

HAVING ANY MENTAL HEALTH CONDITION BEFORE THE COVID-19 PANDEMIC AS A RISK FACTOR OF COVID-19 CONTAGION DURING THE FIRST YEAR OF PANDEMIC: A SPANISH ADULT COHORT

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ABSTRACT

Background: Numerous studies suggest that subjects suffering from a mental health condition before the COVID-19 pandemic were at higher risk of contagion, but mostly are cross-sectional or retrospective.

Method: The BIOVAL-D-COVID-19 is a longitudinal cohort study design with 922 subjects who full filled two evaluations from an online survey of Spanish residents before and during the pandemic. Mental health conditions assessed were: Major Depressive Episode (MDE), Generalised Anxiety Disorder (GAD), Suicidal Thoughts and Behaviours (STB) and subthreshold of panic and bipolar disorder. Mental health screening instruments used were: the Spanish version of the Composite International Diagnostic Interview (CIDI) version 3.0 for the evaluation of MDE, the GAD-7 scale to evaluate GAD; STB was evaluated with 4 items from the CIDI questionnaire. Panic Disorder and Bipolar Disorder were screened from a modified and self-reported version of the CIDI. A bivariate plus five logistic regression models were developed for each mental health condition adjusted by socio-demographic variables; employment status; general and physical health; comorbidity; and including all previous variables and the other mental health conditions.

Results: We found in bivariate model that MDE; GAD and STB were statistically significant risk factors of contagion of COVID-19. The logistic regression models developed reveal that having a previous GAD (aOR 3.30 1.31 - 8.31) or STB (aOR 2.16 CI 95% 1.01 - 4.62) was statistically significant associated with COVID-19 contagion, independently of all variables included. MDE was not a risk factor of contagion when it was adjusted by comorbidity (aOR 0.99 CI 95% 0.47- 2.09).

Conclusions: It is recommended to detect those subjects with previous GAD or STB as vulnerable groups of infection to reduce contagion rates.

KEY WORDS

COVID-19; Depression; Generalized Anxiety Disorder; Mental health; Suicide

INTRODUCTION

During the first year after pandemic onset, 709,557 confirmed cases and 14,319 deaths were reported worldwide (*World Health Organisation*, 2020). During COVID-19 contagion, a cytokine storm causes severe somatic complications. Furthermore, the central nervous system (CNS) is also affected, primarily due to the body's inflammatory response. When there is an overproduction of cytokines, it can lead to disruptions in neurotransmission, influencing both mood and cognition. Research suggest that inflammatory processes contribute to the development of mood disorders (Dantzer et al., 2008). Moreover, stressful experiences, depression and anxiety can boost inflammatory cytokine production (Glaser & Kiecolt-Glaser, 2005; Raison et al., 2006; Steptoe et al., 2007). In particular, this factor is often found in subjects suffering from atypical depression or suicidal ideation (Black C, 2015; Lamers F, Milaneschi Y, de Jonge P, Giltay EJ, 2018). All these mechanisms, such as alterations in neurotransmission and the involvement of inflammatory processes in mental health conditions, could contribute to the increased vulnerability to COVID-19 contagion in subjects with pre-existing mental health conditions (Moreno et al., 2020; Nemani et al., 2021; Tang et al., 2020; Taquet et al., 2021; Wang et al., 2021; Yang et al., 2020). However, other studies reported mental health conditions as a protective factor of COVID-19 contagion (Azar et al., 2020; Jeon et al., 2021; Nemani et al., 2021; Salvatore et al., 2021). The mixed findings observed in various studies might be

partially explained by some limitations inherent in the research conducted. Many of these studies have methodological limitations. For instance, they often rely on cross-sectional or retrospective designs, or they lack control groups for comparison. Additionally, some potentially confounding variables could influence the results. Certain socio-demographic factors have been recognized as increasing the likelihood of COVID-19 contagion. For example, elderly age groups have been associated to higher disease severity and also higher mortality rates during COVID-19 (Xiaoyu Fang et al., 2020). When comparing gender, men with COVID-19 were face a higher risk of adverse outcomes and death, regardless of age (Jin et al., 2020). Regarding employment status and related variables, research findings vary. Some studies reported that subjects in precarious employment situations, are especially susceptible to the effects of the COVID-19 pandemic (Matilla-Santander et al., 2021). Other studies indicate that working from home (Xiao et al., 2021) may lead to an increase in physical and mental health conditions. Otherwise, current research indicates that populations with a high prevalence of comorbidities are likely to face more severe outcomes and higher mortality rates among COVID-19 patients (Xiaoyu Fang et al., 2020) and it is also documented the negative impact of COVID-19 pandemic on quality of life, behaviour and mental health in subjects suffering from chronic diseases and disability (Consonni et al., 2021) and in the general population (Cerami et al., 2020; Chudasama et al., 2020; Consonni et al., 2021; Solomou & Constantinidou, 2020).

