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Editorial

Società Italiana di Psichiatria

Editorial

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Massimo di Giannantonio

Enrico Zanalda

This volume is entirely devoted to an in-depth examination of aspects of the COVID-19 pandemic in psychiatry. It deals with psychopathology, suicide, Post Traumatic Stress Disorder, Delirium, the field of addiction, child neuropsychiatry and psychogeriatrics. I would like to remind you that the 2021 national congress will be held in virtual mode from 23 to 25 November and will deal with the changes brought about by the COVID-19 pandemic in psychiatry.

At the same time, thanks to the widespread use of the vaccine in Italy, we are returning to normal and have finally been able to schedule our 49th congress in Genoa. This congress, which should have been held in October 2020, is now scheduled for May 2022, so we are confident that we will be able to meet as many members as possible, given that we will be able to use the congress facilities in full by then. The desire to be able to meet in safety and in the presence of members can finally be realised in a city like Genoa, which has shown that if a bridge is quickly rebuilt, the country and of course our society can quickly restart.

We are going through a complicated period because of the difficulty in finding psychiatrists in the Mental Health Departments. On the one hand, there is an increase in both ordinary and complex requests for the ever-increasing number of patients who have committed crimes, while at the same time it is difficult to find staff willing to be employed in mental health departments. The COVID pandemic has further highlighted the criticality of community services, which require significant economic and cultural investments. Our scientific society has contributed to bringing together the directors of the Italian Mental Health Departments and with them has prepared a draft “Progetto Obiettivo Tutela della Salute Mentale” for the period 2021-2130. The Department of Mental Health must be an inclusive, technologically advanced, non-rigid organisation capable of attracting also young people in order to prevent mental illness as much as possible. The inclusion of addiction services and child neuropsychiatry in the Departments of Mental Health makes it possible to better manage young people in the 16-28 age group, when psychotic disorders are more likely to occur and must be intercepted at an early stage if they are to be treated successfully. In addition to this situation, it should be remembered that COVID-19 has led to an increase of about a third in depressive and anxious disorders, with the need to involve psychology services and General Practitioners in order to intervene early when therapy is most effective.

In the next few years there will be the economic investments of the Recovery Plan and it will be crucial for mental health to be adequately considered. For example, it has been shown that some SPDCs can no longer physiologically contain any patients. This is possible, however, if there are adequate spaces and wards with a large number of staff who are well trained in emotional reduction techniques. Even the opening hours of the community services will only become more flexible if there are more staff working there. Personally, I believe that for a mental health centre, 8 hours every weekday is a timetable that allows to visit a sufficient number of patients and to collaborate as a team,

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because it does not oblige to work in shifts. This organisation provides for the 24-hour presence of an emergency service at the Emergency and Acceptance Department, which also has the Psychiatric Diagnosis and Treatment Service (SPDC).

The recent increase in the number of psychiatric trainees should overcome the current difficulty in finding psychiatrists in mental health services over the next three years.

Our scientific society is made up of both professions and can help formulate hypotheses for integration between the Ministry of Health and the Ministry of Scientific Research and Universities in the field of mental health. Greater integration in the training of Mental Health Departments and greater use of advanced technologies such as tele-psychiatry are possible solutions to the current operational difficulties of the services.

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Original article

Società Italiana di Psichiatria

COVID-19 and psychopathology: the impact of the pandemic on suicide

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Summary

Background. COVID-19 pandemic led to a radical change in habits and interpersonal relationships that, together with a sense of uncertainty for future and the economic crisis, had a noticeable impact on mental health, with an increase in cases of anxiety, depression, substance abuse. As in previous outbreaks in history one of the most important risks is the possible increase in suicidal behaviors.

Current data. An initial assessment of suicide rates showed different trends in countries all over the world, with a majority of them reporting a decrease in the first phase of the lockdown, followed by an increase. Biological and psychosocial factors affect different levels of risk and particular populations like health workers, elderly and young people, psychiatric patients and abuse victims seem to be most vulnerable.

Prevention strategies. Identifying risk factors is essential to implement preventive strategies, enhancing mental health services and creating new specific measures like COVID-19 help-lines and telemedicine, to ensure continuity of care for patients.

Discussion. Authors of various countries reported a general decrease in suicidal behaviors in the first period of the pandemic emergency, followed by a tendency for them to rise again in the period immediately afterwards. A similar trend has been reported after other catastrophic events and an explanation can be find in the so called "honeymoon period". It is crucial to analize suicide rates of the other stages of the pandemic, still in progress.

Introduction

The COVID-19 pandemic represents a global health emergency that will leave a permanent mark on each of us, with millions of people affected and hundreds of thousands of deaths around the world. Since December 2019 up to now, every country has been facing an unprecedented health crisis that has which made it necessary to take various measures aimed at the containment of the contagion. These measures, such as social distancing, general lockdown, restriction of movement, closure of various businesses, led to a radical change in interpersonal relationships and the way each individual relates to society; these changes, together with the pervasive sense of uncertainty for the future and the economic crisis correlated with the pandemics, had a noticeable impact on the mental health of the population, with an increase in the levels of anxiety, depression, insomnia and substance abuse, as highlighted in some studies [1]. The rise in psychological discomfort and a lack of prevention program could determine an increase in suicidal behaviors in the general population, as already highlighted in previous outbreaks throughout history [2,3] or in other economic crises [4] and as shown

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by some preliminary data in relation to the COVID-19 pandemic [5].

In this article we will try to examine the complexity of suicidal behavior during the pandemic, providing the epidemiological data currently available in the literature, as well as some hypotheses concerning the genesis of this phenomenon and which categories end up being most at risk of developing self-injurious behaviors. Finally, the prevention strategies adopted by different countries to promote mental health and limit the increment of suicidal behaviors will be analyzed.

Comparison with the former world disasters

All major world disasters in history have caused profound cultural, economic, and psychosocial changes: the latter determines the increase in frequency and severity of risk factors for the occurrence of mental disorders and, in particular, suicidal ideation and behavior.

Public health emergencies related to infectious disease outbreaks on a global scale may play a crucial role in this matter, with an impact greater than that of the World Wars [3]. Zortea et al. [6] authored a systematic review collecting the existing evidence on the impact of epidemics occurred between 1889 and 2016 on suicidality, including completed suicides, suicide attempts, suicidal ideation, and self-injurious acts. Regarding suicide-related deaths, it was possible to observe an upsurge during the 2003 SARS outbreak in Hong Kong, with a higher significance for the female gender and a steadily high rate for about one year after the end of the epidemic. Two further studies analyzed focused on the Great Influenza Pandemic of 1910-1920 in America and on the Russian Influenza and its impact on the British population in the period between 1889 and 1893: these cases also showed increased suicide rates compared to the same period in previous years and reasonably correlated with epidemic-related risk factors. Suicide attempts appeared elevated as well, and correlated with the consequences of the SARS, Ebola, and Influenza B outbreaks [6]. Among the numerous studies on SARS and suicide, Tzeng et al. described a group of patients affected by SARS who were at higher risk for developing anxiety, depression, sleep disturbances, PTSD, and suicidal behaviors compared to the control group at a 12-year follow-up [7]. In their review of major respiratory epidemics and suicide risk, Kahil et al. highlight how SARS led to an increase in psychiatric disorders and suicide rates in affected populations, although a reliable association between these two factors appears difficult given the large inhomogeneity of the analyzed studies [8]. Devitt, in his historical paper, after reviewing the data regarding suicides correlated with the greatest disasters in human history, such as World War II, the terrorist attack on the Twin Towers on September 11, 2001, and in London on 7, July 2005, Hurricane Katrina, SARS, and some major economic depressions, concludes that these have been the main causes of the rise in suicide rates over the centuries, proving that protection from recession could also be useful during the pandemic we are currently going through [9].

Comparison with past disasters can lead to the identification of risk and protective factors given by the ongoing pandemic, but it is true that each situation has its own peculiarities, also due to the historical period and current necessities.

Data on suicidal behavior related to the current pandemic

The SARS-CoV-2 pandemic has shown different trends in suicidal behavior in the various countries hit by the virus, and it is now possible to make an initial assessment, bearing in mind that much will remain to be judged in the months and years following the end of the pandemic itself. In Japan, suicide risk was evaluated at different times during the pandemic, showing an initial decrease in the number of suicides of about 20% compared to the same period of the previous year (April), followed by an increase in July, August, and September, with the female gender being the most affected [10,11]. Another Japanese study shows that in the first five months of the pandemic (February to June), the rate was 14% lower than in previous years, attributed to the generous subsidy from the government, the lower burden given by a reduction in working hours and closure of schools, followed by a 16% increase from July to October, which was higher in females (37%) and in children and adolescents (49%) [12]. This trend, displaying an initial decline in the suicide rate in the first phase of the pandemic and switching to an increase during the second phase, fits the “honeymoon” theory; this is characterized by a “protective” period based on the development of a sense of belonging and social cohesion, as well as government-provided assistance, followed by a period of great economic difficulty and psychosocial suffering. These problems, together with the risk factors directly linked to the virus (fear of becoming infected, losing loved ones, etc.), tend to lead to a higher number of suicides in the second phase. This tendency has also been highlighted subsequently to other disasters, such as Hurricane Katrina and the September 11, 2001 terrorist attack [12], and, during the current COVID-19 pandemic, early stage studies conducted in several other countries did show lower rates of suicidality compared to earlier years. In Ireland, fewer hospital admissions due to self-harm are observed in the first period (March-April 2020), which grow exponentially, peaking in mid-May [13]. In Norway, Qin et al. showed a reduction in the number of suicides in the period March-May 2020 compared to the same period in the previous five years, which was attributed to an increase in social cohesion and financial and psychosocial preventive measures implemented by the government [14]; the trend revealed in Austria displayed as well a decrease in the number of suicides between April and September with respect to the same months

from 2006 to 2019 [15], and the same phenomenon was detected in the city of Leipzig, Germany, where a decline in the suicide rate coincided with the enforcement of more restrictive measures [16]. In Paris, a retrospective study examined how admissions due to suicidal behavior among children and adolescents decreased during the lockdown compared to the previous two years, likely due to a reduced tendency to seek help by going to hospitals during the pandemic, but also due to the adoption of coping mechanisms and feelings of belonging and social cohesion [17]; the same result was obtained in Spain, where fewer accesses were found for both suicidal ideation and suicide attempts, in a context of a decrease in accesses for all psychiatric causes in general, probably due to fear of contagion and the presence of restrictive measures [18].
On the contrary, in some countries, an increase in the number of suicides or suicidal behavior in general was highlighted even in the earliest stages of the pandemic. In China, one of the countries most affected by the COVID-19 outbreak in the early stages, an increase in suicidal ideation and attempts has been noted among students in rural areas of the country [19] and among the elderly [20]. In India, Pathare et al. showed an increase in suicide cases reported in the media between March and May 2020 compared to the same period in 2019, but it is unclear whether this is due to a higher focus of the media on suicides during the pandemic [21]; Singh, during a September 2020 commentary, identifies three 'waves of suicides' in India: the first during the period of the first lockdown in March-May, the second during the reintroduction of quarantine at the end of May, and the last at the end of the lockdown due to the economic impact; these would have affected people of different ages, social backgrounds and geographical locations [5]. In the UK, one of the surveys carried out between March and April 2020 confirms the suicide rate generally found in the most vulnerable populations (women, ethnic minorities), with the addition of some new cases deriving from economic problems, the presence of previous psychiatric or chronic illnesses and SARS-CoV-2 infection diagnosis [22], while O'Connor et al. warn of a significant increment in suicidal ideation among young adults in the same period [23].
Many studies were conducted in the United States to identify trends in suicide rates during the pandemic, some of which ending with conflicting results. One of the first surveys (March-April 2020) highlighted how suicidal ideation was more frequent in people with risk factors such as legal problems, conflict with a partner, particular concern about becoming ill, but decreased among people with economic difficulties, as often seen at the beginning of a financial crisis [24]. Ammerman et al. found that 45% of individuals with suicidal ideation early in the epidemic associated it with pandemic-related risk factors, and 9% of the population reported intentional suicidal exposure to the virus [25]. In the state of Texas, visits to a pediatric emergency department were evaluated and it was found that visits related to suicidal ideation or attempts increased significantly during the months when the restrictive measures implemented by the government caused the most stress in the population [26], while in California, the number of calls received by the main Poison Control Center for attempted suicides due to drug use in the first months of the pandemic decreased significantly compared to the same period in the previous two years [27]. In Connecticut, suicide mortality was 13% lower during the lockdown period than during the same months in the former five years, involving nevertheless a relative increase in suicides among racial minorities, suggesting greater social and economic impacts of the pandemic on these populations [28]. A study conducted by a group in New York evaluated the trends of words searched by Americans on Google during the early stages of the outbreak encountering fewer terms that were closely correlated with suicide, but more terms that were related to risk factors for suicide during the pandemic, such as "I lost my job", "unemployment" or "layoff" [29]. The same type of study was conducted in Canada in March, with results showing a reduction in searches for words related to anxiety, suicide and hopelessness, while searches for words associated with survival, hope, resilience, but also sadness, were more numerous [30]. On the other hand, in South America, particularly in Colombia, a survey of 700 people aged between 18 and 76 years showed that 7.6% of the sample had a high risk of suicide, which was related to other depressive symptoms and pandemic-related stressors [31].
Finally, some countries exhibited unchanged rates from previous years; this is the case of Greece [32] or Australia, Queensland, where suicide mortality rates obtained from police reports were unchanged in February-August 2020 compared to 2015 to 2019, but a proportion (n = 36) of suicides committed in 2020 were significantly associated with COVID-related risk factors [33].

Risk factors and most affected populations

Suicidal ideation and suicidal behavior are conditions whose genesis is known to be multifactorial. In the context of the COVID-19 pandemic, there are many causes that may lead to an increase in suicidal behavior, in the short term and in the future. In fact, many different mechanisms come into play in the correlation between the epidemic and the risk of suicide, starting from the biological ones, which depend on the changes caused by the virus or the therapies implemented, to the psychosocial ones, which are related to the restrictions imposed by the pandemic on daily life, to the no less important aspect of the "pre-pandemic" personality of the subject, which can determine, in a certain way, a predisposition to suicide risk in this context. It is therefore important to bear in mind that the increased risk of suicide simultaneously affects not only those directly affected by COVID-19, but also those who have experienced this pandemic indirectly.

Suicidality in COVID+ patients: neuroinflammation and possible side effects of the pharmacological treatment

It is known in the literature that exposure to infectious diseases can cause an increased risk of committing self-harming acts [34].
The underlying causes may be several: the infection and the inflammatory changes themselves might increase the risk of suicidal behavior through neuroinflammation-related processes [35]; the modification of the microbiota, due to the use of antibiotics and antivirals and their influence on the central nervous system, could also be involved [36] or again, the idea of having to fight, for example, an invisible enemy may represent an enormous distress for patients, increasing the risk of anti-conservative ideation.
Data from other respiratory viral infections identify certain clinical phenotypes at risk of suicide. A strong association was found between mood disorders and the presence of antibodies directed against influenza A and B viruses and a strain of coronavirus (HCov-NL63) compared to the control group; in addition, influenza B seropositivity appeared to be significantly associated with a history of anticonservative attempts [37].
Regarding the COVID-19 pandemic, recent evidence in the literature suggests the existence of a possible medium-term neuropsychiatric impairment of patients who contract this virus [38]. A strong association between coronavirus seropositivity and the onset of psychotic symptoms has also been reported (OR = 3.10, CI = 1.27-7.58) [39]. Several mechanisms are likely to participate to the brain involvement secondary to infection: retrograde axonal transport from the respiratory mucosa, peripheral inflammation modulating brain function [40], migration of mononuclear cells carrying the virus across the blood-brain barrier [38].
Recent data in the literature have shown that SARS-CoV-2 is able to enter cells through binding to the ACE-2 (angiotensin-2-converting enzyme) receptor, a central enzyme in the Renin-Angiotensin-Aldosterone system (RAAS), and that alterations in this system are implicated in SARS-CoV-2-induced lung disease and acute respiratory distress syndrome [41].
Previous research has also established that alterations in the RAA system may increase suicide risk, including those secondary to the use of angiotensin receptor blockers [42].
In addition, it appears that certain gene polymorphisms of the ACE enzyme (such as D/D) are associated with an increased risk of suicidal ideation and acts [43]. This preliminary evidence suggests that there is a link between the RAA system and suicidal ideation and, considering the role of this system in the pathogenesis of SARS-CoV-2 infection, further studies are needed to test a possible hypothesis linking the RAA system, SARS-CoV-2 infection and suicidal ideation.
COVID-19 infection appears to be characterized by moderate to severe cytokine storms, caused by an overall dysregulation of the immune system, which seem to be responsible for the death of many patients with this disease. In particular, Interleukin-6 (IL-6) seems to play a key role in the so-called Cytokine Release Syndrome (CRS) and it has been hypothesized that blocking the cascade that leads to increased levels of this cytokine may somehow treat the more severe forms of COVID-19. This is the basic rationale for using monoclonal antibodies, such as Tocilizumab, to treat the cytokine storm induced by COVID-19 in the most severe forms [44]. Interestingly, high levels of IL-6 in the CSF have been associated with impulsive behavior and an increased risk of suicide attempts [44,45]. In the context of COVID-19 disease, increased IL-6 levels may therefore be somewhat related to increased suicide risk.
The evidence currently available thus points to the presence of a psychoneuroimmune alteration in the brain in COVID-19 patients, which may be relevant in determining the psychiatric symptoms of these patients, particularly with regard to the increased suicide risk. The extent to which biological aspects are relevant in determining suicidal behaviour in these patients is currently not known, so further studies correlating disease severity, blood markers of neuroimmunity, and suicide risk are needed to better understand the direct or indirect effect of these elements on suicide risk [46].
The pharmacotherapy currently available for the treatment of COVID-19 is mainly based on the use of antivirals and antibiotics (e.g. Azithromycin, Remdesivir, lopinavir/ritonavir) monoclonal antibodies (tocilizumab), antimalarials (chloroquine, hydroxychloroquine). Numerous studies have been carried out on the possible side effects of currently used treatments, some of which have highlighted possible psychiatric symptoms as collaterals to treatments, particularly with hydroxychloroquine [47]. Even before the COVID-19 pandemic, studies had shown an increased suicide risk in patients with Rheumatoid Arthritis, Malaria or Systemic Lupus Erythematosus treated with Hydroxychloroquine [48,49].
The increased suicidal risk with hydroxychloroquine seems to be secondary to a higher incidence of mood disorders in patients treated with this drug; several pharmacodynamic mechanisms have been hypothesized, such as a dysfunction of serotonergic neurotransmission induced using hydroxychloroquine [50].
A recent pharmacovigilance study showed that in patients with COVID-19 there was an increased incidence of psychiatric manifestations, with increased suicidal behavior and suicidal ideation, in those treated with hydroxychloroquine compared to other available treatments [47]. Although this is an interesting finding, further investigation is needed considering the critical aspects of this study (lack of stratification of patients by severity of illness, absence of assessment of pre-morbid personality and any pre-existing psychiatric disorders).

Psychosocial hypothesis

The COVID-19 pandemic profoundly and dramatically revolutionized the lives of people around the world,

changing habits and customs. Measures that have been taken to control the spread of the virus, such as social distancing, lockdowns, closing businesses, restaurants, and recreational activities, have proven effective in controlling the spread of the virus in individual countries [51]. However, these measures, combined with the impact the pandemic has had on the economy, with a dramatic crisis affecting multiple countries and significantly reducing jobs, have led to a significant raise in psychosocial stress in the general population.

Anxiety, fear of infection, social isolation, uncertainty about the future, and chronic stress linked to rapid changes in infection rates are common feelings that have affected much of the population during this pandemic period, as is now evident in the literature [1].

Such elements may cause an increase in suicidal ideation and anti-conservative acts, as demonstrated in previous epidemics, such as Spanish flu [3], SARS [2] or Ebola [52].

Starting from the measures taken to limit contagions, several theories on psychosocial models of suicide (e.g. Durkheneim's theory, Joiner's interpersonal theory) link the feeling of not belonging to a social group, the feeling of being 'excluded' from society or the presence of extremely rigid rules limiting individual freedoms, to an increased risk of suicidal ideation [53,54].

All this fits perfectly into the reality of the COVID-19 pandemic, where the distancing rules, quarantine, travel restrictions, the deconstruction of normally known social customs and rituals, may have increased feelings of hopelessness, loneliness, low hope and uncertainty for the future, as well as suicidal thoughts and self-harming behaviors experienced as an escape route from a reality perceived as inadequate and frustrating.

In this context, economic uncertainty linked to the crisis in financial systems secondary to the pandemic may be an additional factor in increasing suicide risks. The regulations undertaken to contain the pandemic have led to the closure of many businesses and a major increase in unemployment rates worldwide.

These elements are known to be correlated with an increase in suicide risk, as shown by previous studies that have analyzed the impact of economic crises on mental health and suicide risk [4,55]. In particular, some studies have observed that high rates of unemployment are associated with a higher prevalence of major depression, alcohol and substance use disorder and deaths by suicide [4], with the risk of self-harming behavior being up to 20-30% higher in the unemployed than in the employed [56].

The loss of employment, economic security and uncertainty about the future could therefore be important determinants of increased suicide risk, not only in the short term, but also in the long term when the health emergency is over.

In the context of the psychosocial impact of the COVID-19 pandemic on the increase in suicide risk, one should not forget the so-called "infodemic", a true epidemic of information, often "fake news", that abound on the web and on television. If, on the one hand, social networks and television programs can represent a way to reduce the sense of 'marginalization' and discouragement deriving from social isolation, on the other hand, it is necessary to prevent 'fake-news' and misinformation from spreading, leading to a potential increase in the risk of developing mental problems in categories potentially at risk. In this context, the continuous reporting of negative news about the pandemic increases people's anxiety levels and feelings of hopelessness, both of which may increase suicidal behavior [57].

