

Original Article

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Hospitalization for SARS-CoV-2 and the risk of self-harm readmission: a French nationwide retrospective cohort study

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Abstract

Aims. The impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection on the risk of self-harming behaviours warrants further investigation. Here, we hypothesized that people with a history of hospitalization for self-harm may be particularly at risk of readmission in case of SARS-CoV-2 hospitalization.

Methods. We conducted a retrospective analysis based on the French national hospitalization database. We identified all patients hospitalized for deliberate self-harm (10th edition of the International Classification of Diseases codes X60–X84) between March 2020 and March 2021. To study the effect of SARS-CoV-2 hospitalization on the risk of readmission for self-harm at 1-year of the inclusion, we performed a multivariable Fine and Gray model considering hospital death as a competing event.

Results. A total of 61,782 individuals were hospitalized for self-harm. During the 1-year follow-up, 9,403 (15.22%) were readmitted for self-harm. Between inclusion and self-harm readmission or the end of follow-up, 1,214 (1.96% of the study cohort) were hospitalized with SARS-CoV-2 (mean age 60 years, 52.9% women) while 60,568 were not (mean age 45 years, 57% women). Multivariate models revealed that the factors independently associated with self-harm readmission were: hospitalization with SARS-CoV-2 (adjusted hazard ratio (aHR) = 3.04 [2.73–3.37]), psychiatric disorders (aHR = 1.61 [1.53–1.69]), self-harm history (aHR = 2.00 [1.88–2.04]), intensive care and age above 80.

Conclusions. In hospitalized people with a personal history of self-harm, infection with SARS-CoV-2 increased the risk of readmission of self-harm, with an effect that seemed to add to the effect of a history of mental disorders, with an equally significant magnitude. Infection may be a significantly stressful condition that precipitates self-harming acts in vulnerable individuals. Clinicians should pay particular attention to the emergence of suicidal ideation in these patients in the aftermath of SARS-CoV-2 infection.

Introduction

Suicide remains a major cause of death worldwide, accounting for 1.4% of premature deaths (Bachmann, 2018; Reinke 2023), while a history of self-harm increases the risk of subsequent suicide death, thus representing the most important risk factor for completed suicide (WHO 2024). It is worth noting that the number of non-lethal self-harming acts is 10–30 times higher than the number of completed suicides (Bachmann, 2018). Moreover, non-lethal self-harm is associated with an increased risk of subsequent non-lethal self-harm, with around 16% recurrence within 1 year (Carroll 2014). It is therefore essential for prevention to better understand the factors associated with self-harm. Suicide and non-lethal self-harm are associated with various social, psychological and biological factors, some of which may be common to somatic diseases, e.g. the implication of the inflammatory pathways (Song 2023). Overall, it has been postulated that self-harming acts result from a complex interaction between risk factors (proximal adverse life events or depression, for instance) and vulnerability factors (a personal history of self-harm, for instance).

In this respect, a severe respiratory infection could represent a significant stress factor, through both psychological, physical and biological mechanisms (fear of death, difficulty

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breathing, inflammation, etc.). It can therefore be assumed that infection with severe acute respiratory syndrome coronavirus 2, known as SARS-CoV-2 (Piroth 2021; Winkler 2021), as an inflammatory neurotoxic virus (Barthorpe 2022; Spudich 2022; Merad 2022; Aschman 2022), could be a risk factor for self-harm. Although the pathophysiology of the long-term consequences of SARS-CoV-2 infection remains poorly understood, a body of epidemiological evidence suggests that SARS-CoV-2 infection can lead to multifaceted outcomes, including a marked neuropsychiatric impact (Pierce 2020; Barthorpe 2022). More generally, an increase in mental problems (mostly depression and anxiety) was observed during this pandemic (Winkler 2021; Liao 2021; COVID-19 Mental Disorders Collaborators 2021; Gloster 2020), including increases in non-lethal self-harming behaviours in young people (Jollant 2022a, Jollant 2022c; Madigan 2023). While the psychological impact of the pandemic has been highlighted, particularly at its onset and during the various lockdowns, the mechanisms linking SARS-CoV-2 infection and the risk of self-harm are still under debate. Many researchers initially focused on the consequences of collective measures (e.g. lockdown, closure of non-essential activities), which may have exacerbated loneliness or led to lasting breaks in social relationships, and self-harm behaviours (Ayuso-Mateos 2023; Farooq 2021; Jollant 2021; Jollant *et al.*, 2022c). However several recent studies have suggested an association between SARS-CoV-2 infection itself and self-harm, particularly in work focusing on specific populations (Reinke 2023; Hynes 2023). In this respect, a very recent study we carried out on the French hospital database between March 2020 and March 2021 on all patients hospitalized in France (10,084,551) showed that hospitalization for SARS-CoV-2 had no overall significant influence on the occurrence of subsequent hospitalization for self-harm (Chauvet-Gelinier 2023). However, this study also revealed an interaction between hospitalization for SARS-CoV-2 and a self-harm episode at inclusion relative to the risk of subsequent self-harm, suggesting that there may be a particular influence of SARS-CoV-2 infection (as a stress factor) on the risk of self-harming in those who are more vulnerable to these acts (Chauvet-Gelinier 2023). Those results were consistent with a recent meta-analysis from Yuan *et al.* who demonstrated that SARS-CoV-2 may cause adverse psychiatric outcomes in people with pre-existing mental health problem (Yuan 2022).

