Original Research

Evolution of Anxiety and Depression in Men during the First Six Months of the COVID-19 Pandemic and Factors Associated with Worsening of Mental Health: Retrospective Longitudinal Study

Ana Lear-Claveras[1], Alejandra Aguilar-Latorre[1], Bárbara Oliván-Blázquez[1,2,3,]*,
Sabela Couso-Viana[4], Ana Clavería-Fontán[3,4,5]

[1]Aragonese Primary Care Research Group (GAIAP, B21_20R), Institute for Health Research Aragón (IIS Aragón), 50009 Zaragoza, Spain
[2]Department of Psychology and Sociology, University of Zaragoza, 50009 Zaragoza, Spain
[3]Network for Research on Chronicity, Primary Care and Health Promotion (RICAPPS), 08007 Barcelona, Spain
[4]I-Saúde Group, South Galicia Health Research Institute, 36201 Vigo, Spain
[5]Vigo Health Area, SERGAS, 36201 Vigo, Spain
*Correspondence: bolivan@unizar.es (Bárbara Oliván-Blázquez)

Abstract

Background: The Coronavirus disease (COVID-19) pandemic has had a huge impact on the psychological wellbeing of the population, however, few studies have analysed the psychological consequences for the most vulnerable groups, particularly those suffering from depression and anxiety, and specifically in men. The objective of this study is to analyse the changes in a population of men undergoing active treatment for depression or anxiety and factors associated with these changes. **Methods**: Retrospective, longitudinal and observational study of a population of 28,294 men in northern Spain. The study variables were sociodemographic variables, chronic comorbidities, COVID-19 infection, anxiolytic and antidepressant drug consumption, and use of healthcare resources. These variables were collected from the Primary Health Care electronic records for the two distinct periods (6 months before and 6 months following the end of the lockdown). To compare drug patterns and the use of healthcare resources a paired Student's *T*-test was used. To analyse associated factors related to a deterioration of mental disorders, a multivariate logistic regression was performed. **Results**: In relation to changes in drug patterns, 40% of men saw an increase in at least one Defined Daily Dose (DDD) of their prescribed drugs during the 6 months following lockdown and the number of appointments at health centres and home visits significantly decreased. Factors associated with a deterioration of mental disorders are being under 60 years old, having an income of less than 18,000 euros/year and suffering from more than one comorbidity. **Conclusions**: The pandemic had a significant impact on men with a previous diagnosis of depression and/or anxiety.

Keywords: depression; anxiety; men; COVID-19 pandemic; anxiolytic; antidepressant; drug consumption; use of healthcare resources

1. Introduction

Depression is considered the principal cause of disability worldwide, with anxiety being the sixth most prevalent cause. Both these conditions, especially depression, contribute to the overall global morbidity and mortality burden, and generate high levels of disability as well as economic and social costs [1]. By 2030, depression is expected to be the leading cause of morbidity in the world [2–5]. The prevalence of depression in Spain is 13% over one's lifetime and 4% per year [6]. From the healthcare system perspective, approximately 25–35% of all primary health care (PHC) patients suffer from psychiatric disorders, and over 80% of these patients suffer from depression or anxiety disorders [7]. It is well known that General Practitioners (GPs) only refer approximately 5–10% of psychiatric patients diagnosed in primary care settings to mental health services [8]. Therefore, these mental health disorders are managed chiefly at the PHC level.

It is a common belief that the probability of experiencing a depressive or anxious episode increases when certain genetic [9,10], demographic and psychosocial factors [11–14], as well as environmental factors [15–17] are present, among which the size of an individual's residence is considered [18,19]. Gender is prominent among these factors, with women having typically double the risk of developing severe depression than men [20–24]. Consequently, few studies have been conducted on the diagnosis, evolution and treatment of depression specifically in men [25,26]. Other frequently studied sociodemographic factors related to depression are: old age [27–31]; having a lower cultural and educational level [32–34]; experiencing a lack of relationships and social support [35–38]; and having a lower socioeconomic level [35,39,40]. Another analysed risk factor is the comorbidity of depression with other physical and psychiatric diseases [41,42].