In addition, receiving continuous news about pandemic-related suicides may increase the risk of suicide by emulation, especially when the methods used to commit the self-harming act are described in detail [58].

The previously analysed determinants of increased suicide risk, such as fear of contagion, social isolation, feelings of uncertainty and hopelessness, economic uncertainty, anxiety and chronic stress secondary to the pandemic, should be placed in the context of the individual's premorbid personality. There are, in fact, some categories of individuals who are more vulnerable and at risk of developing psychiatric problems and suicidal ideation under conditions of particular stress, such as during a pandemic. Subjects with a personality structure characterised by low levels of resilience, for example, have a higher risk of developing suicidal behaviour [57].

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In addition, a recent study on family members of patients infected with COVID-19 demonstrated that lower psychological flexibility (reduced adaptability, perception of living on the margins of society) is correlated with an increased risk of developing suicidal ideation [59].

With regard to patients who have developed COVID-19, there is growing evidence in the literature of a higher risk of suicidal behavior than in the general population, especially for those who have developed more severe forms [60]. Stressful experiences such as being diagnosed with COVID-19, fear of infecting others, and hospitalization, especially in intensive care, can lead to the development of anxiety, depressive disorders and post-traumatic stress disorder (PTSD) [61,62].

In addition, a recent review showed that neurological issues (such as stroke, ataxia, headache, seizures, dizziness) are present in about 25% of patients with COVID-19 [63] and many patients continue to have widespread pain and aches for a long period of time after the acute phase of the disease. Neurological disorders such as stroke, seizures, headaches as well as physical symptoms such as algias and pain, are associated with increased suicidal risk [64,65]. The increase in suicidal behavior in COVID-19 patients thus appears to be of multifactorial genesis, depending not only on the emotional and psychological impact that the experience of COVID-19 leaves on those that were infected, but also on the direct physical consequences that the disease has on the body.

Populations most at risk

Health workers

International attention focused on the psychological condition of health workers on the frontline during the battle against COVID-19. At first defined as heroes and thanked, then exposed to complaints, stigmatized, and discriminated due to the higher chances of getting infected [66] soon afterwards. Chronic stress caused by exposure to the virus, guilt and fear of infecting the loved ones, forced isolation, and pressure at work are all conditions that can contribute to the onset of depression, anxiety, insomnia, burnout, and frustration. Doctors are in themselves a category most at risk of depression, anxiety, and self-harming acts with high lethal rates [67]. In addition to the stress caused by increased workload, isolation and fear of infection, they face the significant emotional cost of increased patient deaths, feelings of helplessness and loss of control, and feelings of self-accusation for not being able to do more [68]. Numerous studies have shown an increase in hopelessness, lowered self-esteem, feelings of guilt and insomnia among workers engaged in fighting SARS-CoV-2 [69]. The international press has reported numerous cases of suicide among health workers involved in emergency management [70]. Anxiety, depressive symptoms, insomnia, and self-harming thoughts have also been reported among family members of frontline emergency responders [71].

Elderly and young people

The elderly population is a particularly vulnerable group to the consequences of the COVID-19 pandemic. In fact, old age, as well as being an important risk factor for severity and mortality from SARS-CoV-2 infection, is a predisposing factor for psychosocial difficulties. The suicide rate of elderly individuals is higher than that of the general population [72] and is particularly high among socially isolated individuals [54]. Social distancing measures dictated by the need to contain the spread of infection may lead to an increase in such isolation and a higher risk of loneliness, depression and suicidality among older people [73]. In the current situation, policies of social distancing and ethical issues related to the need to select patients who are candidates for treatment given the extreme emergency and scarcity of health resources, could favour the perception of being a burden to society and the decrease in the sense of belonging among the elderly [74]; these conditions, according to the interpersonal theory of suicide, can drive an individual to want to commit suicide [54]. On the other hand, among young people there has been an increase in the rate of depression related to the COVID-19 epidemic which could lead to an increase in suicidal acts due to greater economic insecurity [75]. Recently, there has been growing alarm at the increase in self-harm and suicide among children and adolescents [76]. The social disconnection and the difficulty of building a sense of belonging related to the drastic reduction of socialization activities (distance learning, closure of gyms and meeting places) would facilitate the progressive withdrawal and the tendency to take refuge in a virtual world to find some relief.

People with psychiatric disorders or addictions

The presence of psychiatric disorders is an important risk factor for suicidal ideation and behaviour. Cavanagh and colleagues [77] analyzed several studies using the psychological autopsy method and found that 85-95 % of those who died by suicide were likely to have suffered from known or unknown psychiatric problems that may have contributed to their suicidal conduct. People with psychiatric illnesses are among those most affected by the psychosocial effects of the pandemic [78,79] and those at greatest risk of infection and complications due to widespread risky lifestyle habits such as cigarette smoking, poor adherence to suggested precautionary measures and alcohol use [80]. Alcohol and other substances of abuse are a risk factor for suicide both because of their influence on mental health and the risk of dependence they carry, but also due to their potential to be used as lethal means or as facilitators of self-harm; indeed, as many as one third of suicide deaths have a positive toxicological test for substances of abuse [81]. There is ample evidence on the association between alcohol use and suicidal behavior [82]. Psychosocial issues exacerbated by the pandemic, such as family conflict, financial issues and unemployment, may favor alcohol abuse which increases suicidal risk by increasing impulsivity, aggression, feelings of loneliness and loss of hope [80].

Abuse and violence victims

Lockdown policies adopted in various countries have led to an unprecedented situation where households have been forced to share time and space beyond normal routines. Pre-existing conditions of domestic violence, abuse and conflict between family members have been exacerbated by current conditions. Indeed, there has been an increase in reports of domestic violence and abuse often accompanied by suicidal ideation [83].

Prevention strategies

Suicide prevention during the COVID-19 era must be targeted not only to specific risk factors dictated by the pandemic but also to pre-pandemic risk factors that are often inadequately addressed.

Effective prevention strategies require a combination of health, governmental, social and media forces. Government, community and media actions remain the cornerstones of universal suicide prevention interventions, i.e. those interventions targeting the whole population and focusing on specific risk factors. Among them, the following measures have proven effectiveness in suicide risk prevention: restricting access to lethal means, campaigns to reduce hazardous alcohol use, school awareness programs, media accountability in reporting suicide-related news, and government policies to mitigate economic crisis, unemployment and poverty [80]. Among selective interventions, i.e. those interventions targeting individuals at high risk of suicide, the timely pharmacological and psychological treatment of depression and the chain of care and follow-up of patients have a proven preventive effectiveness [80]. In order to cope with the challenges posed by the pandemic emergency, it is necessary to update and adapt preventive strategies by adopting special measures targeted at risk factors specifically induced by the COVID-19 emergency. Suggested special measures include increasing the number of mental health help-lines linked to COVID-19 information services, increasing the number of untraceable domestic violence support hot-lines and raising the awareness of those involved in responding to domestic violence calls (e.g. police). Specific training of primary care professionals for early detection of warning signs [83] and creative collaboration between mental health professionals and media experts to increase the dissemination of anti-stigma messages that encourage help-seeking would also be helpful [84]. Specific interventions on high-risk populations include the strengthening of mental health and addiction services, with a focus on reinforcing telemedicine methods, to ensure continuity of care for patients in need, the increase of treatment options and the opportunity to identify high suicide risk individuals.

Specific training in suicide prevention techniques for mental health and addiction service workers and encouraging the telematic provision of specific screening and treatment for suicide risk would also be desirable [83]. There is a need to ensure immediate and job-neutral access to mental health services for frontline workers and to disseminate suicide prevention programs in schools and workplaces [84]. The promotion of social contacts is another specific intervention essential to mitigate the increased risk brought about by the need for physical distancing. Some authors have demonstrated a high reduction potential (up to 50-60%) in the risk of suicide attempts in a high-risk population by sending 'caring messages' in various forms (letters, postcards, emails or telephone messages) [85]. In this sense, it might be useful to encourage large-scale use of technology (e.g. phone, video calls, texting) to regularly check up on friends and family members. The use of media campaigns to promote social cohesion and the encouragement of community telematic services for communication with individuals living alone, the elderly or marginalized people may also represent effective strategies [84]. Another important aspect to consider in suicide risk prevention during COVID-19 is the media impact of suicide news and its potential "contagious" effect, if reported incorrectly. Collaboration between the media and health services is crucial during this period to fight misinformation and the broadcast of wrong messages about suicide [83]. It is also crucial to raise media awareness on the use of guidelines [86] on the most appropriate and safe way to report suicide news [84].

Discussion

From the early stages of the pandemic emergency there was global alarm for the possibility of a rapid increase in suicidal acts as a result of COVID-19 related issues [87]. In the literature, we have observed a general decrease in anti-conservative acts in the first period of the pandemic emergency, with a tendency for them to rise again in the period immediately afterwards, a phenomenon reported by authors in various countries. It is not unusual to find a stationarity or often a decrease in suicidal acts after catastrophic events involving the entire population of a nation or, as in this case, the world [15]. A similar effect has been reported following terrorist attacks [88], wars [9] and natural disasters [89].

The increase in social cohesion, the so-called 'pulling together' phenomenon [90], could partly explain this trend. In the face of the danger caused by an invisible virus, individual problems may take a back seat, at least for a limited period [15]. The 'honeymoon period' [91], fostered by increased social and community cohesion and mutual support, may have moderated the unfavorable psychosocial impact of the pandemic [92]. From a psychodynamic point of view, the decreased need to transform outward aggression into self-aggressive acts, due to the real perception of an external enemy, may have transiently reduced self-injurious impulses [15]. The COVID-19 period embodies a dual phenomenon, composed of elements belonging to global catastrophes, during which the honeymoon effect was found, and elements typical of periods of deep economic crisis, characterized by a surge in suicide rates [9]. The combination of these elements is unpredictable and could act differently in different populations depending on the stage of the pandemic.

In this historical moment it seems sensible to act expecting the worst and hoping for the best, strengthening as much as possible the suicide prevention systems and mental health services that are lacking in many countries, activating social shock absorbers able to mitigate the devastating effects of the likely imminent global economic

crisis and implementing policies aimed at strengthening social cohesion and encouraging mutual aid among citizens.

The health emergency we are facing has the potential to trigger a series of changes in the structure of society, and therefore a strong institutional and individual commitment is required to ensure that the changes triggered are aimed at improving the protection and integration of the populations most at risk, especially those marginalized and in economic difficulty, using the destructive wave of change to lay the foundations for a new world.

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Original article

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How the COVID-19 pandemic changed the world of addiction: considerations on the impact on substance use and treatment

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Summary

The CoronaVirus (CoViD)-19 pandemic has affected life and mental health, in relation to several factors, including fear, uncertainty, anxiety, social isolation, loneliness, trade and movement disruption, and economic consequences. In these circumstances vulnerable categories having a higher risk of mental illness could be considered the elderly (> 80 years), individuals residing in disadvantaged areas, minority in disadvantaged areas, ethnic minorities, children/adolescents and pregnant women, health workers, and in general individuals with a positive psychiatric history. For sure, a peculiar situation is that of people diagnosed with a Substance Use Disorder (SUD), as they may experience: a) quantitative changes in substance use, e.g. an increase in drug use related to the negative impact of the stressful situation; b) a switch to other substances if access to those previously used is limited; c) relapsing into alcohol and/or alcohol and/or substances if they had stopped. Drug users might have a higher risk to become infected with COVID-19, either because of a possible physical comorbidity, e.g. pulmonary or cardiovascular diseases, HIV, viral hepatitis infections; or because of a psychological/psychiatric comorbidity, which includes a state of general distress, sleep disturbances, anxiety disorders, mood disorders, psychotic symptoms; and by any disadvantaged social condition (homelessness, prisoners, etc.), or more generally, socio-economic problems arising from drug dependence. Thus, the purpose of the present article is to show the impact COVID-19 had on people with SUDs and the intervention strategies that addiction services have then adopted. A reorganisation of addiction services and facilities, and the use of telemedicine are strategies for reducing or impeding COVID-19 transmission among drug users, avoiding overcrowding and ensuring continuity of care for people with SUD.The development of multidisciplinary support could be useful to reduce mental distress due to misinformation and teach strategies to cope with possible pandemic-related problems.

Introduction

After over one year of COVID-19 outbreak we have observed how this pandemic affected the mental health of the general population, in relation to various factors including fear, the sense of uncertainty, constant apprehension, social isolation, loneliness and possible economic repercussions [1-3]. Previously, in the 2003 outbreak of Severe Acute Respiratory Syndrome (SARS) [4,5], an increase in suicidal behaviors (suicidal ideation, suicide attempts and actual suicide) [6-8] and an increase in anxiety and mood disorder were recorded, with a prevalence

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Conflict of interest
The Authors declare no conflict of interest.

of traumatic-type disorders such as post-traumatic stress disorder (PTSD) [1,6,9-17]; these complications appeared evident in subjects with Substance Use Disorders (SUDs) [18,19].

A recent study [19] estimated that unemployment, isolation and high levels of stress due to the COVID-19 pandemic could cause up to 75,000 "desperate deaths" from substance use and / or alcohol and suicide [19]. The elderly (> 80 years), individuals residing in disadvantaged areas, ethnic minorities, children/adolescents and pregnant women can also be considered vulnerable categories [1,14,16,20] although previously the high risk of mental illness was identified only in individuals with a positive psychiatric history [1,14,16,20]. Healthcare workers should also be considered vulnerable subjects, as they have experienced emotional overload due to organizational problems related to the lack of adequate personal protective equipment, the reduction of human resources and relentless work shifts [21-24]. Stress caused by fear of becoming infected and infecting family members and friends, high mortality rates, grieving the loss of patients and colleagues, and separation from families are other possible vulnerabilities for healthcare workers [23-25]. The female gender seems to be a category at greater risk for the incidence of anxiety and post-traumatic symptoms and the category of nurses more affected than medical personnel [26]. The aim of the present study is to show the impact that COVID-19 had on the people with SUDs and the intervention strategies that the Services dedicated to addiction have adopted.

Consumption of substances and COVID-19

In this scenario, SUD patients could be particularly vulnerable, being able to experience: a) quantitative changes in substance consumption, for example a reactive increase to the negative impact of the stressful situation; b) the transition to other substances if the access to those previously used is limited; c) a relapse in consuming alcohol and/or substances if they had stopped. Attention should be done to the high risk for drug users to become infected with COVID-19, either because of a possible possible physical comorbidity, e.g. pulmonary disease or cardiovascular disease, HIV, viral hepatitis infection; or because of a psychological/ psychiatric comorbidity, which includes a state of general distress, sleep disturbances, anxiety disorders anxiety disorders, mood disorders, psychotic symptoms; or because of possible disadvantaged social conditions (homeless people, prisoners, etc.), economic difficulties or, more generally, socio-economic problems more generally socio-economic problems resulting from drug addiction [8,12,27-29]. Moreover, abusers can hardly adhere to the rules and limitations imposed by the pandemic, for example under the influence of alcohol/substances they may be more likely to violate protocols, not to respect social distancing, not to adapt to the use of the mask, not to carry out proper hand hygiene also due to their increased levels of impulsiveness [30]. In relation to alcohol consumption, it should be noted that online and takeaway alcohol sales during the pandemic have greatly increased [31]; this data, combined with the fact that socialization opportunities are limited, can lead the subject to use alcohol mainly at home and in solitude, leading to more alcohol consumption than social drinking [30].

The COVID-19 pandemic has hit drug markets, causing on the one hand an increase in the prices of some of the illicit substances sold on the black market, and on the other a reduction in purity. For example, the availability of some synthetic substances, such as methamphetamine, has drastically reduced due to air travel restrictions and flight cancellations, while cocaine, which mostly traveled by sea, continues to be detected in European ports [32], like heroin and opioids. Finally, cannabis appears to be less available, due to restrictions on movement across regions. There is the possibility that these disruptions will become increasingly severe and that the risks to people who use substances increase, for example by affecting the purity of substances, adulterating them, or contaminating them with synthetic compounds, as in the case of heroin contaminated with opioids synthetics such as fentanyl. Consequently, there is a risk of switching to the consumption of more dangerous substances, street drugs and new psychoactive substances, such as synthetic cannabinoids [33]. In fact, due to the disruption of drug markets, the reduction in supply and restrictions on access to drugs, the search and purchase of drugs on the web could increase. In line with this, the use of common drugs such as narcotics has emerged in some countries, in this case both prescription drugs, such as opioids, benzodiazepines, some anbtipsychotics (e.g. quetiapine and olanzapina), the gabapentinoids pregabalin and gabapentin, Z-drugs (for example, zolpidem) [34-36]; and some over-the-counter drugs, such as some antihistamines, for example promethazine, some codeine-based cough syrups, and/or ephedrine, and the antidiarrheal loperamide [34,35].

The crisis brought about by COVID-19 is likely to increase the need for access to drug treatments and services, despite the general overload of health systems and emergency services [28,33]. In fact, access to drug addiction treatment services has sometimes been interrupted by the need for self-quarantine, social isolation and other public health measures taken to contain COVID-19 contagion [28,33,37]; the same drug addiction structures such as the SerD must face the shortage of personnel due to self-isolation and the disorganization of services [28,33,38]. Therefore, to counteract the possible negative effects [5,14,20,28,33], some preventive interventions have been adopted, including: a) an increased supply for home pharmacological treatment of opioid-dependent patients (suboxone/methadone) in cases that allowed it [39-41]; b) support in the management and prescription of controlled substances [27,33,42]; c) tele-health for monitoring drug addicted patients; d) participation in remote employee support groups via online meetings [17,27,38].

Telemedicine and SUD

Although patients with SUDs had an increased requirement of support during the COVID-19 pandemic a decrease in their access to services was recorded: both rehabilitation facilities and employee support groups interrupted programs and limited new admissions [18,28,38,41] Self-help support options, such as Alcoholics Anonymous (AA) and Narcotics Anonymous (NA), which typically represent the primary treatment option in SUD, have become even less accessible. The regulations related to the virus's spread prevention created the urgent need of alternative approaches to treat addiction [43,44]. Telemedicine, providing remote healthcare through telecommunications technology, may guarantee services continuity, on the one hand satisfying the needs of patients with SUDs and on the other reducing the risk of infection [45-47]. The four most common telemedicine modalities in SUDs treatment programs are computer assessments (45%), telephone support during recovery (29%), telephone therapy (28%) and video call (20%). Tools such as texting, smartphone app and virtual reality interventions are less used [48-50]. Several studies reported the positive effects of this kind of intervention in patients with SUDs [43]. Patients should be encouraged to participate to virtual 12-step group meetings and other self-help meetings, as well as professional-led groups. Useful is the presence of an online sponsor or the maintenance of a virtual connection with their current sponsors. However, these methods have limitations, including the virtual type of interpersonal relationship and the unavailability of a reliable telephone service or access to the Internet or the necessary devices. Some patients may also have some concerns about their privacy and security [50-52].

This difficult period led to a rapid increase of technology use in a short period of time. For this reason, many clinicians have been inadequately prepared to use telemedicine tools, causing a significant delay or even the interruption of patient support. Telemedicine is a necessary and valid response to the crisis, but its role in ensuring clinical care in post-pandemic health systems will depend on the characteristics of the health systems in which it is applied. In order to evaluate the short and long-term outcomes of such interventions in patients with SUD it will be necessary to compare personal assistance with that in telemedicine. Adherence to treatment, occurrence of relapses, maintenance of abstention, comorbidities, access to Emergency Services and the results of toxicological tests must be evaluated [43].

COVID-19 and craving

The first Italian study conducted during the lockdown in the SUDs population, found that the subjects had the same psychopathological burden of the psychiatric population, the subjects with double diagnosis, the subjects with SUD and the general population. An increase of stress, anxiety and depression was reported. On the other hand, the level of craving was lower than that of the general SUD population. In the study it is hypothesized that this unexpected finding may be the result of: (i) a perception of reduced availability of the substance during the lockdown. In fact, this phenomenon could have reduced craving priming; (ii) a possible reduction in social pressure induced by the increase in the sense of belonging of the dependent patient who is in a moment of emergency shared with the rest of the population. For this reason, the sense of marginalization and rejection, which often contribute to increasing the craving and use of the substance in the addicted patient, could be decreased [53].

Another Italian study conducted on the population affected by pathological gambling found a reduction in craving during the first phase of the emergency; one of the causes could be the reduction of certain environmental stimuli such as the inability to access electronic gambling machines (EGMs) [54]. In a second phase craving may increase due to persistent stressors caused by the pandemic. The craving assessment is helpful in the management of the SUD patient, not only for the current period, but also for a better understanding of the craving itself.

The clinical practice

Innovative and effective interventions should be planned to address the social effects of the pandemic and from the point of view of physical and mental health.

Patients should be properly informed and aware of the most common psychological effects of a pandemic, and healthcare professionals play a crucial role in this process. COVID-19, associated with common environmental factors such as stress or trauma, can contribute to both the development of a psychiatric disorder and the development of a SUDs. Urgent action is needed to improve mental health care, emergency preparedness and a prompt and effective response to people with SUDs. Therefore, mental health services should develop and evaluate: (i) psychoeducational strategies that particularly concern the possibility of self-injurious/suicidal behaviors, overdose and domestic violence; (ii) staff training to support new work methodology; (iii) valid tools for remote diagnostic evaluation; (iv) care pathways for people at risk [1,10,14]. Healthcare professionals should develop prevention strategies for the transmission of COVID-19 among drug addicts, such as preventing overcrowding and ensuring continuity of care for people with SUD [55-57].

