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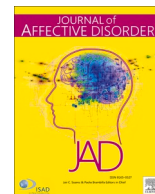


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Research paper

Lower risk of hospitalisation for depression following hospitalisation for COVID-19 versus for another reason



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ABSTRACT

Introduction: Although hospitalisation for COVID-19 is associated with a higher post-discharge risk of mood disorders, including major depressive disorder (MDD) and bipolar disorder (BD), this risk has not been compared to that following hospitalisation for a reason other than COVID-19.

Methods: Using data from France's National Health Data System (SNDS) database, we compared patients hospitalised for mood disorders in the 12 months following COVID-19/another reason hospitalisation.

Results: 96,313 adult individuals were hospitalised for COVID-19, and 2,979,775 were hospitalised for another reason. In the 12 months post-discharge, 110,976 (3.83 %) patients were hospitalised for mood disorders. In unadjusted analyses, patients initially hospitalised for COVID-19 (versus another reason) were more likely to be subsequently hospitalised for a mood disorder (4.27 % versus 3.82 % versus, respectively, $p < 0.0001$). These patients were also more likely to have a history of mood disorders, especially depressive disorders (6.45 % versus 5.77 %, respectively, $p < 0.0001$). Women, older age, lower social deprivation, a history of mood disorders, longer initial hospitalisation (COVID-19 or other), and a higher level of clinical care during initial hospitalisation were all significantly associated with the risk of subsequent hospitalisation for MDD and BD. In contrast, after adjusting for all these factors, persons initially hospitalised for COVID-19 were less likely to be subsequently hospitalised for MDD (OR = 0.902 [0.870–0.935]; $p < 0.0001$). No difference between both groups was observed for BD.

Limitations: Other reasons were not separately studied.

Conclusions: After adjusting for confounding factors, initial hospitalisation for COVID-19 versus for another reason was associated with a lower risk of hospitalisation for a mood disorder.

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1. Introduction

The COVID-19 pandemic has led to worldwide concern about populations' mental health, with many reports highlighting increased psychiatric disorders such as depression, anxiety, sleep and posttraumatic stress symptoms (Bertrand et al., 2022; Bo et al., 2021; Huang et al., 2021; van den Borst et al., 2021; Veazie et al., 2022). Prior to COVID-19, brain conditions - including major depressive disorder (MDD), which is a severe illness - affected up to 20 % of the general population (Bakish, 2001; Kessler et al., 2005; Malhi and Mann, 2018). MDD is a major public health problem; it is one of the three main causes of time spent with disability (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018), and is associated with both suicide (Lopez-Castroman et al., 2015) and considerable economic burden (Wang et al., 2003). Affecting 1–4 % of the population worldwide before the pandemic, bipolar disorders (BD), like MDD, are also frequent mood disorders with a chronic evolution (Merikangas et al., 2007). They present one of the greatest disease burdens (Whiteford et al., 2013).

Using the Global Burden of Disease Study (GBD) model in one of the largest conducted studies to date, Santomauro et al. reported a significant increase in MDD prevalence after the 2020–2022 COVID-19 pandemic. Specifically, they estimated there were an additional 53.2 million [95%CI 44.8–62.9] cases worldwide (i.e., a 27.6 % [25.1–30.3] increase on pre-COVID-19 levels) (Santomauro et al., 2021). In another study using data on 69 million individuals, 62,354 persons were diagnosed with COVID-19; the authors found that compared with six other health events, COVID-19 was associated with a higher incidence of first-time diagnosis of a mood disorder in the 14 to 90 days following COVID-19 diagnosis (Taquet et al., 2021).