This prompted us to conduct a study on adults with a recent history of self-harm to investigate the hypothesis that a severe SARS-CoV-2 infection (defined as necessitating hospitalization) may increase the risk of self-harm readmission in the short-term, in addition to the already increased risk of self-harm readmission in this vulnerable population. To this aim, we analyzed the large and exhaustive French national hospital database at the beginning of the pandemic in 2020–2021.

Methods

Database

We conducted a retrospective analysis of prospectively collected data in a national cohort of all hospitalizations in France. Data were extracted from the national *Programme de Médicalisation des Systèmes d'Information* (PMSI) database, which includes discharge summaries for all inpatients admitted to public and private hospitals in France (Goldberg 2012). Inspired by the American diagnosis-related group model, the information in these abstracts is anonymous and covers both medical and administrative data.

Diagnoses identified during the hospital stay are coded according to the 10th edition of the International Classification of Diseases (ICD-10), and procedures done during hospitalization are coded according to the French Common Classification of Medical Procedures. The fact that these national data are used for the allocation of hospital budgets encourages improvement in data quality in terms of coherence, accuracy and exhaustiveness. Therefore, these hospital data have been used in medical research for many years (Abdulmalak 2015; Creuzot-Garcher 2016; Goueslard 2018; Goueslard 2022; Jollant 2022b; Le Teuff 2015; Lorgis 2013; Maitre 2018; Quantin 2013; Quantin 2021; Vuagnat 2019; Duriez 2023; Goueslard 2023; Jollant *et al.*, 2022c; Goueslard 2022b), and their quality has been confirmed in recent studies on SARS-CoV-2 (Piroth 2021; Jollant *et al.*, 2022c; Mariet 2020; Beltramo 2021; Simon 2021; Quantin 2022; Karila 2021).

Population

The main objective of this study was to explore the association between hospitalization with a SARS-CoV-2 viral infection and readmission for a self-harm in patients recently hospitalized for deliberate self-harm (Fig. 1).

We included all patients aged 18 years or older admitted to hospital with a self-harm code between 1 March 2020 and 31 March 2021.

Hospital stays for self-harm were identified by ICD-10 codes X60–X84 in the primary, related, or associated diagnoses. Self-harm includes the following categories: poisoning (X60–X69), hanging (X70), drowning (X71), firearm (X72–X75), fire (X76–X77), sharp/blunt objects (X78–X79), jumping (X80), vehicle (X81–X82), other or unspecified (X83–X84).

The first stay identified during the inclusion period was considered to be the index hospitalization so that the patient was counted only once.

Exposure

During the year following the index hospitalization, we extracted hospitalization for SARS-CoV-2, identified by ICD-10 codes U07.10, U07.11, U07.12, U07.14, or U07.15 in the primary, related, or associated diagnoses.

Outcome and follow-up

The outcome was any hospitalization for self-harm identified with at least one ICD-10 code X60–X84 filled in a hospital discharge abstract during the 1-year period following the index hospitalization.

Co-variables

The following variables were extracted for all individuals included in the study. At baseline (i.e. during the index hospitalization), we collected: age, sex, admission to intensive care unit (ICU), somatic disorders according to the main category (all chapters of ICD-10) and psychiatric disorders (F10–F69 ICD-10 codes). Age was taken into account in different ways. Firstly, we established several age categories (18–29, 30–39, 40–49, 50–59, 60–69, 70–79, 80–89, ≥ 90 years) using disjunctive variables. Indeed, in many papers, the frequency of self-harm was shown to differ according to age group (Jollant 2021; Knipe 2022). Secondly, we