As a result of the COVID-19 pandemic, which has devastated the entire world, the global population has been exposed to an endless number of stressful events such as restriction of social activities, limited mobility and/or lockdowns. These restrictive measures have been useful in reducing the spread of the virus, but they have had a huge impact on the physical and psychological wellbeing of the population [43]. Numerous studies have analysed the psychological consequences of the pandemic and lockdown on the mental health of the general population. Several meta-analyses concluded that the COVID-19 pandemic has increased mental health issues among the global population, mainly the prevalence of depression, anxiety and sleep disorders [44–47]. Factors associated with experiencing these symptoms are being female, a healthcare worker, suffering from a non-infectious chronic disease, contracting COVID-19 disease or having a high risk of doing so, having lower socioeconomic status, as well as being socially isolated.

However, few studies have analysed the psychological consequences of the pandemic for the most vulnerable groups, particularly those suffering from pre-existing mental disorders [48]. The lockdown, social and physical distancing measures and difficulty in maintaining daily routines during the pandemic may also have had an acutely negative impact on people with mental health disorders [48–52]. Furthermore, the collapse of PHC services at the onset of the pandemic and during each subsequent wave may have interrupted these patients' ongoing healthcare [49,53], causing a deterioration of their mental disorder and an imbalance in health service usage.

Given the lack of research on the consequences of the pandemic for those suffering from pre-existing mental disorders, especially in the case of men, the objective of this study is to determine and analyse the changes between 6 months prior to lockdown and 6 months after it was lifted in a population of men undergoing active treatment for depression or anxiety. We will also examine factors associated with these changes, looking at patients' electronic clinical history (ECH), held by PHC services. The use of this data from PHC records allows us to quantify the use of drugs such as anxiolytics and anti-depressants as well as how patients accessed healthcare resources, which may indicate a change in their condition.

The alternative hypotheses for this study are the following:

H1: Men with a previous diagnosis of depression and/or anxiety, who had undergone active treatment for these mental disorders at least six months before the beginning of the COVID-19 pandemic, experienced a worsening of their mental health status during the six first months of the pandemic.

H2: Men with a previous diagnosis of depression and/or anxiety, who had undergone active treatment for these mental disorders at least six months before the beginning of the COVID-19 pandemic, experienced a decrease in the number of consultations with health professionals during the six first months of the pandemic.

H3: There are associated factors between the worsening of mental health in men and having a previous diagnosis of depression and/or anxiety when these individuals had undergone active treatment for these mental disorders at least six months before the beginning of the COVID-19 pandemic.

2. Materials and Methods

This is a retrospective, longitudinal and observational study of a population of men in northern Spain (Aragon) over the age of 16, undergoing active treatment for depression and/or anxiety, according to their ECH.

Aragon is an autonomous community (one of Spain's 17 main administrative and political divisions) with a population of 1,328,753. Its territory takes in 47,719 square kilometres, and it has a population density of 28.20 people per square kilometre. It has an ageing population which is concentrated in rural areas, with the main cities having a younger population structure. The capital city of the region (Zaragoza) accounts for half of the population, and rural nuclei (with less than 2000 residents) account for 86% of municipalities, but only 16.8% of the overall population [54].

2.1 Sample and Sample Size

The sample consisted entirely of men with open electronic medical records held by health centres in the Autonomous Community of Aragon, with a diagnosis of depression and/or anxiety, who had undergone active treatment for these mental disorders (antidepressants and anxiolytic medication), prescribed by their GP at least 6 months before the declaration of the state of emergency in Spain (i.e., on or before 14/09/2019). Accordingly, the inclusion criteria are: men over 16 years of age, who have experienced episodes of depression and anxiety (codes F30-F39 and F41 of the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10)), and who, during the study period, were prescribed some of the active ingredients used to treat these two disorders. According to the Anatomical, Therapeutic, and Chemical Classification (ATC), the following codes were included: N05B (anxiolytic drugs), N05C (hypnotics and sedatives), and N06A (antidepressants).

Records containing inconsistencies in the database were excluded from the study. The total sample that met inclusion criteria consisted of 28,294 men.