To mitigate the adverse effects of COVID-19 contagion, it is recommended to identify vulnerable population groups and implement preventative measures accordingly. The aim of this study is to evaluate prospectively if individuals with previous mental health conditions: Major Depressive Episode (MDE); Generalised Anxiety Disorder (GAD); Suicidal Thoughts and Behaviours (STB) and subthreshold of panic (PD) and bipolar

disorder (BD) symptoms before the pandemic are at higher risk of COVID-19 contagion in general population during the first year of COVID-19 pandemic, independently of socio-demographic, employment status, general and physical health, and comorbidity variables.

METHOD

Participants

A nationally representative population-based sample of Spanish subjects aged 18 years or older was chosen based on geographical zones, socioeconomic status, age and sex using a stratification sampling. At the baseline evaluation (T0), subjects were recruited from a secure online panel data seller, leading to a final sample of 2,005 subjects of which 922 answered the follow-up survey (T1) achieving a 46.6% participation rate. Participants who completed both assessments were included in the longitudinal analyses. To increase the number of participants, an additional 416 participants were recruited at T1, matching the profile of the original base group who did not participate, and were then included. This resulted in a total of 1,338 participants included in the analysis at 12 months. In Table S1, differences between responders and non-responders can be found.

Instruments

Independent variables

Mental health problems

Major Depressive Episode (MDE)

We administered the full screening section of the MDE (8 items) of the Spanish version of the Composite International Diagnostic Interview (CIDI) version 3.0 (Haro et al., 2006; Kessler & Üstün, 2004). Two screening items, which one of them must be positively answered, were used as a filter to enter the diagnosis section. The diagnostic section comprises 37 items divided into 8 sections: depression and anhedonia (6 items); weight (5 items); insomnia (5 items); retardation and agitation (4 items); fatigue (2 items); worthlessness and guilt (5 items); concentration (4 items); suicide (6 items) that evaluate the presence or absence of MDE symptoms for at least two weeks. When five criteria were met, subjects must also have a high disability grade of >50 on the World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2.0) to establish the diagnosis (Luciano et al., 2010; Vázquez-Barquero et al., 2000). The area under the curve was 0.75 (Haro et al., 2006). The CIDI has been translated into many languages, including Spanish (Kessler & Üstün, 2004).

Generalised Anxiety Disorder (GAD)

The GAD-7 scale (García-Campayo et al., 2010) was administered in this study. The GAD-7 consists of 7 items answered on a 4-point Likert scale, with total scores ranging from 0 to 21 during the last two weeks. For the Spanish version, Cronbach's alpha coefficient of 0.93 was obtained. Using a 10-point cut-off, sensitivity values were 86.8% and specificity values were 93.4%. To establish a diagnosis, subjects must also have a high degree of disability, with a score greater than 50 on the WHODAS 2.0 (Luciano et al., 2010). The GAD-7 was administered to all those who had a positive depression screening using CIDI instrument and to a randomized 40% of those with a negative screening in the baseline sample, as well as to the entire sample during the follow-up assessment, which a total of 313 subjects were included in our analyses.

Suicidal Thoughts and Behaviours (STB)

STB (Nock, 2010) was assessed using the CIDI questionnaire, which included items for passive and active suicidal ideation, plan or attempt with a single item for any symptom, resulting in 4 items. The response options were Yes, No, and I don't know. Subjects were considered STB positive if they answered Yes to any of the STB symptoms.

Other mental health problems

We assessed the screening for Panic Disorder (2 items) and Bipolar Disorder (2 items) with the modified and self-reported version of the CIDI version 3.0. According to current research, PD subthreshold positive was categorized as experiencing a panic attack accompanied by related symptoms such as overwhelming anxiety and fear, a feeling of being out of control, or a fear of death or impending doom. BD subthreshold was defined as having 4 or more days of elevated, expansive, or irritable mood, along with symptoms such as inflated self-esteem or grandiosity, increased talkativeness, racing thoughts or engaging in activities that have the potential for negative consequences (e.g., unrestrained buying sprees).

Potentially confounding variables

Socio-demographic variables

We assessed age, gender, and marital status as socio-demographic variables. Age was treated as a continuous variable. Gender had two response options: Male and Female. Marital status was recorded with these following categories: Single, Married or Living with a couple, Separated, Divorced and Widowed.

Employment status

Furthermore, employment status was categorized as Employed, Housework, Student, Retired, Sick leave, and Unemployed. Under these circumstances, these socio-demographic variables were treated as nominal.