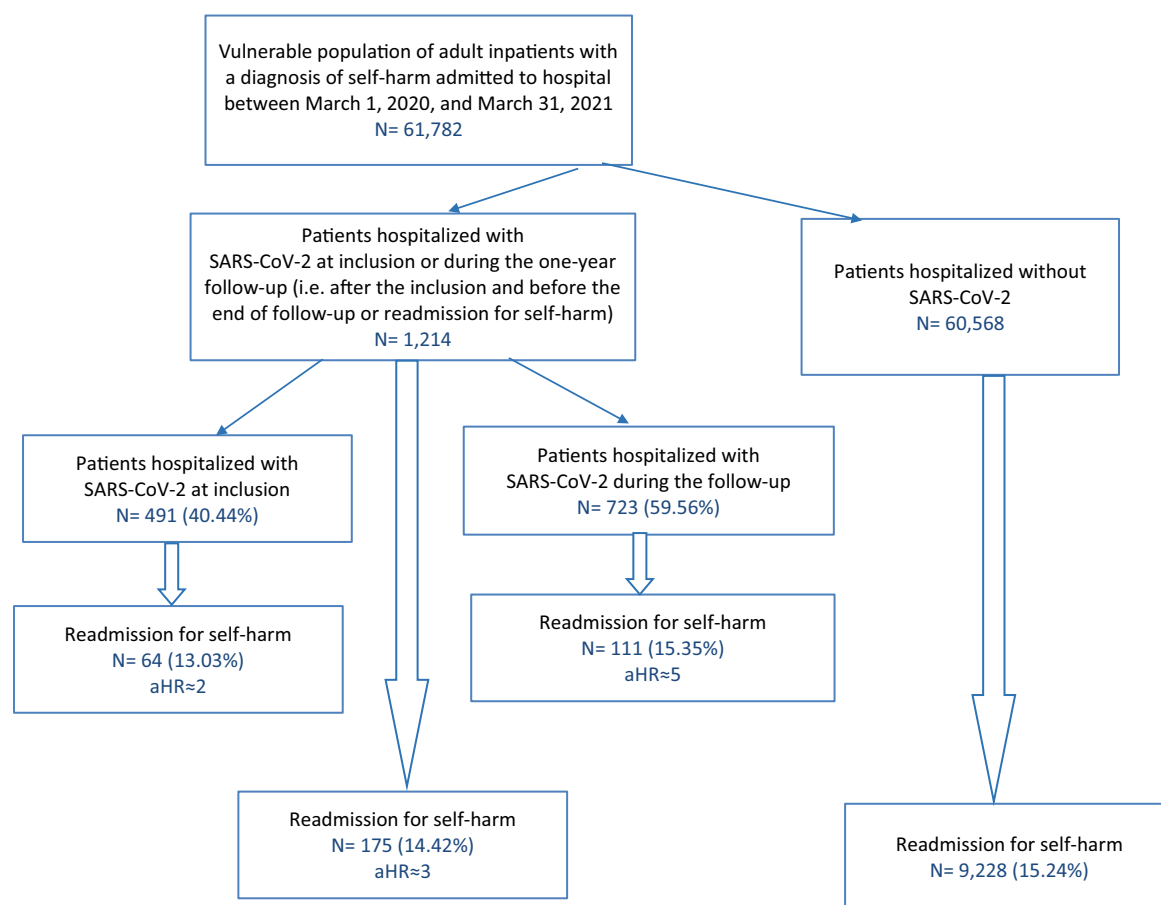


Figure 1. Flowchart.

included age as a continuous variable. Indeed, categorizing an essentially continuous variable may waste information (Altman 2006; Royston 2006) and can lead to implausible models because they expect the effect to remain stable within categories and to take on a new value at the category boundary. Psychiatric disorders included mental and behavioural disorders due to psychoactive substance use (F10–F19), schizophrenia (F20–F29), mood disorders (F30–F39), stress-related disorders (F40–F48), behavioural syndromes associated with physiological disturbances and physical factors (F50–F59), and disorders of adult personality (F60–F69).

We also considered a history of hospitalization in the 7 years preceding the index hospitalization for self-harm, somatic disorders and psychiatric disorders. The 'self-harm in the 7 previous years' variable was obtained using the codes selected only in the discharge abstracts for the previous 7 years before admission. Note that if a person had more than one event, we considered the closest event. The reason we used the past 7 years as cut-off in our retrospective analysis is that, the national hospitalization data collection becomes assuredly comprehensive from year 2014 onwards. Seven years is therefore the longest period during which we can obtain robust and reliable data.

During the year of follow-up after the index hospitalization, we also extracted in-hospital death.

We considered two additional periods, March–September 2020 and October 2020–March 2021, which corresponded to sanitary restrictions in France but also to the arrival of the alpha variant in France at the end of the year 2020. We also added a deprivation index for social disadvantage available in our database and

constructed using national census data from the French national census institute, the *Institut National de la Statistique et des Etudes Economiques* (Rey 2009). This deprivation index estimates patients' probable socioeconomic status based on four variables that depend on the geographical location of residence: median income per consumption unit in the household; the percentage of baccalaureate holders in the population over 15 years old; the percentage of blue-collar workers in the active population; the unemployment rate.

Statistical analyses

Individual characteristics, somatic and psychiatric disorders are presented as proportions, and comparisons between patients hospitalized with and without SARS-CoV-2 were made using a χ^2 test. Age is also presented as means $\pm$ standard deviation (SD) and as medians and interquartile range, and comparisons were made using a Student's t-test.

