

Suicidality and COVID-19: Suicidal ideation, suicidal behaviors and completed suicides amidst the COVID-19 pandemic (Review)

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Abstract. Since the outbreak of the coronavirus 2019 (COVID-19) pandemic, there has been widespread concern that social isolation, financial stress, depression, limited or variable access to health care services and other pandemic-related stressors may contribute to an increase in suicidal behaviors. In patients who have recovered from COVID-19, an increased risk of developing suicidal behaviors may be noted, while post-COVID syndrome comprises another potential risk factor contributing to increased suicidal behaviors. Despite the initial alarming predictions for an increase in suicide rates due to the COVID-19 pandemic, the majority of published studies to date suggest that experienced difficulties and distress do not inevitably translate into an increased number of suicide-related deaths, at least not in the short-term. Nevertheless, the long-term mental health effects of the COVID-19 pandemic have yet to be unfolded and are likely to remain for a long period of time. Suicide prevention and measures aiming at promoting well-being and mitigating the effects of COVID-19 on mental health, particularly among vulnerable groups, should thus be a priority for healthcare professionals and policymakers amidst the evolving COVID-19 pandemic.

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1. Introduction

The outbreak of coronavirus 2019 (COVID-19) was declared by the World Health Organization (WHO) as a global public health emergency on January 30, 2020 (1). Currently, worldwide, there have been >249 million confirmed cases of COVID-19, and >5 million deaths from COVID-19 reported, according to the WHO (2).

From a public health perspective, the current pandemic has underscored that a multitude of predisposing factors may contribute to the rapid spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), particularly among vulnerable individuals. First, environmental pollution and chronic exposure to chemicals, such as fossil fuel derivatives, as well as exposure to particle matters, metals, and ultraviolet (UV)-B and ionizing radiation have been acknowledged as risk factors for immunodeficiency, that may contribute to the manifestation of COVID-19 (3). Second, a number of studies have underlined that distinct cellular mechanisms may be associated with an increased predisposition to COVID-19, including the dysfunction of high mobility group proteins (HMGBs), which belong to a superfamily of nuclear proteins with DNA-binding properties that have been implicated in immunological, pro-thrombotic and viral replicating cascades (4). Third, there is an increasing understanding of the central role of immunological processes, including aberrant inflammatory responses and cytokine release during the initial stages of viral infection, as well as a growing awareness of the pivotal role of humoral and cellular responses in the elimination or conversely, the propagation of COVID-19 (5).

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Of note, the COVID-19 pandemic is considered the most severe pandemic of the 21st century with significant repercussions not only on physical health, but on mental health as well (6-8). It is thus unsurprising, that the development of effective vaccines against SARS-CoV-2 became a priority for the public health agenda from the time of the outbreak of the pandemic. Currently, there are several available vaccines against COVID-19, which have been proven both safe and effective in preventing severe SARS-CoV-2 infection or mortality from COVID-19, while to date, >50% of the world population has received at least one dose of a COVID-19 vaccine (9-17). Although causal treatments for COVID-19 remain unavailable, certain beneficial effects from vitamin supplements, probiotics and minerals have been reported in a number of studies, although their role is considered mostly supportive for the immune system (10,18-20).

Multiple public health interventions have also been implemented worldwide to decrease the transmission of SARS-CoV-2 (21). Nevertheless, measures aiming to attenuate the viral spread, such as self-isolation, quarantine, lockdown and movement restrictions, have led to significant restrictions in daily activities and routines, and along with the threat posed by the pandemic, these measures have propagated feelings of fear, uncertainty, stigmatization, social isolation and loneliness (22-24). Furthermore, there have been reports of a significant increase in alcohol consumption and a significant exacerbation of domestic violence during the implementation of the aforementioned restriction measures (25,26).

Thus, there is a growing concern currently regarding the mental health sequelae of the COVID-19 pandemic (23,27,28). In particular, accumulating evidence has been presented of relapses in individuals with pre-existing mental health issues, who are at risk of further deterioration, new-onset mental illness, increased morbidity or even death, while individuals with no prior psychiatric history are also at risk of developing psychological issues (29,30).