Understanding the relationship between COVID-19 hospitalisation and subsequent mood disorders is a crucial step in delving deeper into the intricate interplay between pandemic-induced mental health effects and the specific impact of COVID-19 infection. This focus on the connection between COVID-19 hospitalisation and future mood disorders is warranted as it not only bridges the gap from general observations about pandemic-related mental health to more specific outcomes but also sheds light on a critical facet of the broader pandemic-mood disorder relationship. Rogers et al. highlighted that severe COVID-19 infection which led to hospitalisation and intensive care greatly impacted mental health (Rogers et al., 2020). We confirmed this finding in a recent article (Decio et al., 2022). Specifically, we found a slightly higher unadjusted rate of hospitalisation for psychiatric disorders (of any type) within the 12 months following discharge after hospitalisation for COVID-19, in comparison to initial hospitalisation for another reason (odds-ratio (OR) = 1.20, 95 % confidence interval (95 % CI) [1.18–1.23]; $p < 0.0001$). Importantly, this increased rate was notable for mood disorders (OR = 1.12, 95 % CI [1.09–1.16], $p < 0.0001$), as well as for psychotic and anxiety disorders, but not for personality disorders. Given these findings, it is pertinent to conduct a more in-depth and personalized examination of these disorders. This approach would facilitate specific analyses and interpretations tailored to their unique characteristics. These disorders exhibit distinct interactions, potential confounding factors, and unique manifestations, all of which justify a separate and dedicated investigation.

Comparing data on the risk of hospitalisation for mood disorders after prior hospitalisation for COVID-19 versus for another reason may highlight whether the COVID-19-related risk is higher or not. Accordingly, in the present study, we used the same dataset as in our previous study (see above; hospital inpatients admitted between 1 January 2020 and 30 June 2020 in metropolitan France) to examine hospitalisation for mood disorders (specifically MDD and BD) following prior hospitalisation for COVID-19 versus for another reason, while adjusting for other risk factors.

2. Material and methods

2.1. Data sources

Data were taken from France's *National Health Data System (Système National des Données de Santé, SNDS)* which covers the country's entire population of 67 million inhabitants. The SNDS contains hospital admission and discharge information for all French public and private hospital stays. As previously described (Decio et al., 2022), for all these hospitalisations, medical diagnoses are coded according to 10th edition of the International Classification of Diseases (ICD-10). Medical and surgical procedures performed are coded according to the Common Classification of Medical Procedures (*Classification Commune des Actes Médicaux, CCAM*). Medical diagnoses are coded as 'principal' diagnosis (i.e., the main reason for the hospitalisation), or 'secondary' (i.e., a comorbidity that was not the main reason for hospitalisation).

For each individual included, data from the Diseases and Expense Mapping database 8th edition (*Cartographie des Pathologies et des Dépenses*) were also used to identify the presence of a history of mood disorders over the five years preceding the study period. Medical algorithms were based on data from the SNDS and are publicly available in French (Caisse Nationale d'Assurance Maladie (CNAM), 2020; Rachas et al., 2022).

2.2. Study design and participants

The present study aimed to compare the risk of hospitalisation for a mood disorder, including MDD and BD, in adult patients (i.e., ≥ 18 years) in metropolitan France, during the 12 months following hospital discharge from a medical, surgical, or obstetrics ward after hospitalisation for COVID-19 between 1 January 2020 and 30 June 2020 versus hospitalisation for another reason in the same period. As previously described (Decio et al., 2022), a reference hospital stay was selected for each patient. For patients with multiple hospitalisations during the study period, the COVID-19-related stay (if any) ($N = 85,514$) was considered the reference hospital stay. For patients with multiple COVID-19-related hospitalisations during the period ($N = 7521$), the reference stay was the COVID-19 hospitalisation where the highest level of clinical care was provided. For patients with multiple hospitalisations for a pathology other than COVID-19, the reference stay was that where the highest level of clinical care was received.

2.3. Outcome

The main outcome was a diagnosed mood disorder (any type) in the 12-month period following discharge for the reference hospital stay. We considered both inpatient admissions for a mood disorder in medical, surgical, and obstetrics wards (MCO), in psychiatric wards (RIM-Psy), as well as in follow-up care and rehabilitation facilities (SRR), with the following ICD-10 codes:

- F30 Manic episode
- F31 Bipolar affective disorder
- F32 Depressive episode
- F33 Recurrent depressive disorder
- F34 Persistent mood disorders
- F38 Other mood disorders
- F39 Unspecified mood disorder

Mood disorders were studied first as a whole (i.e., *F30-F39*), and then separately for MDD (*F32, F33, F34*) and BD (*F30 and F31*).

