lancet, 2020), whereas the institutional/municipal/state instances adopted a pro-quarantine/pro-science perspective. Possibly, political identity and ideology are protective factors since they are cognitive shortcuts to support shared beliefs and similar choices (Pereira et al., 2020), decreasing the mental burden in choosing between difficult options.

Finally, healthcare workers presented no increased odds for psychiatric disorders. Importantly, healthcare professionals in our sample work at the University Hospital, which treated cases of moderate severity, ~~since~~ severe cases of COVID-19 were transferred to a tertiary university hospital. This ~~might have reduced the stress overload of our sample of healthcare workers who worked in relatively less stressful conditions. Also, those~~ with higher risk of COVID-19 morbimortality were kept away from work. ~~Moreover, which might have reduced the stress overload of our sample of healthcare workers who worked in relatively less stressful conditions. In fact, even though several reports have indicated a great mental burden for these professionals, Interestingly,~~ a recent systematic review showed that their rates of depression and anxiety during the pandemic are neither necessarily higher than the general population, nor increased compared to pre-pandemic levels (Liu et al., 2020).

#### *Methodological considerations*

~~Importantly, we also employed modified GAD criteria. This change was done aiming to better reflect the occurrence of acute anxiety disorders during the pandemic, since participants were interviewed 8-16 weeks after the quarantine. Interestingly, using the original criteria, a decrease in the rates of GAD and anxiety disorders between W3 and WC-1 was observed.~~

Our study has some strengths compared to previous ones (Vindegaard & Benros, 2020; Xiong et al., 2020). ~~First, instead of using only symptom-based scales, we also employed our evaluation was centered on a validated questionnaire for diagnosings of mental disorders; therefore, the risk of instrumental bias was low. SecondThird, our longitudinal design allowed us to compare mental health data between two waves, assessing changes of symptoms; conversely, most studies employed cross-~~

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~~sectional evaluations, disallowing the assessment of previous symptoms to characterize whether an actual increase of symptoms occurred.~~

## Limita

### Limitations

~~Study limitations should be underscored.~~ First, the mean age of our sample was ~~approximately~~ around 60 years-old; therefore our results might not be applicable to younger ~~or unemployed~~ populations. ~~Second~~Third, approximately only half of the eligible sample answered to our survey. This is in line with cohorts in the UK and the Netherlands that presented response rates in online assessments during the pandemic of 25-55% (Evandrou et al., 2021; Pan et al., 2020; Pierce et al., 2020) that probably occurred due to the need of rapid organization for collecting timely data during the pandemic. In fact,~~Although this seems low,~~ initial response survey rates are typically around 30% and increase only after many contacts, which usually take several months (Fincham, 2008). As we aimed to capture the mental health of the sample in a short period, we only extended our recruitment for two months. Third, although the ~~e~~ differences between responders and non-responders were mostly small, ~~however,~~ a higher educational level was observed in responders, which probably reflects the spectrum of digital literacy within the sample. Notwithstanding, inherent issues of our sample are its relatively old age and low digital literacy.

### Generalizability

We Used a well-defined cohort, which decreased the risk of selection bias, enhancing the external validity and generalizability of the findings, in contrast with snowball sampling. However, our sample is occupational and not population-based, being composed of public servants of the University of São Paulo. Their income, which is on average higher than the national income, was essentially unaffected during the pandemic. Thus, the rates of psychiatric disorders and symptoms should not be considered as nationally representative, but rather interpreted in the context of longitudinal changes within the same sample and associated risk factors. Nonetheless, even representing a fraction of the Brazilian population, our findings are interesting for similar samples from other developing countries

that continually struggle with huge socio-economic inequalities, with vulnerable safety nets, and having some of the highest COVID-19 excess mortality rates (The Lancet, 2020b). Our results can also be used for mega-cohort analyses exploring whether the observed exposure variables are of worldwide importance or country-dependent, which is important to develop comprehensive early intervention strategies in different contexts.

#### *Final remarks*

—The pandemic-related mental health impact has been much anticipated, based on observations from previous pandemics (Brooks et al., 2020), and factors such as the psychological stress of quarantine and its consequences (Pfefferbaum & North, 2020). Nonetheless, the scenario observed during 2020 is more complex and no consistent evidence of worsening psychopathology was observed. Interestingly, preliminary evidence on suicide, the most severe outcome for psychiatric disorders, also showed no clear evidence for rising rates (John, Pirkis, et al., 2020), despite of previous simulations predicting an increase of up to 145% (John, Eyles, et al., 2020).

Possible explanations for our findings are: (1) we did not assess mental symptoms in the first initial weeks of the pandemic. Possibly, the psychological burden was higher during this early stage, as well as before the quarantine measures, with reports of the pandemic in European countries and less information of COVID-19. Therefore, some psychological stress adaptation could have been already occurring; (2) the quarantine measures in São Paulo were not extremely severe (*Adesão a isolamento social em SP é de 48%, aponta Sistema de Monitoramento Inteligente*, 2020) as domestic travels were not banned, and curfews, fees, and penalties were not imposed; moreover, the population adherence to quarantine was only moderate; (3) reports of quarantine measures nationally and worldwide might have reduced the confinement stigmatization, which is a psychological stressor (Brooks et al., 2020); (4) frustration and boredom might have been attenuated through social media and electronic apps of mental health support, which were not present in previous pandemics; (5) likewise, activities that could be done at home were not stopped, reducing the economic impact of the pandemic; finally; (6) our sample was composed by public servants with job stability, economic security and reasonable public healthcare access.

## Conclusion

During a strict lockdown period in São Paulo in May-July 2020, no major changes in psychiatric disorders and symptoms have been detected compared to [earlier assessments in 2008-2010 and 2016-2018](#)<sup>9</sup>. Moreover, symptoms of depression, anxiety, and stress decreased along 3 assessments performed from May to December in 2020. Risk factors representing socioeconomic disadvantages and ~~usual~~ predictors [associated with distress and loneliness of psychiatric disorders](#) were associated with increased odds of psychiatric disorders. As further quarantine periods may endure in the future, our findings are important to identify subgroups at elevated risk. Finally, follow-up surveys are necessary to identify trajectories of these disorders during the pandemic and post-pandemic phases.

(Please also check the [Supplementary Material](#) for further information)

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## Conflicts of Interest

None to disclose.

## Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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Table 1. Characteristics of the study sample.

		<u>Presence of CMD</u>		
	<u>Overall</u>	<u>No</u>	<u>Yes</u>	<u>P</u>
<u>n</u>	<u>2117</u>	<u>1667</u>	<u>450</u>	
<u>Sociodemographic variables</u>				
<u>Age, mean (SD)</u>	<u>62.32 (8.41)</u>	<u>63.08 (8.57)</u>	<u>59.54 (7.17)</u>	<u>&lt;0.001</u>
<u>&gt; 60 years-old, n (%)</u>	<u>1210 (57.2)</u>	<u>1011 (60.6)</u>	<u>199 (44.2)</u>	<u>&lt;0.001</u>
<u>Educational level, n (%)</u>				<u>&lt;0.001</u>
<u>Below High School</u>	<u>23 (1.1)</u>	<u>16 (1.0)</u>	<u>7 (1.6)</u>	
<u>High School</u>	<u>49 (2.3)</u>	<u>36 (2.2)</u>	<u>13 (2.9)</u>	
<u>Incomplete College</u>	<u>788 (37.2)</u>	<u>578 (34.7)</u>	<u>210 (46.7)</u>	
<u>College University Degree</u>	<u>1257 (59.4)</u>	<u>1037 (62.2)</u>	<u>220 (48.9)</u>	
<u>Self-reported ethnicity, n (%)</u>				<u>&lt;0.001</u>
<u>Black</u>	<u>224 (10.7)</u>	<u>153 (9.3)</u>	<u>71 (16.0)</u>	
<u>Mixed (brown)</u>	<u>361 (17.3)</u>	<u>260 (15.8)</u>	<u>101 (22.7)</u>	
<u>White</u>	<u>1394 (66.7)</u>	<u>1137 (69.1)</u>	<u>257 (57.8)</u>	
<u>Yellow</u>	<u>102 (4.9)</u>	<u>89 (5.4)</u>	<u>13 (2.9)</u>	
<u>Indigenous</u>	<u>9 (0.4)</u>	<u>6 (0.4)</u>	<u>3 (0.7)</u>	
<u>Non-white ethnicity, n (%)</u>	<u>696 (33.3)</u>	<u>508 (30.9)</u>	<u>188 (42.2)</u>	<u>&lt;0.001</u>
<u>Female gender, n (%)</u>	<u>1233 (58.2)</u>	<u>916 (54.9)</u>	<u>317 (70.4)</u>	<u>&lt;0.001</u>
<u>Distress related variables</u>				
<u>Self-reported distress level, n (%)</u>				<u>&lt;0.001</u>
<u>Low (1st quartile)</u>	<u>514 (26.5)</u>	<u>463 (30.2)</u>	<u>51 (12.5)</u>	
<u>Medium (2nd quartile)</u>	<u>534 (27.5)</u>	<u>443 (28.9)</u>	<u>91 (22.3)</u>	
<u>High (3rd quartile)</u>	<u>416 (21.5)</u>	<u>325 (21.2)</u>	<u>91 (22.3)</u>	
<u>Very high (4th quartile)</u>	<u>475 (24.5)</u>	<u>300 (19.6)</u>	<u>175 (42.9)</u>	
<u>Stress relieving practices, n (%)</u>				<u>0.403</u>
<u>None</u>	<u>163 (7.7)</u>	<u>123 (7.4)</u>	<u>40 (8.9)</u>	
<u>Sporadic</u>	<u>1131 (53.5)</u>	<u>886 (53.2)</u>	<u>245 (54.4)</u>	
<u>Frequent</u>	<u>821 (38.8)</u>	<u>656 (39.4)</u>	<u>165 (36.7)</u>	
<u>Concerns about income, n (%)</u>	<u>1210 (62.1)</u>	<u>894 (58.1)</u>	<u>316 (77.6)</u>	<u>&lt;0.001</u>
<u>Increased domestic chores, n (%)</u>	<u>1145 (58.3)</u>	<u>897 (57.7)</u>	<u>248 (60.3)</u>	<u>0.368</u>
<u>Loneliness related variables</u>				