Moreover, an increasing number of studies have suggested that patients with COVID-19 may experience neuropsychiatric manifestations, both during the acute and post-illness stages (i.e., COVID-19 survivors) (31-38). The severity of acute SARS-CoV-2 infection appears to be related to subsequent psychiatric or neurological sequelae, while there may be a tendency towards symptom improvement over time (33).

2. Suicidal behaviors in the context of the COVID-19 pandemic

Since the outbreak of the COVID-19 pandemic, there has been widespread concern regarding its effect on suicidality, as COVID-19 may increase the risk of individuals developing suicidal behaviors through its effects on a number of well-established suicide risk factors (Fig. 1) (39,40).

Several parameters, both at the population and individual levels, modulate suicide risk (41). Factors that are related to an increased number of suicides, include a history of suicide attempts, mental health issues, experiencing social isolation, facing financial stress or professional difficulties, criminal or legal issues, having a serious physical illness, substance use disorder, adverse childhood experiences, a family history of suicide, having experienced sexual violence, barriers to health

care, stigma associated with mental illness or help-seeking, easy access to lethal means and unsafe media portrayals of suicide (42).

It should be noted that during previous infectious disease outbreaks, suicide prevalence appeared to be elevated. Specifically, suicide rates were found to have increased during the bubonic plague, during the Spanish Flu of 1918-1919 in the United States, during the SARS outbreak in China among the elderly, women and lower socio-economic class, as well as during the Ebola infection in Africa (43-46).

Mental, behavioral, financial and psychosocial issues associated with the COVID-19 pandemic may contribute to an increase in suicidal behaviors (39,40). Furthermore, symptoms of psychiatric, neurological and physical illnesses, as well as inflammatory damage to the brain among patients with post-COVID syndrome may be associated with an increased risk of suicidal tendencies in this population, while COVID-19 survivors without post-COVID syndrome may also face such a risk (47).

Suicidal ideation and suicide attempts amidst the COVID-19 pandemic. Suicidal ideation during the COVID-19 pandemic has been associated with loneliness, anxiety, depression, insomnia, impaired family functioning, a history of mental health issues, alcohol misuse, COVID-19-related stress symptoms, concerns over COVID-19, having tested positive for COVID-19, a younger age, an unmarried or divorced marital status, living alone, being a military veteran, previous homelessness, financial strain, housing instability, unemployment, a poor perceived quality of physical health, disability and living with an individual with frail health (48-53). On the other hand, increased social support, resilience, positive feelings regarding the lockdown measures and faith in a supreme being have been identified as significant protective factors against suicidal ideation (48,49,54).

In a previous meta-analysis of 54 studies, including data from 308,596 individuals, that investigated suicide behaviors during the COVID-19 pandemic, increased event rates were found when considered against event rates from pre-pandemic studies (39). Specifically, that study demonstrated during the COVID-19 pandemic, the combined samples' event rate was 10.81% for suicidal ideation, 4.68% for suicide attempts and 9.63% for self-harm, whereas when community, clinical and frontline samples were examined separately, a trend for higher rates was found in the clinical sample. Nevertheless, it should be noted that the majority of the studies were cross-sectional or retrospective chart reviews (39).

A previous longitudinal study examining the trajectory of mental health during the first 6 weeks of lockdown (from March 31 to May 11, 2020) in a UK adult population (n=3,077) revealed increased rates of suicidal ideation during the initial weeks of the pandemic-related lockdown, particularly among young adults (55). On the other hand, a Spanish longitudinal study aiming at examining the suicidal ideation prevalence among 1,103 adults after the pandemic-related lockdown measures were lifted in Spain (May 21, 2020 to June 30, 2020) compared to the pre-lockdown period (June 17, 2019 to March 14, 2020) found no differences regarding the suicidal ideation rates (54).