2.4. Adjustment variables

2.4.1. Sociodemographic characteristics

Age, sex, and region of residence (among the 13 regions in

Table 1

Comparison of patients initially hospitalised for COVID-19 with those initially hospitalised for another reason among patients hospitalised with a mood disorder in the 12 months following discharge after initial hospitalisation.

	Total (N = 110,976)	Hospitalisation for COVID-19 (N = 4115)	Hospitalisation for another reason (N = 106,861)	p-values ¹	
<i>Sex: N (%)</i>					
Male	43,767 (39.44)	1668 (40.53)	42,099 (39.40)	0.1435	
Female	67,209 (60.56)	2447 (59.47)	64,762 (60.60)		
<i>Age group (years): N (%)</i>					
18–39	14,508 (13.07)	160 (3.89)	14,348 (13.43)	<0.001	
40–59	29,198 (26.31)	732 (17.79)	28,466 (26.64)		
60–74	28,738 (25.90)	1183 (28.75)	27,555 (25.79)		
75+	38,532 (34.72)	2040 (49.57)	36,492 (34.15)		
<i>Region: N (%)</i>					
Île-de-France	16,279 (14.67)	1483 (36.04)	14,796 (13.85)	<0.001	
Centre-Val de Loire	4024 (3.63)	127 (3.09)	3897 (3.65)		
Bourgogne-Franche-Comté	5530 (4.98)	237 (5.76)	5293 (4.95)		
Normandy	7072 (6.37)	159 (3.86)	6913 (6.47)		
Hauts-de-France	9582 (8.63)	328 (7.97)	9254 (8.66)		
Grand Est	8759 (7.89)	565 (13.73)	8194 (7.67)		
Pays de la Loire	5984 (5.39)	148 (3.60)	5836 (5.46)		
Brittany	7471 (6.73)	88 (2.14)	7383 (6.91)		
Nouvelle-Aquitaine	12,069 (10.88)	171 (4.16)	11,898 (11.13)		
Occitanie	9912 (8.93)	151 (3.67)	9761 (9.13)		
Auvergne-Rhône-Alpes	14,582 (13.14)	446 (10.84)	14,136 (13.23)		
Provence-Alpes-Côte d'Azur	9293 (8.37)	204 (4.96)	9089 (8.51)		
Corsica	419 (0.38)	8 (0.19)	411 (0.38)		
<i>Social deprivation index (FDep, quintiles): N (%)</i>					
1 (least deprived)	19,148 (17.48)	1150 (28.24)	17,998 (17.06)		<0.001
2	20,054 (18.30)	695 (17.07)	19,359 (18.35)		
3	22,973 (20.97)	690 (16.94)	22,283 (21.12)		
4	23,515 (21.46)	697 (17.12)	22,818 (21.63)		
5 (most deprived)	23,870 (21.79)	840 (20.63)	23,030 (21.83)		
<i>History of mood disorders: N (%)</i>					
No	65,472 (59.00)	2709 (65.83)	62,763 (58.73)	<0.001	
Yes	45,504 (41.00)	1406 (34.17)	44,098 (41.27)		
<i>Duration of reference hospital stay (median [Interquartile interval], in days)</i>					
	3 [1–9]	10 [4–18]	3 [1–8]	<0.0001	
<i>Level of clinical care received during reference hospital stay: N (%)</i>					
General hospital ward (medical, surgery, obstetrics)	94,781 (85.41)	3120 (75.82)	91,661 (85.78)	<0.001	
Intensive care unit	12,373 (11.15)	529 (12.86)	11,844 (11.08)		
Intensive care unit with invasive procedure	3822 (3.44)	466 (11.32)	3356 (3.14)		

Legends: ¹chi-square tests or *t*-tests.

metropolitan France) were considered. Age was calculated from the individual's year of birth and categorized into one of four age groups (18–39, 40–59, 60–74, 75+ years old). We used the French Deprivation Index (Fdep) as a proxy of individual measure of socioeconomic status. It is an indicator based on median household income, the percentage of higher education graduates in the population over 15 years old, the percentage of manual workers in the labour force, and the unemployment rate of the individual's city of residence (Rey et al., 2011).