<u>Living with child in school age, n (%)</u>	<u>371 (19.1)</u>	<u>276 (17.9)</u>	<u>95 (23.4)</u>	<u>0.016</u>
<u>Living with &gt; 60 year-old, n (%)</u>	<u>704 (33.3)</u>	<u>570 (34.2)</u>	<u>134 (29.8)</u>	<u>0.088</u>
<u>Married, n (%)</u>	<u>1270 (63.9)</u>	<u>1034 (65.8)</u>	<u>236 (57.0)</u>	<u>0.001</u>
<u>Relationship quality, n (%)</u>				<u>&lt;0.001</u>
<u>Worsened</u>	<u>458 (23.4)</u>	<u>325 (21.0)</u>	<u>133 (32.4)</u>	
<u>Maintained</u>	<u>964 (49.2)</u>	<u>794 (51.3)</u>	<u>170 (41.4)</u>	
<u>Improved</u>	<u>537 (27.4)</u>	<u>429 (27.7)</u>	<u>108 (26.3)</u>	
<u>Living alone, n (%)</u>	<u>334 (16.8)</u>	<u>266 (16.9)</u>	<u>68 (16.4)</u>	<u>0.868</u>
<u>Comorbidities</u>				
<u>Previous mental disorders, n (%)</u>	<u>551 (26.0)</u>	<u>330 (19.8)</u>	<u>221 (49.1)</u>	<u>&lt;0.001</u>
<u>Good physical health, n (%)</u>	<u>677 (34.2)</u>	<u>600 (38.3)</u>	<u>77 (18.6)</u>	<u>&lt;0.001</u>
<u>Obesity, n (%)</u>	<u>582 (27.5)</u>	<u>430 (25.8)</u>	<u>152 (33.8)</u>	<u>0.001</u>
<u>Chronic diseases, n (%)</u>				<u>0.002</u>
<u>None</u>	<u>1102 (52.1)</u>	<u>897 (53.8)</u>	<u>205 (45.6)</u>	
<u>One</u>	<u>672 (31.7)</u>	<u>521 (31.3)</u>	<u>151 (33.6)</u>	
<u>More than one</u>	<u>343 (16.2)</u>	<u>249 (14.9)</u>	<u>94 (20.9)</u>	
<u>Active tobacco smoker, n (%)</u>	<u>176 (8.9)</u>	<u>123 (7.9)</u>	<u>53 (12.8)</u>	<u>0.002</u>
<u>Alcohol abuse, n (%)</u>	<u>251 (11.9)</u>	<u>206 (12.4)</u>	<u>45 (10.0)</u>	<u>0.197</u>
<u>Behaviors related to COVID-19</u>				
<u>Obedience to quarantine, n (%)</u>	<u>1595 (81.3)</u>	<u>1249 (80.5)</u>	<u>346 (84.2)</u>	<u>0.105</u>
<u>Adopting adequate preventive measures, n (%)</u>	<u>981 (49.5)</u>	<u>770 (49.1)</u>	<u>211 (51.1)</u>	<u>0.516</u>
<u>Adequately informed about COVID-19, n (%)</u>	<u>1094 (55.2)</u>	<u>888 (56.6)</u>	<u>206 (49.9)</u>	<u>0.016</u>
<u>In agreement with federal measures, n (%)</u>	<u>943 (48.1)</u>	<u>761 (49.1)</u>	<u>182 (44.3)</u>	<u>0.093</u>
<u>In agreement with municipal and state measures, n (%)</u>	<u>1069 (54.5)</u>	<u>866 (55.9)</u>	<u>203 (49.4)</u>	<u>0.022</u>
<u>COVID-19 exposure</u>				
<u>Presented COVID-19 symptoms</u>	<u>620 (29.3)</u>	<u>397 (23.8)</u>	<u>223 (49.6)</u>	<u>&lt;0.001</u>
<u>Working at the office, n (%)</u>	<u>343 (16.2)</u>	<u>271 (16.3)</u>	<u>72 (16.0)</u>	<u>0.953</u>
<u>Working from home, n (%)</u>	<u>798 (37.7)</u>	<u>622 (37.3)</u>	<u>176 (39.1)</u>	<u>0.52</u>
<u>Being retired, n (%)</u>	<u>491 (23.2)</u>	<u>403 (24.2)</u>	<u>88 (19.6)</u>	<u>0.046</u>
<u>Working on healthcare, n (%)</u>	<u>108 (5.1)</u>	<u>81 (4.9)</u>	<u>27 (6.0)</u>	<u>0.392</u>

<u>Other CIS-R diagnoses</u>				
<u>Anxiety disorders, n (%)</u>	<b><u>169 (8.0)</u></b>	<b><u>29 (1.7)</u></b>	<b><u>140 (31.1)</u></b>	<b><u>&lt;0.001</u></b>
<u>Depressive disorders, n (%)</u>	<b><u>60 (2.8)</u></b>	<b><u>0 (0.0)</u></b>	<b><u>60 (13.3)</u></b>	<b><u>&lt;0.001</u></b>

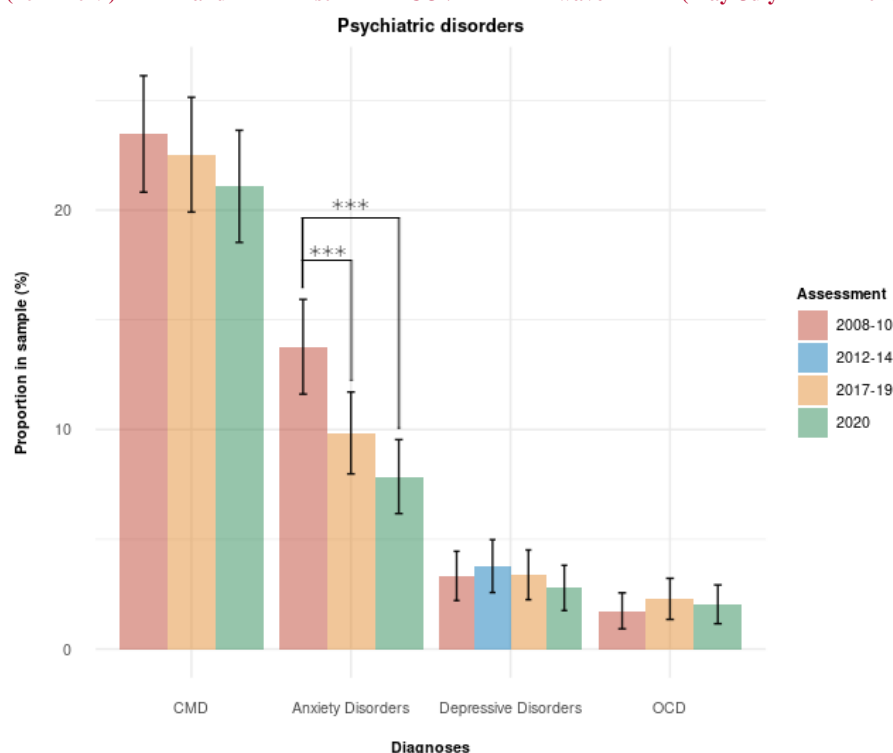
values are highlighted in bold when a significance of 0.005 was achieved in t-tests or Chi-squared tests for continuous and categorical variables, respectively. Preventive measures for COVID-19 included hand washing with soap, using alcohol gel, using facial masks, and others. Knowledge about COVID-19 included knowledge on transmission, symptoms and hygiene measures. COVID-19 symptoms included fever, cough, shortness of breath, sore throat, fatigue, anosmia, and ageusia. Alcohol abuse was defined as >1 dose/day for women and >2 doses/day for men during a given week. Obesity is a Body Mass Index  $\geq 30$ . Adherence to quarantine was leaving home only when strictly necessary. Close relationships included family and close friends. Stress-alleviating practices included mindfulness, praying, gardening, physical activity at home, reading, writing, painting, playing games, watching TV/streaming, hearing music, playing musical instruments, and taking care of a pet. Risk factors for severe COVID-19 disease were older (>60 years-old) age, obesity, cardiovascular risk factors (e.g. hypertension, diabetes) and chronic clinical conditions.

**Figure 1. ELSA-BRASIL São Paulo center flow chart.**

CIS-R; Clinical Interview Schedule-Revised. DASS; Depression, Anxiety, and Stress Scale. The full version of the CIS-R was applied in all waves, except for Wave 2, when only questions regarding depressive symptoms were applied.

Figure 2. Rates of psychiatric disorders and CIS-R total symptom scores at Wave 1 (2008-2010), Wave 2 (2012-2014), Wave 3 (2016-2018) and 1st COVID wave (May-July 2020), and DASS depression, anxiety, stress and overall total mental scores at 1st (May-July 2020), 2nd (July-September 2020) and 3rd (October-December 2020) COVID waves.