Monitoring of the need for care and support of vulnerable patients and social workers should be carried out [2,3,8,57,58]. Telemedicine needs to be strengthened and supported with adequate funding in the post-pandemic. Healthcare professionals should be educated on the use of telemedicine and should have adequate equipment. Physicians should be alerted to a possible drug misuse, with increased prescription requests or over-sales of over-the-counter products that can be abused. The development

of multidisciplinary support platforms could be useful to reduce mental distress due to disinformation and teach strategies to cope with possible problems related to the pandemic [15]. These precautions and strategies can be helpful in supporting post-pandemic mental health.

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Original article

Post-Traumatic Stress Disorder (PTSD) and the COVID-19 pandemic

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Summary

Health crisis, such as that occurred during the COVID-19 pandemic, generally shows a significant impact on individual mental health, setting the stage for the development of a condition of significant mental distress that could lead to the development of a psychiatric disorder or could exacerbate the symptoms of an already diagnosed psychiatric disorder too. In the specific case of our work, we have focused our attention on the COVID-19 and PTSD pandemic relationship. We reviewed the available evidence and examined the aforementioned relationship in the general population and also in COVID-19 survivors, in family members of COVID-positive patients, in healthcare workers and in psychiatric patients. We have also considered the development of PTSD in the same categories of subjects also during previous pandemic crises, in order to have a broader view of what are the factors that, in conditions of an infectious disease pandemic, can induce the development of PTSD. Finally, we focused on how to treat the aforementioned disorder in a context in which mental health services have had to reorganize and reorganize their standard models of care delivery.

PTSD and health crisis

Post-Traumatic Stress Disorder (PTSD) is a psychiatric disorder that can develop following exposure to traumatic events. The term trauma derives from the Greek word τραῦμα (wound) which in turn derives from τιτρωσχω (to pierce). Trauma can be defined both in physical terms and in psychological ones. From a physical point of view, a common definition of trauma is that of a severe physical injury or injury experienced as painful. In psychological terms, a useful definition is that of an overwhelming stimulus, stressor, or event that is so excessive in its psychological upheaval that it significantly compromises psychological functioning itself. Traumatic events can include sexual violence, wars, natural disasters or other types of threats to a person's life. The effects of this events on the person do not depend exclusively on the trauma itself, but also on the subject's ability to adapt to stress and to cope with adversity. The aforementioned ability is what is typically named resilience. This latter can be considered a progressive process of psychological and physiological adjustments that can be implemented to better enable the traumatic experience to be dealt with. Resilient individuals would then develop techniques and strategies that allow them to more effectively deal with adversity and even crises. They would be also characterized by a certain amount of optimism that would help to effectively balance negative emotions. To date, a series of factors have been identified that would favor individual resilience and which have therefore taken on the name of resilience factors. These include: an optimistic but realistic outlook, seeking and accepting social support, solid role models as an inner compass, religious or spiritual practices, acceptance of what cannot be changed, mental acuity, emotional strength, the ability to actively solve problems by seeking their meaning and opportunity, and even humor. Finally, resil-

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ient people tend to take responsibility for their emotional well-being and use the traumatic experience as the basis for personal growth [1].

Specifically, PTSD is characterized by the development of negative symptoms after exposure to one or more traumatic events [2]. According to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), an essential condition for the existence of this pathology is "exposure to actual death or threat of death, serious injury or sexual violence" (criterion A). Intrusive symptoms of the stressful event (criterion B), symptoms of avoidance of stimuli associated with the traumatic event (criterion C), negative distortions of persistent and exaggerated thoughts and emotions with respect to oneself and the world (criterion D) and symptoms of hyperactivation (criterion E) can be objectified (DSM-5) [3]. Symptoms of PTSD typically include distressing and intrusive memories, trauma-related nightmares, irritability, hypervigilance, difficulty sleeping, poor concentration, isolation and avoidance of places and/or activities that could remind the subject of the trauma. These symptoms, in patients with PTSD, have a duration greater than 1 month. The severity of the disturb can be worsened by the concomitant presence of substance abuse, depressed mood, anxiety disorders, self-harm, impulsive, dangerous, or suicidal behaviors. PTSD is also associated with significant medical comorbidities, including chronic inflammation and pain, cardiometabolic disorders, and increased risk of dementia. Thus, the total burden of the disease, in terms of disability and premature mortality, is extremely high.

Although exposure to trauma is the precipitating event for the development of PTSD, numerous endogenous and environmental risk factors appear to be related to the development of the disorder as well as to the onset, the severity and the possible chronicity of the symptoms. Regarding to endogenous risk factors, it is necessary to consider the genetic predisposition to the development of the disorder, as well as the dysfunctions in the main systems involved in its pathogenesis such as the hypothalamic-pituitary-adrenal axis (HPA), the noradrenergic immune, that of pro-inflammatory cytokines, that of endocannabinoids and that of glucocorticoids. Furthermore, neuroimaging studies conducted on patients with PTSD have shown alterations in the cerebral circuits involving the hippocampus, amygdala, medial prefrontal cortex, cingulate gyrus and insula [4]. Considering the environmental risk factors, the psychosocial variables associated with this disturb include personality traits (particularly neuroticism), a low socioeconomic and educational level, and female sex. Finally, several studies have shown that fear represents, the risk factor mainly related to the development of PTSD, among the numerous risk factors of the disorder [5,6].

During a health crisis such as the one that is occurring during the COVID-19 pandemic, declared by the WHO Director-General on March 11, 2020, the degree of fear can be influenced by the likelihood of contracting the disease from the new Coronavirus SARS-CoV-2, as well as the consequences that it could derive from it [7]. On the basis of the available evidence, it is well known that exposure to epidemics of infectious diseases can cause a particular type of psychological trauma which can be traced back to the direct symptoms of the disease and their traumatic treatment (dyspnoea, respiratory insufficiency, altered state of consciousness, threat of death, tracheostomy, etc. are the main traumas of patients with severe COVID-19 disease). This same type of trauma can also be associated with the experience of assisting patients who suffer, struggle and die from infectious disease and that of the realistic or unrealistic fear of infection, social isolation, exclusion and stigmatization [8].

The above is confirmed by the fact that several epidemiological studies, conducted after an epidemic of infectious diseases such as SARS, MERS, Ebola, H1N1 flu and HIV/AIDS, have shown a high prevalence of mental health disorders among survivors, victims' families, health workers involved in emergency and in the general population. Specifically, a study of long-term psychiatric morbidity among SARS survivors revealed that PTSD was the most prevalent disorder. The cumulative proportion of patients with PTSD was 47.8%, and 25.5% of patients continued to meet the diagnostic criteria of PTSD [9] with sleep disturbance and recall of traumatic memories [10], 30 months later [9]. Similarly, a systematic review of the psychological consequences of the 2003 SARS epidemic, the 2009 H1N1 epidemic and occupational exposure to HIV indicated that the average prevalence of PTSD among healthcare workers was approximately 21% (from 10 to 33%), with 40% of the same presenting persistent symptoms 3 years after exposure [11]. It is interesting, in this regard, to consider in this category the complications of PTSD arising in the long term and, above all, the correlation between the persistence of PTSD symptoms and the development of alcohol dependence in health care workers who had been exposed to the SARS epidemic 3 years previously [12]. The characteristic and the level of exposure to psychological trauma appear to be the most reliable predictor of PTSD after an infectious disease epidemic. Most epidemiological studies indicate that survivors have a higher prevalence of the disorder, followed by the families of the victims and medical professionals who provide care to affected patients [9].

PTSD in the general population

During the COVID-19 pandemic, multiple online surveys were conducted to assess the impact of this sanitary emergency on the mental health of general population. Several studies conducted in Italy [2,13-15] Spain [16], China [17-19], India [20], Ireland [21] and Israel [22] have evaluated the presence of PTSD symptoms in general population. The results of these studies demonstrated that the pandemic can be considered a traumatic event [13], with an incidence of PTSD ranging from 7 to 53.8% [23]. This disorder would mainly affect subjects under the age of 50, those of female sex (presumably also due to an overload related to the

role of caregiver to be balanced with work and household chores), those with a psychiatric or neurological background, infected subjects and those who are faced with situations of uncertainty about the risk of contagion. Of all the risk factors, the main predictors of PTSD in general population appear to be loneliness and discrimination, while the greatest protective factor should be a condition of spiritual well-being [14-16]. As previously explained, female sex represents one of the main risk factors for the development of PTSD. In particular, health crises and natural disasters represent traumatic events capable of increasing stress in the perinatal period and making pregnant women particularly vulnerable to the development of the disorder. During the COVID-19 pandemic, conditions of isolation and of freedom's loss together with the impact of the virus on pregnancy, the possible vertical transmission of the infection and unfavorable obstetric outcomes, can lead to psychological distress for the pregnant. In this sense, a recent study conducted in Italy shows that the prevalence of PTSD symptoms among women who gave birth during the pandemic was higher than that reported in studies prior to the pandemic itself. Specifically, 42.9% of women who reported the presence of mild symptoms and 29.4% reported the presence of moderate symptoms. The psychological impact of the pandemic on pregnancy could explain the increase in PTSD during the postpartum period, in association with avoidant and anxious attachment. These psychiatric conditions are characterized by a combination of avoidant and anxious tendencies, low self-esteem and an active search for intimate relationships and emotional closeness, with an inability to trust others. COVID-19 stress during the perinatal period could also trigger a reactivation of traumatic memories, thus favoring the development of PTSD, in a general climate of alarm and concern [24].

PTSD in disease survivors

Based on information relating to previous human Coronavirus outbreaks (especially SARS and MERS), a high incidence of PTSD in COVID-19 survivors can certainly be hypothesized. Indeed, 42% of MERS survivors passed the PTSD cut-off one year after the outbreak [25] and, likewise, nearly 26% of SARS survivors met full diagnostic criteria for PTSD 30 months after the outbreak beginning [26,27]. In particular, the SARS epidemic of 2002-2003 highlighted that the media coverage of high death rates together with the stigma against survivors and their families for spreading the disease, the guilt of the survivors, the fear of infecting loved ones and the death of close family members are stressors that can have important implications for psychological outcomes in COVID-19 survivors [28].

Based on the evidence currently available, it is estimated that 96% of COVID-19 survivors experience the symptoms of PTSD with the possibility to develop cognitive impairment and suicidal ideation as complications of these symptoms [29]. From the onset of the pandemic, about 1 in 5 infected people were hospitalized and 1 in 10 people were hospitalized in an intensive care unit (ICU). Most of the latter experienced acute respiratory distress syndrome (ARDS) which required mechanical ventilation. Up to 80% of patients who survive acute respiratory failure, after receiving mechanical ventilation in the ICU, experience new disorders or worsening of pre-existing disorders of an internal, cognitive and/or psychic nature. These may persist beyond hospital discharge and develop into the clinical picture of post-ICU syndrome [26]. Among patients requiring mechanical ventilation in the ICU, the most common psychiatric symptoms include guilt, mood swings, sleep disturbances and memories of panic and suffocation [26,30], with PTSD estimated to occur in between 15 and 51% of intubated and mechanically ventilated patients. In addition, 79% of ARDS patients treated in an ICU recalled vivid nightmares and hallucinations [26]. Although older age, pre-existing physical frailty, psychological symptoms such as anxiety, depression, and cognitive impairment (e.g., dementia) are risk factors, even those without these can experience long-lasting sequelae. In fact, one quarter to one third of ICU survivors can develop psychiatric disorders, including PTSD, whose symptoms can persist 5 years after the onset. Changes in the hospital environment, such as reduced access to family members and pleasant activities and isolation from contact, can lead to a greater risk of negative psychological symptoms. In addition to these already mentioned causes, in the current pandemic, those of PTSD in survivors include the experience of being about to die, delirium and trauma related to ICU treatments. The threat of actual or potential death, as a fundamental criterion for the traumatic experience associated with PTSD, is evident in the words of affected patients and survivors: "you seem to be drowning ... you think you are going to die" and "I am not going to sleep for three days because I was afraid ... I would not wake up" [26]. Another potential cause of PTSD in COVID-19 survivors is delirium, which can occur due to a confluence of factors related to both virus and hospitalization/intensive treatment [31,32]. In elderly and mechanically ventilated populations, delirium can occur in 80% of cases [33], suggesting that survivors of severe COVID-19 infection, often elderly and ventilated [34], may be particularly at risk of delirium itself. In particular, prolonged duration of delirium (> 40 days) has been associated with a higher risk of PTSD [35]. More specifically, further studies have demonstrated that, not delirium in the strict sense, but rather painful memories in the ICU, would contribute to the development of PTSD in survivors [36-38]. Among the other possible mechanisms involved in the development of PTSD in survivors of the disease, we can consider the brain lesions on a hypoxic-ischemic basis with the consequent neuro-psycho-cognitive deficits [39]. Further contributing causes could be the alterations of the circadian rhythm related to intensive treatments [40,41], which may also persist even after discharge [42,43].

Consistent with the foregoing, an online survey conducted in China revealed a high incidence of PTSD in COVID-19

survivors. Specifically, out of a total of 126 subjects included, the mean PTSD self-rating scale (PTSD-SS) scores were found to be 45.5 ± 18.9; 9 (31.0%) survivors also met the minimum score for clinically significant stress response symptoms. Infected family members, social support, retirement, and female gender had significant associations with the PTSD-SS score. In particular, being a woman, having infected family members and having poor social support were associated with hyperactivation, intrusive thoughts and avoidance; retirees, that is survivors aged 60 and over, experienced less severe symptoms than younger [44]. Another study conducted in Korea confirmed the high incidence of PTSD in COVID-19 survivors one month after hospital discharge. In particular, 10% of subjects reported symptoms of PTSD and, of these, the most severe ones were associated with a high perceived stigmatization. In fact, 40% of the participants were worried about infecting others and being discriminated against by neighbors because of their COVID-19 history [45]. A study conducted in Italy, on 402 surviving patients, after one month of follow-up revealed an incidence of PTSD of 28%, underlining that patients with a psychiatric background showed higher scores in the various psychopathological spheres investigated, including PTSD anxiety and depression. To demonstrate the results of the aforementioned study, the testimony of one of the patients is interesting: "After three weeks of treatments, I was recovering from COVID, at home, I had no fever, just a little cough. But sometimes at night, my breath could suddenly disappear, making me feel like I was going to die. I knew what it was because I had suffered from panic attacks in the past. I stood out there on the balcony, for hours, trying to get fresh air into my lungs. It was terrible. The panic made me suffer more from COVID". A patient's report at follow-up [46].

PTSD in family members of COVID-19 patients

During the COVID-19 pandemic, family members of patients affected by the disease and especially those of patients admitted to the ICU, are conventionally subjected to considerable psychological pressure. Because of this reason they have a considerable risk to develop symptoms of PTSD [47-49]. The same are forced to face further hardships, with the moment of end of life which is certainly the most traumatic of all. The main difficulties they face are represented by the insecurity that their family members can be adequately cared for and at the same time treated with affection, by understanding their health conditions in order to be able to make appropriate decisions on their behalf by telephone and by the acceptance of the death of loved ones. The psychological impact of COVID-19-related separation on the families of ICU patients could therefore presumably lead to the development of PTSD symptoms in the long term [50].

PTSD in healthcare workers

Being a healthcare worker during the COVID-19 pandemic comes with enormous pressure, especially with regards to exposure to a risky environment, resulting in concerns about contracting the virus and passing it on to others [51]. This claim is primarily supported by the fact that during epidemics, a high percentage of health workers (up to 1 in 6 of those who provide care to affected patients) develops significant stress symptoms [52]. It is worth considering that in epidemic contexts health workers are the first to face the clinical challenges intrinsically linked to the course of the disease, under the constant personal threat of being infected or representing a source of infection. In this sense, health workers put their health at risk, as well as their life, to fulfill their professional duty [53]. Those who work in emergency structures are, among all, particularly at risk of PTSD due to highly stressful work situations to which they are exposed. These include management of critical medical situations, assistance to severely traumatized people, frequent reports of death and trauma and altered circadian rhythms due to shift work [54,55]. Under these conditions and due to the need to confront an unprecedented number of critically ill patients, with an often unpredictable disease course, with high mortality rates and with the lack of effective treatment or treatment guidelines [17,56] the same operators are at significant risk of developing PTSD. Looking at previous outbreaks of infectious diseases, several studies have shown that PTSD rates in healthcare workers ranged from 10 to 20% [57-59], with the highest rates (8 to 30%) among ICU staff [60-63]. In this regard, a systematic review of the literature, which highlighted in health workers involved in the SARS and MERS epidemics, an incidence of PTSD ranging from 9.6 to 51%, with higher rates in operators engaged in emergency units. Furthermore, the symptoms of PTSD continued to be present in 2-19% of healthcare workers 1-3 years after the outbreak of the epidemics [64]. Based on the above evidence, it is presumed that working in emergency departments is associated with higher levels of PTSD, as confirmed by the comparison, relative to the SARS epidemic of 2003, of the levels of PTSD in emergency department operators (21.7%) compared to those who practiced their profession in the other operating units (13%). Regarding marital status, some studies point out that not being married would correlate with a higher risk of PTSD [65] while others would conclude that being married, separated or widowed would be associated with a higher risk of PTSD [66]. It also appears that healthcare professionals who [25,52,67,68] were quarantined those who felt stigmatized or rejected because of their work [68] and those with prior mood disorders [69,70] were found to be most at risk of developing PTSD. The resilience factors were, on the other hand, the presence of social and family support (in particular the support of supervisors and colleagues), a good work organization and the use of positive cooping strategies such as the use of humor, the planning of activities, the acceptance of the

risks associated with them and the presence of religious beliefs [63]. Although most individuals prove resilient after being exposed to a traumatic event [71] different risk factors can compromise the effectiveness of the adaptation, including a previous psychiatric history, female sex, lack of social support [72,73] having young children [4,74], experiencing feelings of helplessness during trauma and experiencing negative emotions such as anger and peritraumatic distress [75,76]. On the other hand, resilience plays a key role in mitigating the impact of traumatic events and thus reducing PTSD [77,78].

During the current pandemic, several studies have investigated the presence and risk of PTSD among healthcare professionals. Specifically, a literature review conducted from December 2019 to June 2020, which included 44 studies out of a total of 69,499 healthcare professionals, found an incidence of PTSD that ranged from 7.4 to 37.4% [79]. Among the included studies, three of these identified that direct exposure to positive patients would be the main risk factor. First, frontline workers have the greatest risk of exposure and, having seen firsthand the effects of SARS-CoV-2, they experience fear of being infected and passing the infection on to colleagues, friends and family members, as well as other patients [79]. Secondly, the use of Personal Protective Equipment (PPE) for many hours is associated with excessive sweating, dehydration and discomfort, while the lack of PPE leads to a greater risk of contracting infection. Finally, given the nature of the infection, health professionals experience a strong sense of helplessness [80,81]. Two studies in the aforementioned review identified nursing as a major risk factor, highlighting higher scores for acute stress and PTSD among nurses [51,82]. A further study also found a strong association between low-moderate social support and symptoms of depression and PTSD [83]. Other presumably associated factors appear to be working in isolation wards for more than 12 hours a day, quarantine, family and/or friends with SARS-CoV-2 and poor sleep quality. It seems that up to 10 years of work experience represents an additional risk factor for PTSD among health professionals [79]. Another review of the literature, in line with the previous one, identified in health workers, and in particular those in first line, a category at high risk of developing PTSD and other psychic symptoms [84]. In particular, some studies have pointed out that the professional category of migrants was more at risk, due to the double negative effect of the adverse work scenario and the COVID-19 pandemic [85,86]. In the same sense, several online surveys have been conducted in China to assess the impact of the pandemic on the mental health of healthcare workers. A survey conducted in the first period found an incidence of PTSD of 9.8%. Being a nurse, having an intermediate technical qualification, working on the front line with little confidence in protective measures were risk factors for the disorder [87]. Another survey compared the symptoms of PTSD in health care workers that work in hospitals directly involved in the emergency compared to healthcare personnel not directly involved and, also in this case, the first group was found to be at greater risk of PTSD [88]. These data were confirmed by a further study which highlighted the presence of symptoms in 40.2% of health workers, with a higher incidence among nurses [89]. Finally, a large survey of a total of 14,825 doctors and nurses in 31 mainland China provinces showed an incidence of PTSD of 9.1%. Male subjects, middle-aged subjects, those with less work experience, and those with longer working hours and lower levels of social support were most at risk of developing PTSD. Again, being a nurse was associated with a higher risk [83]. Studies on the impact of COVID-19 on health workers have also been conducted in other Asian countries and it was found that the prevalence of PTSD among health workers was relatively low in India (2.1%), Malaysia (6.3%), Indonesia (11.6%), Singapore (12.3%) and Vietnam (15.0%) 91. As for Europe, a survey conducted in Norway on 1773 healthcare workers showed an incidence of PTSD of 28.9% and also in this case the operators who worked directly with COVID-19 patients reported more severe symptoms [91]. In Spain, on the other hand, the number of healthcare workers infected with COVID-19 was among the highest in the world and, analyzing cross-sectional data on 1422 healthcare workers, 56.6% of them presented symptoms of PTSD. The typical profile of a health worker with symptoms is represented by a person who works in a hospital in the Autonomous Community of Madrid, is a woman, thinks that it is very likely to become infected and therefore fears that a person with whom she lives could be infected in turn [92]. As for the United States, an online survey conducted among healthcare professionals from 25 hospitals showed an incidence of PTSD of 23.1% [93]. Another survey, conducted exclusively among nurses, to try to determine the association between access to adequate PPE and mental health outcomes, found that those of staff who did not have access to adequate PPE were more likely to report symptoms of PTSD [94]. Confirming that nurses are particularly vulnerable to stress during the COVID-19 pandemic, an online survey of a total of 448 Jordanian nurses (73% women) found that the majority (64%) were at risk of developing PTSD [95]. In general, among all emergency operating units, ICUs have had to face the most rapid reorganization both in terms of bed capacity and in terms of staff management and training. In a situation of this type, associated with the conditions of confinement and isolation imposed since the emergency, the personnel of these units were exposed to a greater risk of PTSD [96,97]. In this regard, the presence of PTSD was highlighted in between 7.4 and 27% of ICU operators, especially in women, among nurses, in case of inadequate preparation and where there were previous anamnestic episodes of burn-out [98,99].