As regards suicidal ideation during the pandemic, a longitudinal study from Greece in a community sample of 811 adults, investigated suicidal ideation rates during the first (April 7

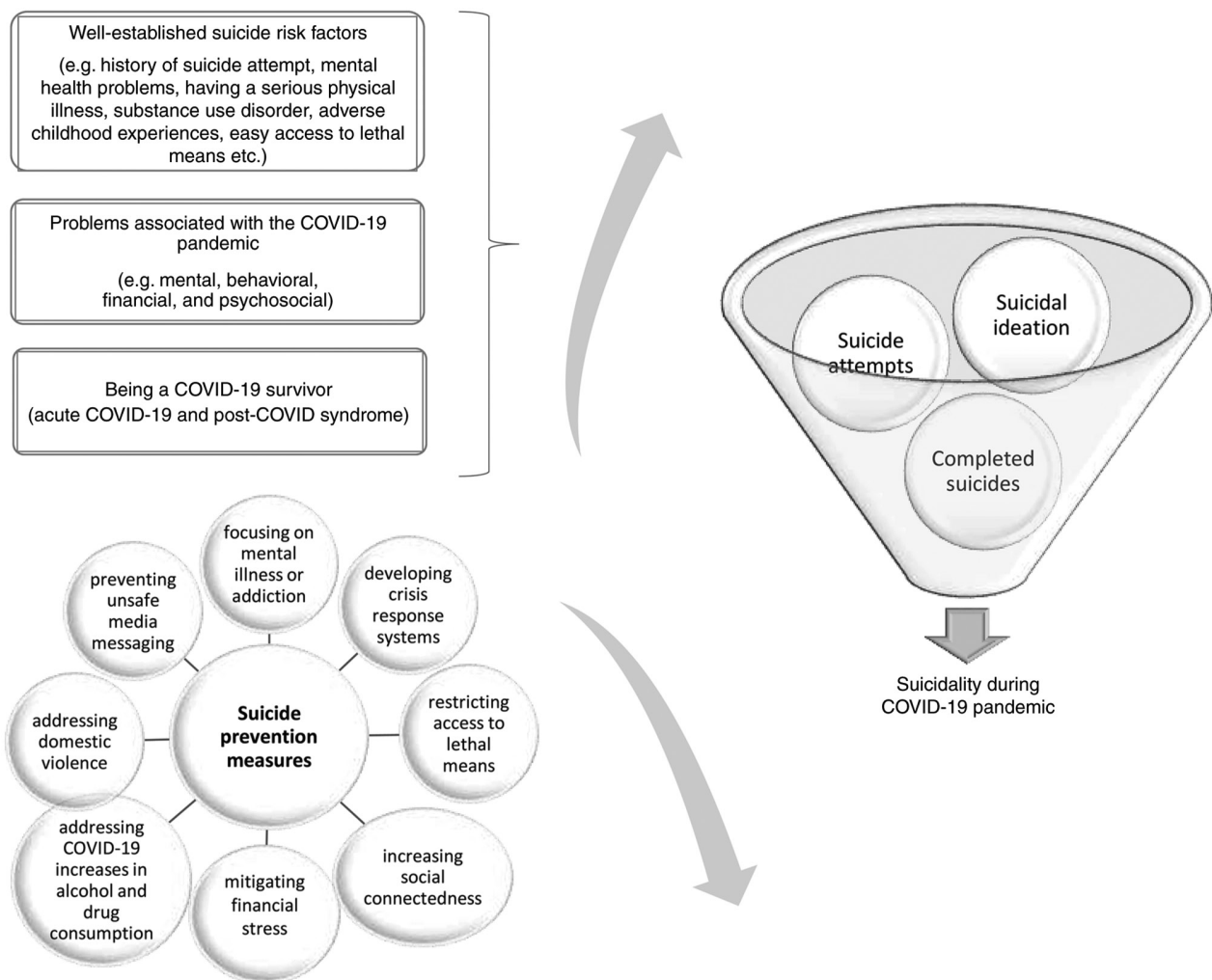


Figure 1. Risk factors for suicidality during COVID-19 pandemic and suicide prevention strategies.