Due to the universal nature of the healthcare system and the absence of other PHC providers, the data obtained in the study is considered to be representative of practically 100% of the population under study.

2.2 Study Variables

Data on sociodemographic variables, chronic comorbidities, COVID-19 infection, drug consumption, and use of healthcare resources were collected from the PHC records for the two distinct periods. The first measurement was taken from the records from the 6 months before the onset of the strict lockdown (14/09/2019 to 15/03/2020) and the second was taken from the records from the 6 months following the end of this lockdown during the first wave (03/05/2020 to 04/11/2020).

- Sociodemographic variables that are associated with the etiopathogenesis of depression and could be collected through the PHC record were: age, data on prescription charges which allowed us to determine peoples' income (less than 18,000 euros/year, 18,000 to 100,000 euros/year, over 100,000 euros/year, free prescriptions and uninsured), and residence in a rural or urban area (the latter is defined as having over 10,000 inhabitants).

- Chronic comorbidities; data on the following conditions were collected: arrhythmias, heart failure, ischemic cardiopathy, dyslipidaemia, obesity, excess weight, vein and artery disease, cerebrovascular disease, diabetes, chronic bronchitis, chronic obstructive pulmonary disease (COPD), asthma, chronic kidney disease, hypo and hyperthyroidism, tobacco addiction, alcoholism, insomnia, attempted suicide, anaemia, neoplasia, dementia, deafness, cataracts, glaucoma, arthrosis, osteoporosis, and back pain. These comorbidities present a prevalence of over 5% among the general population [55], and the data were collected at points six months before the start of lockdown, and six and twelve months after the end of the lockdown.

- Infection with COVID-19 during the study period, recorded as yes/no.

- Changes in drug consumption patterns have been assessed via the variation in defined daily dose (DDD) dispensed under medical prescription by pharmacies. These changes in drug consumption were coded negatively when there was an increase in the DDD of the active ingredient. The pharmacological treatments in the data have been grouped according to therapeutic group (ATC classification) [56] as: N05B (anxiolytic drugs), N05C (hypnotics and sedatives), and N06A (antidepressants). These Benzodiazepines are all first-instance medications for treating these disorders according to the Spanish Society of Family and Community Medicine [57]. They are listed as follows: (a) anxiolytics: diazepam, potassium clorazepate, lorazepam, bromazepam, clobazam, ketazolam, alprazolam, pinazepam, Bentazepam; (b) hypnotics and sedatives: flurazepam, triazolam, lormetazepam, midazolam, brotizolam, quazepam, loprazolam and (c) antidepressants: (ci) non-selective monoamine (MAO) reuptake inhibitors: imipramine, clomipramine, trimipramine, amitriptyline, nortriptyline, doxepin, maprotiline; (cii) selective serotonin reuptake inhibitors (SSRIs): fluoxetine, citalopram, paroxetine, sertraline, fluvoxamine, escitalopram.

- The patients' use of healthcare resources was assessed through looking at how they used PHC services (number of ordinary or ongoing care visits to the health centre or home visits by the nurse or GP, and number of visits to a social worker at a health centre. Use of hospital services was also examined (number of specialised care visits, number of visits to accident and emergency (A&E) services, hospitalisations, admission to intensive care units (ICU) and the duration of these stays) for each of the periods in question.

2.3 Statistical Analysis

The sample size allowed for the use of parametric methods [58]. Firstly, a descriptive analysis of the study variables was carried out using frequencies, means and standard deviation (SD).

To determine variations in drug consumption, the difference in DDD for each period was calculated using a paired Student's T-test. For those variables observed in less than 100 cases, the Wilcoxon rank test was used. To compare the differences in the use of healthcare resources between the baseline measurement and the measurement taken 6 months following the end of lockdown, the same statistics were used.

To analyse associated factors related to the possible deterioration of mental disorders, changes in drug consumption patterns assessed via the increases in defined daily dose (DDD) were analysed as a dependent variable in a multivariate logistic regression. This indicator could be an indirect means of revealing the variation in this population's psychological suffering. The independent variables were age (under 40, 40 to 60, and over 60), income bracket (determined via prescription charges), residence in a rural or urban area, chronic comorbidities (grouped into those not presenting comorbidities or other chronic diseases, and those presenting 2 or more chronic diseases), and COVID-19 infection.