In the category of health workers, it seemed important to emphasize the role of stigma, as well as trauma, in affecting their mental health. Emblematic, in this regard, seem to be the words of Dr. Wei and Dr. Roy Perlis respectively. “I feel like it’s something that has been incredibly traumatizing to our frontline workers - this desperation” says Dr. Wei. “I think part of the battle is recognizing that healthcare workers may be less comfortable seeking care. Al-

though we are better educated about mental health, we are not immune from worrying about stigma and what our colleagues will think of us", adds Dr Perlis [100]. In addition, among health professionals in direct contact with infected patients, a clinically significant association between levels of PTSD and perceived stigma, particularly with respect to the hypervigilance, avoidance and intrusion subscales [101]. Can access to care be undermined by concern about stigma? "I think part of the battle is recognizing that healthcare professionals may be less comfortable seeking care. Even though we are more educated about mental health, we are not immune from worrying about stigma and what our colleagues will think of us" [100].

PTSD in psychiatric patients

The consequences of the COVID-19 pandemic could have a worsening effect on the symptoms of patients with psychiatric disorders [102] and, being the pandemic itself a traumatic event, it could lead to the development of PTSD symptoms. What we want to underline is that, at the current state of knowledge, the evaluation of the COVID-19/PTSD correlation in patients with psychiatric disorders has been poorly studied, as in the past, in the case of previous pandemics/epidemics of infectious diseases. On the basis of the available evidence, in psychiatric patients the risk of PTSD is positively correlated to female sex, to a low level of education, to the presence of sleep disorders in anamnesis [34], to isolation [102] as well as to concerns about the health status of loved ones [103]. To these risk factors, which also occur in the other categories of subjects previously considered, in psychiatric patients are added the greater susceptibility to stressful events and difficulties in accessing mental health services [29,104]. During this period, in fact, psychiatric patients underwent a quantitative and qualitative reduction in care services, as most of the services were not organized to carry out consultations through telepsychiatry, for the home delivery of psychotropic drugs and to screen the patients by performing rapid tests for the diagnosis of COVID-19. In comparing the aforementioned category of patients with the general population, a Chinese study showed that the former had higher scores on the psychometric scales for the evaluation of PTSD, anxiety, depression and insomnia. In the same study, more than a quarter of the patients evaluated reported symptoms of PTSD, as well as moderate to severe insomnia. Psychiatric patients were, among other things, significantly more likely to report concerns about their health, anger, impulsivity and suicidal ideation [106]. Particularly susceptible to developing PTSD, among all, appear to be those patients who may be more vulnerable to the stressful effects of social isolation measures, on the basis of their pre-existing psychopathological characteristics [105,107,108]. In this regard, a category exposed to significant risk seems to be that of patients with Eating Disorder (ED). In this sense, a study conducted in Italy is particularly interesting to evaluate the effects of the pandemic on the aforementioned category of patients. The study compared, in terms of psychopathology, a group of patients with ED and a group of healthy control subjects, further investigating the possibility that the recovery process was deeply affected by the effects of the lockdown. It was also assessed whether a remission obtained before lockdown had a protective role on the psychopathological effects of the pandemic and whether a history of childhood trauma or a particular attachment style were associated with the development of PTSD symptoms. The results of the study showed that, although the lockdown had a lower impact on patients with Anorexia Nervosa than those with Bulimia Nervosa, there was an exacerbation of eating and pathological compensatory behaviors in both categories. As regards the symptoms of PTSD, however, there was an increase in the same, probably due to recurrent exposure to interpersonal and family conflicts during the period of isolation, especially in patients with a history of childhood abuse and with an avoidant and insecure attachment style [109].

Treatment of PTSD during COVID-19 pandemic

During epidemics of infectious diseases, it is essential to reorganize mental health services, in order to be able to provide adequate assistance to all those who suffer from mental illness. In this regard, in 2007, the Inter-Agency Standing Committee (IASC) defined the guidelines for mental health and psychosocial support to be followed in emergency health contexts. The aforementioned guidelines provide for the restoration of basic services and for the safety of the affected populations, the strengthening of family and community networks and the implementation of psychosocial support measures as well as specialized mental health interventions.

However, to date, there are no specific interventions for the prevention of the development of PTSD in all those who are exposed to an emergency condition, such as the health one currently underway [8].

Most of the guidelines for the treatment of PTSD include psychopharmacological interventions with anxiolytic and antidepressant drugs (SSRIs are the most used) and psychotherapy interventions. Among the numerous psychotherapeutic techniques, the most effective and therefore most used seem to be Cognitive Processing Therapy (CPT) and Eye Movement Desensitization and Reprocessing (EMDR) [110].

During the COVID-19 pandemic, the field of providing psychotherapy services has undergone profound changes, resulting in a shift from face-to-face sessions to sessions performed virtually remotely. Telemedicine had until now represented an optional therapeutic approach, valid for those patients who were in geographically isolated contexts and therefore did not have access to personal assistance. During the context of pandemic telemedicine itself has assumed the dimensions of a vital therapeutic tool. Through this tool, professionals working of mental health

have been able to continue to guarantee assistance to their patients in safety, respecting the social distancing protocols currently in force [111-113]. On the basis of the evidence currently available, it seems that telemedicine represents a safe and effective therapeutic option during the pandemic [114,115], as well as substantially comparable to face to face psychotherapy in the treatment of anxious, depressive and PTSD symptoms [112,116,117]. Therapists should therefore encourage patients not to let social distancing measures hinder their relationships. Through telemedicine it is possible to use traditional phones, smartphones, apps and online video calls performed through compliant platforms the rules of the Health Insurance Portability and the Accountability Act (eg Zoom) [111,113] compliant platforms the rules of the Health Insurance Portability and the Accountability.

Considering the psychotherapeutic options for the treatment of PTSD, CPT is a form of cognitive behavioral psychotherapy (CBT) with a focus on trauma [113]. First of all, treatment involves psychoeducation of the patient regarding both exposure to trauma and consequently developed PTSD. Then we proceed with the identification of the so-called "blocked points" of the traumatic experience and of the "declaration of impact", or rather of the ways in which the traumatic experience affects the patient's thoughts. Subsequently, through the Socratic dialogue and the use of a progressive series of worksheets, "the blocked points" are challenged, and cognitive strategies are used to elaborate issues related to the traumatic experience. The treatment ends with a review of the patient's progress, with the elaboration of a conclusive "impact statement" which is used to compare pre- and post-treatment thinking and with a discussion on future goals.

During the pandemic, the symptoms of PTSD develop more frequently among individuals affected by traumatic events related to COVID-19 [17,118]. Among these we can consider, for example, having witnessed the death of patients or co-workers, having been subjected to involuntary quarantine, having worked in high-risk environments without adequate PPE and having been forced to make important and difficult decisions regarding the treatment of positive patients. For events of this type, the "blocked points" can lead to the development of prejudices on the ways in which the index event could be prevented, or to that of feelings of guilt towards oneself and/or towards others. Through the Socratic dialogue these beliefs would be addressed at the beginning of the CPT, in the same way in which other index traumas are faced or taking into consideration the context and the probable options and information that the individual had available at the time of the trauma [113]. The evidence currently available have fortunately been shown that CPT, performed through telemedicine, has an efficacy essentially comparable to that of the same performed in person [113,119-121]. In order for the treatment via telemedicine to be equally effective, it would be important that patients are adequately informed about the psychotherapy procedure, through documentation that can be sent by ordinary mail or via secure messaging systems. At the same time, patients should be educated to assume, towards the sessions and the psychotherapist, a commitment and behavior comparable to what they would assume if the sessions were in person. Equally important, is the monitoring phase of any progress made by the patient. In this regard, during the last session, it would be useful to take advantage of the shared screen mode to display a graph that highlights the aforementioned progress [113].

EMDR, on the other hand, is a form of psychotherapy which aims to reduce the recall of intrusive traumatic memories characteristic of PTSD [122]. This type of psychotherapy has proven to be particularly effective in the treatment of PTSD itself [123]. EMDR lays the foundations in the fact that, by focusing on traumatic memories and by simultaneously moving the eyes (for example by following the movements of the therapists' fingers), the intensity and emotionality of traumatic memories is reduced [122].

In the specific case of COVID-19 pandemic, this psychotherapeutic technique could represent a useful tool for the treatment of all those who have developed symptoms of PTSD. Interesting, in this historical context, particular efforts have been made to evaluate its feasibility and its effectiveness electronically. It seems essential that the therapist has sufficient experience and expertise in EMDR therapy before considering proposing sessions through telemedicine. In this regard, a French study in which the telematic application of the URG-EMDR [124] protocol was evaluated in the treatment of a group of health workers operating on the front line during the COVID-19 pandemic, is interesting. In a single session, the treatment resulted in a reduction in anxious and depressive symptoms, as well as in mental distress reported by health professionals. The latter, although generally perceiving a certain lack of intimacy and concentration, have expressed a good acceptance towards this type of therapeutic approach [125].

Conclusions

In conclusion, the evidence on the high incidence of PTSD in previous MERS and SARS outbreaks as well as in the current SARS-CoV-2 pandemic suggests the need for early recognition of risk and protective factors for its possible development. Furthermore, the need for proper treatment of the disorder itself is emphasized in order to avoid possible comorbidities and complications such as depression, anxiety, substance abuse and suicide.

In particular, although PTSD was found in all investigated groups, including the general population, caregivers and psychiatric patients, the groups most at risk are health care workers and survivors of the disease. In the first group, the subjects most at risk of developing PTSD are mainly those who work on the front line in ICUs and nurses due to direct exposure to the trauma represented by direct contact with COVID-19 positive patients and the resulting deaths. This population also suffers from the powerlessness of managing the pandemic and above all the fear of being infected and of infecting patients, family and friends in turn. In this

sense, the concept of stigmatization and its close relationship with the possibility of developing PTSD are inserted. Despite being health workers, these subjects can in fact experience a "double stigmatization", that linked to their profession, that is to be really removed from the rest of the community or perceive that they are, and that linked to the difficulty of accepting recourse to psychiatric treatment. In this direction, psychiatry is called upon not only to provide tools for treatment, but also to provide tools to accept and request initial access to care through a profound work of unhinging the stigmatization that culturally accompanies it, in order to make it usable for all. The other group at high risk of developing PTSD, primarily due to direct contact with the risk of death, is represented by survivors of the disease. These people also experience quarantine, isolation, mechanical ventilation, delirium, the fear of being able to infect other people and, often, important physical and psychological sequelae even after overcoming the disease. COVID-19 therefore appears to be not only a physical disease but also a disease that affects the psyche and, in this sense, the challenge for psychiatry is to be able to intervene early during the treatment process in order to avoid the onset of important psychic sequelae, including PTSD.

In a context such as the current one, psychiatric services also find themselves operating in conditions of profound emergency. In fact, they had to reorganize the typical methods of providing their performances in compliance with the social distancing regulations in order to continue to guarantee adequate assistance to patients already in care. At the same time, this reorganization is necessary to make the psychiatric services able to accommodate all those who are experiencing symptoms typical of psychiatric disorders. In this sense, the fundamental tool is that of telemedicine. This makes it possible to provide an alternative, but still valid and effective psychotherapy support. In the specific case of all those who experience symptoms of PTSD, psychotherapy via telemedicine allows us to intervene promptly and adequately, allowing us to process the traumatic experience of COVID-19. At the same time, this therapeutic instrument makes everyone feel less alone in a moment in which isolation and distancing are essential paradigms for the protection of health.

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Original article

Psychopathological consequences of the COVID-19 pandemic on the mental health of children and adolescents worldwide

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Summary

The COVID-19 pandemic has had a massive impact on world's population, including children and adolescents. National containment, including lockdown and the main restriction measures such as closure of schools, educational institutions and areas of activity has led to deep changes in daily life and routine activities as well as bringing significant health, economic, financial and social consequences. The nature and extent of the effect on the mental health of children and adolescents depend on numerous vulnerability factors. In the present work we aim to address the mental health disorders induced by the COVID-19 pandemic in children and adolescents and subsequently its impact on the pre-existing neuropsychiatric disorders in the population of this age group. Finally, we report intervention strategies to deal with this situation and the advices of the experts.

The general framework

The COVID-19 pandemic has had a strong impact on the lives of the entire world population, including children and adolescents, in an unexpected way in history. There are more than 2.2 billion children in the world, representing about 28% of the population and those between the ages of 10 and 19 representing 16% overall [1]. Worldwide, the main ways of preventing COVID-19 infection have been isolation and social distancing [2]. Since January 2020, several countries have carried out regional and national containment measures or complete lockdowns. Main restriction measures were the closure of schools, educational institutions and areas of activity. According to UNESCO monitoring, more than 160 countries have implemented nationwide closures, involving more than 87% of the world's student population [3], leading to radical changes in daily life and routine activities [4,5], as well as bringing significant health, economic, financial and social consequences [6]. In addition, the huge pandemic induced changing of life-styles and the fear of contagion have had a negative effect on the lives of children and adolescents [6-11], together with long-term consequences for this section of the population [2], to a greater extent than for adults. The nature and extent of the effect of the COVID-19 pandemic on the mental health of children and adolescents depend on numerous vulnerability factors such as evolutionary age, level of education, special needs, pre-existing mental health conditions, economic disadvantage and quarantine of the child and/or parent for the prevention of contracting the infection.

The negative effects resulting from the pandemic situation have been detected even before the baby is born. During pregnancy, parents, especially pregnant mothers, may experience anxiety and depression [12] that could affect the health

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Conflict of interest
The Authors declare no conflict of interest.

of the unborn child [13]. A particular situation is that of women who have contracted COVID-19 infection during pregnancy. A recent study conducted in Turkey reported that 14.7% of women who had had a pregnancy marked by COVID-19 infection developed postpartum depression within 48 hours of birth and that the mother-baby bond in depressed women was more evident when compared to that of women who had not developed a mood disorder [14]. Furthermore, infection in pregnant woman often causes a mother-child separation after childbirth. A Chinese study [15] showed a link between separation days and an early developmental delay in many domains such as communication, coarse drive, problem-solving, personal-social and social-emotional development. In addition, although there was no evidence of a connection between mother-child separation and maternal mental disorders, the same study found that more than a fifth of patients had developed Post-Traumatic Stress Disorder (PTSD) or depressive disorder 3 months after childbirth or abortion.

Pandemic and lockdown in children and adolescents have had a major impact on emotional and social development. In particular, younger children (3-6 years) seem to have shown a greater chance of expressing symptoms of attachment and fear due to the possible infection in older family members (6-18 years). The latter, on the other hand, have easily developed problems of inattention, together with the attitude to request continuously information about COVID-19. Beyond these subtle distinctions, serious psychological conditions of increased irritability, inattention and separation anxiety have been highlighted in all children regardless of their age group [16], together with sleep disturbances, nightmares, poor appetite, insecurity and a sense of isolation [17].

Globally, pre-lockdown learning for both children and adolescents mainly involved interaction with teachers and peer groups. Restriction measures such as home confinement in children and adolescents is associated with uncertainty and anxiety related to the interruption of their education, physical activities and socialization opportunities [17]. The prolonged absence of a structured and organized setting, such as the school, resulted in routine changing, boredom and lack of innovative ideas to engage in the various academic and extracurricular activities. Some children have shown a reduction in mood tone due to the fact that they can no longer play outdoors, meet friends and engage in school activities [18-20]. They have also developed phenomena of attachment and dependence towards parents. These limitations have had immediate consequences on learning [21] and children may encounter difficulties in returning to school and re-establishing relationships with teachers and classmates, with the potential risk of a long-term negative effect on their overall psychological well-being [18]. Older teenagers and young people have experienced concern about the cancellation of exams, exchange programs, academic events [18] and their working future [22].

During the pandemic, the adolescent also saw an increase of shopping activities [23] and accumulation phenomena [24], as a survival mechanisms looking for security in material goods.

In addition, because of the restriction measure, an increase in internet and social media use has been recorded in children and adolescent, with the risk of compulsively use and addiction to the Internet, accessing questionable content and being more easily bullied or abused [25,26]. Moreover, during the lockdown, while schools were closed and legal and preventive services not fully functioning, children had experienced more possibilities of violence, abuse and harm caused by a possible hostile domestic environment [27]. Confinement could be a trigger for intra-family violence, as families have found themselves spending almost all of their days at home in a stressful situation that can cause emotional distress in parents and consequently less attention towards children, with a more punitive behaviour towards them. Several countries have reported an increase in domestic violence [28]. Women and girls have also reported to be more exposed to gender-based violence, including sexual violence [29].

Excessive internet and social media use seem to be related to depression, anxiety, psychological discomfort [30] and sleep problems [31].

Trends like poor physical activity and the tendency to an unhealthy diet, with the prevalence of ultra-processed foods, have been reported during the COVID-19 pandemic among the population of children and adolescents in many countries of the world [32].

As a mechanism of dealing with stress, some authors point out to the possibility risky behaviors such as drug abuse and dangerous sexual relationships [33]. The same can happen for the development of gambling addiction.

One in six children between the ages of 2 and 8 show neurological, behavioral or emotional development difficulties [34]. These children, suffering from autism, Attention Deficit Hyperactivity Disorder (ADHD), cerebral palsy, learning difficulties, developmental delays and other behavioral and emotional difficulties, have peculiar needs and, together with their families, have experienced major trouble during the pandemic and lockdowns.

Severe lockdown, fear of infection and related consequences have worsened symptoms even in patients with other psychiatric disorders. Adolescents with mental health problems are less able to tolerate a lockdown than their peers who are not affected by such pathologies [35]. The interruption of psychological and/or institutional assistance represent an important adverse factor. A survey involving 2111 adolescents with a history of psychiatric disorders in the UK reported that 83% agreed that the pandemic had worsened their disorders and that 26% had had difficulty accessing treatment and psychological support [36].

Social inequality has contributed to the risk of developing mental health problems. The pandemic and lockdowns have led to a global economic crisis, worsening pre-existing social inequality. An increasing number of poor families have lost their daily wages, developing frustration, feelings of helplessness, conflictuality and violence. As result,

children have become more vulnerable to depression, anxiety and suicide [17,37,38]. Finally, the closure of schools combined with economic crisis could expose children to the risk of child labour and exploitation, especially for those without parents or guardians [39].
During the lockdown, many schools offered students distance or online training courses. However, disadvantaged children could miss these opportunities, in particular if they cannot access to the online material to study. In disadvantaged families, girls, compared to boys, have no access to computer and related education platforms [40]. Due to this gender inequality, an increasing number of girls could drop out of school when normal teaching activities resume [25,41].
A good socio-economic level of the family is protective for the mental health of both parents and children [42].
Despite the numerous data on adults, data concerning on the development of psychiatric disorders in adolescents during economic crises are deficient. In adults periods of economic crisis are associated with an increase in suicides and depression, anxiety and addiction disorders [43]. During the economic crisis in Greece, teenagers reported more tensions and lack of harmony within the family [44].
COVID-19 infection occurs less frequently and is less aggressive in children and adolescents. However, cases of infection and related quarantine have been reported worldwide in minors. In addition, during the quarantine parents and children have been separated. Although quarantine measures are strongly necessary to deal with the pandemic, they can have significant negative psychological effects [45]. Children in isolation are at risk of developing mental health problems due to the lack of the relationship with the key figures during phases of growth [17,25]. They could develop feelings of sadness, anxiety, fear of parental death and isolation in the hospital. These findings colud have an important relevance on their psychological development [34,46,47]. Finally, the condition of isolation can even trigger the development of hallucinatory symptoms [48]. Death of one or both parents, as a frequent occurrence during this pandemic, especially in the most affected areas, represents a risk factor for depressive disorder in adolescents [49]. At the same time adolescents with a history of depression are exposed to prolonged psychological suffering in relation to the sudden loss of a parent [50,51], with the risk of an exacerbation of the pathology.
In conclusion, an alarming phenomenon is spreading , as the media are constantly reporting: a significant increase in self-harm practices and suicide attempts among young people [52].
In the following paragraphs, this paper examines the mental health disorders induced by the COVID-19 pandemic in children and adolescents and subsequently its impact on the pre-existing neuropsychiatric disorders in the population of this age group. Finally, we report intervention strategies to deal with this situation and the advices of the experts.

Pandemic-induced disorders

Sleep disorders

According to the first studies carried out on sleep disorders of preschoolers during the first phase of the COVID-19 pandemic, after a critical period corresponding to the first month, there is a decreased sleep quality, afterword there would be a stabilization of the night routine. However, sleep quality never match that of the pre-lockdown period [45].
Subsequent studies have revealed a significant increase in sleep disorders among young children [45].
A Chinese study [53] revealed a high prevalence of sleep problems in adolescents and young adults, particularly among high school and university students. The highest levels of insomnia were found in combination with anxiety, depression and pessimistic viewing of the pandemic.
Sleep disorders result as a relevant problem not to be underestimated during the current pandemic: they represent a risk factor for the development of mental illness in children and adolescents with neuropsychiatric disease are very vulnerable to as well [54].