To study the effect of hospitalization with SARS-CoV-2 on the risk of readmission for self-harm, we performed a survival analysis using Fine and Gray modelling and comparing patients with and without a hospitalization with SARS-CoV-2. This model avoids a bias in the estimation of risk considering competing events such as in-hospital death. Indeed, this type of event may prevent the observation of the event of interest: self-harm. This model was adjusted for age, sex, admission to ICU, history of self-harm, somatic disorders and psychiatric disorders. Hospitalization for SARS-CoV-2 was considered as

Table 1. Characteristics of patients hospitalized with self-harm between 1 March 2020 and 31 March 2021 with or without SARS-CoV-2 hospitalization

	Patients hospitalized with self-harm		With SARS-CoV-2 hospitalization ^a		Without SARS-CoV-2 hospitalization ^a		<i>p</i> -value to compare patients with and without SARS-CoV-2
	61,782		1,214		60,568		
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Socio-demographic characteristics							
Age							
Mean (SD)	45 (18)		59 (21)		45 (18)		<0.0001
Median [Q1–Q3]	45 [30–56]		60 [43–78]		45 [30–56]		
Age categories							<0.0001
18–29	14,472	23.42	132	10.87	14,340	23.68	
30–39	10,482	16.97	119	9.80	10,363	17.11	
40–49	12,683	20.53	158	13.01	12,525	20.68	
50–59	11,638	18.84	191	15.73	11,447	18.90	
60–69	6,179	10.00	183	15.07	5,996	9.90	
70–79	3,273	5.30	162	13.34	3,111	5.14	
80–89	2,370	3.84	188	15.49	2,182	3.60	
≥90	685	1.11	81	6.67	604	1.00	
Sex = Men	26,624	43.09	572	47.12	26,052	43.01	0.004
Medical characteristics							
Admission to intensive care unit at inclusion	8,828	14.29	244	20.10	8,584	14.17	<0.0001
Somatic disorders at inclusion or in the 7 previous years	47,332	76.61	1,036	85.34	46,296	76.44	<0.0001
Psychiatric disorders at inclusion or in the 7 previous years	48,015	77.72	979	80.64	47,036	77.66	0.01
Self-harm in the 7 previous years ^b	14,664	23.74	259	21.33	14,405	23.78	0.047
Outcome							
Readmission of self-harm at 1 year after inclusion	9,403	15.22	175	14.42	9,228	15.24	0.4306

SD = standard deviation; Q1 = first quartile; Q3 = third quartile.

^aBefore self-harm readmission or the end of follow-up.

^bSelf-harm at the inclusion stay was not considered for this variable as it was already used as an inclusion criterion.

a time-dependent variable. Therefore, SARS-CoV-2 was taken into account either at index hospitalization, or during follow-up, i.e. before readmission for self-harm (our outcome), or before the end of follow-up (1 year after index hospitalization) for patients who were not readmitted for self-harm. For this analysis, we presented the effect of all adjustment variables, but it should be noted that only the effect of SARS-CoV-2 infection is considered as the total effect on the risk of readmission for self-harm (Westreich 2013).

Moreover, in order to refine our findings, we considered, in addition to the overall results, the outcomes obtained by distinguishing between patients with SARS-CoV-2 at inclusion and those who contracted SARS-CoV-2 after their inclusion.

We then performed a first sensitivity analysis according to the March 2020–September 2020 and October 2020–March 2021 periods. We performed a second sensitivity analysis adding the deprivation index as an adjustment variable.

The results are reported as adjusted hazard ratios (aHR) and 95% confidence intervals (95% CI).

Results

61,782 individuals were hospitalized for self-harm between 1 March 2020 and 31 March 2021, of which 15.22% were again hospitalized for self-harm in the following year (Table 1, Fig. 1). Moreover, 1,214 patients were hospitalized for SARS-CoV-2 either at index hospitalization or during follow-up (1.96%). Among these 1,214 patients, 14.42% (175 patients) were readmitted for self-harm.

A comparison with 2019 data found that the characteristics of patients in 2019 and in our inclusion years (March 2020–March 2021) were very similar, with the exception of patients hospitalized for SARS-CoV-2 infection (Table S1).

In our inclusion period (March 2020–March 2021), patients hospitalized with SARS-CoV-2 were significantly older than those who were not (59 vs 45 years). There were also significantly more men (47.12% vs 43.01%), more index hospitalizations in the ICU (20.10% vs 14.17%), and more histories of somatic disorders in the 7 previous years in the SARS-CoV-2 group (85.34% vs 76.44%).