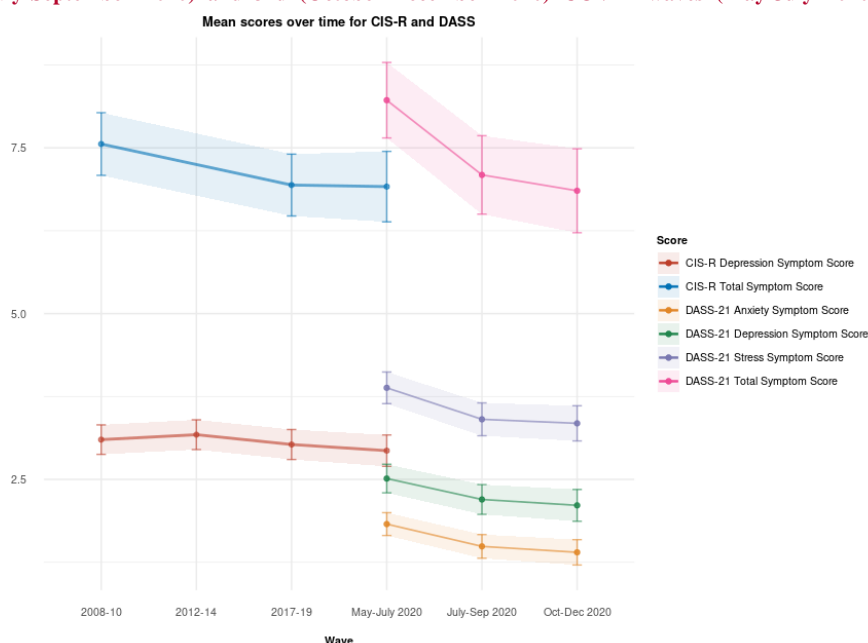
**Figure 2. Rates of psychiatric disorders at Wave 1 (2008-2010), Wave 2 (2012-2014), Wave 3 (2017-2019) and 1st COVID wave (May-July 2020).**



(A) For psychiatric disorders, significant changes were only observed for anxiety disorders. (B) For symptoms, DASS scores decreased along COVID waves. Diagnoses were evaluated using the Clinical Interview Scheduled - Revised and are based on the International Classification of Diseases, 10th version (ICD-10). F32.xx diagnoses were collapsed in “depressive disorders”, and F40.xx and F41.xx diagnoses were collapsed in “anxiety disorders”. Common Mental Disorders is a CIS-R based classification that describes people with relevant mental symptoms (CIS-R score >11). CIS-R (Clinical Interview Schedule-Revised). DASS; Depression, Anxiety, and Stress

Scale. Error bars represent 99.5% Confidence Intervals.~~No significant changes were only observed for anxiety disorders. Bars represent 99.5% Confidence Intervals. Diagnoses were evaluated using the Clinical Interview Schedule Revised and are based on the International Classification of Diseases, 10th version (ICD-10). F32.xx diagnoses were collapsed in “depressive disorders”, and F40.xx and F41.xx diagnoses were collapsed in “anxiety disorders”. Common Mental Disorders is a CIS-R based classification that describes people with relevant mental symptoms (CIS-R score >11).~~

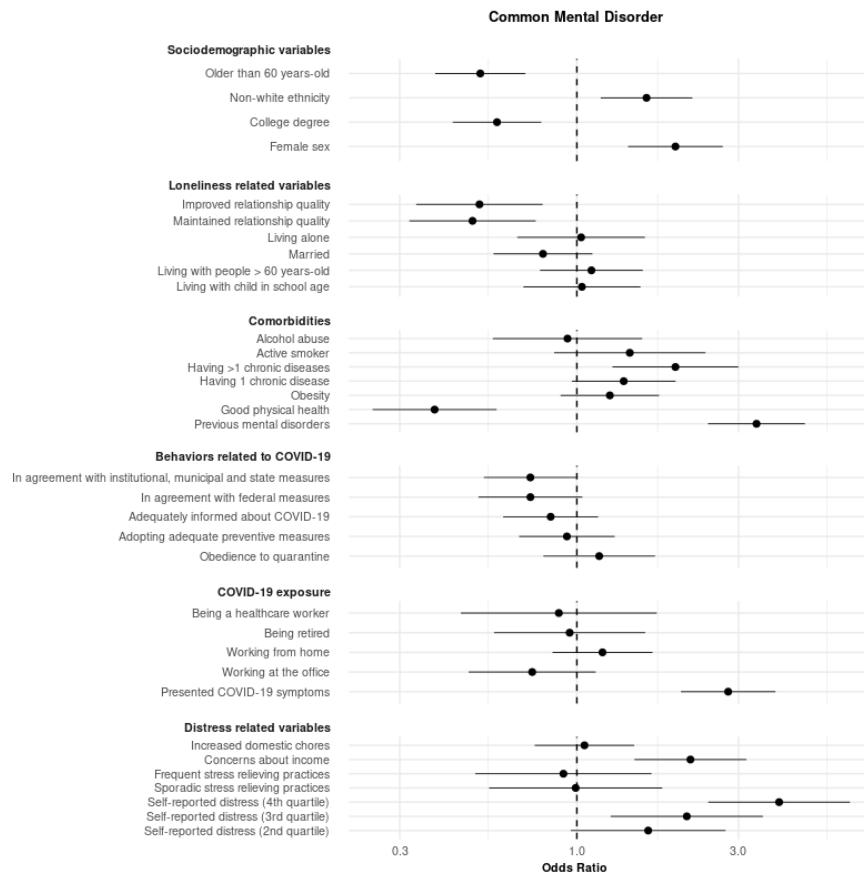
**Figure 3. CIS-R total symptom scores at Wave 1 (2008-2010), Wave 2 (2012-2014), Wave 3 (2017-2019) and 1st COVID wave (May-July 2020) and DASS dDepression, aAnxiety, sStress, and overall mental scores at Wave 1 (2008-2010), Wave 3 (2017-2019) and 1st (May-July 2020), 2nd (July-September 2020) and 3rd (October-December 2020) COVID waves (May-July 2020).**



CIS-R (Clinical Interview Schedule Revised). DASS; Depression, Anxiety, and Stress Scale. The figure shows stable CIS-R total symptom and depression scores from 2008 to 2020, and a decrease of DASS symptom scores measured during 2020. Error bars represent 99.5% Confidence Intervals.

Figure 3. Association of several exposure variables with common mental disorders.

**Figure 34. Association of several exposure variables with common mental disorders, depressive disorders, and anxiety disorders.**



Association was measured using Odds Ratios (ORs) and 99.5% Confidence Intervals. ORs > 1 and <1 indicate variables associated with increased and decreased risk, respectively. Models were adjusted by age, sex, ethnicity and educational level.



## General information

**A) Abstract (where applicable) must be structured using our standard subheadings only (Background, Methods, Results, Conclusions), not to exceed 250 words (including the 4 subheadings). NB: Review articles only may have an unstructured abstract not exceeding 250 words. Editorials and correspondence do not require an abstract but may include one at authors' discretion.**

**B) Figures, which must be uploaded only as a separate file and not combined with any other element of the submission, should be produced using size 8 point Arial font for the legend. Any wording within a figure should ideally be in Arial - 8 point size is standard, but this may vary depending on space limitations within individual figures. Wherever possible figures for print should be monochrome although colour figures are acceptable for online. You will be asked to pay for unnecessary colour printing. If you wish you may have colour online and black-and-white in print at no charge, in which case you should submit two copies of the figures, identical in every respect other than the colour. Figures should NOT be embedded or included in the main text file.**

**C) We are using the APA\* referencing format, listing all authors up to 7 in number, or the first 6 authors plus the last author, date, article title, journal title in full, volume, page numbers and/or DOI.**

**D) Appendices and supplementary material also should be submitted as a separate file from the main text. These will be published online exactly as they are received, so a clean version without track changes showing, etc, must be submitted. Authors may upload two \*clearly labelled\* versions of supplementary material, one clean and one showing changes if they feel this appropriate.**

**E) Text files (and tables) should be uploaded in editable form (ie word processor files, not pdf).**

**F) A clean copy of ALL files will be required prior to final acceptance. If you send a tracked changes copy of your revised manuscript (useful for editors and reviewers to see where you have made changes), you MUST also send a clean copy. The clean copy should be indicated as the main document, with the TRACKED copy as "RESPONSE TO REVIEWERS". You can have more than one file for each designation so it is possible to have both a tracked copy of the manuscript and a letter explaining your changes both indicated as response to reviewers. The tracked copy should NEVER be the main document.**

**G) You must include in the main document a declaration about any Conflict of Interest. If there is none then please state none.**

We stated that there are no conflicts of interest to disclose.

**Reviewers' and editor's comments:**

- ***The reviewers and I feel this is a potentially important paper but needs a lot of work to reach this potential. I would ask you to especially attend # 1's comments. This should be edited by a native English speaker before re-submission. It is likely I will ask # 1 to look at your revision. I will give you up to 5000 words of text so you have some room to expand here if you need it.***

Dear editor, thank you for the opportunity to review our work. We are confident that we addressed all questions raised by the reviewers. Our manuscript was also read and edited by a native speaker.

***Reviewer #1: This study analyzed pre- and peri-COVID data from employees at the University of Sao Paulo, one of the six universities in the ELSA-Brasil project that began in 2008. Data were collected from this cohort 3 times between 2008 and 2018. The 2018 assessment included the CIS-R administered by a rater. In the second half of 2020, 50% of participants agreed to complete additional questionnaires that included COVID items, the CIS-R, and the DASS, on-line, 3 times. Rates of common disorders were not significantly different before and during COVID. Symptom severity was basically stable over the 2020 waves, declining a bit. The expected demographic risk variables, but not most COVID items, were associated with greater anxiety and depression.***

Dear reviewer, thank you for your complete assessment of our work. Your evaluation is completely correct. Note that in this revised version we now present data from earlier assessments of our cohort (not only 2016-2018, but also 2008-2010 and 2012-2014) and that we discuss in more details the COVID items that were actually associated with the outcome.

- 1) ***The paper was very difficult to read because of language issues (uncommon words and odd phrases), abbreviations that weren't intuitively obvious (i.e., WC for covid wave ??), awkward sentence construction, irrelevant phrases (intention to treat?), and most importantly, the lack of a conceptual model for the 3 aims (especially aim 3) that would have given the aims coherence and depth.***

Thank you for your feedback. Regarding the issues regarding grammar and style, the manuscript was carefully reviewed by the authors and a native English speaker.

We have also now clearly specified each of our aims and have better stated our hypotheses and rationale, particularly for the 3rd aim:

“Another issue is that the mental impact of the pandemic in communities from low- and middle-income countries has not been addressed. For instance, female sex, income, educational level, psychiatric comorbidities, and worse physical health have been associated with unfavourable mental health outcomes

in these countries (Musliner *et al.*, 2016; Alonso *et al.*, 2018) and might be risk factors in the pandemic. Also, studies in China and developed countries explored whether age, severity of lockdown and disruption of daily activities, physical distancing, chronic diseases, and worries associated with contracting or having severe presentations of COVID-19 were associated with mental outcomes, with mixed findings (Pierce *et al.*, 2020; Prati and Mancini, 2021).