Anxiety disorders and mood disorders

To date, depression and anxiety are the most common mental disorders in children and young people, with significant functional impairment and associated risk of suicide [55].
A recent Chinese study suggested an early increase in the prevalence of COVID-19-related issues, although the full impact is currently unknown [56]; the potential evolutions of this framework will be better assessed as events evolve.
During this pandemic many child and adolescent had to interrupt many of the activities they regularly and daily carried out, with the possibility of worsening depressive symptoms and strengthing the social withdrawal, anhedonia that represent the symptomatologic core of these disorders [55].
In addition, many of them are experiencing a new period of insecurity: concerns about the health and work of their relatives, issue of death, sudden separation from friends, and school closure [57]. In this context, parental figures play a fundamental role in guiding, protecting the youngest and giving physically and emotionally support. Therefore, stressful events of life can lead to emotional distress even in parents, resulting in less availability towards children [27].
A survey of 8079 Chinese teenagers aged 12-18 found a high prevalence of symptoms related to depression (43%), anxiety (37%), depression and anxiety combined (31%) [58].
In a Spanish sample of university students, a considerable proportion (34%) showed depressive symptoms during the first few weeks of confinement [57].
Based on the data currently available, an increase in the incidence of mood and anxiety disorders associated with the COVID-19 pandemic is expected.
Providing mental health care for children and young people

in the near future will be crucial. In recent years, different innovative approaches have spread among mental health services, such as Telemedicine and Telepsychiatry: randomised and controlled studies indicate that Internet-based care can be effective in treating young people with depression [59,60], in order to adapt the traditional elements of therapy to the new needs dictated by the pandemic situation. In addition, a strategy could be helping families and parents to identify distress situations and to propose new forms of creative activities for their children as an alternative to those precluded by the current safety regulations [55].

Post-traumatic stress disorder

In this pandemic, in all age groups an increased risk of developing PTSD has been recorded. A study of American families exposed to H1N1 and SARS-CoV viruses reported the onset of PTSD in 30% of children exposed to quarantine measures [61]. The prevalence of Post-Traumatic Stress Symptoms in the most affected areas of China a month after the COVID-19 outbreak was 7% [62].
These disorders have a potential impact on the mental health of children and adolescents, affecting the physiological development of the brain, acting at the level of the fronto-limbic circuits, and thus determining greater responsiveness to threats and weaker regulation of the emotions [63].
Childhood and adolescence are crucial periods of brain development and that is why the psychological effects of traumas related to the disasters experienced in early life can be long-lasting [64].
Confinement, indispensable for the control of the COVID-19 pandemic, represents an important stress factor in the lives of children and adolescents. It has led to a deterioration in daily routine, social restrictions, inability to attend school, and feeling uncertainty towards psychophysical well-being [65,66]. These negative elements resulted in a greater propensity of developing an Acute Stress Disorder, an Adjustment Disorder, or PTSD [66]. An increase in the incidence of the latter is supposed to develop in the long term, even if it is difficult to predict the size of this phenomenon [67].
In order to reduce the risk of developing these disorders, it is particularly important to promote the well-being and safety of children and adolescents, providing adequate reassurances and information, increasing moments of dialogue to improve understanding of what is happening and relieve anxiety. As the main caregivers, parents represent the figures who can better perform this function [68].

Effects of the pandemic on pre-existing neuropsychiatric disorders

special needs: autism spectrum disorders and attention deficit hyperactivity disorder

It could be particularly difficult for children with special needs to fully understand the changes due to the current pandemic. They may also have great difficulty in expressing their emotions, like fear, anxiety or frustration for the unknown [69].
In patients with Autism Spectrum Disorder (ASD), the pandemic, the suspension of treatment and lockdowns can have a very important impact [70]. Disruption of the life routine is particularly problematic for these subjects, since inflexible behaviors, habits and rituals are often very important symptoms. Children with ASD find significant difficulties to adapt to changes, becoming more anxious, agitated and exasperated. They could also show an increase of their behavioural problems and present acts of self-harm. Before the pandemic, thanks to special schools, they had learned to develop a routine to follow daylong [71,72]. Managing autistic children at home without the support of centers and specialized operators has represented a big challenge for parents [73], especially those with mental health disease [74], like depressive symptoms [75]. Moreover, parents often lack necessary professional skills. With the closure of special schools and day centres, these children no longer have access to material resources, interactions with peer groups or the opportunity of learning and developing important social and behavioral skills [47]. Aquired skills could also be declining [18]. Children with Specific Learning disorders often find difficulties in learning through online sessions [71]. The difficulties are also noticed in patients with high functioning autism, who easily acquire academic notions through forms of remote learning, but not social rules and norms [76]. It is therefore necessary that health professionals should take care of the mental and physical health of the children's parents providing them with useful advice for managing their children at home during the lockdown phases [77]. Subsequently, the development of innovative approaches to ensure continuity of care is essential, also providing programs in order to look after the needs of children and their families. The creation of a virtual helpline and health communities, such as hospitals and care centers, supported by a multidisciplinary team, should be considered [70].
An increase of ASD cases related to COVID-19 infection contracted during pregnancy has been hypothesized, as long as the COVID-19-induced reduction of IGF-1, which also seems to be involved in the pathogenesis of autism [78].
Children with ADHD struggle to conceive what is happening around them, trying to understand the input they receive from their caregivers. Moreover, an improvement in anxiety related to lower school tension and flexible hours seems to be observed in these patients [79], even if it is difficult for them to remain confined to a place and not touch things that could be infected. Being forced in quarantine, staying in one place, increases their hyperactivity and leads to the development of opposition/provocation attitudes and emotional explosions [79], and in some cases even to a reduction of mood tone [80]. Involving these children in significant activities became difficult [72]. Implementation of interventions focusing on monitoring parents' mental health and their education in managing the problems

caused by the limitations imposed by the pandemic on children with ADHD should be considered [72]. Early attempts in training group of tele-psychology are providing good results [81] and the use of tele-psychiatry also seems to be promising [82]. In this particular situation, the risks and benefits of drug therapy should also be carefully considered [72]. Some studies report significant difficulties with forms of remote learning [83]. According to others [80] hyperactivity symptoms would decrease as the hours of study in online mode increase: this represents a factor that has to be considered for the management of this problem both in this specific situation and in the future.
Again, an increase in the incidence of ADHD cases is expected, as long as the residual effects of COVID-19 disease could selectively affect brain regions underlying attention and motivation and which are insufficient in ADHD, as had already happened during the 1918 flu pandemic [84].

Obsessive-compulsive spectrum disorders

Obsessive Compulsive Disorder (OCD) is a psychiatric disorder characterized by unwanted thoughts, images or impulses and by mental acts or repetitive behaviors that occur in response to anxiety or unpleasant feelings. It affects about 0.5-3% of children and adolescents [85,86].
In children and adolescents, OCD often has an important impact on daily life [87] and is known to be a trigger for OCD symptoms or may contribute to a worsening of symptoms in people already affected [88,89].
Although there are studies that have clearly reported cases of adult patients with OCD who have had a worsening of symptomatology during the COVID-19 pandemic [23], the effects in young populations suffering from OCD have not been thoroughly examined
However, it is suspected that children with OCD among those with mental disorders are supposed to be the most affected by this pandemic. Due to obsessions and compulsions related to contamination, accumulation and somatic concern, they are expected to experience greater discomfort, also because cleaning is a key protective measure against the spread of COVID-19 [90].
However, the worsening of anxiety and depressive symptoms, as well as avoidance behaviors [91] and an increase in contamination obsessions and cleaning/ washing compulsions [92] have been documented.
The World Health Organization has suggested a number of possible preventive approaches for young people with OCD:

- limit or avoid over-exposure to issues related to the COVID-19 pandemic reported by the media or social environments in order to prevent fear and concern;
- encourage parental communication skills to address their children's concerns;
- anticipate the worsening of any symptoms of OCD;
- encourage adherence to treatments.

Eating disorders

It is well known that Eating Disorders (ED) represent a pathology that is able to determine important consequences not only at the psychiatric level, but also at the medical and psychosocial ones.
Anorexia nervosa, for example, is often complicated due to immunodeficiency caused by chronic malnutrition [93], which generally leads to greater vulnerability to infections. EDs affect about 2.8-10.5% of adolescents and young adults [94-97]. During the COVID-19 pandemic, in this category of patients and in particular in those with anxiety related to their state of health and the fear of "contamination", commonly found in this population [98], a worsening of the disorder in question was observed [99].
Anxiety can increase the difficulties in this group of patients in controlling their eating behavior [100].
A study conducted in Spain [101], reported that a considerable number of patients with ED and belonging to the National Health Service (41.9%) presented an exacerbation of symptomatology during lockdown. In particular, food restriction, excessive exercise, concerns about fear of weight gain and increased emotional symptoms have been reported.
The role of stressful events in inducing a worsening of symptomatology in patients with EA is well known [102] and it seems to be closely related to "intolerance towards uncertainty" that characterizes these patients [103] with a psycho-pathological function of primary importance during this pandemic. In addition, fears of losing control on various life situations, postulated by some as an etiological factor of these disorders, can also trigger an increase of weight control behaviors as a compensation mechanism [104].
In view of this, it is clear how critical a diagnosis and effective treatment are for these patients, especially during a delicate period like the COVID-19 pandemic. The use of Telemedicine web-based platforms could be a valuable therapeutic tool [105].

Induction or deterioration due to the pandemic of substance and behavioural addictions

During the pandemic, digital entertainment increased dramatically: among games and apps, the volume of downloads reached record levels [106,107].
Thanks to quarantine and staying at home, gaming not only represents a diversion but can also be used to cope with the psychological stress of the pandemic, thus being able to contribute to the risk of developing gaming disorders. In times of great distress such as a pandemic, people make efforts to find tools to deal with anxiety and stress, since the most popular activities commonly used to distract themselves from daily problems, such as participation in sporting events, celebrations and gatherings of various kinds have become prohibited or impassable. Given these limitations, gaming can be used as a way to escape

from unpleasant and painful emotions, shaping up as a short-term adaptive coping strategy. However, on the long term, instead of a habitual coping strategy at the expense of more beneficial alternatives for health, it can become maladaptive and expose to the risk of developing a gaming disorder or other problems [108]. School closures, the limitation of many activities and social interaction have particularly affected younger subjects, increasing and favoring the isolation in their rooms playing video games. By the way, teenagers should be adequately monitored in their gaming activities in front of a screen, particularly taking care of their physiological sleep-wake rhythm [109].

About the alcohol consumption, a study [110] conducted on adolescents and young adults in the weeks immediately before and after the Italian lockdown and in the same period of 2019 resulted indicative. Young people's hospital treatment was investigated for alcohol abuse, psychomotor agitation and other mental problems. The frequency of severe alcohol poisoning increased from 0.88% during the last part of the block to 11.3% after the end of the block. Comparing these figures with those of 2019, a big difference emerged, as alcohol poisoning in the previous year stood at 2.96%. The average blood alcohol level was 2.4 g/L and 32% of the study sample had a combined intake of alcohol and drugs, mainly cannabinoids. This may have been determined by an uncontrolled emotional response at the end of the lockdown, associated with the resumption of social interactions with peers. Based on this experience, the authors suggest that both pediatric and adult services should be prepared for a possible spike in alcohol-related emergencies.

Another study [111] highlights the patterns, contexts and correlations of substance use in adolescents during the COVID-19 pandemic. For most substances, the percentage of users has decreased; however, the frequency of alcohol and cannabis use has increased. Although the highest percentage of adolescents had consumed the substances alone (49.3%), many used them with peers through technology (31.6%) and, surprisingly, also "face to face" (23.6%). It has also been shown that the first mode was more used by adolescents with medium-high popularity among peers, while the latter by those with low self-declared popularity. This shows that adolescents are very sensitive to the influence of their peers in being approved, accepted or rejected [112,113].

Finally, it has been noticed that the highest percentage of adolescents was found to using substances alone (49.3%); this is a surprising fact since the use of substances during adolescence typically occurs among peers [114]. Using in solitude was found to be related with to the fear of contracting COVID-19 infection and to arousing of a depressive symptomatology as a result of the period of social isolation.

Expert advice and intervention strategies

Since every disorder and every patient represents a peculiar case, requiring specific and dedicated attention, several general considerations can be made regarding to what could be the best measures to be implemented in the immediate and future in order to ensure the psychological well-being of children and adolescents who are facing this pandemic with such a strong impact that on humanity. It is also essential to identify possible intervention strategies to ensure the continuity of care for those suffering from neuropsychiatric problems, whether or not this pandemic situation is posthumous.

With the aim of universal prevention and mental health promotion, International Organizations and advisory bodies have issued various guidelines that consider children's mental health needs during the COVID-19 pandemic. Parents were therefore advised to interact constructively with children by giving them explanations about the current pandemic, based on their level of maturity and their ability to understand the ongoing crisis, and leading them to understand their social responsibilities. Parents should also plan their children's homework, engage them in various household activities, educate them to follow hygiene habits and social distances, engage in indoor games and creative activities with them [115]. The activities of children and adolescents should include a well-structured home education which reproduces the regularity normally imposed by the school. In order to cope with the closure of schools, children should be encouraged to socialize with their friends and classmates through digital forums, under the supervision of an adult [116]. While it is true that the increase in "screen time", inevitable in this period, can be a harmful factor for health, it could also be a valuable tool. Typically associated with sedentary lifestyle, it could instead promote the practice of physical activity through platforms that perform online lessons, applications for exercises on mobile devices or video games that have a component of physical activity. The increase in the latter, together with the precaution of not spending the evening hours in front of the screen, could also have a beneficial effect on sleep (Nagata et al., 2020). If combined with correct eating habits, physical activity could also have positive effects on weight control, immune system and mental health [32].

It is therefore strongly recommended to promote balanced lifestyles, in particular sleep patterns (Guichard et al., 2020). The World Health Organization has published recommendations aimed at adolescents to help them cope with stress: identify normal emotional reactions, engage in dialogue and social exchange, maintain appropriate lifestyles and social contacts, avoid smoking, alcohol and other drugs, seek the help of necessary health workers, seek information from reliable sources, limit media exposure, develop strategies for emotional regulation [117].

Beyond prevention, it is crucial to plan strategies to improve access for children and adolescents to mental health services during and after the current crisis. It is equally important to support parents and monitor their mental health [118]. It is therefore necessary to establish a direct and digital collaborative network involving parents, teachers, pediatricians, community volunteers, the health system

and policy makers. Adapting the mental health system with integrated services designed for young people can be a big challenge [119]. In many countries, rehabilitation services and mental health centers for adolescents have closed or reduced their activity due to lockdown [47,118]. This inevitably led to a period of discontinuation of care, but it was also the stimulus to develop new therapeutic methodologies, such as psychiatry consultations, psychotherapy, psychoeducational interventions for children, adolescents and families, and rehabilitation programs promoted through the use of tele-psychiatry [8,120,121]. The first results obtained with the use of these therapeutic innovations are encouraging, it is now necessary to work to make them more and more functional and usable by everyone [122].

Finally, in this vast and complex scenario, we must not forget the most basic resources and possibilities for intervention: some studies [123] have highlighted the remarkable, healthy and certainly unexpected emotional balance of the new generations facing a sudden and unpredictable phenomenon capable of endangering life itself. While understanding the seriousness of the phenomenon, adolescents still seemed to express an excellent ability to manage situations of insecurity and to face unfavorable and adverse conditions by adapting to the new routine and finding alternative and innovative ways to meet their social and psychological needs. This capacity is an important resource, which should be enhanced by interventions aimed in promoting mental health during the current health emergency, in order to allow the acquisition, by children and adolescents, of a good degree of resilience [124] that allows their healthy psychological development in the years to come.

With regard to the containment of violence, social connection is an important strategy during periods of isolation [125]. In addition, information on services available locally, such as tele-help provided by healthcare professionals, must be promoted and made well known to everyone, to improve safety and connect people with relevant support service [126].

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COVID-19 pandemic and mental health of the elderly in the world

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Summary

Although the virus responsible for the coronavirus pandemic (COVID-19) can affect people of any age, the elderly are particularly vulnerable to serious infections and death [1], due to an age-related decline in the immune system and the increased likelihood of having more comorbidities than younger individuals [2]. Each Country has taken steps to preserve the mental health of the population during the COVID-19 pandemic. Social distancing, loneliness, forced isolation and fear of contracting the disease are all major challenges for the general population facing the spread of the epidemic. The role of technology is relevant and has emerged as an important factor in maintaining social connection and accessing mental health services, especially for the elderly. The psychiatrists of the elderly age need to recognize the importance of non-drug approaches, which are more effective than drug therapy in the treatment of chronic stress, anxiety and prolonged pain. Such approaches include: cognitive-behavioral therapy as well as the promotion of physical activity, increased connection, compassion training and commitment to spirituality as appropriate.

Introduction

Although the virus responsible for the coronavirus pandemic (COVID-19) can affect people of any age, the elderly are particularly vulnerable to serious infections and death [1], due to an age-related decline in the immune system and the increased likelihood of having more comorbidities than younger individuals [2].

The mental health of elderly population is also particularly under pressure: elderly, in fact, often feel frightened by news about the pandemic and aware that, if infected, they would not receive the same attention (e.g. intubation, bed in intensive care unit, etc.) of younger subjects.

Among the elderly, those with pre-existing psychiatric disorders need even more attention, due to the high risk of exacerbating mental health problems during the COVID-19 pandemic. To reduce the risk of disease transmission, certain preventive measures, such as quarantine and travel restriction, could trigger or worsen mental health in older people with psychiatric problems.

As a result of the quarantine and travel restriction, patients have had difficulty attending hospitals, which can trigger mental health problems, such as depression and anxiety. Additionally, older psychiatric patients usually suffer from chronic physical illnesses, such as cardiovascular disease and metabolic disease, which also require long-term medical reviews. Limited access to health services could lead to a deterioration of their physical illnesses and increase the risk of mental health problems.

Older people with mental health problems feel more fragile and vulnerable than before even as contact with caregivers is now minimized, with loneliness and

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neglect becoming a reality for many people. Controlling the regular intake of drug therapies can become problematic; Eating right and maintaining personal hygiene at a sufficient level can also be difficult. This could increase the sense of demoralization and despair in people. Some cases of suicide have been reported by the media [3].
The aim of this work is to review the scientific literature produced in these months of the pandemic to identify which specific problems have emerged and which answers have been formulated at an international level to address the problem of mental health in the elderly following the COVID-19 pandemic. Given the global nature of the pandemic, we focused on comparing the characteristic situations of different states.

Methods

A bibliographic search was carried out on the Pubmed database using the keywords "COVID-19", "mental health", "older adults". The results obtained were evaluated first by the abstract and then by the text for inclusion in the narrative review.

Results

In Italy, each region has established autonomous strategies to protect citizens and fight the disease. The frail elderly, and in particular those with mental health problems, were certainly the subjects who suffered most from the difficulties of the Italian health system. In the most severe months of the pandemic, the elderly who often stayed at home even when the first symptoms of the disease appeared and were in most cases entrusted to themselves or to the care of loved ones. The primary care system is often skipped and families have had to choose independently whether to call the emergency services, fearing to see the family member get on the ambulance and not be able to say goodbye before dying.
On the other hand, in the current situation, caregivers of older people with mental health problems are also exposed to stress: limited opportunities to offer the usual level of care; management of the most problematic food and cleaning; concerns about the possibility of contaminating an older adult who would not survive the disease; and, in a situation like the Italian one, many carers without a regular contract [4], now blocked from reaching the homes of the elderly they take care of.
As for the situation in the US, interesting results on the impact of the pandemic on mental health have emerged from some recently published studies. In August 2020, the Centers for Disease Control and Prevention (CDC) published a survey, conducted June 24-30, 2020, of 5,412 adults residing in the United States, noting that 933 participants aged 65 and over had reported significantly lower rates of anxiety disorder (6.2%), depressive disorder (5.8%), or trauma or stress disorder (TSRD) (9.2%) than participants in younger age groups. Elderly people, compared to other age groups, also reported lower rates of suicidal ideation in the previous 30 days [5].
A similar cross-sectional study involving 3,840 seniors between the ages of 18 and 80 found that older age (60-80 years) versus younger age (40-59 years) was associated with lower rates of anxiety, depression and post-traumatic stress disorder (PTSD).
A study involving 776 adults living in US and Canada who used a 7-day daily diary to monitor affection and stress found that older adults (> 60 years; n = 193), compared to younger adults (18-39 years; n = 330) and middle-aged adults (40-59 years; n = 253) esperienced fewer negative affects and more positive ones and reported positive daily events more often than younger groups, despite the similar level of perceived stress [6,7].
These findings could be explained by the fact that older adults tend to have less acute stress responsiveness and, in general, better emotional regulation and well-being than young adults. Furthermore, not all the USA had severe restrictions as Europe, leading to a lower emotional impact of the pandemic.
In Canada, the lockdown policy led to several changes in the mental health care system, also for the elderly. One of the most important changes was the expansion of the use of virtual assistance, via video or telephone. Indeed, Canada already had a well-developed telemedicine infrastructure. The social distancing policy led to the suspension of groups and daily programs for the elderly, while home care services continued, but with reduced frequency and with health workers wearing PPE. Access to pharmacies has not been hindered, with many pharmacies expanding their home delivery service. Mental health and caregiver organizations have expanded their online presence, with information on the potential effect of the pandemic and related public health measures on mental health [8,9].
In Spain, a country heavily affected by the first wave of the pandemic, an online survey was conducted from 29 March to 5 April 2020 investigating anxious symptoms (Hamilton Anxiety Scale), depressive symptoms (Beck Depression Inventory) and acute stress symptoms (Acute Stress Disorder Inventory) in a population over 60 years of age. The influence of various factors on mental health was assessed: gender differences, the condition of loneliness and the presence of interpersonal relationships, the presence of regular physical activity, the economic condition, and the use of anxiolytic drugs. The group of subjects aged 60 or older showed lower BDI and ASDI scores than the younger population. It has been hypothesized that a possible explanation may be the greater resilience of the elderly Spanish population, which lived through the post-Spanish civil war period (1939-1960) facing social and economic difficulties, and thus developing coping strategies that have also proved useful during the pandemic.
In the United Kingdom, to address the pandemic greater caution has been used in prescribing drugs potentially capable of precipitating respiratory depression, in

particular benzodiazepines and depot antipsychotics (LAI reduction/interruption, favoring oral administration and allowing greater flexibility also in terms of dosage); an increase in preventive pharmacological prescriptions in order to avoid continuous outpatient visits and therefore the possibility of becoming infected was also observed.