to May 3, 2020) as compared to the second (November 22 to December 21, 2020) pandemic-related national lockdown, and found no differences between the two time periods; depression emerged as the only significant prognostic factor for suicidal ideation incidence (i.e., among individuals who experienced suicidal thoughts during the second, but not the first lockdown) (50). Nevertheless, Veldhuis *et al* (56), using a global longitudinal convenience sample (n=1,567), surveyed both in April and September, 2020, reported a significant increase over time in suicidal thoughts and behaviors from baseline levels [mean (M)=2.6; standard error (SE)=0.72] to the 5-month follow-up (M=4.89; SE=0.91; P<0.05).

In another study, temporal trends in primary care-recorded self-harm monthly counts (from January, 2019 to May, 2021) were examined using a time series analysis of electronic healthcare records for 2.8 million patients in the North West of England (Greater Manchester conurbation). According to the results of that study, an initial marked reduction in overall self-harm was identified in April, 2020, while a sustained decrease was also observed to the end of May, 2021. The greatest overall reductions were observed during the first national lockdown, while longer-term reductions were largest among males and individuals residing in the most deprived areas; however, an increase emerged in

the reports of self-harm among adolescents (10-17 years of age) (57).

A time-trend study in Denmark using health records from hospitals and emergency medical services (covering 46% of the Danish population), compared the number of psychiatric in-patients, referrals to mental health services and suicidal behavior in the years prior to the COVID-19 pandemic to levels during the first lockdown (March 11 to May 17, 2020), the inter-lockdown period (May 18 to December 15, 2020) and the second lockdown (December 16, 2020 to February 28, 2021). The study did not identify any significant differences with respect to suicidal behavior or referral rates. However, during the pandemic, the rates of psychiatric in-patients decreased compared with the pre-pandemic levels, with the largest decrease being recorded during the first lockdown (58).

Accordingly, a retrospective cross-sectional study in a large, integrated, community-based health system in the USA, on suicide-related encounters in the emergency department demonstrated that the overall rates within 2020 did not increase, and at times the rates decreased, in comparison to those in 2019; however, an increase was observed in 2020 for patients with a substance use disorders (59).

Of note, apart from the psychosocial aspects of suicidality amidst the COVID-19 pandemic, SARS-CoV-2 infection