Therefore, there is mixed evidence of worsening psychopathology during the pandemic. Thus, we further examined pandemic-related changes in mental symptoms and diagnoses, and their determinants, in the Brazilian Longitudinal Study of Health (ELSA-Brasil), a well-characterized Latin American cohort. Our aims were threefold:

(1) to compare the rates of psychiatric disorders and changes in symptomatology between pre-pandemic and pandemic assessments. We hypothesized that an increase in psychiatric diagnoses and symptoms would be observed, as previously reported (Vindegaard and Benros, 2020);

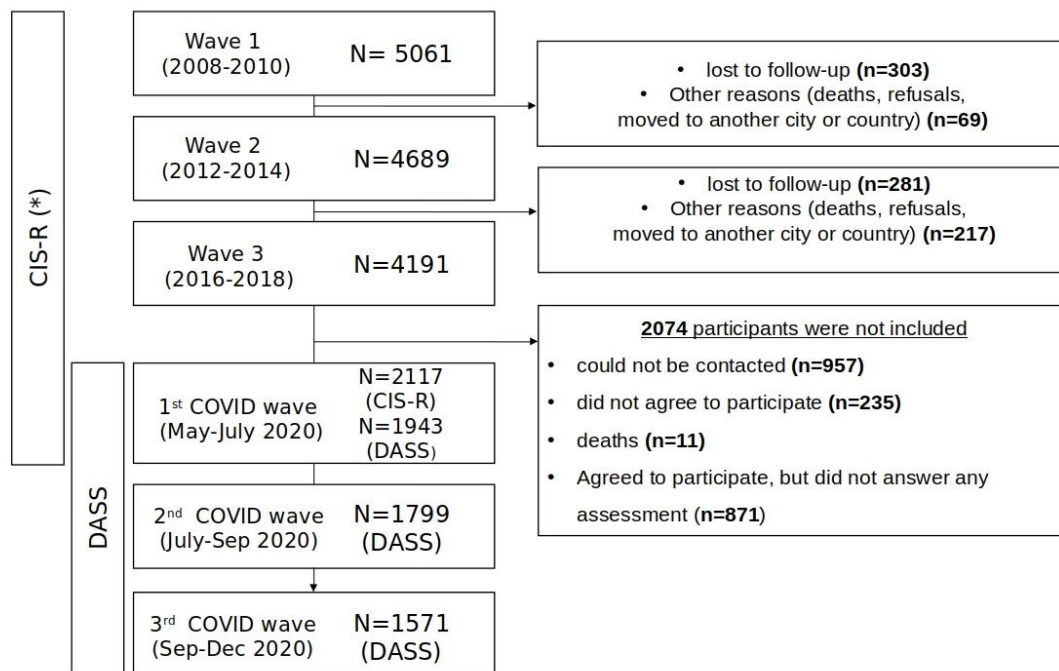
(2) to assess the overall changes of psychiatric symptomatology during intra-pandemic assessments; likewise, we hypothesized that psychiatric symptoms would increase, according to the literature (Salari and Hosseini-Far, 2020);

(3) to assess whether variables such as age, sex, ethnicity, educational level, clinical and psychiatric comorbidities, exposure to COVID-19, adherence and agreement to physical distancing and other quarantine measures, leisure activities, employment status, and financial impact, would be associated with mental disorders. We hypothesized that female sex, lower educational level, non-white ethnicity and psychiatric comorbidities would be risk factors for mental disorders, as observed in earlier ELSA-Brasil studies (Brunoni *et al.*, 2019; Librenza-Garcia *et al.*, 2020). We also hypothesized that the elderly, people with low physical health, and those with risk factors for severe forms of COVID-19 would be more stressed and thus being at greater risk for developing mental disorders. Moreover, we expected that variables associated with loneliness and stress would be associated with greater mental disorder risk (Killgore *et al.*, 2020), and those associated with leisure and stress-alleviating practices, with decreased risk for mental disorders. Finally, we hypothesized that a greater understanding of the COVID-19 (including hygiene and

physical distance behaviors and agreement with the quarantine) would protect from mental illness, as this could decrease the fear of the pandemic (Brooks *et al.*, 2020) and enhance general cooperativeness (i.e., “collective effervescence”, as characterized by Durkheim) (Zumeta *et al.*, 2020).”

**2) Design: The original response rate at time 1 (2008) and attrition bias between time 1 and 3 were not provided. However, the 2020 participants represented 50% of the time 3 sample. Sample biases included more women, younger, better educated, and fewer psychiatric symptoms. Limitations noted the 50%, stating that it's better than 30%. But (a) it seems high for an established occupational cohort and (b) it's not clear to whom the findings from this study can be generalized.**

We have now described attrition rates throughout the cohort in the new Figure 1:



The ELSA-Brasil cohort was also described in more details:

“ELSA-Brasil is a prospective, longitudinal cohort of 15,105 participants from six universities in major Brazilian cities (São Paulo, Rio de Janeiro, Salvador, Belo Horizonte, Vitoria, and Porto Alegre). At its inception, it was the first, largest cohort in Latin America. Its aims were to identify the clinical and sociodemographic determinants of mortality and of the development of chronic diseases within a population

of a low-/middle- income country. It initially aimed to recruit 15,000 out of 52,137 potential participants, stratified by sex, age and occupational category. Recruitment goals were defined by sex (50% each), age (15% aged 35–44, 30% aged 45–54, 40% aged 55–64 and 15% aged 65–74 years) and occupational category (35% of support level, with incomplete elementary school; 35% with high school and 30% with higher education/teaching level). From 16,43 interested participants, 15,821 were pre-enrolled, and gave written consent, responding to an initial pre-interview. Only 716 (4.5%) of them did not complete the baseline examination, achieving a final sample of 15,105 participants. The recruitment goals were fully achieved in all centers (Schmidt *et al.*, 2014).

The cohort began in August 2008, when eligible participants were all active or retired employees of these universities, who were between 35 and 74 years-old, and free of major neurocognitive disorders at enrollment (Aquino *et al.*, 2012; Schmidt *et al.*, 2014). Posterior waves did not recruit new participants. The 1st, 2nd, and 3rd waves occurred in 2008-10, 2012-14, and 2016-18, respectively. During each wave, onsite assessments comprised clinical interviews and examinations, collecting information on sociodemographic variables, clinical history, family history of diseases, lifestyle factors, and anthropometric measurements. Laboratory tests were also collected during the visits (M. I. Schmidt *et al.*, 2014; Aquino *et al.*, 2012).

In 2020, “COVID-19 wave” assessments were carried out only by the São Paulo research center. Data collected during 2020 consisted of 3 online assessments (c1, c2, and c3 waves, respectively, performed between May 18th to July 18th ;July 20th to September 30rd; and October 1st to December 22nd). The most severe lockdown measures in São Paulo started on March 22nd, 2020 and continued through July 10th, 2020 (Quarentena, n.d.); therefore, the c1 wave corresponds to the 8th to 16th quarantine weeks; the c2 wave corresponds to an exponential increase of deaths and cases in Brazil, with some flexibility on quarantine measures adopted by the end of September. and the c3 wave corresponds to a moderate decrease in the rate of daily deaths and cases and greater quarantine relaxation measures in Brazil.

This study was approved by the Local Ethics Committee at the University Hospital, University of São Paulo and is reported according to the STROBE guidelines (von Elm *et al.*, 2007). All patients provided electronic informed consent for participation in the study. “

Regarding (a), we agree that it would be ideal if the recruitment rate had been higher. However, please note that this issue was faced by several cohorts worldwide, especially those that, as ours, had not a planned assessment in 2020. As examples, note that the combined response rate of 3 Dutch Cohorts was only slightly higher than ours (55%), (Pan *et al.* 2020). Moreover, in a cohort study (also published in Lancet Psychiatry as Pan *et al.*) the response rate was 41-48% (Pierce *et al.* 2020). In another study, the combined response of 4 UK cohorts was only 25.7% ([Evandrou \*et al.\* 2021](#)). Moreover, additional issues were: (1) the relatively old age of our sample; (2) low digital literacy due to the socio-economic status; (3) the need for fast data collection as to capture the moment of the acute pandemic period; (4) organizing the study during the pandemic, transitioning to online meetings and workspaces.

These issues are now commented in the revised manuscript version:

“First, the mean age of our sample was around 60 years-old; therefore our results might not be applicable to younger populations. Second, approximately only half of the eligible sample answered our survey. This is in line with cohorts in the UK and the Netherlands that presented response rates in online assessments during the pandemic of 25-55% (Pan *et al.*, 2020; Pierce *et al.*, 2020; Evandrou *et al.*, 2021). These modest rates probably occurred due to the need of rapid organization for collecting timely data during the pandemic. In fact, initial response survey rates are typically around 30% and increase only after many contacts, which usually take several months (Fincham, 2008). As we aimed to capture the mental health of the sample in a short period, we only extended our recruitment for two months. Third, although the differences between responders and non-responders were mostly small, a higher educational level was observed in responders, which probably reflects the spectrum of digital literacy within the sample. Notwithstanding, inherent issues of our sample are its relatively old age and low digital literacy. “

Regarding (b), in the revised manuscript version, we discuss that our absolute rates should be interpreted in the context of longitudinal changes within the same sample. Nonetheless,

considering that developing countries present huge socioeconomic disparities, our findings might also provide insights in samples with similar characteristics in these countries. Finally, our individual participant data results can be analysed in the context of mega-cohort analyses to explore whether the observed risk factors are of worldwide importance or country-dependent:

“We used a well-defined cohort, which decreased the risk of selection bias, enhancing the external validity and generalizability of the findings, in contrast with snowball sampling. However, our sample is occupational and not population-based, being composed of public servants of the University of São Paulo. Their income, which is on average higher than the national income, was essentially unaffected during the pandemic. Thus, the rates of psychiatric disorders and symptoms should not be considered as nationally representative, but rather interpreted in the context of longitudinal changes within the same sample and associated risk factors. Nonetheless, even representing a fraction of the Brazilian population, our findings are interesting for similar samples from other developing countries that continually struggle with huge socio-economic inequalities, with vulnerable safety nets, and which have some of the highest COVID-19 excess mortality rates (The Lancet, 2020b), and for mega-cohort analyses exploring whether the observed exposure variables are of worldwide importance or country-dependent, which is important to develop comprehensive early intervention strategies in different contexts.”