2.4.2. History of mood disorders

Using the “Cartographie des Pathologies et des Dépenses” (8th version) database, we considered the history of mood disorders in the 5 years preceding the study period (Rachas et al., 2022). We defined an individual as having a history of mood disorders if the SNDS contained one of the following: i) a declaration by a healthcare professional that the patient had a mood disorder officially recognised as a long-term disease; ii) hospitalisation(s) for a diagnosed mood disorder in an

RIM-Psy and/or non-RIM-Psy ward or an MCO/SSR in at least one of the previous two years; iii) hospitalisation(s) for a diagnosed mood disorder in an RIM-Psy and/or non-RIM-Psy ward or an MCO/SSR in at least one of the previous five years (*n* to *n-4*) and receiving prescribed mood stabilizers and antidepressants on at least three different occasions during year *n*. Of note, these criteria encompass individuals who may have experienced mood disorders over five years ago and have since achieved remission.

2.4.3. Characteristics of the initial hospital stay

The initial hospital stay (i.e., for COVID-19 or another reason) was characterised by the median duration (in days) and the level of the clinical care received. We defined three levels of care intensity for hospitalizations for COVID-19 and for other reasons. These three levels were defined according to care provided in general for different degrees of COVID-19 severity (more information concerning this data is available elsewhere (Decio et al., 2022)):

Table 2

Number of hospitalizations for a diagnosed mood disorder (principal or secondary diagnosis) in the 12 months following discharge for COVID-19 hospitalisation versus hospitalisation for another reason.

	Total sample N (%)	Hospitalisation for COVID-19 N (%)	Hospitalisation for another reason N (%)	p-value
	(n = 2,894,088)	(n = 96,313)	(n = 2,799,775)	
<i>Mood disorder (any type)</i>	110,976 (3.83)	4115 (4.27)	106,861 (3.82)	<0.0001
Manic episode	1509 (0.05)	35 (0.04)	1474 (0.05)	0.0289
Bipolar affective disorder	17,001 (0.59)	549 (0.57)	16,452 (0.59)	0.4718
Depressive episode	80,875 (2.79)	3059 (3.18)	77,816 (2.78)	<0.0001
Recurrent depressive disorder	20,750 (0.72)	705 (0.73)	20,045 (0.72)	0.5744
Persistent mood disorder	2859 (0.10)	105 (0.11)	2754 (0.10)	0.3039
Other mood disorder	501 (0.02)	12 (0.01)	489 (0.02)	0.2444
Unspecified mood disorder	1155 (0.04)	37 (0.04)	1118 (0.04)	0.8135
BD (Manic or bipolar affective disorder)	17,933 (0.62)	576 (0.60)	17,357 (0.62)	0.3851
MDD (depressive episodes or recurrent depressive disorders)	94,907 (3.28)	3560 (3.70)	91,347 (3.26)	<0.0001
Mood disorder history (F30 > F39)	180,211 (6.46)	6891 (7.15)	180,211 (6.44)	<0.0001
Bipolar disorder history (F30–31)	37,343 (1.29)	1228 (1.28)	36,115 (1.29)	0.6685
Depressive disorder history (F32 > F39)	167,731 (5.80)	6211 (6.45)	161,520 (5.77)	<0.0001

Bold values denote statistical significance at the p-value <0.05 level.

1. The first level corresponded to patients with the mildest level of respiratory difficulty and admitted to a general hospital ward; they required no or low-flow oxygen (up to 15 L/min).
2. The second level corresponded to patients admitted to an ICU, irrespective of the level (i.e., type and flowrate) of oxygen supply therapy, and patients who received high-flow nasal oxygen or non-invasive ventilation.
3. The maximum level of care corresponded to patients who were hospitalised in an ICU and required at least invasive ventilatory support.

2.5. Statistical analysis

We used logistic regression models to estimate and compare the risk of hospitalisation with a diagnosis of i) MDD, and (ii) BD according to hospitalisation for COVID-19 or for another reason. For these outcomes, four nested models were successively performed as follows:

- *Model 1* described the crude associations between outcomes, and the reason for initial hospitalisation (i.e., COVID-19 versus another reason);
- *Model 2*: model 1 plus socio-demographic variables;
- *Model 3*: model 2 plus the 'history of mood disorders' variable;
- *Model 4*: model 3 plus two characteristics of the initial hospital stay variables (specifically, duration and the level of clinical care received).