General health status

Self-perceived general health, smoking status, and body mass index (BMI) were self-assessed. Self-perceived general health was measured using the MOS 36-Item Short-Form Health Survey (SF-36) questionnaire (Ware & Sherbourne, 1992). The SF-36 questionnaire is a widely used patient-reported measure of health status. This is a multipurpose, short-form health survey with 36 questions, providing an 8-scale profile of scores and summary measures. It is a generic health status measure, not targeting any specific age, disease, or treatment group (Alonso et al., 1998). Physical and mental health were assessed with 2 items, each offering 5 response options: Excellent; Very Good; Good; Fair; Poor. Health transition was evaluated with response options: Much better; Somewhat better now; About the same; Somewhat worse now; Much worse. These variables were considered ordinal. Smoking status was categorized as non-smoker, ex-smoker, and smoker. Self-reported BMI was calculated using the formula: $BMI = \text{mass (kg)} / \text{height}^2 \text{ (m)}$. BMI was treated as a quantitative variable.

Comorbidity

The short version of the WHODAS 2.0 (12 items) is a questionnaire which was used to assess disability, and is recommended for epidemiological studies. This self-administered scale includes 12 items grouped into 6 domains: Understanding and communicating with the world; Moving and getting around; Self-care; Getting along with people; Activities of daily living (domestic responsibilities, leisure, and work); and Participation in society. Scoring ranges from 12–60, where 12 indicate no disability and

60 indicates the highest level of disability. Responses were recorded using a Likert Scale (None = 1; Mild = 2; Moderate = 3; Severe = 4; Extreme or cannot do = 5). The scale has been validated for the Spanish population (Vázquez-Barquero et al., 2000). Internal consistency in our sample was good in both assessments (baseline, $\alpha = 0.93$; follow-up, $\alpha = 0.87$). The distribution of disability using WHODAS 2.0 ranged from 12 to 58 at T0, and from 12 to 49 at T1, showing a normal distribution. This variable was considered continuous.

Physical comorbidities were assessed using The European Study of the Epidemiology of Mental Disorders/Mental Health Disability (ESEMeD) (Alonso J, Angermeyer MC, Bernert S, Bruffaerts R, Brugha TS, Bryson H, de Girolamo G, Graaf R, Demyttenaere K, Gasquet I, Haro JM, Katz SJ, Kessler RC, Kovess V, Lépine JP, Ormel J, Polidori G, Russo LJ, Vilagut G, Almansa J, Arbabzadeh-Bouchez S, Autonel, 2004) which screened for the presence of chronic physical diseases.

Dependent variables

COVID-19 contagion

Items regarding COVID-19 exposure were specifically developed for this study, which included collecting information on whether subjects had been tested for or diagnosed with COVID-19. COVID-19 clinical status was classified into four groups: Group 1 consisted of subjects who had not been tested and had no COVID-19 symptoms; Group 2 included those who had not been tested but had COVID-19 symptoms; Group 3 comprised subjects who had been tested and received a negative result; and Group 4 consisted of those who had been tested and received a positive result. Due to the small number of subjects in some groups, the COVID-19 clinical status was consolidated by merging Group 1 and Group 3 (Negative) vs. Group 2 and Group 4 (Positive).

Procedure

We carried out a longitudinally and representative cohort study design with a sample of 922 individuals who filled in two evaluations from an online survey of Spanish residents. This study was developed from a former project study, the BIOVAL-D-COVID-19 study (ISCII-FEDER Exp: PI16/00165) which the baseline cross-sectional data (T0) were assessed again transforming it as a cohort sample. The baseline evaluation was done during October/November 2019, before the SARS-CoV-2 outbreak and sociodemographic, employment status, physical and mental health were asked. The follow-up survey (T1) was conducted 12 months later (November/December 2020) using the same questionnaire, with additional dimensions and variables to identify physical and mental health outcomes, as well as their risk and associated protective factors during the SARS-CoV-2 outbreak and post-lockdown period. This survey included clinical characteristics of people diagnosed with COVID-19. Participants took 30 minutes to complete the survey, approximately. Each subject signed an informed consent form using an online version. Data were recorded in a centralized database, anonymized before statistical analysis, and shared among all authors. Details on the rationale and methods of the BIOVAL-D-COVID-19 project have been published elsewhere (Miranda-Mendizabal A, 2021). Actually, there are some results based on BIOVAL-D-COVID-19 study (Castellví P et al., 2021; Miranda-Mendizabal A, 2021) showing that the incidence of MDE was 5.1%, of GAD was 9.9% and of STB was 2.0%.