**3) *Many measures were inadequately described in the text, especially the determination of diagnosis on the CIS (is it only based on number of symptoms?) and the COVID items. How did the authors determine that the self-administered version of the CIS produced equivalent values as the rater administered version in this sample? What were the inter-correlations among the COVID items? Having looked at the associations of the individual items, was any consideration given to creating summary covid experiences scales?***

Regarding the CIS-R, we agree that it was insufficiently described in the main text. We added the following information in Methods:

“Psychiatric diagnoses were assessed using the validated Brazilian version of the Clinical Interview Schedule-Revised, CIS-R (Lewis *et al.*, 1992; Nunes *et al.*, 2011), a structured interview for measurement and diagnosis of current non-psychotic psychiatric morbidity in the community. CIS-R has poor sensitivity

for diagnosing mental disorders, which might slightly underestimate the rates of psychiatric disorders, although its specificity is high (Brugha *et al.*, 1999). Due to its length, it was applied only during the first COVID-19 wave assessment.

The CIS-R includes the assessment of 14 symptoms and 13 psychiatric disorders based on the International Classification of Disease, 10th edition (ICD-10). The CIS-R domains are somatic complaints, fatigue, concentration and forgetfulness, sleep disturbance, irritability, worry about physical health, depression, depression ideas, worry, anxiety, phobias, panic attacks, compulsions, and obsessions. Scores for each section range from 0 to 4 (except the score for depressive ideas that range from 0 to 5), therefore the total score ranges from 0 to 57. A symptom is present if the corresponding section score is  $\geq 2$ .

The relevant symptoms are grouped to form, with accessory questions and based on an algorithm following ICD-10 diagnostic criteria, the following diagnoses: mild depressive episode without (F32.00) and with somatic syndrome (F32.01); moderate depressive episode without (F32.10) and with somatic syndrome (F32.11); severe depressive episode (F32.2); agoraphobia without (F40.00) and with panic disorder (F40.01); social anxiety disorder (SAD, F40.1); specific (isolated) phobias (F40.2); panic disorder (PD, F41.0); general anxiety disorder (GAD, F41.1); and obsessive-compulsive disorder (OCD, F42.9). Finally, F32.xx diagnoses were collapsed in “depressive disorders”, and F40.xx and F41.xx diagnoses were collapsed in “anxiety disorders”.

Moreover, the total CIS-R score is obtained by adding the scores of all 14 (non-binarized) symptoms. Based on this score, a diagnosis of common mental disorder (CMD) (CIS-R $>11$ ) is operationally defined (Lewis *et al.*, 1992). Finally, the CIS-R score of depressive symptoms was calculated by summing up symptom scores of depression, depression ideas, fatigue, concentration/forgetfulness and sleep disturbance as used previously (Khandaker *et al.*, 2018; Brunoni *et al.*, 2020).

Due to the quarantine measures, it was impossible to collect CIS-R data onsite, as done in previous waves. Therefore, we used an electronic, self-applied CIS-R format that was identical to the one used in



clinical interviews. Importantly, the online version was self-applied, whereas the onsite version was read by trained personnel. Thus, uncontrolled differences in answering engagement could have occurred. However, previous studies have already validated and compared an electronic, self-applied CIS-R version with its standard format, showing that the electronic version presents valid and reliable performance (Lewis *et al.*, 1988) (Lewis, 1994). In fact, a validation study showed that the performance of both versions was similar (Head *et al.*, 2013). In that study, no differences between mean scores in 12 of the 14 symptom scores were observed. Moreover, both versions presented similar accuracy in diagnosing psychiatric disorders (Head *et al.*, 2013).”

Regarding the COVID questionnaire, in the initial manuscript version all information was provided in the Supplementary Material due to its extensive length. However, we agree that part of this information, due to its importance, should be described in the main text. Therefore, a new Table was added in the manuscript describing how these variables were created:

Exposure Variables		Observations
<b><i>Sociodemographic variables</i></b>		Data from 2008-2010 - 1st ELSA-Brasil wave
Older than 60-years old	Based on Date of Birth	
Non-white ethnicity	Based on self-reported ethnicity	
College degree	--	
Female sex	--	
<b><i>Loneliness related variables</i></b>		Data from 2020 - COVID-19 wave
Relationship quality	Classified into <i>worsened</i> , <i>improved</i> or <i>maintained</i> according to changes in relationship quality with family and friends, in a Likert scale	
Living alone	--	
Married	--	
Living with people > 60 years-old	--	

Living with children in school age --

### **Comorbidities**

Data from 2020 - COVID-19 wave

Alcohol Abuse	Present if women reported taking >1 dose/day and men >2 doses/day during a given week
Active smoker	--
Chronic Diseases	Self-reported presence of one or more of Diabetes, High blood pressure, heart attack, stroke, asthma, chronic bronchitis, or other chronic conditions (*)
Obesity	Body Mass Index > 30, based on self-reported height (2016-2018 3rd wave) and self-reported weight (2020 COVID-19 wave)
Physical Health	Self evaluation of physical health in comparison to others of the same age, in a Likert Scale. Classified into <i>not very good physical health</i> or <i>good physical health</i> .
Previous Mental Disorders	Self-reported presence of one or more mental disorders

### **Behaviours related to COVID-19**

Data from 2020 - COVID-19 wave

In agreement with institutional, municipal and state measures	Participants filled out how much they agreed with measures against COVID-19 adopted by each government instance, in a Likert Scale. "In agreement" was established when the participant completely agreed to measures.
In agreement with federal measures	
Adequately informed about COVID-19	Present when participant reported having high level information about COVID-19 symptomatology, transmissibility and preventive hygiene methods
Adopting adequate preventive measures	Present if participant adhered to recommendations to reduce risk of COVID-19 transmission (**).
Obedience to quarantine	Present if participant adhered to "stay-at-home" recommendations during the quarantine, such as leaving their home only when extremely necessary

### **COVID-19 exposure**

Data from 2020 - COVID-19 wave

Being a healthcare worker	--
Being retired	--
Working from home	--
Working at the office	--
Presented COVID-19 symptoms	Present when at least one COVID-19 symptom was reported (***)

***Distress related variables***

Data from 2020 - COVID-19 wave

Concerns about income	Classified as <i>concerned</i> or <i>not concerned</i> according to the score of three questions evaluating concerns about income changes during the pandemic
Stress relieving practices	Classified in <i>frequent</i> , <i>sporadic</i> and <i>no stress relieving practices</i> based on number and frequency of stress-relieving activities performed per week, in a Likert scale
Self-reported distress	Classified from 1st to 4th quartiles of <i>Self-reported distress</i> according to how much distress they felt about determined situations, in a Likert scale (****)
Increased domestic chores	Present when participant reported doing more chores at home during the pandemic period than they did before

(\*) If a chronic disorder was described, we assessed whether it could be considered as one.

(\*\*) Recommendations were: washing hands frequently, removing shoes before entering their homes, wearing masks, covering mouth and nose when sneezing, refraining from shaking hands or kissing when greeting somebody, washing store bought packages before use, and using alcohol gel.

(\*\*\*) COVID-19 symptoms were: fever, cough shortness of breath, sore throat, fatigue (Physical), loss/decreased sense of smell, loss/decreased sense of taste

(\*\*\*\*) Situations were: staying home, avoiding close contact with other people or crowds, refraining from meeting friends, refraining from meeting other family members, having postponed or canceled important events, having postponed or canceled trips, and hearing news of the COVID-19 pandemic

**4) *The section labeled Exposure Variables is really a "Risk Variables" section. Besides more information on the COVID items in the text, other variables in this section were also not adequately described. For example, BMI is determined from height and weight. Were both obtained concurrently, or was only weight on the 2020 questionnaire? Given the age of the sample (60), height would have changed from the collections before 2020. I may have missed it, but were other relevant risk factors for this cohort included, such as retirement status, income adequacy, and chronic diseases like diabetes, hypertension, and autoimmune diseases?***