Statistical analyses were performed using SAS software, version 7.1 (Cary, NC, USA).

2.5.1. Role of funding source, regulatory approval, and ethical aspects

The present study was conducted as part of the surveillance activities of the French agency for public health (*Santé publique France* (SpF)). No specific grant was received from any funding agency in the public, commercial, or not-for-profit sectors. The SNDS database comprises a set of strictly pseudonymized databases. By law, Article L.1461–3 and R1461–13, SpF has permanent regulatory access to SNDS data to carry out its mission in accordance with the French public health code (*Code de la santé publique, 2019*). Access to personal data in these databases for research purposes is only possible in the SNDS hub, and data cannot be extracted or shared.

3. Results

3.1. Global analyses/clinical characteristics (study population)

Between 1 January 2020 and 30 June 2020, 96,313 individuals in metropolitan France were hospitalised (i.e., reference hospital stay) for COVID-19 infection, and 2,979,775 for another reason. The characteristics of this population are detailed elsewhere (*Decio et al., 2022*). In the 12 months following hospital discharge, of the total 3,076,088 persons discharged, 110,976 (3.83 %) were hospitalised for a mood disorder (any type, principal or secondary diagnosis) (*Table 1*); 94,907 (3.28 %) were hospitalised for MDD, and 17,933 (0.62 %) for BD (*Tables S1 and S2, respectively*).

Among patients hospitalised with a mood disorder, those initially hospitalised for COVID-19 were significantly older, lived in less socially deprived cities, were more likely to have a history of mood disorders, had a longer initial hospital stay, and had received a higher level of clinical care compared to patients initially hospitalised for another reason (*Table 1*). These differences were similar in the subgroups of patients hospitalised for MDD (*Table S1*) and BD (*Table S2*).

Comparison of hospitalisation for a mood disorder for patients initially hospitalised for COVID-19 versus for another reason.

Patients initially hospitalised for COVID-19, compared to those initially hospitalised for another reason, were more likely to be hospitalised for a mood disorder in the 12 months following discharge (4.27 % versus 3.82 %, respectively, $p < 0.0001$). This stronger association was mostly due to a higher likelihood of MDD in the COVID-19 group (See *Table 2* for details).

With regard to psychiatric history, patients initially hospitalised for COVID-19 were significantly more likely to have a history of mood disorders, especially depressive disorders (6.45 % versus 5.77 %, respectively, $p < 0.001$) (*Table 2*).

3.2. Analyses of the risk of hospitalisation for specific mood disorders

3.2.1. MDD

Model 1 (i.e., non-adjusted) (*Table 3*), showed a higher risk of hospitalisation for MDD in the 12 months following discharge after hospitalisation for COVID-19 versus for another reason (OR = 1.14 [1.1–1.18; $p < 0.001$). Model 2, which was adjusted for sex, age and social deprivation index, was consistent with model 1, with a higher risk for those initially hospitalised for COVID-19 (OR = 1.05 [1.02–1.09]; $p = 0.004$).

Table 3
Risk of hospitalisation for diagnosed major depressive disorder (MDD) in the 12 months following discharge for COVID-19 hospitalisation versus hospitalisation for another reason.