This strategy is feasible in the context in which UK psychiatrists operates, characterized by strong partnerships between primary and secondary care and good communication with patients and caregivers. Some Community Mental Health Teams (CMHTs) use mobile technologies such as Kardia (an electrocardiogram mobile app) to support rapid initiation of antipsychotic therapy in patients who need them, or Zaponex Treatment Access System (ZTAS), a clozapine monitoring service in the UK. COVID-19 led to a global shift in the working model of the National Health System (NHS) as a whole and of geriatric psychiatry as a specialty in the UK. A huge concern within the specialty is that of the possible future increase in the need for mental health by older people who have experienced the social isolation due to quarantine and / or hospitalization. Older people may have had little access to technology, which on the contrary has allowed younger members of society to alleviate their isolation to some extent.

In Sweden, the rules have been less restrictive for the general population than in other countries, but more restrictive special measures have been applied to the elderly population. This resulted also in verbal abuse and discrimination towards those who went outside breaking the rules, accused as possible threats to the Swedish infection control system. This created a real stigma for older people, causing negative consequences on the mental health of older people.

A Dutch study tested the hypothesis that lowering the frequency of social contacts, losing personal and normal sociability experiences may impair the perception of well-being in elderly people. This study recruited a population of 1,679 Danes between the ages of 65 and 102, which took part in an online survey lasting about 30 minutes, investigating the social impact of physical distancing. The aim was to quantify the population perception of those Weiss defines: (1) Emotional loneliness as the absence of a close or attachment figure; (2) Social isolation, which is, instead, the absence of strangers to form a social network; (3) Mental health problems defined by Berwick as feelings of demoralization, anxiety, depression, together with the perception of not being calm and happy. Four hypotheses have been formulated to explain the reduction of mental well-being in the study population: the first is the frequency reduction in social contacts, the second is that the pandemic caused loss of somebody or something personal, the third is the pandemic perception as psychological stress, also due to the strong media contribution, and the fourth is the reduced ability to implement coping strategies understood as acts and behaviours aimed at facing a stressful situation that weighs on or exceeds the subjects' resources. The survey results do not support the first hypothesis that the reduced frequency of social contacts impacted well-being. Several reasons may explain this lack of association: partner cohabitation or alternative contact methods such as social media. The second hypothesis about experiencing personal losses found support as various personal losses and an unmet need for (professional) help associated with increased social and emotional loneliness and mental health problems. In support of the third hypothesis, we observed that higher emotional loneliness, due to the perceived general threat, appears as a broader concept than the simple lack of meaningful social relationships. On the other hand, the fourth hypothesis was also rejected by the study. Many seniors have engaged in active behavioural coping strategies without improving the well-being during the COVID-19 pandemic compared to others. Finally, Turkey is among the states adopting the most restrictive measures, and this may also explain the death rates among the lowest worldwide. We should examine many aspects, including the Turkish population's demographic characteristics with a lower percentage of older people (8.2%) than the European average (17.2%). In Turkey, the young population respected the restrictive rules more than the elderly. Therefore, we wondered what the factors behind this behaviour might be, and we thought of a multifactorial genesis linked to cognitive decline, poor compliance, low attitude to change and perception of danger and/or low level of education.

Conclusions

During the pandemic, mental health should be one of the main topics on all nations' agendas, particularly if the home confinement is very long and the risks of the financial, familiar and relational problems aggravate a future now seen with serious concerns deep anxieties. Social distancing, loneliness, forced isolation and fear of contracting the disease are all major challenges for the general population facing the spread of the epidemic, but the risk of psychological consequences may be greater for the frail elderly [9]. Psychological support should be provided to everyone by NGOs and public services, actively establishing contacts with psychiatrists and other doctors. As far as possible, healthcare professionals should contact their patients and make continuity of care a reality. An active involvement appears imperative to oppose the feelings of abandonment and helplessness that COVID-19 is imposing on all community members, especially to the more fragile and older adults [10].

The role of technology is relevant and has emerged as an important factor in maintaining social connection and accessing mental health services, especially for the elderly. The already acting changes in health systems and societies were accelerated during pandemics and included increased flexible working models and the larger use of virtual and remote counselling via online platforms.

This could result in fewer home visits in the future, with potentially more efficient use of resources. Additionally, the psychiatrists of the elderly age need to recognize the importance of non-drug approaches, which are more effective than drug therapy in the treatment of chronic stress, anxiety and prolonged pain. Such approaches include: cognitive-behavioral therapy as well as the promotion of physical activity, increased connection, compassion training and commitment to spirituality as appropriate. These approaches have also been shown to improve adaptability, promote resilience, and reduce loneliness.

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The impact of the COVID-19 pandemic on healthcare workers

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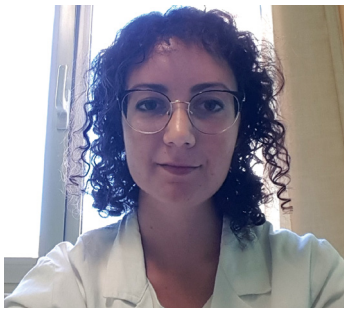

Rebecca Collevecchio

Summary

The pandemic of coronavirus disease (COVID-19) seriously impacts the health and well-being of healthcare professionals, who have been confronted with an unprecedented traumatic experience. In a battlefield-like scenario, facing uncertainty about resources, capabilities and risks, exposure to suffering, death and threats to their own safety, healthcare workers continued to work and care for patients. Literature reveals high levels of distress, anxiety, depression, insomnia and burnout among health professionals. It is, therefore, imperative to promote the implementation of supportive services for mental health and resilience of healthcare workers.

Multiple evidence indicates that the COVID-19 pandemic is having profound psychological and social effects. The psychological consequences of the pandemic are likely to persist for months and years to come. Numerous studies conducted over the past year indicate that COVID pandemic is associated with high levels of distress, anxiety, fear of infection, depression and insomnia in the general population but also among healthcare workers [1].

Although they are accustomed to witnessing traumatic situations and coping with illness and loss, during the COVID-19 pandemic the absence of effective treatments and the consequent restrictive policies implemented in many countries changed the lifestyle and working environment in which healthcare professionals operate. Many of them have experienced feelings of uncertainty, fear, sadness, anxiety, while continuing to care for patients [2].

The first studies about the impact of the coronavirus epidemic on health workers were developed in China [3] but, as the pandemic progressed, other countries began to publish cross-sectional studies aiming to assess the psychological responses of health professionals to the actual crisis [4-7].

Most studies report a high prevalence of anxiety among health workers (ranging from 30 to 70%) and depressive symptoms (with frequencies of 20 to 40%). The highest prevalence of anxiety and depressive symptoms was found among professionals who work in closest contact with infected patients, those with greater clinical responsibility and those who had tested positive for infection. The main cause of stress was found to be the fear of becoming infected or infecting colleagues and family members [2].

The highest exposure to COVID-19 occurs among frontline workers: emergency rooms, intensive care units, ambulance services and primary care staff. Fear of infection, especially among frontline workers, has also been associated with a lack of personal protective equipment [4,8,9].

A recent review of the literature shows a worsening of sleep quality and increased insomnia in healthcare workers compared to the general population; significantly higher levels of fear, depression, somatization and obsessive-compulsive symptoms, irritability, difficulty in managing emotions and stress. Increased levels of anxiety were particularly present in less experienced staff

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compared to professionals with more years of experience, who were more resilient in front of stressful situations [10]. The main cause of stress was the fear of becoming infected or to infect family members [2]. Specific personality traits, such as loneliness, previous mental disorders or the presence of physical disorders, have been linked to a higher risk of anxiety or depression [2,4,11]. Some studies indicate an increased risk for female health workers of both physical and mental health problems during the pandemic [11].

Younger professionals were found to be more concerned about contagion while older professionals were more concerned about the risk of death. Middle aged practitioners, on the other hand, appeared to be less likely to develop psychological symptoms. Fear of being infected, or of infecting their relatives, was higher among those healthcare workers with children. Excessive working hours was found to increase the risk of insomnia and emotional exhaustion [3,12,13]. Finally, the probability of developing symptoms of mental distress was correlated with the different impact of the pandemic in each geographic area and the stage of the epidemic at the time the studies were conducted: a higher incidence of COVID cases was correlated with higher prevalence of anxiety and depressive symptoms [8].

The 2003 MERS epidemic was associated with a 30% increase in suicides in people over 65 years of age; about 50% of hospitalised patients continued to suffer from anxiety and 29% of healthcare workers experienced symptoms of emotional distress [14]. Some consequences of the pandemic on the mental health of health workers, such as post-traumatic stress symptoms or alcohol and/or substance abuse, were also reported after months and years from the onset of SARS, mainly among those with high-risk exposure or who had been quarantined. Social support represented a key protective factor in preventing the onset of psychological distress, particularly during difficult times [13,15,16].

On the other hand, providing the wellbeing of healthcare workers, for example ensuring adequate time to take a break and get enough sleep, organizing resting areas both at work and outside (e.g. in dedicated hotels), helped to reduce the impact of physical and emotional exhaustion and also proved to be more effective than psychological support [17].

Many health workers have been affected by the virus, underwent quarantine or hospitalization. From the experiences of previous outbreaks, it has been found that quarantined health workers tend to feel more anxious, frustrated and helpless than those who do not work in the health sector [18]. In the last MERS and SARS outbreaks, numerous cases of infection and deaths among health workers have been reported and the same happened during the actual epidemic [19]. From the data of previous epidemics, we know that many health workers experienced feelings of worry, for themselves and their families, and painful experiences of fear and anxiety [20]. Professionals who worked closely with COVID-positive patients sought or thought about seeking psychological support significantly more frequently than those who did not work with COVID patients [21]. Nonetheless, healthcare workers continued to work and care for infected patients, even with symptoms of burnout, anxiety and depression [22].

It is of fundamental importance to recognize burnout, particularly in the healthcare sector, as it affects not only the workers but also the patients. Numerous studies have attempted to outline the risk factors and specific prevalence of burnout in different professions and to explore possible individual and institutional interventions to prevent and treat the symptoms of this diseases [23]. In May 2019, the 11th edition of the International Classification of Diseases (ICD-11) defined Burnout as "a syndrome resulting from chronic workplace stress that has not been successfully managed. It is characterized by three dimensions: feelings of exhaustion or depletion of energy, increased mental distance from one's work or feelings of negativism or cynicism about one's work, and reduced professional effectiveness" [24]. In October 2019, the National Academy of Sciences published a groundbreaking comprehensive report outlining the cost and consequences of Burnout among physicians [25].

In a multicentric cross-sectional study, a questionnaire was distributed to physicians, nurses, health care workers, administrative or managerial staff, and support staff in several public hospitals in Singapore [26]. All different health care professionals were found to be susceptible to high levels of Burnout during the current pandemic. Some demographic factors were found to be significantly associated with a higher incidence of Burnout, such as ethnicity and educational level. High levels of anxiety or depression, working shifts of more than eight hours per day and being assigned to a new job were found to be the factors most strongly correlated with higher scores on the Burnout subscale. The analysis did not show significant differences between different healthcare professionals [26]. Modifiable workplace factors to reduce the risk of Burnout include adequate training, avoiding long shifts and promoting safe working environments. Addressing Burnout among healthcare staff should be a priority, to support patient care efforts in the face of a prolonged pandemic [26].

A first attempt to account the psychological and physical impact of COVID-19 epidemic on healthcare workers in Italy is provided by a study, conducted on 1,153 healthcare professionals, who were asked to answer an online questionnaire that included the Maslach Burnout Inventory (MBI) and specific items to assess psychosomatic symptoms and the subjectively perceived health status [27]. Italian healthcare workers reported high levels of work-related psychological pressure, emotional burnout and somatic symptoms. In particular, increased irritability, changes in eating habits, difficulty in falling asleep and muscle tension were experienced very frequently by the majority of the respondents. Healthcare workers directly

involved in the care of COVID-19 patients were found to be at higher risk of developing COVID-related psychological consequences, in line with the results of other studies [6,28]. The levels of emotional exhaustion appeared to be superior than the normal ones and the percentage of workers with Burnout was significantly higher than in other Italian samples before the COVID-19 epidemic. This result needs attention, as emotional stress can be associated with long - lasting effects, including the developing of post-traumatic stress disorder, negatively affecting the level of efficiency in patients care [27].

Therapists usually know how to help others but are less effective in taking care of themselves. However, caring for ours own mental health is crucial in order to be able to do the best to help the patients [29]. In particular, in the field of mental health, the work of professionals (psychiatrists, psychologists, physicians and social workers) is always stressful and can trigger Burnout, but it is even more true during this pandemic period [30]. Occupational stress is detrimental to the psychological and emotional well-being of clinicians, and is related to anxiety, depression and anger, which end up resulting in a reduction of the quality of care provided to patients [29].

Intervention strategies

COVID-19 forced health workers to face unexpected, life-threatening experiences that found them unprepared. Although healthcare professionals are used to deal with the experiences of loss and trauma [31], a lot of new variables characterizing the actual pandemic (high morbidity and mortality rates, lack of protective equipment, fear of infection, the absence of an effective treatment or vaccine available in the short term, together with the restrictions implemented in most countries), changed the normal scenario in which they were accustomed to work [2].

Implementing rapid and effective intervention strategies to improve the mental and physical wellbeing of healthcare workers, is important not only for the present time. In fact, the experience with previous epidemics shows that distress can persist beyond the peak period of the pandemic. During the 2003 SARS outbreak, a study compared levels of perceived stress in health workers with high-risk versus low-risk exposure and found equal (high) levels in both groups [32]. At a one year follow-up and at the end of the epidemic, stress perception decreased in the low-risk group, but increased in the high-risk group, and high-risk workers had significantly higher depression scores [32]. Again from the SARS experience, in a two-years follow-up after the outbreak, it was found that health workers in hospitals that had treated patients with SARS had significantly higher levels of distress and PTSD when compared with health workers in hospitals in the same are, that had not treated patients with SARS [33]. We can therefore probably expect to see a decrease in stress perception in the low risk group, but an increase in the high risk group. We can therefore probably expect that the COVID-19-related psychological distress that has emerged in recent months in healthcare workers will continue to have an impact on their mental health in the years to come. It is also important to underline that there is an association between clinical-environmental stressors in the workplace and long-term cardiometabolic risk [34-36], and in turn, stress can affect health in direct (systemic inflammation, arterial damage, increased blood pressure) and indirect (maladaptive coping strategies such as substance use and poor sleep) ways. Furthermore, prolonged psychological distress and sleep deprivation may alter the physiological balance of the body's stress response system, thus contributing to an additional health risk [37].

From previous experience, we have learned that quarantined healthcare workers tend to feel more anxious, frustrated, powerless and isolated than non-healthcare workers [18]. Human contact and attachment are key factors to well-being, which is why punishments such as isolation in detention centers are considered a form of torture. Anxiety and stress may become more prevalent in individuals experiencing self-isolation or compulsory lockdown. For health professionals such as physicians and psychologists, who support physical health, mental health and well-being, the challenge may become greater during the pandemic phase as they are expected to navigate the crisis while continuing to provide their services in managing patients' physical and psychological health problems, either in person or with the help of virtual platforms [38].

A first level of care for health workers is therefore social support and logistical assistance, which has been shown to be effective in reducing levels of stress, anxiety and depression [39]. Participatory reorganization of the team, adequate debriefing time and the provision of personal protective equipment lead to a decrease in occupational stress. However, practical interventions are also needed to reduce health workers concerns for their loved ones by structuring, for example, childcare services, disinfection protocols, priority access to diagnostic tests for infection and personal protective equipment. It is also important to maintain breaks during work [40,41] and daily dietary and hygiene rules should be encouraged: sleep, physical activity, reducing exposure to screens and mass media, limiting consumption of alcohol, medication or drugs.

During the past SARS outbreak in 2003, meeting sessions with psychologists/psychiatrists proved particularly useful in providing support to health workers, even when psychological support was provided remotely (e.g. by telephone or Skype) when the priority objective was to have as few people as possible on site, thus exposed to infection [42].

Starting from these encouraging data, which have been transferred to the current reality of the COVID-19 pandemic, screening and psychological assistance services have been activated, practically ubiquitously at international level, specifically aimed at health workers

through the creation of dedicated 24/7 telephone lines or virtual platforms [41,43-45].

A different, innovative and structured strategy to support health workers in this rather homogeneous scenario regarding intervention strategies in this difficult historical period has been implemented by the Mount Sinai Hospital System in New York, which has over 40,000 employees across eight member hospitals. The Mount Sinai Center for Stress, Resilience, and Personal Growth (CSRPG), an innovative mental health and resilience-building service whose cornerstones are strong community involvement, screening for symptoms of mental distress, including through a dedicated app created ad hoc, resilience training seminars and, when necessary, specialized care services, was set up for its workers within a few weeks of the start of the pandemic [46].

Based on their previous experiences with disasters, including 11 September 2001 [4,7], it became clear that a long-term program focusing on mental health and especially resilience was not only useful, but necessary. Resilience has been defined in many ways, including the ability to successfully adapt to adversity, and although it has sometimes been seen as a character trait, there is evidence that it can be acquired through learning processes [48].

To this end, CSRPG developed a series of workshops on resilience, comprising an introductory session followed by a discussion and teaching sessions each focusing on one of the 10 resilience factors: Optimism and positive emotions, Coping with fears, Personal morality, Faith and spirituality, Social support, Resilience models to follow, Physical well-being, Cognitive fitness, Cognitive and emotional flexibility, Meaning and purpose [49].

These workshops, organized in several meetings per week, are held to coincide with common work shifts and break times so that it is easier for each operator to be present.

A relevant aspect concerns the long-term sustainability of this program, which will require ongoing federal support, particularly given the economic impact of the pandemic on health systems [50].

It is hoped that through these systematic efforts we will be able to maintain the mental and physical well-being of health workers and, consequently, a high level of care for patients. It will be time, in the years to come, to reveal the effectiveness of this intervention strategy.

A further intervention that stands out for its originality, in some ways also focusing on preventive strategies to promote resilience, at an organizational and personal level, is the result of a multidisciplinary collaboration between the Department of Anesthesiology, Psychiatry and Behavioral Sciences at the University of Minnesota Medical Center. The assumption is that the pandemic has catapulted health workers into a battlefield-like scenario, with health workers facing continued uncertainty about resources, capabilities and risks, exposure to suffering, death and threats to their own safety. A model of peer support, the Battle Buddies, has therefore been borrowed from the US Army. The US Army assigns a 'Battle Buddy' to each soldier, starting with basic training and throughout their military career, thus ensuring that no one is left behind, especially in combat. Each Battle Buddy is supposed to assist their partner in and out of combat. Through their daily contact, they can address and validate each other's professional and personal stressors that could potentially distract them from maintaining focus on their mission. Battle Buddies have reduced suicide rates in the military because, since each person observes their partner's actions over time, a Battle Buddy may be the first to notice a worsening of negative thoughts and feelings and be the first to push for help [51]. The method of 'stress inoculation', which was developed to manage exposure to psychological stress in disaster workers, has also been incorporated [52].

Overall, therefore, this approach is organized into three levels of support:

1. peer support: Battle Buddies (in a 1:1 ratio derived from US Army practice); peers are matched on the basis of demographics, job role, professional experience. The relationship is centered on listening to each other, validating experiences and providing feedback to each other;
2. support of the unit/department by a mental health specialist as a counsellor: during the sessions, the specialist assists the Battle Buddies in identifying their likely risk factors of stress/exposure and planning how they will manage these factors, through their personal resilience plan. Small group sessions are also offered according to the Anticipate-Plan-Deter model [53] on the importance of stress inoculation: cognitively and emotionally preparing healthcare staff for the specific stressors they will face. Briefly, in the Anticipation phase, healthcare staff identify the exact nature of the trauma and the cumulative stressors they will be exposed to, including their expected specific stress responses, such as sleep disturbance, fear and anxiety, grief, anger, etc. In the Planning phase, a personal resilience plan is developed, in which the specific stressors that individual caregivers perceive to be most difficult for them are identified, and a set of personalized coping strategies, responses and adaptive resources are prepared to address them. In the Dissuasion phase, they engage in effective implementation of the action plan and seek further help if needed. The comprehensive APD model was adopted in 2 rescue teams during the 2014-2015 Ebola outbreak in Africa and was found to be effective in protecting high-risk health workers from the negative psychological consequences of exposure to traumatic and cumulative stressors [53]. During the 2003 SARS outbreak in Canada, moreover, this stress adaptation model proved useful in naming and thus normalizing expected stress reactions (e.g., anxiety, worry) and in supporting staff to adapt rather than seeing these reactions as pathological [54];

3. individual support from the mental health specialist assigned to the unit/department, in the form of a confidential conversation, not a clinical meeting, and therefore without opening the medical file for health workers who are experiencing a high degree of stress and who require rapid and specialized access to additional resources. They are referred for further assessment and treatment to immediate mental health support with formal assessment and treatment if necessary [52].