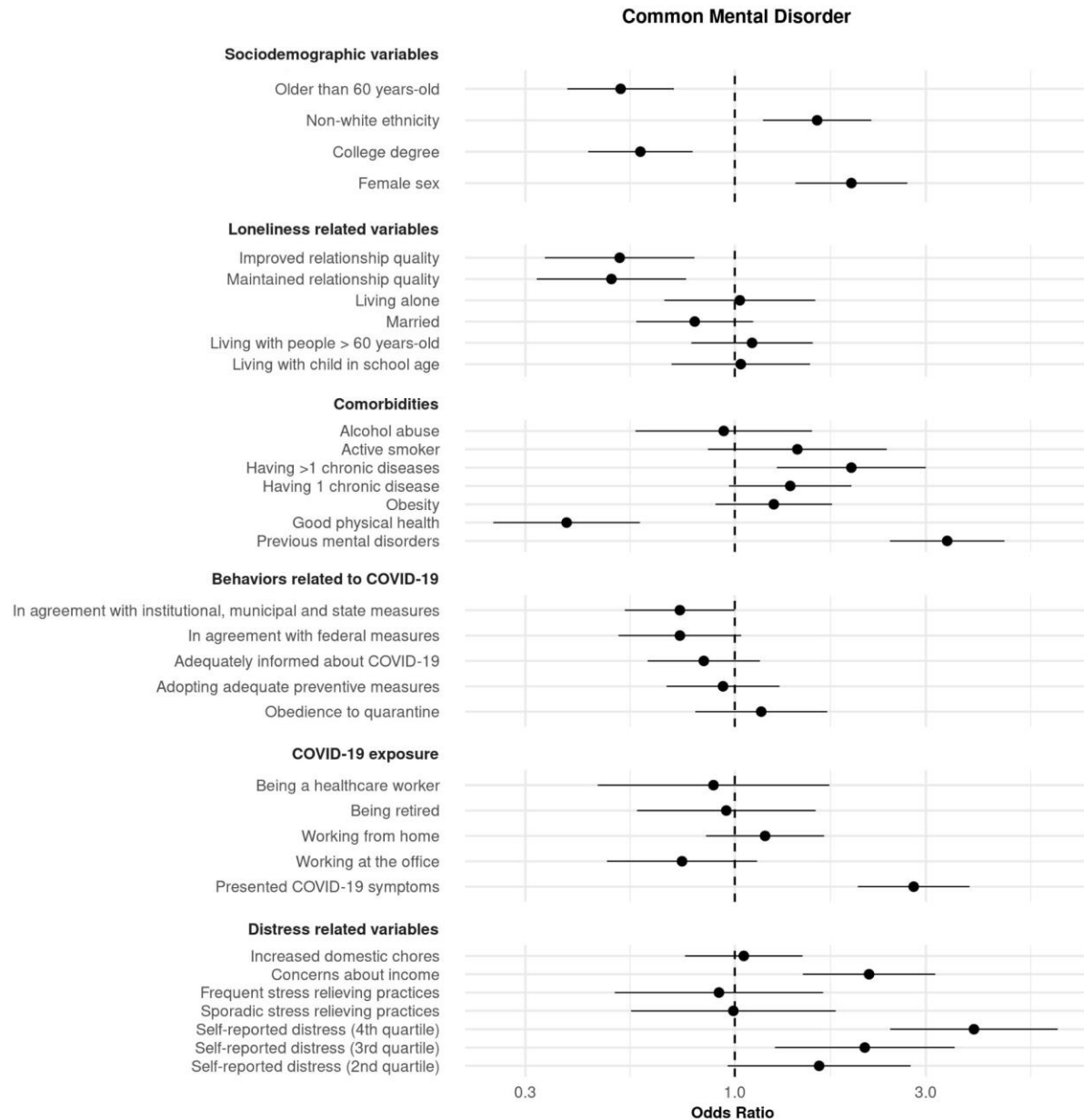
Thank you for your comment. We decided to keep the term “exposure” rather than “risk” in the section as this is a commonly used term in observational studies and is more agnostic regarding causality inference (although “risk” was also used in the manuscript when we considered it appropriate to indicate causality).

We have now provided complete information on all variables used in our analysis in the Supplementary Material and in the new Table 1, including those collected in previous waves and those collected in the COVID assessment. Particularly:

- height (in cm) was obtained from the 3rd wave, since we considered that eventual height changes between 2016-18 and 2020 would still be more accurate than self-reported height, as the 2016-2018 assessment was performed by trained staff.

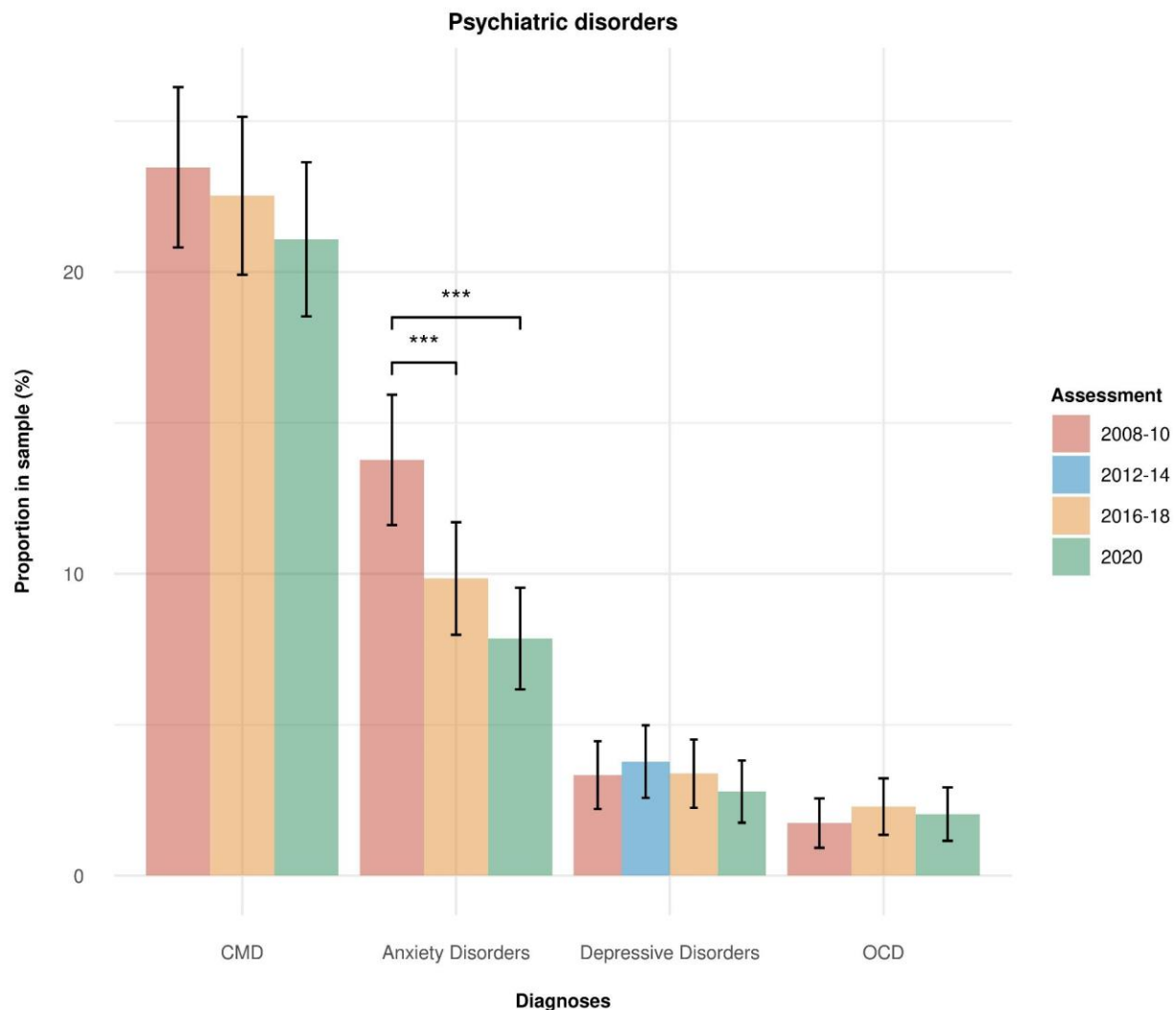
- Chronic diseases such as diabetes and hypertension were surveyed, as well as other diseases associated with greater COVID-19 severity risk. Autoimmune diseases were not surveyed, as we observed, from previous ELSA-Brasil waves, that they were not correctly self-described by participants, and also because the presence of verified auto-immune disorders in ELSA-Brasil is <1%.
- Questions about financial impact of the pandemic and retirement status were indeed surveyed in our study and now clearly indicated in the manuscript.

Also, please note that more than 5000 variables have been collected in previous waves, and therefore the number of analyses that could be taken is endless (future studies will use data-driven and other hypothesis-driven approaches). However, the suggestion of better elaborating Aim 3 helped us to state more clearly why these variables were selected. Also note that Figure 3 was reorganized according to our aim:



5) ***Aim 1 was to examine differences in diagnosis before and at the first wave of the 2020 study. Was it necessary to show every individual diagnosis, as opposed to broader categories, given the comorbidity of the disorders shown in Figure 2? Are there data on diagnosis at time 1 (2008)? If so, were diagnoses stable across the pre-COVID study decade?***

We thank the reviewer for this suggestion. In the revised manuscript version, we only provide description of broad psychiatric disorder categories, and display data regarding the first wave as well:



Summarily, only a decrease in anxiety disorders was observed (but not OCD, depressive disorders and Common Mental Disorders). This is now discussed in the revised manuscript version:

“Our first aim was to compare the prevalence of mental disorders in 2117 participants in the ELSA-Brasil São Paulo study center between two pre-pandemic assessments (2008-2010 and 2016-2018) and the initial phases of the COVID-19 pandemic (May-July 2020). Contrary to our initial hypothesis, the rates of observed psychiatric disorders were not significantly different from previous assessments. Likewise, overall mental symptoms and depressive symptoms did not significantly change over time. In fact, a slight decrease in anxiety disorders was found. We believe that a lower rate in the COVID-19 assessment was

partially observed due to a decrease in the rate of generalized anxiety disorder (GAD), which has a time criterion duration of 6 months or more. As the assessment was performed in May-June and the pandemic started in March 2020, possibly some participants considered that anxiety symptoms only started after the pandemic, even if they were present before (recall bias). In fact, additional analyses changing the time criterion for 2 weeks or more (for all waves) revealed similar rates of anxiety disorders among all waves (data not shown).