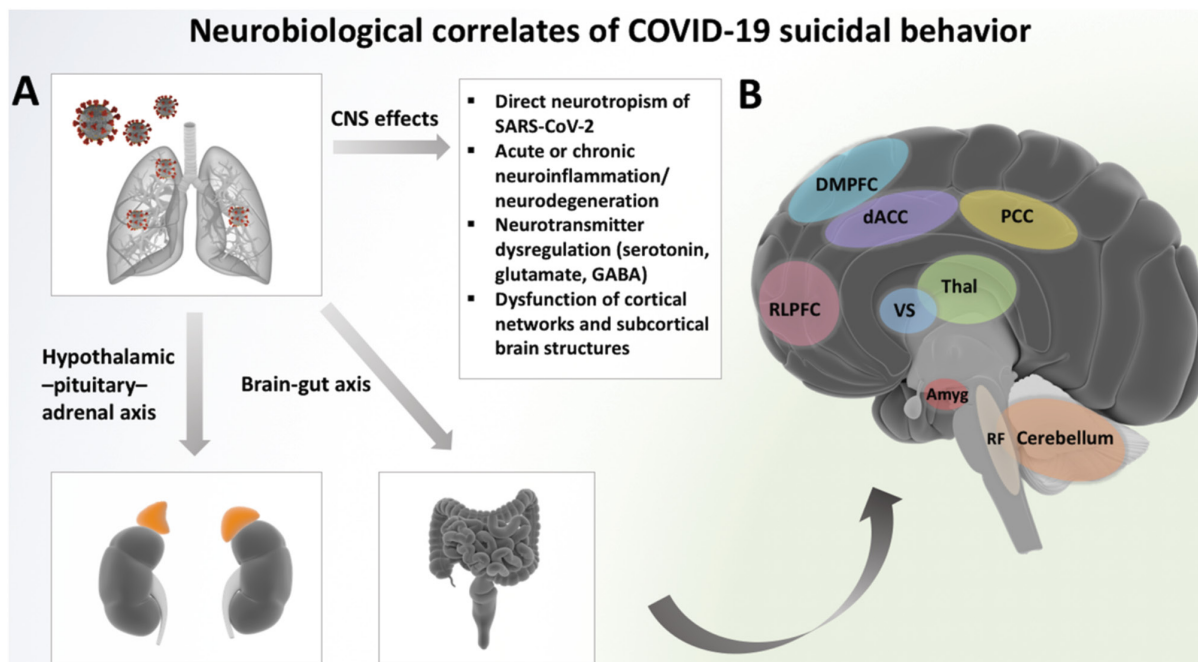


Figure 2. Neurobiological correlates of COVID-19 suicidal behavior. (A) SARS-CoV-2 infection induces distinctive effects in the CNS, which are mediated by the retrograde axonal transport of the virus in the CNS in acute COVID-19, or immune responses, including the cytokine ‘storm’, that precipitate acute or chronic neuroinflammatory and neurodegenerative cascades. Additionally, SARS-CoV-2 may cause the dysregulation of neurotransmitters (i.e., serotonin, glutamate, GABA) and the dysfunction of large cortical networks and subcortical brain structures, which may be linked to an increased risk of suicidality in patients with COVID-19. Further pathways possibly involved in COVID-19-related suicidal behavior involve the hypothalamic-pituitary-adrenal axis. In COVID-19, stress responses and cortisol hypersecretion have been shown to upregulate the hypothalamus-pituitary-adrenal axis (adrenal glands are depicted in orange), while further suggested mechanisms that may contribute to emergence or exacerbation of suicidal behavior involve dysregulation of the gut microbiota and the brain-gut axis. (B) All the aforementioned mechanisms may induce dysfunction in several brain regions, which have been implicated in the pathophysiology of suicidal behavior, and are mainly located in the ventral and dorsal prefrontal cortex, insula, mesial temporal, subcortical and posterior regions. Notably, neuroimaging and histopathological evidence of COVID-19-related suicidality is currently unavailable; thus, the depicted brain regions have been linked with suicidal behavior in previous neuroimaging studies in non-COVID-19 patients with suicidal ideation or behavior. Further brain structures implicated in suicidality include the DMPFC, the hippocampus and the basal ganglia (not shown). Notably, as previously demonstrated, autopsies of patients with COVID-19 have indicated neuronal loss and hypoxic changes in some of the aforementioned brain regions (64). CNS, central nervous system; GABA, glutamate and gamma-aminobutyric acid; RLPFC, rostral/lateral prefrontal cortex; DMPFC, dorsomedial prefrontal cortex; dACC, dorsal anterior cingulate cortex; PCC, posterior cingulate cortex; Thal, thalamus; VS, ventral striatum; Amyg, amygdala; RF, reticular formation.

per se may confer an increased risk of suicidal ideation and behaviors. Although the pathophysiological underpinnings of COVID-19 associated suicidality remain to date poorly elucidated, putative mechanisms have been proposed that may increase suicidal vulnerability and the overall risk of suicidal acts in infected patients (60). Accordingly, several mechanisms may be implicated in infection-associated brain damage as follows: The direct neurotropic effects of SARS-CoV-2 mediated by the retrograde axonal transport of the virus from the respiratory mucosa, hypoxic brain injury, peripheral inflammation and monocyte-macrophage system activation that precipitate neuronal dysfunction, and the disruption of the blood-brain barrier that induces a prolonged state of neuroinflammation and possibly neurodegeneration (60–64). The SARS-CoV-2-induced cytokine ‘storm’ has been shown to play a major role in the propagation of neuropsychiatric symptoms associated with COVID-19, while aberrations in inflammatory cytokines have been proposed as pathophysiological correlates of suicidality (22,63,65,66). In addition, neurotransmitter imbalances, including GABAergic, glutamatergic and serotonergic pathways, as well as widespread neuronal network dysfunction, have been suggested to provide neurobiological links to COVID-19 suicidality. Moreover, COVID-19 related sleep disturbances, neuroendocrine changes, including