	Model 1			Model 2			Model 3			Model 4		
	OR	(95 % CI)	p	OR	(95 % CI)	p	OR	(95 % CI)	p	OR	(95 % CI)	p
<i>Hospitalisation for COVID-19</i>	1.137	1.175	<0.0001	1.052	1.016	1.090	0.004	1.010	0.6042	0.902	0.870	<0.0001
Sex												
Male	1			1			1			1		
Female	1.336	1.318	1.355	1.355	1.318	1.355	<0.0001	1.122	1.106	1.138	1.122	1.154
Age (years)												
18–39	1			1			1			1		
40–59	2.434	2.379	2.490	2.490	2.379	2.490	<0.0001	1.777	1.736	1.819	1.702	1.783
60–74	2.009	1.963	2.055	2.055	1.963	2.055	<0.0001	1.589	1.553	1.627	1.510	1.546
75+	2.458	2.405	2.511	2.511	2.405	2.511	<0.0001	2.047	2.002	2.092	1.913	1.956
<i>Social deprivation index (quintiles)</i>												
1 (least deprived)	1			1			1			1		
2	0.937	0.916	0.959	0.959	0.916	0.959	<0.0001	0.937	0.915	0.959	0.913	0.957
3	0.968	0.946	0.990	0.990	0.946	0.990	0.0047	0.942	0.921	0.965	0.916	0.960
4	0.969	0.947	0.991	0.991	0.947	0.991	0.0056	0.940	0.918	0.962	0.933	0.955
5 (most deprived)	0.992	0.969	1.014	1.014	0.969	1.014	0.4661	0.959	0.936	0.981	0.950	0.972
<i>History of mood disorders (any type)</i>												
<i>Reference hospital stay (days) - median (IQR)</i>												
<i>Level of clinical care received during reference stay</i>												
General hospital ward								9.425	9.289	9.563	1.016	1.017
Intensive care unit												
Intensive care unit with invasive procedure												

Bold values denote statistical significance at the p-value <0.05 level.

Table 4
Risk of hospitalisation for diagnosed bipolar disorder (BD) in the 12 months following discharge for COVID-19 versus hospitalisation for another reason.

	Model 1			Model 2			Model 3			Model 4		
	OR	(95 % CI)	p	OR	(95 % CI)	p	OR	(95 % CI)	p	OR	(95 % CI)	p
<i>Hospitalisation for COVID-19</i>	0.964	0.887	1.048	0.3931	1.072	0.985	1.167	0.1066	1.034	0.948	1.128	0.4506
Sex												
Male	1			1			1		1			1
Female	1.466	1.421	1.512	<0.0001	1.050	1.017	1.084	0.0026	1.060	1.027	1.094	0.0003
Age (years)												
18–39	1			1			1		1			1
40–59	2.410	2.305	2.520	<0.0001	1.130	1.079	1.183	<0.0001	1.118	1.068	1.171	<0.0001
60–74	1.763	1.684	1.846	<0.0001	0.985	0.940	1.032	0.516	0.964	0.919	1.010	0.1238
75+	0.889	0.845	0.934	<0.0001	0.518	0.493	0.546	<0.0001	0.508	0.482	0.535	<0.0001
<i>Social deprivation index (quintiles)</i>												
1 (least deprived)	1			1			1		1			1
2	0.832	0.792	0.874	<0.0001	0.824	0.783	0.867	<0.0001	0.824	0.783	0.867	<0.0001
3	0.884	0.842	0.928	<0.0001	0.819	0.779	0.862	<0.0001	0.819	0.778	0.861	<0.0001
4	0.770	0.732	0.809	<0.0001	0.701	0.665	0.738	<0.0001	0.700	0.664	0.737	<0.0001
5 (most deprived)	0.754	0.716	0.794	<0.0001	0.678	0.642	0.715	<0.0001	0.676	0.641	0.714	<0.0001
<i>History of mood disorders (any type)</i>												
<i>Reference hospital stay (days) - median (IQR)</i>												
<i>Level of clinical care received during reference stay</i>												
General hospital ward					45.603	44.034	47.228	<0.0001	45.449	43.885	47.069	<0.0001
Intensive care unit												
Intensive care unit with invasive procedure												

Bold values denote statistical significance at the p-value <0.05 level.

Model 3, which cumulatively adjusted for mood disorder history, showed no statistically significant higher risk (OR = 1.01 [0.97–1.05]; $p = 0.60$). Finally, Model 4, which cumulatively adjusted for the duration of initial hospitalisation and the level of clinical care received, reversed the association: persons initially hospitalised for COVID-19 had a lower risk of hospitalisation for MDD (OR = 0.90 [0.87–0.94]; $p < 0.001$). Taken separately, longer hospitalisation duration and a higher level of clinical care were both associated with a higher risk of subsequent hospitalisation for MDD (Table 3).

3.2.2. Bipolar disorder

All four models (Table 4), irrespective of the variables adjusted for, were consistent. They showed no difference in the risk of hospitalisation for BD in the 12 months following discharge after hospitalisation for COVID-19 versus for another reason.