As for our second aim, we performed 3 longitudinal assessments from May to December 2020 to evaluate changes in depression, anxiety, and stress scores. Also contrary to our hypothesis, these symptoms were either maintained or slightly decreased during the pandemic. Notwithstanding, our findings are in line with other studies. In a prospective study in the UK with more than 70,000 people examined during the lockdown period in the first semester of 2020, depressive and anxiety symptoms were moderately high at the beginning of lockdown measures but decreased rapidly during the next 20 weeks (Fancourt *et al.*, 2020). A longitudinal study of three Dutch case-control cohorts, with well-characterized psychiatric disorders, employed data from approximately 1,500 subjects and assessed depressive symptoms, anxiety, worry, and loneliness. People without psychiatric disorders showed a slight increase in symptoms during the pandemic, whereas those with the greatest previous mental health burden tended to exhibit a slight symptom decrease (Pan *et al.*, 2020). In a longitudinal assessment in Ireland with over 1000 participants (Hyland *et al.*, 2020), rates of GAD were actually higher in 2019 compared to 2020, and further decreased during the pandemic. In contrast, other studies showed an increase in mental health symptomatology. In a US study comparing matched (but different) adult samples before and during the pandemic, the prevalence of probable depression rose from 8.5% to 27.8% (Ettman *et al.*, 2020). In a UK study with 48,486 respondents, the prevalence of mental health symptoms rose from 24.3% in 2016-2018 to 37.8% in April 2020, further decreasing to 31.9% in June 2020. Interestingly, those with a pre-existing depressive disorder did not experience an increase in mental symptoms (Daly *et al.*, 2020). “

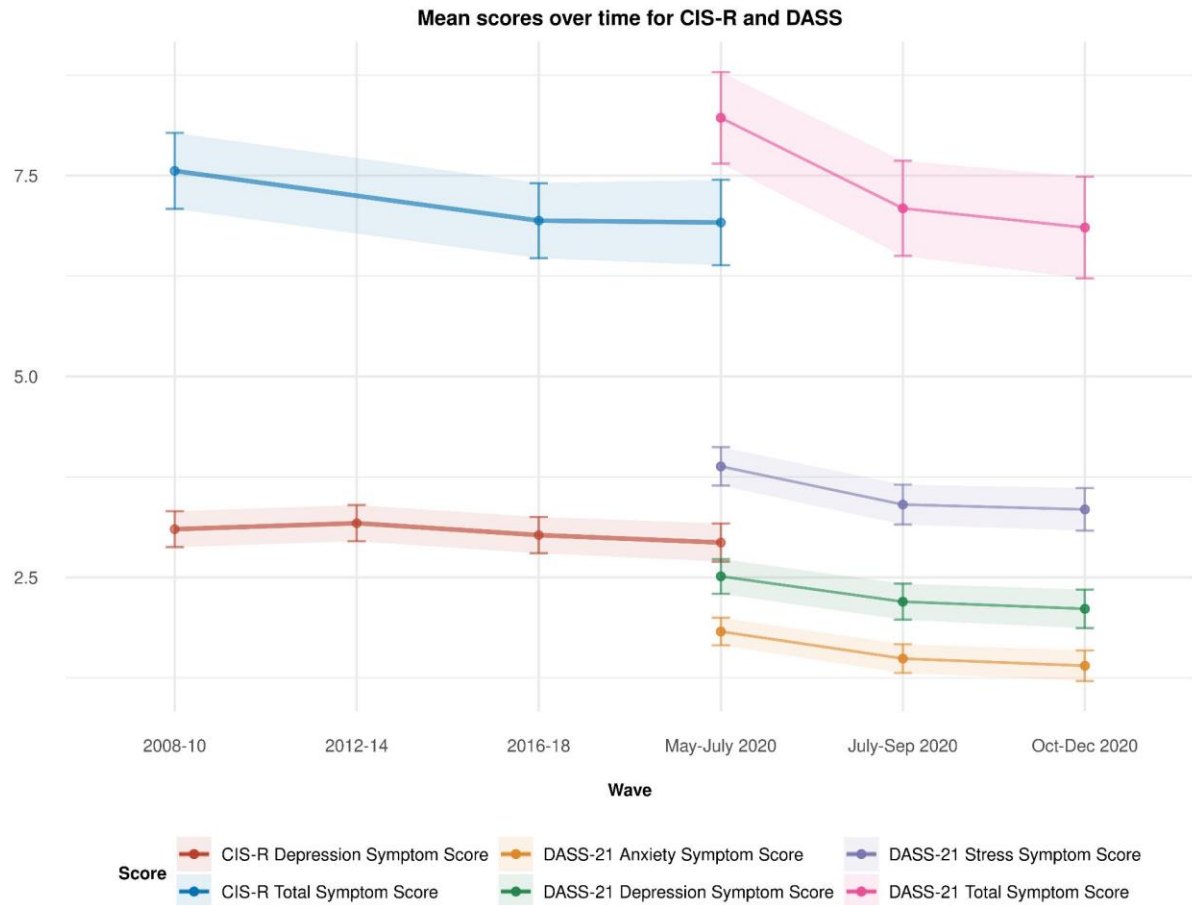
- 6) ***Aim 2 was to examine first whether DASS scores changed across the covid waves, and they basically didn't. Aim 2 also asked about the trend starting in 2018? The problem is that the DASS wasn't included in the 2018 wave. So the authors imputed DASS scores for the 2018 wave. It seems to me that this additional Aim 2 goal goes beyond the data. It's one thing to impute missing values. But to impute missing measures for an entire sample in order to expand what was shown in Aim 1 -- needs further justification. If on the other hand, the 2018 and 2020 assessments both contain other mental health markers, like subjective mental health ratings, this would be a reasonable expansion of aim 2.***

Thank you for your comment. CIS-R (as it is better explained in the present review) was also developed as a continuous score and was used to assess mental health changes between the 3rd ELSA-Brasil wave (2016-18) and the 1st covid wave (May-July 2020). In fact, in this revised version, we also expanded our analyses to include the first ELSA-Brasil wave (2008-2010) as shown in Figures 2A and 2B.

Regarding DASS, it was collected only in 2020, in the 3 assessments. Since we collected DASS and CIS-R at the same time (May-July 2020) and they are highly correlated, we did a equipercentile linking to identify their corresponding scores, as it is done in psychometric studies (e.g., Samara et al., Eur Neuropsychopharmacol, 2014). Based on that, we estimated, in the 3rd wave, the corresponding scores of DASS based on the CIS-R. Therefore, we do not think that these values were necessarily “imputed”, but rather “projected” or “estimated” from known values. Nonetheless, we agree that this approach is not necessary for the present study and therefore this part of the analysis was removed.

In Figure 2B, we kept both DASS and CIS-R in the same graph due to space limitations and to show temporal trends. However, there is no more dash lines indicating a connection between DASS and CIS-R. Also, in Figure 1 the CIS-R and DASS assessments are also indicated.





**7) Aim 3 would benefit from a conceptual model linking established risk factors, prior occupational exposures and COVID experiences, and hypothesized interactions, to mental health during COVID.**

We agree with the reviewer. As indicated above, the Introduction was updated to better show our aim and Figure 4 was reorganized according to the 3rd aim. Also, a new Table 1 was created in order to show the variables assessed. Finally, the discussion was also updated:

“Regarding the third aim, we confirmed, in agreement with our hypothesis, that female sex, non-white ethnicity and lower educational level were risk factors for CMD. These characteristics reflect socio-economic disadvantages and have been observed as risk factors for incident and persistent depression in a previous ELSA-Brasil study (Brunoni *et al.*, 2019)(Xiong *et al.*, 2020). People with lower educational levels also experienced more psychiatric symptoms (Xiong *et al.*, 2020), possibly due to accumulating workload and the impossibility of stopping working and/or working from home, generating distress. In a UK study,

non-white ethnicities (Proto and Quintana-Domeque, 2021) also experienced higher mental distress, in line with our findings. Interestingly, meta-analyses did not find an association between these factors and psychiatric symptoms (Prati and Mancini, 2021; Wu *et al.*, 2021), although meta-analyses are usually underpowered for such analyses. Although we expected that increased age - due to stress of presenting a severe form of COVID-19 - would be associated with psychiatric disorders, what was found was that people younger than 60 years-old presented increased risk. Interestingly, this was also observed in a systematic review (Xiong *et al.*, 2020) and could be explained by factors such as the impossibility of staying at home due to employment, lower financial support and more domestic activities (e.g., taking care of children).

We also analysed several other variables corrected for age, sex, ethnicity, and educational level. Psychiatric comorbidity was a risk factor for presenting CMD, reflecting the greatest mental burden associated with these patients, as demonstrated previously (Pan *et al.*, 2020), and emphasizing the need of maintaining psychiatric care during the pandemic. Regarding clinical comorbidities, exposure variables associated with increased rates of CMD include having had COVID-19 symptoms (tests were not widely available and there were stay-at-home instructions for mild cases when data were collected, so no confirmatory assessment was done), and presenting one or more chronic diseases, while self-reported good physical health was associated with decreased risk. This suggests that participants with greater susceptibility of presenting a severe case of COVID-19 were those more likely to develop psychiatric disorders. Conversely, obesity, being a smoker, and alcohol abuse were not associated with significant increased risk, which could be explained by inadequate perception or awareness of these variables as risk factors for severe COVID-19.

High or very high self-reported distress levels (evaluated by questions such as the distress associated with staying at home, avoiding contact with people, refraining from meeting friends and relatives, and others) and concerns about income were associated with increased odds of presenting mental disorders. However, stress alleviating practices were not associated with decreased risk, or increased domestic chores with increased risk. This possibly reveals that activities at home during the quarantine are

less important for modifying mental health than initially hypothesized by researchers (Pfefferbaum and North, 2020). Notwithstanding, maintaining or improving relationship quality (e.g., using social apps) were associated with decreased risk. In fact, feelings of loneliness might have been attenuated via social media and electronic apps of mental health support; also, activities that could be done at home were not stopped (Williams *et al.*, 2021).

Interestingly, agreement with federal measures (which almost reached statistical significance) or institutional/municipal/state measures were independently associated with lower odds of having mental disorders. This is surprising as the Brazilian president adopted a radical anti-quarantine attitude, promoting mass rallies and systematically undermining the severity of the pandemic (The Lancet, 2020a), whereas the institutional/municipal/state instances adopted a pro-quarantine/pro-science perspective. Possibly, political identity and ideology are protective factors since they are cognitive shortcuts to support shared beliefs and similar choices (Pereira *et al.*, 2020), decreasing the mental burden in choosing between difficult options.