Data analysis

Descriptive analyses were conducted using relative and absolute frequencies in qualitative variables and mean and standard deviation (SD) in continuous variables. The

WHODAS 2.0 was estimated with median and quartiles (Q_1 - Q_3), as homogeneity hypotheses did not hold ($p < 0.05$).

In bivariate analysis (Model 1), we used binary logistic regression analyses to examine the association between having a previous mental health condition (MDE; GAD; STB; PD; BD) and COVID-19 infection defined by a positive test, or positive symptoms and test done using odds ratios (OR). Then, five logistic regression models were conducted to assess if having a previous mental health condition is associated of a higher risk of COVID-19 contagion, independently of: (a) socio-demographic variables; (b) employment status; (c) general and physical health; and (d) comorbidity; (e) Including all previous variables and the other mental health conditions. Five models for each set of variables (Models 2 to 6) and, finally, with all variables were conducted. The risks for multivariate models were assessed using adjusted OR (aOR).

All statistical tests were conducted with R and SPSS v20.0 with a significance level of 5%.

RESULTS

Sample Characteristics

Out of 922 participants, 51.2% were women, most respondents were married or living as a couple (58.9%), most of them were employed or both student and employed (54.0%). The weighted prevalence of mental health problems was 6.1% of MDE, 9.5%, of GAD, and 12.4% of STB. For PD and BD subthreshold was 53.0% and 19.1%, respectively. Results showed that 341 (37.0%) individuals who had a diagnostic test for COVID-19, 30 (3.2%) were positive.

The distribution of all variables included in multivariate regression models are shown in table 1, which summarises baseline characteristics of the 922 participants.

In Table S1 differences between responders and non-responders are shown. Statistically significant differences were found in age, gender, civil status, GAD, STB and general health status between responders and non-responders. There were more missing participants in young people, males, singles, participants with GAD, STB and worst general health status.

Association between major depressive episode (MDE) and COVID-19 contagion

Bivariate model showed a statistically significant association between MDE and COVID-19 contagion (OR 2.37, 95% CI 1.32- 4.26, $p < 0.01$). MDE was also associated of a higher risk of COVID-19 contagion independently of socio-demographic variables (aOR 2.06, 95% CI 1.13 – 3.75, $p = 0.018$), employment status (aOR 2.44, 95% CI 1.33 – 4.47, $p < 0.01$) and general and physical health (aOR 2.25, 95% CI 1.20 – 4.23, $p = 0.012$). Nevertheless, when adjusting by comorbidity, MDE was not a risk factor of COVID-19 contagion (aOR 0.99, 95% CI 0.47- 2.09, $p=0.97$). Furthermore, MDE was not statistically significant including all variables in the multivariate model (aOR 0.42, 95% CI 0.16 - 1.11; $p = 0.081$) either. (Table 2)

Association between generalised anxiety disorder (GAD) and COVID-19 contagion

GAD was associated of a higher risk of COVID-19 contagion in all models, including bivariate model (OR 4.22, 95% CI 2.22-8.01, $0 < 0.01$) and all logistic regression models, which GAD was statistically significant independently of socio-demographic variables (aOR 4.17, 95% CI 2.15 – 8.09, $p < 0.01$), employment status (aOR 4.07, 95% CI 2.11-7.84, $p < 0.01$), general and physical health (aOR 4.74; 95%CI 2.40 – 9.36; $p <$

0.01), comorbidity (aOR 2.73, 95% CI 1.26 – 5.94, $p = 0.011$) and when adjusted by all variables (aOR 3.30, 95% CI 1.31 - 8.31, $p < 0.01$). (Table 2)

Association between suicidal thoughts and behaviours (STB) and COVID-19 contagion

The logistic regression models developed reveal that having previous STB is statistically significant associated of a higher risk of COVID-19 contagion in bivariate model (OR 2.79, 95% CI 1.79- 4.37, $p < 0.01$) and in all logistic regression models when adjusting by socio-demographic variables (aOR 2.58, 95% CI 1.64– 4.07, $p < 0.01$), employment status (aOR 2.98, 95% CI 1.88 – 4.74, $p < 0.01$), general and physical health (aOR 2.68, 95% CI 1.68 – 4.26, $p < 0.01$), comorbidity (aOR 2.08, 95% CI 1.18 – 3.66, $p = 0.012$) and when adjusted by all variables (aOR 2.16, 95% CI 1.01 - 4.62, $p = 0.048$). (Table 2)

Association between panic and bipolar disorder subthreshold and COVID-19 contagion

PD and BD subthreshold were not statistically significant in any bivariate or logistic regression model. PD subthreshold was only statistically significant in bivariate model ($p = 0.042$).