Table 2. Risk of readmission for self-harm at 1 year in patients admitted to hospital for self-harm between 1 March 2020 and 31 March 2021 according to SARS-CoV-2 hospitalization in multivariable Fine & Gray analysis

	Model 1: Age as a categorical variable HR [95% CI]	Model 2: Age as a continuous variable HR [95% CI]	Model 3: Age as a continuous variable (quadratic effect) HR [95% CI]
SARS-CoV-2 ^a	2.86 [2.57–3.18]	3.04 [2.73–3.37]	2.86 [2.57–3.18]
Self-harm in the 7 previous years ^{b,*}	2.02 [1.94–2.11]	2.00 [1.88–2.04]	2.03 [1.95–2.12]
Psychiatric disorders at inclusion or in the 7 previous years ^c	1.65 [1.57–1.74]	1.61 [1.53–1.69]	1.67 [1.58–1.76]

HR = hazard ratio; CI = confidence interval.

^aAdjusted on age, sex, intensive care unit admission at inclusion, somatic disorders at inclusion or in the 7 previous years, self-harm in the 7 previous years, psychiatric disorders at inclusion or in the 7 previous years, period of the epidemic.

^bAdjusted on age, sex, intensive care unit admission at inclusion, somatic disorders at inclusion or in the 7 previous years, psychiatric disorders at inclusion or in the 7 previous years, period of the epidemic.

^cAdjusted on age, sex, intensive care unit admission at inclusion, somatic disorders at inclusion or in the 7 previous years, period of the epidemic.

*Self-harm at the inclusion stay was not considered for this variable, as it was already used as an inclusion criterion.

Moreover, those hospitalized with SARS-CoV-2 were more likely to have a history of psychiatric disorders (80.64% vs 77.66%) but less likely to have a hospitalization for self-harm (21.33% vs 23.78%) in the 7 previous years.

Univariate analyses showed no significant difference in self-harm readmission between those hospitalized with or without SARS-CoV-2 infection (14.42% vs 15.24%, $p = 0.43$).

However, we found that patients hospitalized with SARS-CoV-2 had three times the risk of readmission for self-harm compared to patients hospitalized without SARS-CoV-2 in multivariable analysis adjusted for age and sex, ICU admission at inclusion, somatic disorders at inclusion or in the 7 previous years, self-harm in the 7 previous years, psychiatric disorders at inclusion or in the 7 previous years, and the epidemic period (Table 2, Fig. 2).

In addition, the risk of self-harm readmission was increased in those admitted to ICUs, those with a history of self-harm over the past 7 years, those with a mental or somatic disorder at inclusion and over the past 7 years, and those older than 80 years old (Fig. 2). This risk was decreased in women and individuals aged 50–69 years (Fig. 2).

In particular, we showed that hospitalization for SARS-CoV-2 conferred a higher risk of readmission for self-harm than a history of psychiatric illness or self-harm (Table 2). The results were consistent in both sensitivity analyses, stratifying by period (Tables S2, S3), or adding the deprivation index as an adjustment variable (Table S4). The results were also the same when we adjusted for age as a categorical or continuous variable (linear or quadratic).

Distinguishing between patients with SARS-CoV-2 at inclusion and those who contracted SARS-CoV-2 after their inclusion (Table 3), we found that the results show an even more pronounced effect for patients who developed SARS-CoV-2 after their inclusion stay, seeing as these patients had five times the risk of readmission for self-harm compared to patients hospitalized without SARS-CoV-2.

Discussion

While an association between the COVID-19 pandemic and non-lethal self-harm incidence has been demonstrated in various populations, there is a lack of data focusing on individuals who contracted a severe SARS-CoV-2 infection (Farooq 2021). This study, based on the French national hospital database, showed that

hospitalization for SARS-CoV-2 infection was associated with a significant increase in the risk of readmission for self-harm in people who had recently been hospitalized for self-harm. This association was, however, only significant after multivariate analyses. Moreover, this association remained significant in addition to the effect of comorbid mental disorders. It should also be noted that the recruitment period did not seem to affect the risk of self-harm readmission. As a reminder, March 2020–September 2020 was a period of strict lockdown while October 2020–March 2021 was much less strict. The lack of difference between these periods may suggest that the infection itself may be more important than the social context. Finally, we found that factors such as frailty or vulnerability (older than 80, somatic and psychiatric comorbidity) and a more severe presentation (ICU at admission) were associated with an increased risk of self-harm readmission. The distinct impact of SARS-CoV-2 infection is again illustrated by the fact that a SARS-CoV-2 hospitalization occurring subsequently to the initial hospitalization for self-harm was nearly five times more associated with the risk of self-harm readmission, while hospitalization for SARS-CoV-2 concurrently to the initial hospitalization for self-harm only doubled the risk of self-harm readmission. These unprecedented results highlight how hospitalization for a SARS-CoV-2 infection represents a distinctly identified risk factor for the readmission of self-harm, especially among individuals vulnerable to suicidal behaviours.