Statistical analysis was carried out using IBM SPSS Statistic 21 [59] and R 4.0.5. [60] on a PC with 16 MB of RAM.

3. Results

On 14/09/2019, there were 110,694 patients in Aragon with a diagnosis of depression and/or anxiety who were being actively treated for these mental disorders with antidepressants and anxiolytic medication, prescribed by their GP. Of these, 28,294 were men, 25.56% of the total.

Table 1 represents the sample according to the variables under study. The participants' mean age is 58.76 years old (SD 16.79). Among them, 60.6% had an annual income of less than 18,000 euros, and 53.9% resided in urban areas. In terms of comorbidities, dyslipidaemia (45.1%), hypertension (39.4%), back pain (29.4%), neoplasia (25.4%), and tobacco addiction (23.9%) were the

most frequently found chronic conditions among the study population. Only 4.4% of the participants suffered from a COVID-19 infection.

Table 1. Sociodemographic data, chronic comorbidities and COVID-19 infection in patients suffering from anxiety or depression in Aragon at least 6 months prior to the pandemic outbreak.

	n = 28294
Age, M (SD)	58.76 (16.79)
Income bracket (based on prescription charge data)	
<18000, n (%)	17152 (60.6)
18000–100000, n (%)	10076 (34.4)
>100000, n (%)	181 (0.6)
Free prescriptions, n (%)	1238 (4.4)
Uninsured, n (%)	8 (0.0)
Place of residence	
Urban, n (%)	15248 (53.9)
Rural, n (%)	13046 (46.1)
COVID-19 infection	
Yes, n (%)	1241 (4.4)
Chronic comorbidities	
Arrhythmias, yes n (%)	2239 (7.9)
Heart failure, yes n (%)	784 (2.8)
Ischemic heart disease, yes n (%)	2515 (8.9)
Hypertension, yes n (%)	11139 (39.4)
Dyslipidaemia, yes n (%)	12762 (45.1)
Obesity, yes n (%)	3234 (11.4)
Overweight, yes n (%)	451 (1.6)
Vein and artery disease, yes n (%)	1220 (4.3)
Cerebrovascular disease, yes n (%)	1985 (7.0)
Diabetes, yes n (%)	4296 (15.2)
Chronic bronchitis, yes n (%)	498 (1.8)
COPD, yes n (%)	2127 (7.5)
Asthma, yes n (%)	1698 (6.0)
Chronic kidney disease, yes n (%)	1737 (6.1)
Hypothyroidism, yes n (%)	1529 (5.4)
Hyperthyroidism, yes n (%)	649 (2.3)
Tobacco addiction, yes n (%)	6760 (23.9)
Alcoholism, yes n (%)	1294 (4.6)
Insomnia, yes n (%)	5764 (20.4)
Autolytic attempt, yes n (%)	332 (1.2)
Anaemia, yes n (%)	3105 (11.0)
Neoplasia, yes n (%)	7177 (25.4)
Dementia, yes n (%)	770 (2.7)
Hearing loss, yes n (%)	2575 (9.1)
Cataracts, yes n (%)	2764 (9.8)
Glaucoma, yes n (%)	1892 (6.7)
Osteoarthritis, yes n (%)	1827 (6.5)
Osteoporosis, yes n (%)	545 (1.9)
Back pain, yes n (%)	8330 (29.4)

Note: COPD, Chronic obstructive pulmonary disease.

As for new diagnoses of psychiatric comorbidity in this population in the 6 months prior to the lockdown, there were 253 (0.9%) new diagnoses of tobacco addiction, 50 (0.2%) of alcoholism, 402 (1.4%) of insomnia and 39 (0.1%) of attempted suicide. However, in the 6-month period following the lockdown being implemented, there were 66 (0.2%) new diagnoses of tobacco addiction, 41 (0.1%) of alcoholism, 194 (0.7%) of insomnia, and 23 (0.1%) suicide attempts.