DISCUSSION

Main results

The present study explored the prospective and longitudinal association between having a mental health condition before the COVID-19 pandemic and the risk of COVID-19 contagion during the first year of the onset in Spain. Results show that those individuals with GAD and STB previously are at higher risk of COVID-19, independently of many

potentially confounding variables. The higher risk of COVID-19 in individuals with MDE was explained by disability and comorbidity.

Strengths and limitations

Firstly, we must bear in mind that the results of this study must be taken with caution because its limitations. Firstly, the attrition rate (53.4%) at follow-up might have biased our comparisons between our baseline results of the total Spanish population. To reduce this bias, we applied population-based adjustments and weighting to correct for bias in the comparisons, which proved to be a successful method for reducing bias from a lack of response (Brick, 2013; Dey, 1997). Secondly, the assessment of mental disorders and suicide risk was based on self-reporting and not on direct clinical assessment. Consequently, as a result, they would be better considered as “probable cases” of disorder. In spite of that, good diagnostic agreement was reported with the clinical judgment of the CIDI instrument, which includes an assessment of MDE and STB in our study, with face-to-face (Haro et al., 2006; Wittchen, 1994), and online assessments (Ballester et al., 2019) in the Spanish population. However, although the GAD-7 is a well-validated scale (García-Campayo et al., 2010; Orlando & Marshall, 2002), calibration studies fail to have been carried out on general population samples. In addition, some scales were developed *ad hoc* for this study, such as the COVID-19 variables; consequently, their diagnostic properties for detecting cases are not available. The urgency of the pandemic situation and the need for developing our study to add to the body of knowledge about the impact of the pandemic and the social restrictions during the first year of pandemic motivated us to develop these scales without verifying their validity. Regarding the assessment of PD and BD subthreshold, it was carried out with a newly modified and self-reported version of the CIDI version 3.0. It is a useful screening instrument assessment, not a uniquely diagnostic-oriented tool. So that, the

unexpected prevalence and null results in this study looking for an association between PD and BD subthreshold and COVID-19 contagion should be taken with a certain degree of caution. Thirdly, because of the infrequency of suicide plans and attempts, we had to combine information to avoid numerical problems in statistical analyses. Therefore, it was not possible to analyse them separately, due to the low frequency of these outcomes. Fourthly, non-responders at follow-up were deleted in statistical analysis. Additionally, analyses comparing responders and non-responders showed statistical differences between these two groups. Although, these differences suggest a probable selection bias in the sample, association analyses may not be influenced by this bias. Finally, as the initial BIOVAL study was not developed for assessing the impact of mental health caused by the COVID-19 pandemic, some instruments, such as GAD-7 and WHODAS 2.0 were not administered to the entire sample at baseline, which is the reason why a lower number of participants were included in comorbidity assessment. Fortunately, we administered all the assessments to all the individuals with depression positive screening and a randomized sample with negative screening. Following that, some variables of interest, such as, toxicological history, psychiatric history, sleep status, medication status of the cohort were not included in the assessments.

Despite that, the study has a few strengths. First and foremost, the prospective cohort design, with an assessment before and during the first year of the COVID-19 pandemic covering a wide range of health outcomes, particularly in mental health, has helped to fill in a shortfall in the knowledge and provides a more extensive view of the risk of contagion amongst vulnerable groups, for example those with a previous mental health condition. Secondly, we evaluated two mental disorders (MDE, GAD), and STB using highly adapted and validated instruments. To end up with, the online methodology used

tends to deliver more reliable information about sensitive information, such as suicide risk, than face-to-face assessments (Tourangeau & Yan, 2007). These strengths allow us to establish better inferences about the causality between the evaluated variables. Finally, bivariate and multivariate regression logistics models assessed have shown that some groups of variables have been acting as confounding variables in the association between previous mental health conditions and COVID-19 contagion, such as having any comorbidity and/or disability in the MDE.

Comparison with other studies

Our study has shown an association between previous GAD and STB before the COVID-19 pandemic and risk of contagion among the Spanish population. According to our results, numerous studies showed that people with mental disorders are at higher risk of COVID-19 contagion (Moreno et al., 2020; Nemani et al., 2021; Tang et al., 2020; Taquet et al., 2021; Wang et al., 2021; Yang et al., 2020). On the other hand, conflicting studies reported that suffering from a mental health condition, was a protective factor of COVID-19 contagion (Azar et al., 2020; Jeon et al., 2021; Nemani et al., 2021; Salvatore et al., 2021). These conflicting results could be explained by the biases associated with a retrospective study design, or by those with mental disorders who spend more time at home in self-imposed isolation or in quarantine, more so than in healthy people and thereby reducing the risk of contagion. Additionally, most of the studies previously published used scales and not a diagnostic tool. We used online diagnostic instruments for MDE and STB, but not for GAD.