cortisol hypersecretion and the dysregulation of the hypothalamus-pituitary-adrenal axis, as well as the dysregulation of the gut microbiota and the brain-gut axis may all contribute to the emergence or exacerbation of suicidal behaviors in patients with COVID-19 (Fig. 2) (22,67–69). Nevertheless, SARS-CoV-2-induced neurobiological changes that precipitate suicidality are possibly intertwined with superimposed psychological stressors associated with COVID-19. Thus, further research is warranted to provide neuroimaging and histopathological data from patients with COVID-19 with suicidal tendencies or behaviors.

Completed suicides amidst the COVID-19 pandemic. From the onset of the COVID-19 pandemic, several mental health experts have expressed concerns regarding a possible increase in the rates of suicide and have even warned of a ‘suicide epidemic triggered by COVID-19’, a ‘dual pandemic of suicide and COVID-19’, or a ‘suicide mortality and COVID-19-a perfect storm’ (43,70–72).

Worldwide, cases of individuals who died through suicide have been reported, mainly in the media, linking their deaths to the fear of COVID-19 infection, fear of transmitting SARS-CoV-2 to others, anxiety over COVID-19, fear of isolation due to imposed country pandemic-related lockdown and

a lack of knowledge. Further triggers that have been identified for suicides related to the COVID-19 pandemic are xenophobia, COVID-19-related stigma and social boycott, financial insecurities and uncertainty concerning the future (73,74). In previous a review article on suicide reports, possible factors and predictors of COVID-19-related suicide were categorized according to 'social isolation and distancing', 'worldwide lockdown creating economic recession', 'stress, anxiety and pressure in medical healthcare professionals' and 'social boycott and discrimination' (73).

Pirkis *et al* (75) investigated suicidal trends in the early months of the COVID-19 pandemic (from April 1 to July 31, 2020) by using an interrupted time-series analysis of preliminary data from 21 countries, including national data from 10 countries and data from 25 regions across a further 11 countries. Specifically, real-time data were acquired on suicides for Australia, Austria, Canada, Chile, Croatia, United Kingdom (England), Estonia, Germany, Italy, Japan, Netherlands, New Zealand, Poland, South Korea, Spain, USA, Brazil, Ecuador, Mexico, Peru and Russia. Their study demonstrated that suicide rates remained unaltered or declined in the early months of the pandemic compared with the expected levels based on the pre-pandemic period, in high-income and upper-middle-income countries (75).

Furthermore, other studies using official data and taking into consideration the effect of temporal trends, have also reported no increase in suicide rates during the early months of the pandemic. In particular, studies from Greece, Australia (Queensland) and the USA (Massachusetts) have demonstrated stability in suicide rates, whereas a study from Peru reported a decline in suicides following the implementation of a pandemic-related lockdown (76-79). Another study from Japan demonstrated fluctuations in suicide rates and highlighted their association with pandemic-induced employment shocks (80).

The absence of an increase in suicide figures, at least during the early months of the pandemic, can be connected to a range of factors. From the beginning of the pandemic, its profound mental health consequences were highlighted. This may have led to governments responding rapidly in order to strengthen existing mental health services, while developing telemedicine services, as well as to enact fiscal support initiatives with the aim of moderating the economic repercussions of pandemic-related lockdowns. Furthermore, for some individuals, the stay-at-home period may have offered them the opportunity to avoid everyday life stresses, while the collective feeling of all individuals facing a pandemic may have been beneficial and helped them feel connected and supported (75,81). Nevertheless, there is evidence to indicate that while suicide rates remain stable or decline during times of acute crises, delayed increases may appear in the period that follows. Indeed, a lag effect of exposure to distressing situations on suicide rates has been previously observed for major world events, such as World War I, World War II and other natural disasters; therefore, a timely implementation of effective prevention strategies is required (81-83).