Indeed, our data provide a new perspective on the links, sometimes described as uncertain, between SARS-CoV-2 infection and subsequent self-harm, as highlighted by Erlangsen et al. (Erlangsen 2023). The present study thus refines this Danish work with conclusions identical to our initial investigation (Chauvet-Gelinier 2023), showing that among patients highly vulnerable to suicidal behaviours (i.e., those who have recently self-harmed), hospitalization for SARS-CoV-2 significantly increases the risk of further self-harm readmission. Another major interest of this work lies in encouraging clinicians to pay attention to the risk of recurrent suicidal behaviour in a middle-aged population traditionally less prone to self-harm compared to young adults (Nock 2006; Wang 2022), especially among patients with recent history of self-harm and hospitalized for SARS-CoV-2. The population included in our study has particular characteristics, namely an average age of 45 years and the presence of both psychiatric and somatic comorbidities. Our results therefore allow us to recommend that special attention be paid to middle-aged/elderly patients

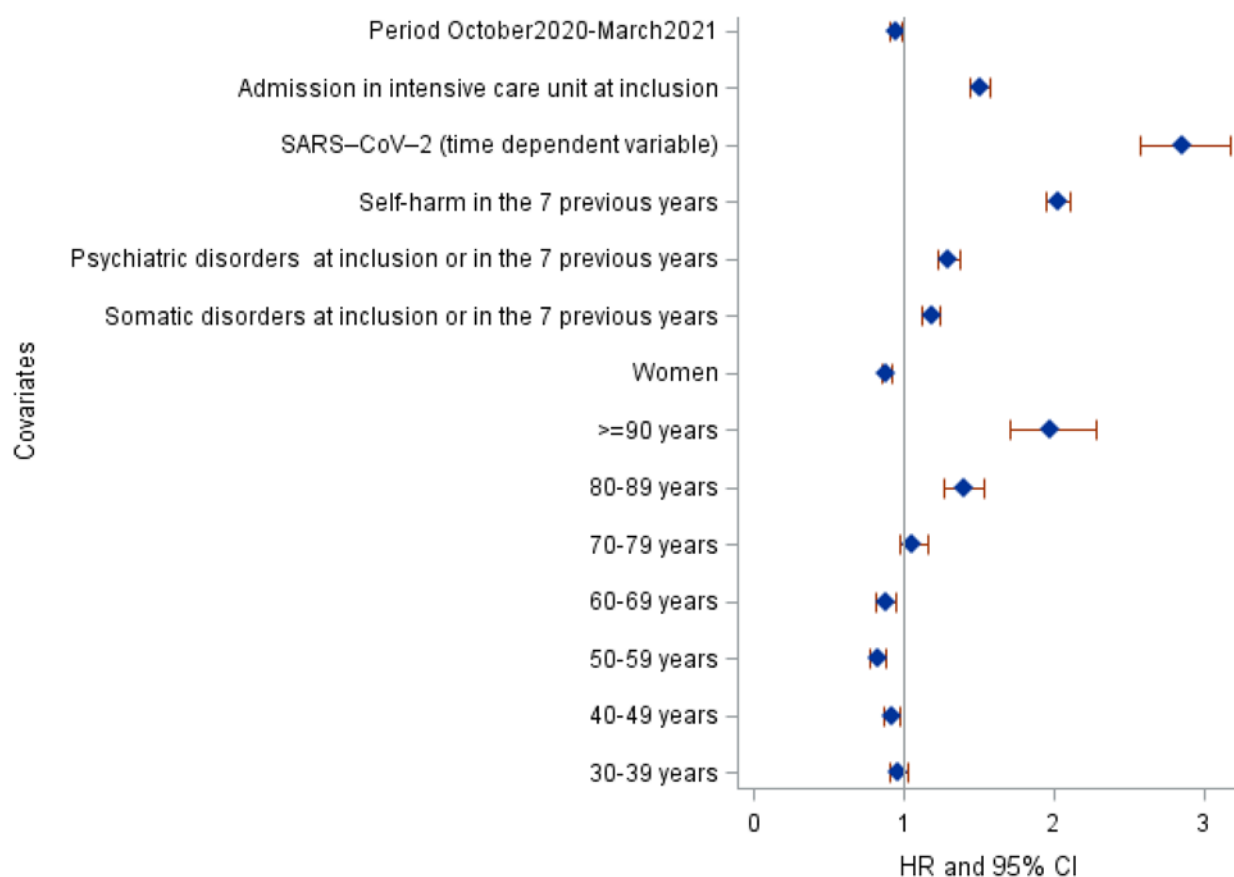


Figure 2. Forest plot of hazard ratio following the application of a Fine & Gray analysis to study the risk of readmission for self-harm at 1 year in patients hospitalized with self-harm admitted between 1 March 2020 and 31 March 2021. Self-harm at the inclusion stay was not considered for the 'Self-harm in the 7 previous years' variable, as it was already used as an inclusion criterion. All estimates are for direct effects, except for SARS-CoV-2, which gives the total effect