Our results, adjusted for many potentially confounding variables, suggest that having a previous GAD or STB have a direct effect on the risk of COVID-19 contagion. Recently carried out studies linked neuroinflammatory pathways involved in COVID-19

to anxiety and depression. Various studies reported how the immune system regulates mood and the potential causes of the dysregulated inflammatory responses in depressed patients. Inflammatory processes have been implicated in and involved in the pathophysiology of numerous diseases, including depressive disorders and a selection of chronic neuropsychiatric complications (Costanza et al., 2022). That dysregulation in immune system could explain the fact that people suffering from a mental health condition, such as, GAD or STB among others, are more likely to be infected by COVID-19. Consequently, there has already been reported an increased prevalence of depression and anxiety during COVID-19 pandemic attributed to the COVID-19 invasion and pain over CNS (Mello et al., 2022). Connection between depressive disorders and inflammation has been studied for potential shared etiological mechanisms that might explain comorbidity between MDE and numerous illnesses. For example, cardiovascular disease, diabetes and cancer (Raison et al., 2006). Therefore, this may be the reason that MDE was not associated with COVID-19 contagion when we included comorbidity in multivariate analysis; higher risk of COVID-19 contagion in MDE may be explained by comorbidity presented in individuals with MDE. The reason for this is that individuals with any comorbidity have higher prevalence of MDE than healthy people, and comorbidity by itself is associated with both the hyper inflammatory effect and MDE. Following this line of thoughts, some studies suggest that as inflammation is likely a critical disease modifier, increasing susceptibility to depression (Beurel et al., 2020).

A recent review reported the molecular and cellular mechanisms of COVID-19-associated neuroinflammation with emphasis on their importance to the inflammatory hypothesis of suicide development. Since inflammatory mediators have also been

accredited as putative biomarkers of STB, hyper and neuroinflammation could be interconnected in the context of COVID-19 (Costanza et al., 2022).

Moreover, a few unmeasured variables should be borne in minds, which are associated between both a deterioration of mental health and a higher risk of COVID-19 contagion. Some biological factors, for example, out of control or chronic responses to stress and dysregulated neuroendocrine-immune interactions which can lead to several disorders (de Figueiredo et al., 2021), as mentioned above, neuroinflammation is involved in mental health conditions, COVID-19 contagion and the interactive relationship between them. What is more, there are other unmeasured socio-demographic and economic variables. Such as, economic status deterioration, lower socio-cultural background or having an unhealthy lifestyle and sub-optimal circumstances, which includes poor housing and lower income. Different groups of population are at higher risk of both mental health's deterioration during the pandemic and COVID-19 contagion. To be more specific, there are reported cases of vulnerable professions, such as, healthcare workers and caregivers, who were seriously impaired by the COVID-19 pandemic, presenting an increased alcohol use, anxiety, depression, sleep problems and deprivation, (Nair & Bulgiba, 2022; Strzelecki et al., 2022). Regarding employment and job status and related variables, a number of studies reported that workers in precarious employment situation, are the most affected by the COVID-19 pandemic (Matilla-Santander et al., 2021). A recent Spanish study found an association between psychiatric morbidity and the use of different types of psychotropic drugs with mortality among COVID-19 inpatients, where high levels of psychiatric comorbidity resulted in high rates of prescription of psychotropic drugs. The history of depressive disorders was associated with an increase in mortality in these patients (Diez-Quevedo et al., 2021).

Ongoing research is needed to assess if individuals with a previous mental health condition are more likely to present higher clinical severity of COVID-19 infection. Additional research about health consequences on COVID-19 survivors are required as immune mediated hyperinflammation could also have long-term consequences in mental health, as happened in previous pandemics and are particularly relevant for patients experiencing post-COVID conditions (Chacko et al., 2020; Rogers et al., 2020; Troyer et al., 2020). Future studies should focus on studying PD and BD using proper diagnostic-oriented tools instead a screening instrument assessment.

In the context of the COVID-19 pandemic, it is recommended to establish preventative measures, such as a surveillance system in conjunction between governments and mental health and primary services that identify those subjects with previous GAD or STB as vulnerable groups of infection, these cases should be grouped in a national database. Furthermore, once the cases are labelled, some restrictive measures as self-isolation in supervised apartments or inpatient and close symptoms monitoring should be taken into account in this group of the population. An unhealthy lifestyle, having lower income and sub-optimal circumstances including poor housing, are more common in people with mental health problems (Phillips et al., 2009; Russ et al., 2012). At the same time, mental health conditions may influence the risk of acquiring COVID-19 infection (Pedrelli et al., 2004) and have an increased risk of severe COVID-19, including mortality (Sörberg Wallin et al., 2022), this increased risk was partly explained by sociodemographic and economic factors.