Finally, healthcare workers presented no increased odds for psychiatric disorders. Importantly, healthcare professionals from our sample work at the University Hospital, which only treated cases of moderate severity, while severe cases of COVID-19 were transferred to a tertiary university hospital. This might have reduced the stress overload of our sample of healthcare workers who worked in relatively less stressful conditions. Also, those with higher risk of COVID-19 morbimortality were kept away from work. Interestingly, a recent systematic review showed that their rates of depression and anxiety during the pandemic are neither necessarily higher than the general population, nor increased compared to pre-pandemic levels (Liu *et al.*, 2020).“

***Reviewer #2: This paper analyzed detection rates of common psychiatric symptoms, depression, anxiety and common mental disorders and their determinants in 3 assessments in Brazil during the COVID-19 pandemic in 2020, and compared those data with the pre-pandemic ELSA-Brasil assessment (2016-2018). The authors found that COVID-19 pandemic did not have much effect on the psychology of the responders in the cohort, detection rates of common psychiatric symptoms had not increased, but slightly decreased along 2020. Risk factors associated with socioeconomic disadvantages were associated with higher risk of psychiatric disorders. The study is interesting and***

***conducive to a comprehensive understanding of the impact of COVID-19 pandemic on occurrence of common psychiatric problems. However, there are too much to be corrected and further explained.***

We thank the reviewer for these comments. We believe that we were able to improve this manuscript after the reviewers' suggestions.

- 1. The authors should further elaborate the ELSA-Brasil longitudinal cohort. If ELSA-Brasil is a sampled and population-representative cohort, the current results would be highly biased due to the high proportion of non-responders at stage WC and the significant difference in detection rates for many common psychological problems between non-responders and responders at baseline 2016 -- 2018 (W3). If it is not a representative cohort, extrapolation of the results of this study should be done with caution.***

Regarding the ELSA-Brasil cohort, we have described it in more details in the Methods section and in the new Figure 1:

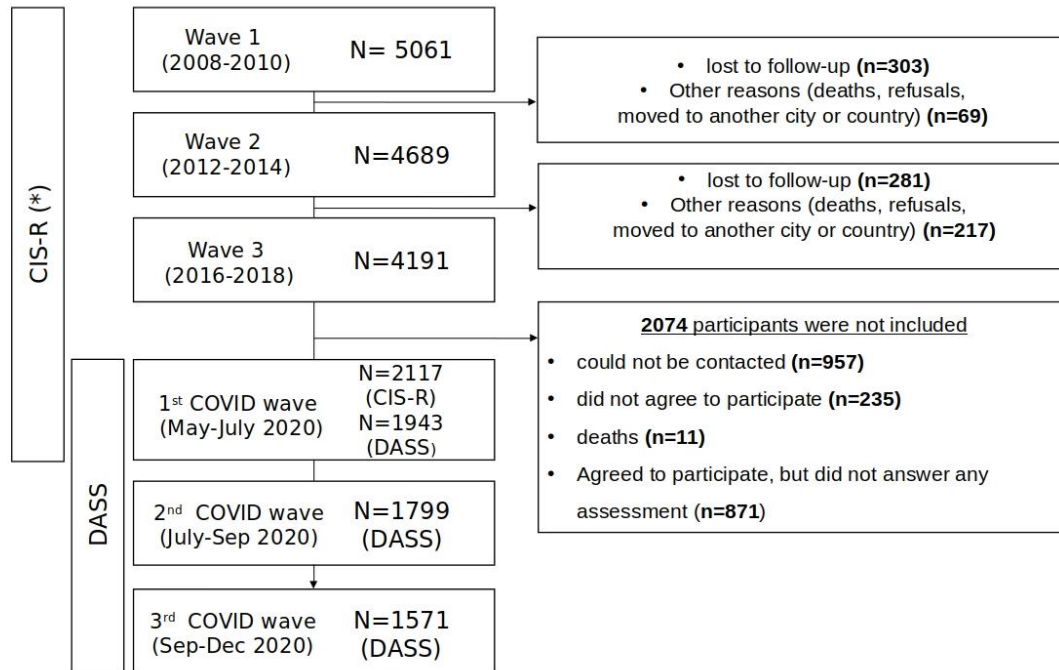
“ELSA-Brasil is a prospective, longitudinal cohort of 15,105 participants from six universities in major Brazilian cities (São Paulo, Rio de Janeiro, Salvador, Belo Horizonte, Vitoria, and Porto Alegre). At its inception, it was the first, largest cohort in Latin America. Its aims were to identify the clinical and sociodemographic determinants of mortality and of the development of chronic diseases within a population of a low-/middle- income country. It initially aimed to recruit 15,000 out of 52,137 potential participants, stratified by sex, age and occupational category. Recruitment goals were defined by sex (50% each), age (15% aged 35–44, 30% aged 45–54, 40% aged 55–64 and 15% aged 65–74 years) and occupational category (35% of support level, with incomplete elementary school; 35% with high school and 30% with higher education/teaching level). From 16,43 interested participants, 15,821 were pre-enrolled, and gave written consent, responding to an initial pre-interview. Only 716 (4.5%) of them did not complete the baseline examination, achieving a final sample of 15,105 participants. The recruitment goals were fully achieved in all centers (Schmidt *et al.*, 2014).

The cohort began in August 2008, when eligible participants were all active or retired employees of these universities, who were between 35 and 74 years-old, and free of major neurocognitive disorders at enrollment (Aquino *et al.*, 2012; Schmidt *et al.*, 2014). Posterior waves did not recruit new participants.

The 1st, 2nd, and 3rd waves occurred in 2008-10, 2012-14, and 2016-18, respectively. During each wave, onsite assessments comprised clinical interviews and examinations, collecting information on sociodemographic variables, clinical history, family history of diseases, lifestyle factors, and anthropometric measurements. Laboratory tests were also collected during the visits (M. I. Schmidt et al., 2014; Aquino et al., 2012).

In 2020, “COVID-19 wave” assessments were carried out only by the São Paulo research center. Data collected during 2020 consisted of 3 online assessments (c1, c2, and c3 waves, respectively, performed between May 18th to July 18th; July 20th to September 30rd; and October 1st to December 22nd). The most severe lockdown measures in São Paulo started on March 22nd, 2020 and continued through July 10th, 2020 (Quarentena, n.d.); therefore, the c1 wave corresponds to the 8th to 16th quarantine weeks; the c2 wave corresponds to an exponential increase of deaths and cases in Brazil, with some flexibility on quarantine measures adopted by the end of September. and the c3 wave corresponds to a moderate decrease in the rate of daily deaths and cases and greater quarantine relaxation measures in Brazil.

This study was approved by the Local Ethics Committee at the University Hospital, University of São Paulo and is reported according to the STROBE guidelines (von Elm *et al.*, 2007). All patients provided electronic informed consent for participation in the study. “



Regarding the generalizability, we discuss that our absolute rates should be interpreted in the context of longitudinal changes within the same sample. Nonetheless, considering that developing countries present huge socioeconomic disparities, our findings might also provide insights in samples with similar characteristics in these countries. Finally, our individual participant data results can be analysed in the context of mega-cohort analyses to explore whether the observed risk factors are of worldwide importance or country-dependent:

“We used a well-defined cohort, which decreased the risk of selection bias, enhancing the external validity and generalizability of the findings, in contrast with snowball sampling. However, our sample is occupational and not population-based, being composed of public servants of the University of São Paulo. Their income, which is on average higher than the national income, was essentially unaffected during the pandemic. Thus, the rates of psychiatric disorders and symptoms should not be considered as nationally representative, but rather interpreted in the context of longitudinal changes within the same sample and associated risk factors. Nonetheless, even representing a fraction of the Brazilian population, our findings are interesting for similar samples from other developing countries that continually struggle with huge socio-economic inequalities, with vulnerable safety nets, and which have some of the highest COVID-19 excess mortality rates (The Lancet, 2020b), and for mega-cohort analyses exploring whether the observed

exposure variables are of worldwide importance or country-dependent, which is important to develop comprehensive early intervention strategies in different contexts.”

- 2. *There are too many grammatical errors and numerical inconsistencies in the manuscript, as page6, line6 "CW "should be "WC", page9, line1-2, figures in parentheses do not agree with those in table S5.***

Thank you for your feedback. Regarding the issues regarding grammar and style, the manuscript was carefully reviewed by the authors and a native English speaker.

- 3. *In page11 line18. The sentence "Although high, these rates do not capture changes in mental symptoms, as no previous data were available" should be rewritten to make it clearer and readable.***

We have rewritten the sentence to: “However, due to the absence of longitudinal data in these studies, changes compared to pre-pandemic levels were not assessed.”

- 4. *What does "participant who answered at least one assessment at WC1" mean in Figure 1 ? Can participant in the cohort be assessed multiple times at WC1 ? Please elaborate it.***

We apologize for being unclear in the Figure. The participant at the 1st covid wave was only assessed once. Because the questionnaire was long, some participants did not complete both CIS-R and DASS - i.e., “all assessments” - this is what we aimed to describe. However, we noticed that this was already described in the box below, in the Figure. Therefore, the Figure was changed to express more clearly that 2117 participants answered the CIS-R and 1943 answered the DASS at the first covid wave assessment.

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**São Paulo, April 13th, 2021.**

**Prof. Kenneth Kendler**

**Editor-in-Chief**

**Psychological Medicine**

**Dear Prof. Kendler,**

We hereby submit our original research article for your consideration to be published at **Prevalence and risk factors of psychiatric symptoms and diagnoses before and during the COVID-19 pandemic: findings from the ELSA-Brasil COVID-19 Mental Health Cohort.**

The COVID-19 pandemic brought several issues to worldwide communities, and a surge in psychiatric disorders and psychopathology was predicted. Although initial evidence from cross-sectional studies supported this hypothesis, other cohorts suggested otherwise. The study design of most studies are generally poor, focused on symptoms and non on diagnoses, without data from before the pandemic, and using convenience, snowball samples

Meanwhile, this issue was not investigated in low-/middle- income countries, where 85% of world population lives. In these countries, chronic social and healthcare difficulties are being aggravated by the COVID-19 pandemic.

These issues were addressed in our study that used data from a large Brazilian occupational cohort with robust methodology. Comparing data from before the pandemic, we observed that psychiatric disorders remained stable in 2020. Moreover, during 3 longitudinal assessments performed along 2020, symptoms slightly declined. We also found that variables associated with socioeconomic disadvantages were associated with increased mental disorder risk. The implication of our findings are further discussed in our manuscript, but present

original and relevant data from a LMIC during a COVID-19 pandemic, possibly having broad implications in mental healthcare.

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