When considering pharmaceutical treatments, the active ingredients most often prescribed to men with depression and/or anxiety are anxiolytics (lorazepam, diazepam, alprazolam) hypnotics and sedatives (lormetazepam) and antidepressants (escitalopram, paroxetine, sertraline, fluoxetine, and amitriptyline). In relation to changes in drug patterns, as shown in detail in Table 2, it is relevant to highlight that 11,038 men (40%) saw an increase in at least one DDD of their prescribed drugs during the 6 months following lockdown. Looking at the active ingredients, 15% of the men that took diazepam saw an increase in DDD during the six months after lockdown ended, as did 11.1% of those who took alprazolam, 12% of those who took lormetazepam, 14% of those who took amitriptyline, 16.9% of those who took fluoxetine, 11.3% of those who took sertraline, 9.5% of those who took escitalopram, and 8.2% of those who took paroxetine.

As seen in Table 3, the number of ordinary and continuous PHC nursing appointments at health centres and the number of ordinary care GP home visits significantly decreased during the six months after the end of the lockdown. The number of PHC appointments attended for ongoing and ordinary care, as well as appointments with specialists, did not show significant differences. Finally, visits to hospital (no. of visits to urgent care and no. of hospitalisations), also decreased during the study period ($p < 0.001$).

In terms of factors associated with a deterioration of mental disorders, considering men that see an increase or decrease in their prescribed DDD as an indicator of heightened psychological suffering, a multivariable logistic regression was performed, the results of which are displayed in Table 4. Being under 60 years old, having an income of less than 18,000 euros/year and suffering from more than one comorbidity are associated with an increase in the DDD of anxiolytic drugs (N05B), hypnotics and sedatives (N05C), and/or antidepressants (N06A).

4. Discussion

This study analyses a sample consisting of patients that had been diagnosed with depression and/or anxiety who were being actively treated for these mental disorders with antidepressants and anxiolytic medication prescribed by their GP, at least six months before the lockdown. Of these patients, 25.56% were men, which means that there were 3 women for every man with depression in Aragon. This percentage has remained stable over the last ten years,

Table 2. Number and percentage of men taking each active ingredient with a stable, reduced or increased DDD.

Active ingredient	N (%)	Stable or reduced DDD N (%)	Increased DDD N (%)
Benzodiazepines			
Anxiolytics			
Diazepam	4656 (16.4)	3947 (84.8)	709 (15)
Potassium clorazepate	1434 (5.1)	1271 (88.6)	163 (11.4)
Lorazepam	11157 (39.4)	10612 (91.8)	945 (8.2)
Bromazepam	161 (0.6)	141 (87.6)	20 (12.4)
Clobazam	52 (0.2)	49 (94.2)	3 (5.8)
Ketazolam	499 (1.7)	449 (90)	50 (10)
Alprazolam	3903 (13.8)	3470 (88.9)	433 (11.1)
Pinazepam	2 (0.0)	2 (100)	0 (0)
Bentazepam	550 (1.9)	506 (92)	44 (8)
Hypnotics and sedatives			
Flurazepam	119 (0.4)	102 (85.7)	17 (14.3)
Triazolam	13 (0.0)	0 (0)	13 (100)
Lormetazepam	3973 (14.0)	3496 (88)	477 (12)
Midazolam	161 (0.6)	141 (87.6)	20 (12.4)
Brotizolam	16 (0.0)	0 (0)	16 (100)
Quazepam	4 (0.0)	3 (75)	1 (25)
Loprazolam	52 (0.2)	46 (88.5)	6 (11.5)
Antidepressants			
Non-selective monoamine reuptake inhibitors			
Imipramine	19 (0.0)	11 (57.9)	8 (42.1)
Clomipramine	426 (1.5)	387 (90.8)	39 (9.2)
Amitriptyline	993 (3.5)	854 (86)	139 (14)
Nortriptyline	52 (0.2)	40 (76.9)	12 (23.1)
Doxepin	6 (0.0)	5 (83.3)	1(16.7)
Maprotiline	8 (0.0)	2 (25)	6 (75)
Selective serotonin reuptake inhibitors			
Fluoxetine	1377 (4.8)	1144 (83.1)	233 (16.9)
Citalopram	780 (2.7)	732 (93.8)	48 (6.2)
Paroxetine	2757 (9.7)	2531 (91.8)	226 (8.2)
Sertraline	2525 (8.9)	2239 (88.7)	286 (11.3)
Fluvoxamine	99 (0.3)	82 (82.8)	17 (17.2)
Escitalopram	5383 (19.0)	4873 (90.5)	510 (9.5)