This is an especially promising path for future research, assuming that measures taken to prevent contagion and infections themselves may contribute to psychiatric disorders (Taquet et al., 2021). Consequently, implementation of preventative measures (self-isolation, in forced quarantine, in forced sick leave, prophylactic treatment...), is a

controversial, problematic issue because of the consequences on the mental health's population. It is about balancing the risks and/or benefits of isolating or not isolating and treating vulnerable groups to reduce infection rates against the possible worsening of mental health in these groups due to the application of coercive measures, such as imposed quarantine. We must consider here the lethality and transmissibility of the virus and how it affects the general population versus the morbidity caused in vulnerable groups suffering from a mental health condition particularly in old people's homes/retirement homes and mental institutions.

CONCLUSION

To sum up, identifying and labelling people who suffer from mental health illnesses, as vulnerable potential groups of infection, could reduce contagion rates and would help to implement more effective and efficient preventative measures among old people homes/retirement homes and mental institutions. The knowledge acquired during the COVID-19 pandemic should be appropriate for establishing preventative measures such as voluntary self-isolation and in forced quarantine in future related pandemics. In our study we found that having a previous GAD or STB was statistically significant associated with COVID-19 contagion, independently of all variables included.

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Table 1. Description of the sample included in the analysis (absolute numbers and weighted proportions)

Variables	Total N= 922 N (%)
At baseline	
Mental health condition	
MDE	53 (6.1)
GAD (<i>Missing= 609</i>)	36 (9.5)
STB (<i>Missing= 18</i>)	112 (12.4)
PD subthreshold (<i>Missing= 30</i>)	476 (53.0)
BD subthreshold (<i>Missing= 2</i>)	166 (19.1)
Socio-demographic variables	
Age	
18-25	41 (4.5)
26-40	146 (15.8)
41-65	534 (57.9)
66 or older	201 (21.8)
Gender	
Men	450 (48.8)
Women	472 (51.2)
Civil status	
Single	244 (26.5)
Married/Living with a couple	544 (58.9)
Separated	15 (1.7)
Divorced	64 (6.9)
Widowed	55 (6.0)
Employment status	
Employed	481 (52.2)
Sick leave (>3 months)	12 (1.3)
Unemployed	70 (7.6)
Housework	59 (6.4)
Student	22 (2.4)
Student and employed	16 (1.8)
Disability allowance	26 (2.8)
Retired	236 (25.5)
General health status	
Self-perceived general health	
Excellent	50 (5.4)
Very good	180 (19.5)
Good	536 (58.2)
Fair	140 (15.2)
Poor	16 (1.7)
Smoking status	
Non smoker	805 (87.3)
Smoker	117 (12.7)
BMI (<i>Missing= 3</i>)	
Underweight	18 (2.0)

Normal	415 (45.2)
Overweight	359 (39.0)
Moderately obese	104 (11.3)
Severely obese	19 (2.1)
Very severely obese	4 (0.4)
Comorbidity	
Chronic Diseases	
AIDS or HIV infection	2 (0.2)
Allergy	222 (24.1)
Back pain	188 (20.4)
Cancer	44 (4.7)
Cardio-vascular	33 (3.6)
Diabetes	51 (5.5)
Fibromyalgia	27 (3.0)
Gastrointestinal	26 (2.8)
Headache	135 (14.6)
Hypertension	177 (19.2)
Neurological	9 (1.0)
Osteoarthritis	147 (15.9)
Respiratory	32 (3.5)
Stroke	15 (1.6)
Thyroid	59 (6.3)
None of the above	305 (33)
Number of chronic diseases	
0	326 (35.5)
1	275 (29.8)
2	172 (18.6)
3	82 (8.9)
>3	67 (7.2)
	Median (Q₁ – Q₃)
WHODAS -12 (<i>Missing</i> = 455)	17.0 (13.0 – 24.0)
At 12-month follow-up	
COVID-19 contagion	
No COVID test done and no symptoms	556 (60.3)
COVID-19 symptoms without COVID test done	25 (2.7)
COVID-19 test done and negative result	311 (33.8)
COVID-19 test done and positive result	30 (3.2)

AIDS= Acquired Immunodeficiency Syndrome; BD= Bipolar Disorder; BMI = Body Mass Index; COVID-19= Coronavirus Disease 2019; GAD= Generalised Anxiety Disorder; HIV= Human Immunodeficiency Virus; MDE= Major Depression Episode; PD= Panic Disorder; STB= Suicidal Thoughts and behaviour; WHODAS= World Health Organisation Disability Assessment Schedule.