Conclusions

Given the abundant evidence available in literature on the long-term effects of psychological stress on healthcare workers involved in pandemic emergencies, it becomes imperative to decisively and systematically address these risks and actively promote resilience in healthcare workers. The hope is that, by collecting data on the subject, the long-term benefits of prevention programs such as those outlined above, can be discovered in order to better cope with future emergency situations. Human beings are, by their nature, remarkably adaptable to change, and it is our belief that the majority of us will emerge stronger, wiser, with many new relationships and skills, and with a renewed sense of strength in our community. The positive side of all this, might be found in the "post-traumatic growth", a phenomenon reported in literature that takes the form of positive responses to significant adversity. Taking one last example from the 2003 SARS outbreak, health workers who worked during that outbreak subsequently reported improved relationships with family members and co-workers, had a renewed sense of priorities (including a new respect for their profession), and perceived a significant increase in altruism [55].

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Original article

Denial as a psychological process underlying non-compliance with public health recommendations for the prevention of COVID-19

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Summary

During the COVID-19 pandemic, phenomena such as denial, skepticism and conspiracy have occurred with great negative repercussions in the management of the pandemic itself. This work analyzes the presence of the psychic mechanism of denial as a common root underlying many individual and group behaviors, also considered the consequence of the difficulty of many individuals to manage the feelings and emotions caused by the pandemic. Psychoanalytic theory was the first to describe and study defense mechanisms such as denial and it can be useful not only for treating the distress of individuals or groups, but also for understanding the complex dynamics underlying denial social phenomena in order to implement better awareness and prevention strategies.

In the present work we aim to address the role of denial in relation to some phenomena that occurred during the COVID-19 pandemic, analyzing the implications on the experience of the individual and in the collective, with important repercussions in the management of the pandemic itself. In this historical moment, the problem of denial is becoming very evident in relation to the subjective experience and the overall management of global impact issues such as climate change, poverty, immigration, up to the issue of health. Very often we see skeptical positions, up to the frank contestation of the scientifically reliable and significant evidence that is proposed for discussion, while "alternative facts" are evoked in spite of all the available data. Undesiderable feelings related to various problems can trigger the implementation of defense mechanisms at various levels, by the single individual, by the community and sometimes by the institutions. The most frequently engaged defense is denial, a very common and characteristic reaction of human being.

The term "defense mechanism" refers to a mental operation that occurs mostly unconsciously and whose main function is to protect the individual from experiencing excessive anxiety. Any perceived stress can also be faced thanks to the use of psychological defense mechanisms. The concept of defense mechanism is formulated within the definition of psychic functioning as conceived by psychoanalytic theory, as a function of the Ego through which the Ego protects itself from excessive libidinal demands or from too intense instinctual experiences. Psychoanalytic theory defines a defense mechanism as an unconscious psychological process, with or without resulting behavior, which therefore aims to reduce or eliminate anxiety resulting from unacceptable or potentially harmful stimuli. In other words, defense mechanisms protect the mind, Self and/or Ego from perceived negative consequences and provide

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protection from a situation that cannot currently be coped with [1].

Freud was the first to theorize the overall function of different defense mechanisms in psychic development, but many subsequent authors, starting with Anna Freud [2], expanded this theory, thanks to the observation of what were the most common reactions not only in pathological field, but also towards common life situations, considered particularly painful or impossible to face. The defense mechanisms, as unconscious processes, have as their primary purpose to exclude from the conscience an experience perceived as unacceptable or dangerous for one's psychic stability. In most cases, different defense mechanisms can be employed to deal with the event. These are therefore fundamental functions, which cross the psychic life of the individual in a continuum between physiology and pathology, designed to promote a better adaptation of the individual to life. The defense mechanisms, therefore, should not be classified as necessarily pathological, since they are the basis of a normal psychic development. They can present themselves such as rigidity, inflexibility, intensity, inadequacy with respect to the psychic age and irreversibility that overall contribute to a maladaptive or frankly pathological condition.

Denial is one of most common defense mechanisms, defined as the refusal to recognize the existence of a real situation or the feelings associated with it [3]. If implemented qualitatively and quantitatively, denial can compromise a reality examination, up to the complete scotomization from the consciousness of events perceived as excessively conflictual or intolerable, undergoing a mental process without being aware of it. If on a pathological level there can be a serious impairment of contact with reality, such as in psychosis or serious trauma, even in individuals with a psychic functioning that is not frankly pathological it can produce negative consequences rather than the possibility of solving a problem, while protecting the subject from distress. It is therefore a mechanism that can become severely dysfunctional and maladaptive.

If the first and original formulation belongs to Freudian psychoanalytic theorization, there are a variety of other terms that are used in part as synonyms of denial. These are conceived within different theoretical frameworks, which however highlight above all the perceptual aspect that is, the inability to grasp the most disturbing element of a field of observation, in addition to banishing an uncomfortable thought from our awareness. In the 1960's it was theorized the so-called "spectator effect". The literature on this subject was stoked in part by the case of Kitty Genovese, a woman murdered in 1964 in New York, in which it was found that a substantial number of bystanders who had heard or seen "something" apparently "chose" not to intervene or report the event, thinking that the others would take care of it, or they came to the conclusion that no action was necessary, since not even the neighbors had reacted to it. Another concept formulated in those years was about a "psychic numbness", coined by Robert Jay Lifton to describe people traumatized by the atomic bombing of Hiroshima [4].

The reference to their way of being able to "turn off" emotions almost undergo a "paralysis of the mind", actually takes on the characteristics of the defense mechanism called Dissociation. However more subtle forms of psychic numbness can operate even in less catastrophic environments, as a means of shielding oneself from the "stimuli bombing" of everyday life. This is interesting for the purpose of this paper and highlights the complexity and heterogeneity of the psychic reactions that an individual can implement in the face of distressing situations. Another term often used in the literature is "disavowal", conceived as a disavowal of a responsibility or knowledge of something. Freud himself used the verb *verleugnen* to refer to the mental act of rejecting a perception as inconceivable and his translator James Strachey translated it just as "to disavow". In this concept, as can be deduced from Freud's work on Fetishism [5], it is highlighted that disavowal does not cancel the idea or perception in question, but rather its meaning and can therefore allow a sort of suspension of the function of judgment. This term has also been more widely and loosely used to indicate a refusal to think, a propensity to simply put aside what cannot be integrated, thus ignoring painful evidence [6].

The innovative contributions to psychoanalytic theory by post Freudian authors have helped to formulate a broader function of defense mechanisms. For example by highlighting how they are structured in the child's relationship with caregivers from the earliest stages of life, as argued by Melanie Klein [7-10], then undergoing an evolution in the course of psychic development, with gradual re-dimensioning of the most primitive mechanisms, which nevertheless never disappear and can return to have a greater influence even in situations of adult life that put the individual back in contact with ancient anguish.

A particularly important and innovative contribution to psychoanalytic theory must be acknowledged to Wilfred Bion, mainly for his discoveries deriving from the study of group dynamics, very central for the purposes of the present work. Among the various notations, Bion observes how a group can silently and collectively "accept" not to notice, as it were an elephant in the room or an emperor without clothes [11]. He differentiates "work groups" which are able to function more thoughtfully and creatively from "groups in basic assumptions" which are dominated by schizoid and paranoid mechanisms. Groups can work to share the radical distortion of reality and also its "scotomization", or the creation of a mental blind spot. A group, as postulated by Bion, can oscillate between such states, just as an individual can. Bion's work can be particularly useful in considering how institutions can also be constituted and maintained thanks to an operation based above all on "not seeing and not knowing" [11]. Throughout history, there have been numerous collective events that can be interpreted thanks to the knowledge of social groups functioning, from

the Holocaust to the most recent revelations on the sexual abuse of children by Catholic priests around the world.
Theodor Adorno also deserves special attention in light of his attempts to understand the psychology of the masses during fascism and to explore its combined state of knowing and not knowing. For example, while examining the catastrophe of interwar German history, Adorno imagined political subjects who did not truly believe what they claimed to believe, having to obey the idea that Jews were the enemy and that the "final solution" was therefore necessary. However, they knew it was false, so their performance was particularly frantic: "If they stop thinking for a second," Adorno wrote, "the whole performance would fall apart and they would panic" [12]. They behaved like actors in a play, psychologically unable to afford to do otherwise.
In this sense, the vocabulary suggested by the psychoanalyst John Steiner, who explores the psychological dynamics of "turning a blind eye", is useful. Steiner begins by reminding us of the many ways we can distort and misrepresent reality and uses the Oedipus myth to examine a situation where there is access to reality, but it is ignored for reasons which may then be susceptible to analytic work. "I refer to this mechanism as turning a blind eye," he writes, "because I think this conveys the right degree of ambiguity about how conscious or unconscious the knowledge is." He is interested in the theme of disavowal through the study of those ambiguous situations in which we can have a vague awareness of the choice not to look at the facts, but we proceed anyway to evade this awareness. These evasions can lead to a series of maneuvers "that deny or hide what happened by creating a cover". Steiner draws attention to the social and political implications of turning a blind eye and the dangers it could bring [13].
Also interesting is the well-known reading that Jacques Lacan gives of Edgar Allen Poe's short story *The Purloined Letter*. He focuses on an object, the epistle in question, placed in plain sight on a mantel where no one (except the detective) can see it [14]. Randomly leaving a secret object in an easily accessible place can be, in general, a great hiding place. Similarly, for historians, archives may be technically open, but no one bothered to look for them for reasons that could include, among other things, an unacknowledged discomfort to the consciousness related to what it might contain.
Returning to focus on denial, the contemporary meaning of the term, starting from the psychoanalytic conceptualization, also contains within itself what was already expressed in 1755 by Johnson, who in his dictionary had concentrated on the multifaceted meaning of the term, defining the denial "refusal" or even "abjuration", conceived as the opposite of a recognition of membership. Johnson also included an entry for the term "denier", which means contradictor, opponent, who holds the negation of a proposition, "one who does not possess or recognizes", or even "one who rejects" [15]. The word denial itself, therefore, can mean that something is not happening, does not exist, is not true or is not known.
Denial is therefore an unconscious constitutive mechanism of the individual and within certain limits it is functional to his adaptation to the relational environment, becoming part of the functioning of groups, institutions or even states [16].
We can therefore think that the mechanism of denial significantly intervenes in all situations when something is believed to be false. It can also mean disbelief in the existence or reality of a thing, disbelief about a natural, social or economic phenomenon ("climate deniers" or, to quote another phrase that became a common part of British political discourse in the 2010s, "deficit deniers").
According to a theoretical point of view aimed not so much at identifying deep psychic processes, as at the study of the operational strategies that an individual implements in relationships under stressful conditions, the concept of Coping appears to be important.
Lazarus (1966) hypothesizes that in a stressful situation an individual uses the strategy he perceives has the best chance of countering the threat and the one he feels most able to use. In other words, we use the coping strategy perceived as most vital in a specific situation [18]. According to the most recent guidelines, there are two distinct types of coping that the individual can employ: *problem-focused coping*, which actively or behaviorally alters the external person-environment relationship, and *emotion-focused coping,* which modifies the personal, internal or relational significance underlying the stressful event [17]. To these two broad categories, another defined *avoidance-focused* has been added, a proactive strategy, aimed at escaping from the stressful situation and which is therefore implemented before the event takes place. According to Aspinwall and Taylor [19], this latter strategy would have advantageous adaptive consequences as it minimizes the impact of stress, however it could lead to a long-term not very adaptive strategy, as the stressful event may not never be confronted.
Therefore, to better understand some of the phenomena that occurred during the COVID-19 pandemic, it is essential to focus the attention on the main stressor, and then subsequently analyze individual and collective responses. In fact, the current pandemic has worked as a multifactorial stressor, characterized by chronic anxiety and lack of control over the succession of unpredictable environmental events, which include not only the spread of the infection but also the psychological impact of quarantine measures. In January 2020, the Coronavirus had caused the deaths of over 2,221,949 people, with a total of 102,673,378 global cases, of which 2,541,783 in Italy [20]. In addition, necessary government countermeasures such as curfews and border closures have negatively impacted the economy, bringing personal restrictions and uncertainty into daily life. The context of the pandemic can then be seen as a breeding ground for amplified distress and anxiety [21].
United Nations Secretary António Guterres has called COVID-19 disease as the greatest threat since World War II [22]. In response to this we have observed a succession of very different reactions: initially the irrational hoarding

of assets, an increase in identification and support for one's national ingroup, resentment against outgroups (in particular those associated with COVID, such as non-EU citizens), attitudes of defense and justification of the political *status quo*, but also denial and phenomena such as increased belief in conspiracies linked to the virus and the outbreak of the pandemic. Despite the diversity of defense reactions presented, they all had in common the fact that they did not have the ability to reduce or diminish the threat posed by COVID-19, nor did they provide a remedy for it [23]. In fact, the denial process in the COVID-19 epidemic seems to have had a negative impact on the mental health of the individual, as well as implications for the community. A study conducted in Poland in the first week of the pandemic assessed the mental health of citizens by administering specific psychometric tests. The results shown that subjects with significant reduction in mental well-being used non-adaptive strategies, including denial [24]. Another study conducted in Japan during the second wave of the pandemic showed that 18.35% of the subjects analyzed were depressed and in particular the attention was paid to how subjects who implemented denial-based coping strategies had an increased vulnerability of developing depressive symptoms [25].

In the context of the COVID-19 pandemic, there has been a negative effect on the mental health of the entire world population and in particular health workers have had a considerable increase in the levels of psychological distress. In a recently published Case Series, we have the opportunity to observe the mechanism of reaction to the stressogenic stimulus by the individual, due to denial. It is described the case of a psychiatrist who, when the frequency of news about the virus increased, found it particularly difficult to accept this reality. In fact, it was too threatening and a moderate amount of anxiety aroused in him; it was therefore easier from a cognitive point of view to deny the existence of the virus, since this represented a real threat. This caused the psychiatrist to speak to colleagues about his lack of precautions, resulting in frustration and annoyance among other team members who could not understand why their colleague did not take this threat seriously [26].

On a collective level, of course, the psychic dynamics are much more complex and, as previously postulated, take into account the unconscious interaction between the individuals in the group. What is observable on a collective level can be characterized by a homologation of emotional and behavioral responses, which lead the group to function as a single subject. On the level of emotional expression we can observe a "Mutual induction" which, as Slavson notes [27,28], occurs above all in groups in which there is a certain cohesion and in which people can interstimulate each other, causing each to exacerbate the emotional intensity in the other subjects. This phenomenon is described as "Emotional contagion", a condition in which the emotional excesses of some stimulate similar emotional reactions in the other members of the group, by mutual identification.

The "Emotional contagion", defined by Hoffman as "global empathic distress", is that phenomenon attributable to various forms of immediate and instinctive emotional sharing, which occurs before a cognitive awareness can be achieved, therefore an automatic human reaction to an emotional stimulus expressed by a similar person, a direct and not vicarious emotional sharing [29]. To use a more popular terminology, in this phenomenon the emotions of others, positive or negative, become "viral" in a group of individuals, being able to influence their thoughts or actions. From a psychopathological point of view, emotional contagion is one of the possible phenomenal derivatives of unconscious group dynamics, but what is of absolute importance is its value in being able to determine group behavioral modifications in particular social contexts.

Even emotional contagion, like the psychic dynamics underlying it, represents a fundamental function for the human being, for its phylogenetic and ontogenetic development [29], an absolutely frequent and common phenomenon, which each of us experiments in his own life, easily identified in contexts such as the couple relationship, in the family, in peer groups where we know each other and live common and sharing experiences. However, it can oscillate towards frankly pathological polarities especially when the social group expands, going to include unknown people, to whom one is not linked by bonds of friendship or kinship. In this case the emotional contagion can become maladaptive and dangerous for both the group and the individual. The growing emotional current can favor more primordial or impulsive behaviors in the community, unreasonable and unmated and of which, by definition, we are little or not at all aware [30]. In the pandemic context, feelings such as anxiety and fear that we all know as negative feelings, can spread via social media as negative emotional sources capable of emotionally infecting people, immersed in an unfavorable climate and amplified by messages conveying adverse feelings [31]. It follows that when the level of anxiety rises excessively in people and groups, just as unconsciously one can be led to use defense mechanisms such as denial or minimization, with resulting maladaptive behaviors, such as even failing to take adequate protection measures [32], since the stressful object once denied no longer represents a danger.

Skepticism is also a phenomenon that is worth analyzing in this light, as it can be conceptualized as a derivative of the denial of disease severity, with the perception that the pandemic is exaggerated or invented. It is easy to see how such dynamics, once triggered, can pose a threat to public health, as people who do not perceive COVID-19 as a threat to their own health and the health of others can hinder efforts to reduce transmission of the disease, adopting high-risk behaviors and becoming a disease vector. Those who are unable to feel at risk of contracting a disease and denying it at various levels, in its existence

or in its consequences, to defend themselves from anguish cannot consider it as a serious threat to themselves and to others.

A recent study investigated, through a survey administered during the lockdown period, whether or not people skeptical of COVID-19 engaged in preventative behaviors, such as wearing a mask and reducing contact. The correlations between COVID-19 skepticism and political ideology, social norms on distancing, perceived risk, information-seeking behaviors and conspiracy theories was also assessed. At the time of data collection, conducted through a survey administered between May 5 and May 14, 2020 [33], COVID-19 cases in the United States totaled more than 1 million. Younger, healthier, and politically more conservative individuals were more likely to support claims of skepticism regarding COVID-19; People who reported greater skepticism found it hard to believe that those close to them could die from COVID-19 and therefore engaged less in preventative behaviors, including spending time in their home and wearing a face mask outside. Those who were more skeptical were also more likely to believe the conspiracy theory that China government had intentionally spread the virus.

Some researchers have studied in particular the phenomenon of conspiracy, analyzing some motivational drives [34], such as the socio-psychological satisfaction of individuals, epistemic motivations (understanding one's environment), existential (feeling safe and having the control) and social (maintaining positive images of oneself and one's group). In relation to the COVID-19 pandemic, it is also described how conspiracy theories manage to overcome people's existential problems by helping them to feel safe in their environment [35]. A conspiracy theory can be described as "a subset of false beliefs in which the ultimate cause of an event is believed to be due to a plot of multiple actors working together with a clear goal in mind, often illegally and secretly" [36]. Among the psychological factors positively associated with belief and adherence to conspiracy theories we find the perception of individual risk, anxiety, negative emotions with external blame attribution; among the negatively associated factors we find instead a greater perception of control and analytical thinking.

In light of this, it is clear that individuals are more likely to believe conspiracy theories when they feel anxious, helpless, or unable to control their emotions. Likewise, people who perceive the world as dangerous and uncontrollable can benefit by alleviating their anxiety through conspiracy theories; in fact the perceived risk is positively correlated to the beliefs in conspiracy theories. From a psychological perspective, believing in a conspiracy theory is one of the unconscious ways to reduce the level of anxiety and stress, particularly intense and unsustainable if caused by an important and collectively perceived external event, and COVID-19 is a perfect example of this. Conspiracy theories functionally provide very simple causal explanations for distressing events; in other words, they help to control the acute stress level and thus to instill order, a sense of control and predictability [37].

With regard to these phenomena it is obviously right to consider the type of society in which an individual finds himself, in order to better understand the collective dynamics: in this sense it is important to analyze, for example, the cultural factors that regulate relations with others. Western civilization, for example, tends to enhance individualism and the perception of a person's uniqueness and independence from others; conversely, in oriental cultures, such as China and Japan, the connection between individuals is instead greatly emphasized, giving great value to conformity and interdependence [30]. In this sense, a close collective cohesion can prove to be very useful in overcoming adversity: allying oneself around a "common cause" and accepting restrictions spontaneously or even under government induction can prove to be a healthy coping strategy, mitigating part of the anxiety experienced and achieve beneficial outcomes for the mental health of all [38].

The public health response of the United States, on the other hand, can in some ways be considered an example of how individualistic and disruptive behaviors, even connected to higher levels of personal denial, have not helped to overcome the COVID-19 problem. Numerous no mask, no vax movements and various conspiracy theories on the origins of the virus have flourished. Less than half of people in the United States initially heeded health recommendations to wear a face mask when out in public. The psychological dynamics that have triggered skepticism towards COVID-19 can be considered an important causal part of the reduction in the commitment to preventive behaviors [33]. The unscientific rhetoric based on denial and skepticism has dramatic consequences: while only 4% of the world's population resides in the United States, in September 2020 the United States accounted for 20% of COVID-19-related deaths worldwide, thus achieving less positive compared to many other wealthy nations [39].

A similar behavioral reaction, equally attributable to attitudes based on denial, occurred in Brazil, where the rapid spread of COVID-19 and the consequent dramatic health emergency had as its political scenery the denialist behaviors and choices of President Bolsonaro, as well as the uncoordinated actions between federal and local governments, which functioned as independent and opposing groups. The interruption, on 6 June 2020, of the explicit official communication of registered cases and deaths [40] also seems to have played a fundamental role in non-prudent behaviors, in a further impetus of denial of reality data.

Brazil, the United States and the United Kingdom initially showed a political model based on distraction and denial, with consequent negative effects on the management of the pandemic [41]. In fact, the distrust of scientific evidence and guidelines issued by the government is related to political affiliation, just as there is evidence of the fundamental role played by scientific denial on institutional

behaviors assumed in relation to a series of issues of collective interest, including climate change, hesitation about vaccines, hurricanes and, more recently, the risks related to COVID-19 [42].