For both BD and MDD, being a woman, older age, lower social deprivation, having a history of mood disorders, longer duration of initial hospitalisation and receiving a higher level of clinical care, were all significantly associated with a higher risk of subsequent hospitalisation for BD (Table 4).

4. Discussion

In the present study, patients who were initially hospitalised for COVID-19 were more likely to have subsequently been hospitalised for a mood disorder (any type) in the 12 months following discharge, compared to patients initially hospitalised for another reason. Moreover, patients initially hospitalised for COVID-19 had more risk factors for mood disorders including a longer hospital stay and a higher level of clinical care. However, after adjusting for all the observed risk factors (i.e., duration, level of clinical care, being a woman, older age, lower social deprivation, and having a mood disorder history), persons initially hospitalised for COVID-19 had a lower risk of subsequent hospitalisation for MDD. This phenomenon was not observed for BD, as no elevated risk between COVID-19 hospitalisation and the onset of BD was detected in any of the models.

Our unadjusted results reflect those in other studies (Gao et al., 2021; Vahey et al., 2021). Instead, after adjustment for confounding factors, all other things therefore being equal, COVID-19 infection by itself (versus another reason) was associated with a lower risk of subsequent hospitalisation for a mood disorder. Previous findings suggested that having a diagnosed psychiatric disorder might be an independent risk factor for contracting COVID-19 (Bo et al., 2021; Taquet et al., 2021; Wang et al., 2020). Indeed, patients with a history of psychiatric disorders have more risk factors for developing severe forms of COVID-19. These factors include obesity, smoking, cardiovascular and pulmonary diseases (BPCO), venous thromboembolism, hypertension, and diabetes (Godin et al., 2018; Kowal et al., 2020). Our study confirmed that patients previously hospitalised for COVID-19 were more vulnerable, including a higher likelihood of having a history of mood disorders. These factors align with the expected predictors of incident hospitalisation for MDD, such as being female and of older age, both of which are widely recognised as MDD risk factors (Malhi and Mann, 2018). The association of a lower deprivation index was also observed in our work focused on psychotic disorders (Pignon et al., 2023). The nature of this relationship appears to be complex, and its role as a risk factor in MDD has demonstrated inconsistent findings when elevated, especially in women (Remes et al., 2019). Furthermore, the level of care received during the initial hospitalisation, especially intensive care (which is significantly more frequent for hospitalisation for COVID-19 than for another reason), is a known factor of psychological stress, in particular in MDD (Rai et al., 2019). The identification of these risk factors for incident MDD provides valuable insights for targeted prevention and intervention programs, and should be considered by mental health policymakers.

Our results highlighted that COVID-19 infection by itself was not related to a higher risk of subsequent hospitalisation for a mood

disorder, when compared to other causes of hospitalisation. Several hypotheses may explain this observation. First, unlike most studies to date, ours compared hospitalisations over the same period and not before/after the COVID-19 pandemic (Dubé et al., 2021; Santomauro et al., 2021; Taquet et al., 2021; Veazie et al., 2022). This is an important point as the pandemic impacted all individuals and healthcare systems. Stress brought on by the pandemic and its economic, social and health consequences led to significant disturbances in sleep and emotion regulation, which in turn contributed to a higher incidence of mood disorders (Baglioni et al., 2011; Bertrand et al., 2022; Christodoulou et al., 2023; Wirz-Justice and Benedetti, 2020). For example, in the general Chinese population, 54 % of those interviewed reported the pandemic impacted them psychologically; 16.5 % of the latter reported depressive symptoms (Wang et al., 2020). Accordingly, our choice to compare mental health outcomes over the same period and after hospital discharge for COVID-19 infection removed the influence of the high level of stress associated with this period.