% weighted follow-up sample weight (inverse probability weighting and post-stratification).

Screening instruments were used for mental health indicators. Cut-off used to establish diagnosis of: (a) MDE: achieve 5 criteria in the CIDI and >50 points in WHODAS score; (b) GAD: a 10-point-cut-off in the GAD-7 scale and >50 in WHODAS score; (c) STB: Positive in any passive or active ideation, and suicide plan or attempt; (d) PD subthreshold: A panic attack with related symptoms and overwhelming anxiety and fear, or a feeling of being out of control, or a fear of death or impending doom; (d) BD subthreshold: 4 or more days with elevated, expansive, or irritable mood with inflated self-esteem or grandiosity, increased talkativeness or racing thoughts or engaging in activities that hold the potential for painful consequences (e.g., unrestrained buying sprees).

Table 2. Association between mental health problems and COVID-19 contagion

Mental health condition	Model 1: Bivariate	Model 2: Sociodemographic	Model 3: Employment status	Model 4: General health	Model 5: Comorbidity	Model 6: All variables
	N OR (95% CI)	N aOR (95% CI)	N aOR (95% CI)	N aOR (95% CI)	N aOR (95% CI)	N aOR (95% CI)
MDE	n=934 2.37 (1.32-4.26)**	n=934 2.06 (1.13 – 3.75)*	n=934 2.44 (1.33-4.47)**	n=934 2.25 (1.20- 4.23)*	n=516 0.99 (0.47- 2.09)	n=305 0.42 (0.16 – 1.11)
GAD	n=319 4.22 (2.22-8.01)**	n=319 4.17 (2.15-8.09)**	n=319 4.07 (2.11-7.84)**	n=319 4.74 (2.40- 9.36)**	n=319 2.73 (1.26-5.94)*	n=305 3.30 (1.31-8.31)**
STB	n=916 2.79 (1.79 - 4.37)**	n=916 2.58 (1.64-4.07)**	n=916 2.98 (1.88-4.74)**	n=916 2.68 (1.68- 4.26)**	n=503 2.08 (1.18- 3.66)*	n=305 2.16 (1.00 - 4.62)*
PD sub-threshold	n=904 1.51 (1.02- 2.25)*	n=904 1.36 (0.91- 2.04)	n=904 1.46 (0.98 -2.19)	n=904 1.46 (0.97- 2.19)	n=505 0.93 (0.54- 1.60)	n=305 0.42 (0.16-1.11)
BD sub-threshold	n=932 1.46 (0.94- 2.28)	n=932 1.34 (0.85- 2.11)	n=932 1.38 (0.88- 2.16)	n=932 1.43 (0.91- 2.25)	n=515 0.90 (0.52- 1.56)	n=305 0.59 (0.29 -1.25)

95% CI= 95% Confidence Interval; MDE= Major Depression Episode; GAD= Generalised Anxiety Disorder; STB= Suicidal Thoughts and behaviour; PD= Panic Disorder; BD= Bipolar Disorder

n= number of participants included in the logistic regression models.

Variables included in the logistic binary regression models: - Model 2.- Sociodemographic: Age, Gender and Civil Status; - Model 3.- Employment status: Employed, Sick leave, Unemployed, Housework, Student, Student and employed, Disability allowance, and Retired; Model 4.- General health: Body mass index, Smoking status and Self-perception of physical health; Model 5.- Comorbidity: Number of chronic diseases and Disability; Model 6: All variables including other mental health problems.

**p-value* <0.05

***p-value* <0.01

Screening instruments were used for mental health indicators. Cut-off used to establish diagnosis of: (a) MDE: achieve 5 criteria in the CIDI and >50 points in WHODAS score; (b) GAD: a 10-point-cut-off in the GAD-7 scale and >50 in WHODAS score; (c) STB: Positive in any passive or active ideation, and suicide plan or attempt; (d) PD subthreshold: A panic attack with related symptoms and overwhelming anxiety and fear, or a feeling of being out of control, or a fear of death or impending doom; (e) BD subthreshold: 4 or more days with elevated, expansive, or irritable mood with inflated self-esteem or grandiosity, increased talkativeness or racing thoughts or engaging in activities that hold the potential for painful consequences (e.g., unrestrained buying sprees).

COVID-19 clinical status was classified into 2 groups: (a) Positive, those with no COVID-19 test done but with COVID-19 symptoms, or those with COVID-19 test done and positive result; (b) Negative, those with no COVID-19 test done and no COVID-19 symptoms, or those with COVID-19 test done and a negative result.

Figure 1: Association between dependent variable (COVID-19 contagion) with independent variables