which can be seen when comparing these data to other studies using data from PHC clinical records in Aragon [61].

Epidemiological studies suggest that there are considerable differences between men and women in terms of the prevalence and presentation of depression. Women are more than twice as likely to be diagnosed with depression and may also report more atypical and anxiety-like symptoms than men [62,63]. Several studies support the argument that these epidemiological differences are related to psychological, neurochemical, anatomical, hormonal, genetic, and personality-related factors [26,63], but also to the nature of the roles that men and women perform [36].

Furthermore, the sample for this study presents high comorbidity with other chronic conditions, which is consistent with other studies. In fact, just as comorbidity with other chronic conditions is high (64.9–71.0%) (diabetes, hypertension, cardiovascular diseases and cancer, among others) [64–66], so is comorbidity with other psychiatric diseases (40–66%) [67]. A noteworthy result is that in the

6 months after lockdown ended there were fewer new diagnoses of psychiatric comorbidities in comparison with the 6 months prior to lockdown. Except for attempted suicide, these results have to be considered with caution, given that the decrease in the use of health services may have led to an underdiagnosis bias. In the case of attempted suicides, 39 (0.1%) men with diagnoses of depression and anxiety had attempted suicide in the six months prior to lockdown, while this number dropped to 23 in the subsequent 6 months. According to recently published studies [68,69], in the countries hit worst by the pandemic, an increased prevalence of depression and anxiety was anticipated, and several questionnaire-based studies of the general population have shown this to have been the case [70]. Both of these disorders and, even more so, comorbidity between the two, are considered to be major risk factors in suicidal behaviour [71]. Suicide data published in Spain in 2020 showed an increase of 7.4% on the previous year [72], but this increase has not been reflected among men diagnosed with depres-

Table 3. Number of consultations with health professionals in the six months prior to lockdown, and the six months after it ended.

	N	Six months prior	Six months after	95% CI	p
		Mean (SD)			
No. of nursing appointments at health centre or by telephone (ordinary care)	10676	4.15 (5.12)	3.83 (4.96)	0.22; 0.41	<0.001
No. of nursing home visits (ordinary care)	922	6.02 (8.19)	5.95 (8.29)	−0.45; 0.58	0.811
No. of nursing appointments at health centre (ongoing care)	980	2.51 (4.55)	2.14 (4.20)	0.19; 0.54	<0.001
No. of nursing home visits (ongoing care)	163	2.35 (2.88)	2.58 (5.83)	−1.18; 0.71	0.628
No. of GP appointments at health centre or by telephone (ordinary care)	22595	5.87 (5.26)	5.86 (5.70)	−0.06; 0.08	0.818
No. of GP home visits (ordinary care)	628	3.39 (3.36)	3.02 (4.04)	0.08; 0.66	0.012
No. of GP appointments at health centre (ongoing care)	2282	2.17 (3.23)	2.08 (2.88)	−0.01; 0.19	0.060
No. of GP home visits (ongoing care)	197	1.99 (1.73)	1.79 (1.48)	−0.06; 0.46	0.143
No. of visits to PHC social worker	185	2.50 (2.13)	2.72 (2.98)	−0.67; 0.13	0.188
No. of visits for specialised care (first consultation)	955	1.50 (0.87)	1.54 (0.90)	−0.11; 0.04	0.384
No. of visits for specialised care (successive consultations)	7261	2.70 (2.27)	2.68 (2.48)	−0.03; 0.07	0.492
No. of visits to A&E department	1946	2.03 (2.11)	1.82 (1.77)	0.12; 0.29	<0.001
No. of hospital admissions	1948	1.32 (0.74)	0.35 (0.80)	0.92; 1.01	<0.001
No. of days spent in hospital	463	17.28 (39.42)	19.02 (36.38)	−4.15; 0.68	0.159
No. of ICU admissions	2	1.00 (0.00)	1.00 (0.00)		*
No. of days spent in ICU	2	82.5 (6.36)	82.5 (6.36)		*