Furthermore, we might have hypothesized that COVID-19, due to its immuno-inflammatory effects, would be linked to a higher likelihood of developing mood disorders. This hypothesis reflects observations by Taquet et al., who found a significant relationship between COVID-19 and mood disorders, even after comparison with six other health events (including respiratory tract infections and skin infections) (Taquet et al., 2021). Autoimmune diseases and severe infectious diseases are recognised risk factors of psychiatric disorders (Benros et al., 2013, 2011; Khandaker et al., 2012; Nielsen et al., 2014). It also has been proposed that the immune system's response and neuro-inflammation (i.e., inflammation not caused by the infection itself) contribute to the emergence of psychiatric disorders (De Picker et al., 2017; Leboyer et al., 2016; Malhi and Mann, 2018; Pape et al., 2019; Phillips and Kupfer, 2013). Nevertheless, in our study, hospitalisation for COVID-19, when compared to those for other causes, did not appear to be a supplementary risk factor for mood disorders after controlling for other risk factors, including more severe and longer hospitalisation. This finding leads us to suppose that irrespective of the cause (i.e., COVID-19 or another reason) for the initial hospitalisation, the principal risk factors associated with the subsequent onset of mood disorders were a history of mood disorders, the duration of the initial hospital stay, and the level of care received during that stay. However, it is worthwhile to explore how various causes of hospitalisation (COVID-19, cardiovascular issues, accidents, etc.) are linked to future mood disorders in order to definitively establish and generalize these risk factors for mood disorders.

Finally, our findings concerning hospitalisation for BD did not highlight any difference between patients previously hospitalised for COVID-19 and those hospitalised for another reason. Few studies to date have investigated patients with BD in the context of COVID-19; those that have, mostly assessed the impact of the pandemic or of related lockdowns, rather than the impact of the disease itself (Barrett et al., 2022; Dalkner et al., 2022, 2021; Fornaro et al., 2021). A case series reported three situations of patients with BD who suffered a relapse after being hospitalised with COVID-19 (Panda et al., 2021). It is therefore difficult to relate our results to the literature.

Several limitations of this work should be acknowledged. The most important one is that the reasons for hospitalisations other than for COVID-19 were not individually listed or separately studied. This control group was therefore non-specific (Decio et al., 2022). Having said that, other studies which did examine different reasons for hospitalisation found no difference in between-group (i.e., COVID-19 versus a specific other reason) findings (Taquet et al., 2021). In addition, we did not study different follow-up durations. Although 12 months may be considered reasonable to estimate the risk of MDD, it might be insufficient for BD given that the risk factors involved can impact for years before the disorder presents (Geoffroy et al., 2013). Accordingly, our results concerning the influence of COVID-19, especially on the risk of BD, should be interpreted with caution, especially given the smaller

sample size compared to those with MDD. Lastly, it's important to note that our study focused solely on hospitalised individuals and did not include outpatients. Therefore, the findings should be regarded, at most, as a proxy for incident severe MDD.

Despite these limitations, the study has several strengths, the most important being the exhaustiveness of the data. More specifically, all public and private hospitalisations in metropolitan France were included, thereby limiting selection and memory biases, and ensuring analyses with good statistical power.

In conclusion, we observed that close to 4 % of patients hospitalised during the beginning of COVID pandemic - whether for COVID-19 or for another reason - were subsequently hospitalised for a mood disorder in the 12 months following discharge. Interestingly, initial hospitalisation for COVID-19 versus another reason was associated with a lower risk of subsequent hospitalisation for a mood disorder. Being a woman, older age, lower social deprivation, and a history of mood disorders, were all associated with a higher risk of subsequent hospitalisation for MDD and BD. In addition, the duration of initial hospitalisation and the level of clinical care received were associated with the risk of being hospitalised for both disorders.

CRedit authorship contribution statement

PAG, VD, PP, NR & ST designed the review. VD & ST performed the statistical analyses. PAG, ST & BP performed the literature search and study selection. PAG wrote the first draft of the manuscript. All the authors participated in the text redaction and the interpretation of the results. All approved the final version of the manuscript.

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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.

Declaration of competing interest

The authors declare no conflicts of interest related to this work.

Data availability

The National French administrative healthcare database (*Système national des données de santé* (SNDS) database comprises a set of strictly pseudonymized databases. By law, SpF has permanent regulatory access to SNDS data for the performance of its missions (article L.1461-3 and R1461-13) and following of the French public health code (*Code de la santé publique, 2019*). Access to personal data in these systems for research purposes is only possible in the SNDS hub and cannot be extracted and shared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jad.2024.01.121>.

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