There is research evidence to support this pattern of an increase in suicides. Following an initial reduction in Japan, where monthly suicide rates decreased by 14% early stages of the pandemic (February to June, 2020), a subsequent increase

in these rates was observed during the second wave (July to October, 2020) by 16%, with a larger increase among females, children and adolescents (84). In addition, while a first report on the short-term effects of the COVID-19 pandemic on suicides, including data from Mexico City, had suggested no increase in the respective rates following the declaration of a national emergency, a second report, following the initial analysis and employing an interrupted time-series analysis indicated that the number of monthly suicides increased during the first 8 months of the pandemic; however, most of the increase occurred beyond June, 2020, and concerned males regardless of their age (85).

Moreover, it is worth noting, that each suicide may affect 5-80 individuals, including nuclear family members, relatives, friends and acquaintances, which are known as 'suicide survivors'. Suicide survivors face an increased risk of prolonged or persistent complex bereavement (with rates reaching up to 40%), depression, anxiety and substance-abuse disorders, as well as suicidal behaviors, while social stigma and feelings of shame may discourage them from seeking mental health-related assistance (74,86). The suicide of a 'significant other' amidst the COVID-19 pandemic is even more challenging for suicide survivors, who are already struggling to adjust to new conditions and are likely experiencing psychological difficulties. Feelings of confusion, doubt, non-acceptance, hopelessness, helplessness and stigmatization may emerge, while the fact that death and grief rituals, that would facilitate adjustment to bereavement and a healthy adaptation to the loss, have either been suspended or modified due to pandemic-related regulations, rendering it even harder for suicide survivors to mourn their loved ones and 'say their goodbyes' (74,87).

Suicide prevention during the COVID-19 pandemic is a global priority and requires addressing not only pandemic-specific suicide risk factors, but also pre-pandemic ones. Interventions proposed to significantly mitigate the negative impact of the pandemic on the risk of increased suicidal behaviors include focusing on the needs of individuals with mental illness or addiction, increasing social connectedness, developing robust, accessible and culturally inclusive crisis response systems, restricting access to lethal means, addressing COVID-19-related increases in alcohol consumption and drug overdoses, mitigating financial stress, addressing domestic violence issues and preventing unsafe media and entertainment messaging (Fig. 1) (40).

3. Conclusion

The present review has illustrated the impact of the various aspects related to the COVID-19 pandemic on suicidal behaviors, while presenting a comprehensive overview of epidemiological data, as well as evidence on pathophysiological mechanisms implicated in suicidal ideation and behaviors in patients infected with SARS-CoV-2. Improving the current understanding of risk factors that contribute to suicidality is important as it may help mental health professionals in identifying patients at high risk, and can eventually facilitate the development of targeted interventions and prevention strategies.

Despite the initial alarming predictions and warnings regarding an 'epidemic' of suicides due to COVID-19, the

majority of studies presented in the present review article suggest that difficulties and experienced distress related to the pandemic do not inevitably translate into increased suicide-related deaths, at least not in the short-term. However, it should be pointed out that, even if suicide figures have remained at mostly stable levels, they represent '*real lives lost, real families devastated*' (88). Moreover, the long-term mental health effects of the COVID-19 pandemic have yet to be unfolded and are likely to remain for a long period of time or even appear after the actual pandemic. Thus, long-term data are urgently required to reflect the possible long-term repercussions or late-effects of the pandemic. The limitations of the present review thus include the scarcity of available data on long-term outcomes of patients who recovered from acute COVID-19, but continue to suffer from major psychological effects of the pandemic. Future research is urgently required to enable the characterization of risk factors and the early identification of predictors of suicidal behavior during the ongoing pandemic of COVID-19.

Suicide prevention and measures in order to promote mental health and well-being, as well as to mitigate COVID-19 psychological consequences, particularly among vulnerable groups and populations at a higher risk, should be a priority for health care professionals and policymakers.

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Ethics approval and consent to participate

Not applicable.

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Not applicable.

Competing interests

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