Note: CI, Confidence Interval; ICU, Intensive Care Unit; PHC, Primary Health Care; A&E department, Accident and Emergency department.
* The correlation and t cannot be calculated because the standard error of the difference is 0.

Table 4. Multivariable logistic regression of factors associated with a deterioration of depression and anxiety.

	B	Exp (B) Odds ratio	95% Confidence Interval for Exp (B)	p-value
Intercept	−0.487			<0.001
Aged under 40 years	0.266	1.241	1.206; 1.413	<0.001
Aged 40 to 60 years	0.216	1.241	1.177; 1.308	<0.001
Aged over 60 years		Ref		.
Income <18,000 euros/year	0.062	1.064	1.011; 1.120	0.017
Income >18,000 euros/year		Ref		.
One comorbidity	−0.112	0.094	0.820; 0.975	0.011
Two or more comorbidities		Ref		.
Residence in urban area	−0.021	0.979	0.933; 1.028	0.394
Residence in rural area		Ref		.
No COVID-19 infection	−0.064	0.938	0.835; 1.054	0.282
COVID-19 infection		Ref		.

sion and/or anxiety before the pandemic began.

According to the results of the study, the hypotheses for this study have been verified. Men with a previous diagnosis of depression and/or anxiety, who had undergone active treatment for these mental disorders at least six months before the beginning of the COVID-19 pandemic, experienced a worsening of their mental health status and experienced a decrease in the number of consultations with health professionals during the six first months of the pandemic. It is relevant to highlight that 40% of the participants saw an increase in at least one of the DDD of their prescribed drugs during the 6 months after lockdown ended. We chose to analyse changes in the status of depression and anxiety in men over a 14-month period (from 6 months prior to until 6 months after the end of lockdown, i.e., from 14/09/2019 to 04/11/2020) by collating changes in the use of healthcare system resources and consumption of anti-depressant and anxiety drugs, starting with the hypothesis that increases in use or consumption may reflect an increase in psychological suffering in these patients. However, 60% of the patients saw their DDD remain stable or decrease. These data may be related to the natural evolution and treatment of depression and anxiety, but may also indicate the abandonment of treatment. According to a study conducted by Serna *et al.* [73], 78% of patients who take antidepressants abandon treatment within 6 months, with men being more likely than women to do so. The National Institute for Health and Care Excellence (NICE) guide recommends continuing treatment with antidepressant drugs for at least 6 months after remission of the episode [74]. The mainte-

nance dose should be the same as that which obtained the improvement, as it has been observed that those patients who have their dose reduced have higher rates of relapse than those who continue with the same dose. The cessation of antidepressant treatment should be done by reducing the dose gradually, usually over a period of 4 weeks [75]. Given that the total monitoring period of this study is approximately 14 months, maintenance or even reduction of medication can be considered as an indication that clinical practice guidelines are have been followed [75], depending on the evolution of the patient's condition.

The fact that 40% of the participants saw an increase in at least one of the DDDs of their prescribed drugs during the 6 months after the lockdown ended, cannot be related to a progressive increase in prescription, as the diagnosis was made almost 8 months prior. Therefore, these data confirm an increase in psychological discomfort during the first wave. Some previous studies show a higher psychological effects of the pandemic and the lockdown (fear, anxiety, sadness, sleep quality) in people with previous mental illness compare with the general population [50,76–78]. This could explain the increse of the consumption of anxiolytic drugs and antidepressants not only among the general population [44,47,69,79] but also among vulnerable people such as patients with depression and anxiety [48–52]. The restrictions of the pandemic forced to modify clinical practice. In Spain and other countries [78] care for patients with these pathologies was diminished. Togheter, the fear of contagion, that among this group was higher according to some studies [50,77] could also explain the decrease in the number of PC and hospital care visits observed in our study.