Table 3. Risk of readmission for self-harm at 1 year in patients admitted to hospital for self-harm between 1 March 2020 and 31 March 2021 according to when the SARS-CoV-2 hospitalization is observed in multivariable Fine & Gray analysis

	Model 1: Age as a categorical variable HR [95% CI]	Model 2: Age as a continuous variable HR [95% CI]	Model 3: Age as a continuous variable (quadratic effect) HR [95% CI]
SARS-CoV-2 at inclusion or during follow-up	2.86 [2.57–3.18]	3.04 [2.73–3.37]	2.86 [2.57–3.18]
SARS-CoV-2 at inclusion	1.75 [1.48–2.06]	1.86 [1.58–2.20]	1.75 [1.49–1.59]
SARS-CoV-2 only during follow-up	4.82 [4.21–5.52]	5.14 [4.49–5.88]	4.81 [4.20–5.51]

Adjusted on age, sex, intensive care unit admission at inclusion, somatic disorders at inclusion or in the 7 previous years, self-harm in the 7 previous year, psychiatric disorders at inclusion or in the 7 previous years, period of the epidemic.

with SARS-CoV-2 who have medical and psychiatric histories, especially a recent history of self-harm.

This study provides additional evidence of the damaging impact of SARS-CoV-2 infection. Our results are consistent with another large cohort study based on electronic medical records. The authors found that 18% of the 62,354 included patients received a psychiatric diagnosis (mainly anxiety and mood disorders) in the 3 months following a diagnosis of SARS-CoV-2, which was significantly higher than in matched controls with other medical conditions, including respiratory infections such as influenza (Taquet 2021a; Taquet 2021b). In addition, recent reports have underscored the extent to which hospitalization for SARS-CoV-2 can lead to profound psychological upheavals in the following months,

such as the unmasking or relapse of bipolar disorders (Del Casale 2022).

Above all, the present study supports the notion that hospitalization for SARS-CoV-2 infection may cause particularly detrimental neuropsychiatric events (here, self-harm readmission) in individuals with pre-existing mental health issues and vulnerability (here, recent and past hospitalization for self-harm). These findings are consistent with those of Wang *et al.*, who recently reported that pre-infection psychological distress was associated with the risk of post-SARS-CoV-2 conditions and impairment of daily living, suggesting the prospective impact of psychiatric status surrounding SARS-CoV-2 infection on physical and mental outcomes (Wang 2022).

Although our study does not allow us to conclude that there is a causal link between hospitalization for SARS-CoV-2 infection and an increased risk of self-harm readmission, and we did not investigate the mechanisms of this association, the inflammatory neuropsychiatric impact of this virus is worth mentioning (Conejero 2021). Immuno-inflammatory hypotheses have been evoked as potential mechanisms associated with psychiatric decompensation, notably in individuals at risk of mood disorders (Brundin 2017). Like other inflammatory respiratory viruses such as influenza, SARS-CoV-2 could have a highly deleterious influence in terms of suicidality. In a study illustrating the links between influenza and suicidal ideation, Jung et al. suggested that the inflammatory hypothesis must be considered in the biological approach to the link between viral infection and suicidal ideation/behaviour (Jung 2021). More specifically, the disruption of the serotonergic system by inflammatory cytokines could partly explain suicidal ideation or behaviour in people with affective disorders. Some inflammatory cytokines have been associated with the neurotoxic kynurenine pathway in people with suicidal behaviour (Sublette 2011; Brundin 2016). This pathway is known to disrupt the serotonin system (Pariante 1999), which may lead to major depressive disorders (Vaswan 2003; Yuan 2019). Interestingly, a recent meta-analysis (Vasupanrajit 2022) exposed a robust link between activated immune-inflammatory pathways and recent self-harm or suicidal ideation in a study including 4,034 suicide attempt/suicide ideation cases and 12,377 controls. We speculate that the central and peripheral inflammatory effects of the SARS-CoV-2 infection could lead to an increased risk of self-harming ideas and acts in people who have previously responded to stress with self-harm. In addition, it has been shown that patients hospitalized for SARS-CoV-2 with metabolic (i.e. lipid metabolism dysregulation) and inflammatory alterations have a worse prognosis (Aparisi 2021; Li 2021). Additionally, it has been shown that inflammation and certain metabolic disorders (i.e. lipid metabolism dysregulation) are associated with the recurrence of self-harm (Aguglia 2020). Therefore, our study allows us to hypothesize that a SARS-CoV-2 infection occurring a significant time after an initial self-harm incident constitutes a detrimental psychobiological factor, likely to cause inflammatory and metabolic disturbances in the brain and the entire body, potentially triggering new self-harm incidents. The specific psycho-biological impact of SARS-CoV-2 infection, as described previously (Conejero 2021; Taquet 2021b), was again illustrated by the fact that hospitalization for SARS-CoV-2 infection occurring distant from initial hospitalization for self-harm appears to be nearly 5 times (aHR of 5.14) more associated with the risk of self-harm readmission, compared to the risk of self-harm readmission in people initially hospitalized for both self-harm and SARS-CoV-2 (aHR of 1.8). These data thus allow us to distinguish between the various risk factors and the timing of their emergence, illustrating the discernible impact of SARS-CoV-2 infection on suicidal behaviour among subjects at high risk of self-harm readmission. Beyond the biological hypothesis, we cannot rule out the possibility that hospitalization with SARS-CoV-2 may constitute *per se* a traumatic event or at least a factor of psychological stress. Indeed, being affected by SARS-CoV-2 has been associated with increased feelings of guilt (Hamama 2022), which in turn has been described as increasing suicidal ideation (Kealy 2021). Hospitalization for SARS-CoV-2 infection, with all that it implies in terms of septic isolation, may serve as a kind of trigger for people who have recently self-harmed. In addition, several studies maintain that the fact of believing oneself to be affected by the virus (either as a result of a diagnosis, or as a