"The USA's failure to contain COVID-19 has been spectacular from every angle. Looked at as a case of mass non-adherence to medical advice, however, it's unique in modern history. Never before have so many citizens had so much access to information and simultaneously protested public health recommendations with such full-throated denial of the medical facts", Austin Ratner and Nisarg Gandhi affirm in a paper published in the journal Lancet. Failure to contain this serious infection can therefore be seen as a case of mass failure to adhere to medical recommendations, a direct consequence of a psychological process of denying the medical evidence itself. The authors of the work published in the important scientific journal highlighted the need for a strong intervention in the field of public health that cannot fail to consider the unconscious psychological factors underlying the effectiveness or otherwise of the choices relating to the pandemic. The invitation is to exploit the insights provided by psychoanalytic theory to better understand the internal dynamics that regulate the adaptive responses implemented at the individual and societal level.

Psychoanalysis was the first to describe defense mechanisms as denial and thanks to its individual and group mental functioning model, which takes into account what is unconscious, but extremely powerful, can be set in motion in relation to deep anxieties, therefore represents a valid ally in attempting to solve the various problems that pile up the current pandemic scenario. This turns out to be of fundamental importance at a time when psychological denial has unfortunately been in the spotlight multiple times, marking a dramatic moment of public health crisis. Denial currently surrounds us ignoring the existence of such dynamics in these circumstances could be interpreted as another example of denial. In order to acquire greater containment and greater awareness, It is necessary to educate people to acknowledge their psychological structure and the resulting defenses, which work to remove danger and anxiety from consciousness and which can be difficult to contemplate. It follows that, although psychoanalysts cannot treat all cases of denial individually, they can educate health care professionals and government bodies about denial and work with them on an effective model of communication. Finally, active participation in care teams dealing with the public health crisis and global issues so strongly affected by dysfunctional defense mechanisms would be important [43].

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Delirium in COVID patients: recommendations for assessment and treatment

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Summary

COVID-19 patients, particularly those admitted to an Intensive Care Unit, are at high risk of Delirium due to the frequently observed concomitant presence of a series of factors which, taken together, constitute an increased risk factor. Factors thought to play a key role include: a direct action of the virus and state of inflammation on the Central Nervous System; secondary effects of organ failure; effect of sedative treatment; prolonged exposure to mechanical ventilation; prolonged immobilisation; environmental factors including social isolation and restricted interaction with relatives and healthcare operators. Bearing in mind the potential impact of delirium on clinical outcome, with an increased risk of death, appropriate prevention and management of this condition, particularly complex in COVID patients due to the frequently observed concomitant presence of numerous predisposing and precipitating factors, is fundamental.

Definition of delirium

Delirium is a severe neuropsychiatric syndrome characterised by an acute and fluctuating attention deficit. The condition develops in association with other cognitive or perceptual deficits as the direct physiological consequence of an ongoing medical condition, substance intoxication or withdrawal (substances of abuse or medications) or ingestion of prescribed medication, with symptoms manifested as a side effect of treatment. Delirium may be either *Acute* (duration from a few hours to a few days) or *Persistent* (duration of weeks or months) (Tabs. I, II).

Table I. DSM-5 criteria for delirium [1].

- A disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment)
- The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day
- An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception)
- The disturbances in Criteria A and C are not explained by another preexisting, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma
- There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e., due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies

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The Authors declare no conflict of interest.

Table II. Symptoms of delirium.

Hyperactive or hyperkinetic delirium	Psychomotor agitation, mood swings, illusions, hallucinations, delusions, increased response to external stimuli (e.g. light, noise), state of alert, signs of CNS activation (tachycardia, mydriasis, hypertension, sweating)
Hypoactive or bradykinetic delirium	Reduced psychomotor activity, reduced response to external stimuli, somnolence, lethargy
Mixed delirium	Fluctuating characteristics between the hyperkinetic and hypokinetic forms, with an at times "unpredictable" swing between lethargy and agitation

Prevalence

Delirium is very common in the elderly, in hospitalised patients, in patients in intensive or palliative care and in subjects affected by substance abuse. The risk is extremely high in elderly patients admitted to an intensive care unit.

- General population: from 1.2 to 14% (elderly population).
- Hospital population: 6-56%.
- Hospital population: post -surgery in 15-53% of elderly patients; in intensive care 70-87%.
- End-of-life patients: 83%.
- COVID-19 patients: 15% of hospitalised patients; up to 2/3 of patients admitted to intensive care.

How to prevent delirium

- Screen for delirium with periodic reassessment in at-risk subjects.
- Reduce the risk of onset of delirium by limiting known precipitating factors:
  - help the patient to achieve spatial and temporal reorientation;
  - facilitate interaction with relatives by means of phone calls or videocalls;
  - ensure that prescribed visual or hearing aids are used;
  - keep all transfers (room or ward transfers) to a minimum;
  - restrict the use of psychoactive drugs;
  - mobilise the patient as soon as possible;
  - ensure restorative sleep;
  - ensure adequate hydration and nutrition;
  - prevent constipation;
  - prevent urinary retention;
  - provide pain therapy;
  - maintain adequate oxygenation.
- Evidence has been provided relating to the use of melatonin in the prevention of delirium in patients in intensive care, leading to a proposed use of melatonin in COVID-19 patients [2].

Clinical assessment

Assess

- Vigilance, altered levels of awareness and attention, presence of cognitive disorders and fluctuation of symptomatology.
- Support assessments through use of rating scales (Confusion Assessment Method, CAM - Tab. III) [3].

Predisposing and precipitating factors for delirium

- Old age.
- Comorbidities.
- Severity of concomitant illness.
- Brain disorders (cognitive decline, dementia, stroke, Parkinson's disease).
- Cardiac disorders
- Endocranial disorders.
- Infections.
- Surgery.

Table III. The confusion assessment method (CAM) [3].

FEATURE 1: ACUTE ONSET OR FLUCTUATING COURSE
Is there evidence of an acute change in mental status from the patient's baseline? Did the abnormal behavior fluctuate during the day, that is, tend to come and go, or increase and decrease in severity?

FEATURE 2: INATTENTION
Did the patient have difficulty focusing attention, for example, being easily distractible, or having difficulty keeping track of what was being said?

FEATURE 3: DISORGANIZED THINKING
Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?

FEATURE 4: ALTERED LEVEL OF CONSCIOUSNESS
Overall, how would you rate this patient's level of consciousness?

0 = alert (normal); 1 = vigilant (hyperalert), lethargic (drowsy, easily aroused), stupor (difficult to arouse) or coma (unarousable).

The diagnosis of delirium requires the presence of features 1 and 2 and either 3 or 4.

- Sensory deficits (auditory and/or visual).
- History of delirium.
- Malnutrition.
- Dehydration.
- Electrolyte and metabolic imbalances (e.g., hypernatremia).
- Urinary retention.
- Catheterisation.
- Multidrug therapy.
- Ongoing treatment with sedatives, anticholinergics, cortisones, analgesics.
- Introduction of new medications.
- Hospitalisation (particularly if prolonged).
- Admittance to an intensive care unit.
- Prolonged mechanical ventilation.
- Immobility.
- Sleep deprivation.
- Isolation.
- Restricted interaction with relatives or healthcare workers whilst in hospital.
- Restraints.
- Pain.
- Frailty.

Drugs are divided into three categories with a score of 1 to 3 based on the level of cognitive effects: the overall anticholinergic burden is yielded by the algebraic sum of the scores obtained of the relevant drugs (Tab. IV).

Non-pharmacological management of delirium

- Treatment of underlying causes.
- Management of hydration and nutrition.
- Verification of the need for oxygen.
- Treatment of pain as required.
- Treatment of urinary retention.
- Treatment of constipation.
- Correction of any electrolyte imbalances and metabolic alterations.
- Ensure monitoring and continuous assessment of patient's condition.
- Where possible, accommodate the patient in the vicinity of the nurses' station to allow for frequent monitoring.
- If the patient habitually uses glasses or hearing aids, ensure these are used to restore normal sensorial input.
- Excessive exposure to sensory stimuli (lights, noise, voices) and total isolation of the patient's room should be avoided.
- Ensure natural daylight during the day and artificial lighting at night.
- Promote movement whenever possible: keep the patient active (walking, exercises in bed).
- Refrain from prescribing sedatives unless absolutely necessary.
- Assess and re-evaluate ongoing treatments featuring a potential to predispose to/precipitate delirium.
- Promote a 24h presence of relatives where possible, or alternatively, set up phone calls or videocalls with family members.
- Monitor staff attitudes (e.g. ensure patient is not mocked).
- When addressing the patient refer to him/her using their name and explain the procedures being carried out. Avoid discussions with colleagues using strictly scientific terminology to avoid generating persecutory ideas.
- Speak slowly and calmly using an easily understandable terminology.
- Facilitate orientation: ward staff and relatives should provide frequent stimuli both to help the patient in reorientation and in responding to his autonomous interactions.
- Use a calm and reassuring attitude when dealing with the patient.
- Reassure the patient during the period of symptom remission.

Table IV. Anticholinergic cognitive burden scale.

Score 1		Score 2	Score 3	
Alprazolam	Furosemid	Amantadine	Amitriptyline	Orphenadrine
Haloperidol	Fluvoxamine	Belladonna Alkaloids	Atropine	Oxybutynin
Atenolol	Hydrocortisone	Carbamazepine	Chlorpheniramine	Paroxetine
Bupropion	Isosorbide	Cyclobenzaprine	Chlorpromazine	Perphenazine
Captopril	Loperamide	Cyproheptadine	Clemastine	Promazine
Chlorthalidone	Metoprolol	Oxcarbazepine	Clomipramine	Prometazine
Quinidine	Morfin	Pethidine	Clozapine	Propantheline
Cimetidine	Nifedipine	Pimozide	Desipramine	Quetiapine
Chlorazepate	Prednisone		Diphenhydramine	Scopolamine
Codeine	Ranitidine		Flavoxate	Thioridazine
Colchicine	Risperidone		Hydroxizine	Tolterodine
Diazepam	Theophyilline		Imipramine	Trifluoperazine
Digoxin	Trazodone		Nortriptyline	Trihexyphenidyl
Dipyridamole	Triamterene		Olanzapine	Trimipramine
Disopyramide	Warfarin			
Fentanyl				

From Boustani et al., 2008, mod. [4].

- Protect the patient and others by removing dangerous objects from the room and securing the area occupied by the patient.
- Place temporal references (clock, calendar) within sight of the patient.
- Invite relatives to bring the patient's personal belongings from home and leave by the bed.

Pharmacological management of delirium

General principles

- Only resort to pharmacological treatment following the failure of non-pharmacological measures.
- Use the lowest possible drug dose.
- Antipsychotics (APs) should be preferred over benzodiazepines (BDZ) unless delirium tremens is suspected: bear in mind that the sole indication for use of BDZ as monotherapy is delirium related to alcohol withdrawal (delirium tremens); in other cases BDZ as monotherapy should be avoided, being associated with a deterioration of state of confusion.
- Bear in mind that APs, particularly those with a higher sedative effect, as well as the combination of several APs, may increase the risk of respiratory depression.
- Monotherapy is the option of choice.
- Response to treatment should be assessed in the short term.
- Reduce and/or suspend prescribed treatment shortly (a few days) after achieving response.

Pharmacological management of delirium in COVID-19 patients

The following pharmacological proposals are based on the guidelines for delirium and on the recent recommendations relating to the management of delirium in COVID-19 patients.

These suggestions may be updated at any time in line with the continuous updating of scientific evidence.

Wherever possible, all guidelines should be adapted to suit each individual case at the time a need for therapeutic intervention is manifested and in the specific context in which this requirement is determined (Tabs. V, VI).

Table V. Effective drugs for use in clinical practice.

Tiapride
• First generation antipsychotic belonging to the class of benzamides • Indications: Severe Chorea in Huntington's Disease, behavioural disorders with agitation and anxiety, acute and chronic alcoholism, behavioural deficits in the elderly • Good sedative effect, of use in cases of hyperkinetic delirium • May be used in patients taking Lopinavir/Ritonavir (Lo/Ri) • Metabolism: renal • Does not interfere with cytochromes implicated in the metabolism of Lo/Ri or commonly used antibiotics • Therapeutic range: 50-300 mg/day • Available formulations: 100 mg tablets and vials containing 100 mg/2 mL • Indicated for both IM (in the absence of clotting disorders) and IV use (in the case of malabsorption): Tiapride should be commenced at a dose of 100 mg IM to be given up to three times daily • Oral administration should be established as soon as possible: reference dose 50+50+100 mg/day at 8am, 4pm and 10pm, respectively • The risk of prolonged QTc interval should be assessed • Risk of arrhythmias, particularly in association with lopinavir, although relatively slight • Caution should be applied when administering to patients with low K+ and Mg+ (e.g. vomiting and diarrhoea) • SpO_2 should be monitored to prevent onset of respiratory depression
Dexmedetomidine
• Selective alpha-2 adrenoceptor agonist • Sedative, anxiolytic and analgesic effect • Indicated for use in sedating adult patients in Intensive Care Units requiring a relatively superficial degree of sedation (patient able to respond to verbal stimuli: score ranging from 0-3 on the Richmond Agitation-Sedation Scale) • Difficult to manage on a ward: indicated for use solely in a hospital setting by staff specialised in the management of patients in Intensive Care • Does not produce respiratory depression • May be used in the presence of renal failure • Caution should be applied when using in the presence of liver failure • Alterations to blood pressure resulting in both hypotension and hypertension and bradycardia are frequently observed (particular attention should be paid to interaction with beta blockers) • Metabolised by means of oxidation: CYP2A6, 2D6 and others are involved • Possibly inductor of CYP1A2, CYP2B6, CYP2C8, CYP2C9 and CYP3A4: numerous antivirals are eliminated by means of oxidation (3A4 and 2D6); accordingly, dexmedetomidine may reduce the concentration of antivirals if co-administered

Promazine

- Antipsychotic belonging to the class of phenothiazines
- Marked antihistaminic properties and pronounced sedative effect, weak anti-alpha-adrenergic and anticholinergic activity
- Posology ranging from 50 to 300 mg IM/day (evaluate the presence of possible contraindications due to clotting deficiencies)
- Good sedative effect with low cardiovascular risk
- Monitor the risk of respiratory depression
- Metabolised in the liver by CYP1A2, 2C19, 3A4 and 2D6
- Bear in mind that both Lopinavir/Ritonavir and chloroquine/hydroxychloroquine may increase the bioavailability of promazine: implications are fewer if promazine is used only in the short-term (3-4 days), also in view of the short half-life of promazine (6h)
- Absence of significant interactions with antibiotics having a prevalently renal metabolism (tazobactam, piperacillin and doxycycline, the latter having a 50% hepatic metabolism)
- Caution should be applied when administering in association with sulfamethoxazole, clarithromycin, azithromycin and trimethoprim (increased toxicity and/or increased QTc) (association to be avoided preferably)
- Assess the risk of prolongation of QTc
- Low risk of arrhythmias, even in association with Lopinavir
- Low risk of hypotension
- Monitor SpO_2 for risk of onset of respiratory depression (relative risk in the case of short-term administration)
- Monitor K+ and Mg+: particular attention should be paid to patients with low K+ and Mg+ levels

Haloperidol

- Highly potent antipsychotic belonging to the class of butyrophenones
- Half-life: 20-24 hours
- The most widely used drug in the treatment of delirium
- Low risk of respiratory depression: caution should be applied and patients should be monitored
- Lower antihistaminic and anticholinergic effects compared to promazine, but a weaker sedative effect
- Absence of active metabolites
- Does not induce hypotension
- May increase QTc interval: lower risk if administered orally
- Use should be limited in patients treated with chloroquine/hydroxychloroquine and several antibiotics due to the risk of prolonged QTc
- Lopinavir/ritonavir and chloroquine/hydroxychloroquine increase blood plasma levels of haloperidol
- May induce acute dystonia/neurodyslectic syndrome, together with a lowering of the epileptogenic threshold
- Best suited for oral administration (1-15 mg/day: initial dose 0.5-1 mg 3 times daily with a potential increase and adjustment in daily distribution based on symptom evolution)
- Vial formulations should only be used for IM, and not IV, administration due to the increased risk of prolongation of QTc interval and onset of torsades de pointes
- Compared to oral use, IM administration is linked to a higher degree of cardiac toxicity (torsades de pointes)
- 2mg and 5mg immediate release vials are available: initial dosage ranging from 2 to 5 mg which, in the case of non-response or partial response, may be repeated after one hour. Oral administration should be implemented as soon as possible
- Use of a reduced dose should be considered in elderly patients, on the basis of patient's general clinical condition
- Oral administration of a fixed daily dose (rather than "as needed") represents the ideal solution and should be continued up until several days following remission of symptoms and then gradually withdrawn

Aripiprazole

- Second generation antipsychotic
- Long half-life: 75 h
- Immediate release oral or IM formulation (9.75 mg per IM vial)
- Of use in treating hyperkinetic (IM formulation should be used preferably) and hypokinetic delirium
- Low antihistaminic activity
- No anticholinergic activity
- Low risk of arrhythmia
- Low risk of respiratory depression
- Low risk of interactions
- The risk of onset of akathisia should be taken into account
- Metabolised by CYP2D6 and 3A4: blood plasma levels may increase in the presence of CYP2D6 and 3A4 inhibitors (e.g., atazanavir, lopinavir/ritonavir and, to a lesser extent, chloroquine/hydroxychloroquine); when co-administration is required, lower doses of aripiprazole should be used
- For IM administration, in the absence of CYP2D6 and 3A4 inhibitors, the maximum dose corresponds to 3 vials/day at intervals of no less than 2 hours

▶

Quetiapine

- Second generation antipsychotic
- Half-life: 6-12 hours
- Only available in oral tablet form
- The risk of prolonged QTc interval should be considered
- In Europe, association with lopinavir/ritonavir is contraindicated due to the potent inhibitory effects exerted by the drug on CYP3A4, which metabolizes quetiapine, resulting in an increase of quetiapine levels; a decrease of quetiapine to 1/6th of the original dose is recommended in the US
- Latency of action potential exceeding 1 hour
- The risk of hypotension at doses exceeding 100 mg should be taken into account, particularly in elderly patients
- Standard dosage ranges from 25-200 mg/day in one or two daily administrations
- Olanzapine
- Second generation antipsychotic
- Half-life: 33 hours
- Oral or IM formulation
- Association with lopinavir/ritonavir determines a reduction in blood plasma levels of olanzapine, which may result in the need for an increased dose of the antipsychotic in the case of co-administration
- Elevated anticholinergic action should be taken into account
- Displays a good sedative action and rapid onset of action
- IM formulation should not be associated with BDZ
- Standard dosage ranges from 2.5 to 10 mg/day in one or two daily administrations

Risperidone

- Second generation antipsychotic
- Half-life: 24 hours
- The risk of EPS should be considered
- The risk of prolongation of the QTc interval should be considered, particularly in association with Atazanavir, Lopinavir/Ritonavir, Chloroquine and Hydroxychloroquine
- Association with atazanavir, lopinavir/ritonavir, chloroquine and hydroxychloroquine determines an increase in blood plasma levels of risperidone, resulting in a potential need to reduce the dose of the antipsychotic in the case of co-administration
- Standard dosage ranges from 1-4 mg/day in one or two daily administrations

Recommendations for the use of benzodiazepines

- They may induce respiratory depression due to a central (depression of bulbar respiratory centres) or peripheral action (myorelaxant action)
- Use should be avoided in patients at high risk of impaired respiratory performance
- Caution should be applied in patients treated with BDZ with a long half-life, even in the absence of dyspnoea, as the latter may develop rapidly
- If required, use molecules with a short half-life
- The association of midazolam and diazepam with atazanavir and lopinavir/ritonavir increases benzodiazepine levels, thus recommending use of a reduced dosage in relation to the risk of respiratory depression

IM: intramuscolar injection.

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Table VI. Drug interactions between psychotropic drugs commonly used in delirium and drugs used in COVID-19 patients.

	ATA	LPV/RIT	RDV	FAVI	CLO/ICLO	NITAZ	RBV	TCZ	ANTIBIOTICS
Haloperidol	↑HAL ♥	↑ HAL ♥	↔	↔	↑ HAL ♥	↔	↔	↔	♥ with SULF, TRIM, AZI and CLR
Promazine	♥	↑ PRO	↔	↔	↑ PRO ♥	↔	↔	↔	♥ with SULF, TRIM, AZI and CLR ↑toxicity of SULF
Aripiprazole	↑ ARI	↑ ARI	↔	↔	↔	↔	↔	↔	↑ ARI with CLR
Olanzapine	↔	↓ OLA	↔	↔	♥	↔	↔	↔	♥ with CLR
Quetiapine	↑ QTP ♥	↑ QTP ♥	↔	↔	♥	↔	↔	↔	♥ with AZI and CLR ↑ QUE with CLR
Risperidone	↑ RIS ♥	↑ RIS ♥	↔	↔	↑ RIS ♥	↔	↔	↔	♥ with SULF, TRIM, AZI and CLR
Lorazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔
Diazepam	↑ DIA	↑ DIA	↔	↔	↔	↔	↔	↔	↔
Midazolam parenteral	↑ MID	↑ MID	↔	↔	↔	↔	↔	↔	↔

ATV: atazanavir; LPV/RIT: lopinavir/litonavir; RDV: remdesivir; FAVI: favipiravir; CLQ/HCLQ: chloroquine/hydroxycloroquine; RBV: ribavirin; TCZ: tocilizumab; ALO: haloperidol; PRO: promazine; ARI: aripiprazole; OLA: olanzapine; QTP: quetiapine; RIS: risperidone; DIA: diazepam; MID: midazolam; SULF: sulfamethoxazole; TRIM: trimethoprim; AZI: azithromycin; CLR: clarithromycin; ↑: increased exposure of the co-medication; ↓: decreased exposure of the co-medication; ↔: no significant interactions; ♥ : increased risk of QTc prolongation (ECG monitoring is recommended).

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