Related to the third hypothesis, there are associated factors between the worsening of mental health in men and having a previous diagnosis of depression and/or anxiety when these individuals had undergone active treatment for these mental disorders at least six months before the beginning of the COVID-19 pandemic. Among the factors associated with an increase in the DDD are being younger (of working age), having an income of less than 18,000 euros/year and suffering from more than one comorbidity. These results are consistent with the social and economic impact the pandemic has had and evince devastating psychological distress among people from poorer socioeconomic groups. The relationship between depression, anxiety, the economic crisis and unemployment has been well-established in the literature [16,33,35,61,64,80–85]. On the other hand, people suffering from comorbidities during the first wave were more likely to have their DDD increased for their anxiety and depression medication, since these comorbidities are risk factors for developing a serious COVID-19 episode [86–88]. This may explain the higher incidence of anxiety and depression.

Our study has some significant strengths, mainly its PHC context, the healthcare setting where most depression

and anxiety episodes are managed and treated, as well as its ecological nature. Furthermore, while most studies have analysed the psychological consequences of the pandemic and lockdown on the mental health of the general population, our study attempts to shed light on the evolution of men with pre-existing mental disorders (depression and anxiety) who had been undergoing active treatment during the six months of the pandemic. As a result, our paper aims to fill a current gap that exists regarding knowledge about the psychological consequences of the pandemic for the most vulnerable groups, such as those suffering from pre-existing mental disorders. On the other hand, it also has its limitations. For example, the duration of the study may not be long enough to detect variations in the severity of depression. Depression is a disease that develops gradually, whereas anxiety is more variable. But the variations in the patterns of anxiolytic and antidepressant consumption which are not explained by the natural course of the disease are a warning sign. Studies should be carried out to corroborate or refute our findings. Our source of information was clinical records: the ECH. But this is not sufficient to provide objective information on the impact of the pandemic on patients' mental health. In addition, to confirm the diagnosis of depression, the use of validated scales would be necessary. A cohort study using diagnostic tools to perform sampling would be extremely useful in answering the question regarding the impact of the COVID-19 pandemic on the mental health of the population. Finally, the last limitation is that, despite the study including men in Aragón (Spain) who had received a diagnosis for depression and anxiety by their GP and who had undergone active treatment for these mental disorders at least six months before the beginning of the COVID-19 pandemic, the sample is representative of an ageing population and, therefore, presents a large number of comorbid chronic diseases.

5. Conclusions

In summary, after the strict lockdown during the first wave of COVID-19, the pandemic had a significant impact on men with a previous diagnosis of depression and/or anxiety. Of these men, 40% had their prescription for medication to treat these mental disorders increased, demonstrating increased psychological suffering. Their use of healthcare resources also decreased. The presence of comorbidities and a greater vulnerability to economic instability are factors related to this deterioration.

Abbreviations

A&E, Accident and emergency; ATC, Anatomical, Therapeutic, and Chemical Classification; COPD, chronic obstructive pulmonary disease; ECH, Electronic clinical history; DDD, Defined daily dose; GPs, General Practitioners; ICU, Intensive care unit; PHC, (MAO) non-selective monoamine;PHC, Primary Health Care; SSRI, selective serotonin reuptake inhibitors; SD, Standard deviation.

Author Contributions

Ethics Approval and Consent to Participate

The authors declare that all procedures contributing to this work comply with the ethical standards of the Aragon Clinical Research Ethics Committee (part of the Department of Health of the Government of Aragon, Spain) and with the Helsinki Declaration of 1975, as revised in 2008. The Aragon Clinical Research Ethics Committee approved the Study Protocol (PI20-175).

Data on the prevalence of depression were obtained from clinical records, provided in a anonymised format by the Aragon Health Service. The processing, notification, and transfer of personal data were carried out in accordance with Regulation (EU) 2016/679 of the European Parliament and Spanish Organic Law 03/2018 on the Protection of Personal Data and the guarantee of digital rights.

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Conflict of Interest

The authors declare no conflict of interest.

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