result of evocative symptoms independent of the patient's viral status) may be a risk factor for mental disorders or suicidal behaviour (Taquet 2021a; Davaisse-Paturet 2023). Respiratory symptoms may also have a particular contribution to an increased risk of anxiety and depressive symptoms (Gasnier 2022).

Whatever the precise mechanisms explaining the link between hospitalization with SARS-CoV-2 and self-harm in the short-term, this study shows that hospitalization with SARS-CoV-2 should be considered a risk factor for short-term self-harm readmission in those who have previously been hospitalized for self-harm. Thus, SARS-CoV-2 infection could be considered as a factor that precipitates self-harm readmission in vulnerable individuals. Clinicians should be made aware of these findings and exercise particular vigilance in these patients, paying particular attention to the emergence of suicidal ideas in the aftermath of a SARS-CoV-2 hospitalization.

We acknowledge that our study has some limitations, mainly due to its design using a hospital database based on ICD-10 diagnosis codes. Clinical symptoms and specific patient characteristics are not available in the PMSI database, which limits the scope of analyses and the interpretation of results and putative mechanisms. In addition, the use of a hospital database meant that we could not include a population of people who had not been hospitalized as a control group. Of course, many individuals infected with SARS-CoV-2 were not hospitalized. We were not able to detect consecutive self-harm in this ambulatory population, which could have led to an underestimation of the effect of SARS-CoV-2 infection on a self-harm outcome. Moreover, some recent studies suggest that individuals hospitalized for SARS-CoV-2 infection may have a better outcome, both in terms of somatic and psychiatric aspects, than those treated in the community (van der Feltz-Cornelis 2024). Furthermore, many patients who self-harm are not hospitalized, with some recent work suggesting that 40% of self-harm events do not result in hospital admission in France (Jollant 2022d). Our work only considered self-harms admitted to hospital, which may have led to an underestimation of the potential association between hospitalization for SARS-CoV-2 and subsequent self-harm. Additionally, we were unable to distinguish infections that had started before hospitalization from those that were acquired during the inclusion stay for self-harm. To our knowledge, there is no literature on the impact of potential hospital-acquired SARS-CoV-2 infection on the risk of self-harm in this particular population of patients hospitalized for self-harm. However, when we distinguished between patients with SARS-CoV-2 at inclusion and those who contracted SARS-CoV-2 after their inclusion, we found an effect of SARS-CoV-2 on the risk of self-harm in both cases. Lastly, other confounding factors such as the level of social stringency (social restrictions), the infection rate (number of new cases/deaths and associated fear), and economic difficulties (either prior to or during the pandemic) could not be fully incorporated into our analyses despite the use of a deprivation index and the inclusion of two distinct epidemic periods.

Conclusion

This exhaustive nationwide exploration of people hospitalized from March 2020 to March 2021 provides new information about the association between hospitalization for SARS-CoV-2 infection and self-harm. We found an increased risk of self-harm readmission in people with a recent history of hospitalization for self-harm with a subsequent hospitalization with SARS-CoV-2 infection,

which may suggest that SARS-CoV-2 infection is a trigger for self-harm, particularly in vulnerable individuals. Our report underlines the importance of continued research in this field. Clinicians should also consider routinely investigating a recent history of self-harm in any patient hospitalized for SARS-CoV-2 and monitoring the emergence of suicidal ideas during follow-up. This study ultimately suggests that healthcare providers should pay particular attention to middle-aged and elderly patients with somatic and psychiatric histories, especially those with a recent history of self-harm, in the management of individuals admitted for SARS-CoV-2 infection.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S2045796024000568>.

Availability of data and materials. The use of these data by our department was approved by the National Committee for data protection. We are not allowed to transmit these data.

PMSI data are available for researchers who meet the criteria for access to these French confidential data (this access is submitted to the approval of the National Committee for data protection) from the national agency for the management of hospitalization (ATIH - Agence technique de l'information sur l'hospitalisation).

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