UNIVERSITY
OF PAVIA

Scuola di Alta Formazione Dottorale
Dottorato di ricerca in:
Psychology, Neuroscience and Data Science
Coordinatore: Chiar.ma Prof. Gabriella Bottini

MENTAL HEALTH AND EMOTIONAL DISTRESS AMONG HEALTHCARE WORKERS DURING THE FIRST WAVE OF COVID-19 PANDEMIC IN ITALY

Relatore:
Chiar.ma Prof. Cristina Montomoli

Tesi di:
Dott.ssa Mariangela V. Puci

Anno accademico 2020/2021

Table of contents

Abbreviations

COVID-19	Coronavirus Disease-19
CoVs	Coronaviruses
CT	Computed tomography
EID	Emerging infectious disease
HCWs	Healthcare workers
ICU	Intensive Care Unit
ISS	Istituto Superiore di Sanità
LEA	Essential Levels of Assistance
MERS	Middle East respiratory syndrome
NPP	National Prevention Plan
PCR	Polymerase chain reaction
PPE	Personal Protective Equipment
REID	Re-emerging infectious disease
RRRs	Relative Risk Ratios
SARS	Severe Acute Respiratory Syndrome disease
TCS	Technical Scientific Committee
TCs	Therapeutic communities
WHO	World Health Organization

Abstract

Background: the novel coronavirus pandemic has had a considerable impact on public health all over the world causing global health crises, straining the resources of health systems and revealing their vulnerabilities with profound implications for health. Italy was one of the most affected countries, as the first European full-blown outbreak occurred there. The exposure of the Italian healthcare workers to COVID-19 may be an important risk factor for psychological distress and mental health.

Aim: to describe worries, sleep disturbances and risk perception of being infected among Italian Health Care Workers (HCWs) during the first wave of the pandemic.

Methods: a research protocol was prepared in order to be submitted to the reference Ethical committee. It reported the aim and the methods (data collection, statistical analysis, privacy etc.) of the study. The protocol has been prepared in accordance with the guidelines for observational studies (STROBE guidelines) and was developed by a multidisciplinary team including biostatisticians, psychiatrists and prevention technicians. A cross-sectional study – web based open survey was conducted. Data collection was carried out through an *ad hoc* questionnaire administered online using the Google platform "Form". The study population included physicians, nurses, medical staff (radiologic technologists, rehabilitation technicians, physiotherapists and midwives), healthcare support and administrative personnel working in hospitals, nursing homes and therapeutic communities in Italy during the first wave of the pandemic period (February–May 2020). Trainee students, who had not obtained the qualification yet at the time of the interview, could not participate in the study. Data were summarized by descriptive statistics. Multivariable logistic regression was implemented to identify factors associated with sleep disturbances. To explore factors associated with risk perception of being infected a multinomial logistic regression was performed. Statistical significance level was set at $p < 0.05$.

Results: respondents were 2103 but 2078 met the inclusion criteria. Females were 78.8% and mean age was 42.17±10.98. The highest percentage of respondents were physicians (40.75%) and nurses (32.15%), followed by medical (18.00%), healthcare support (4.50%) and administrative (4.60%) staff. In a score range between 0 (not worried) and 4 (very worried), our results showed that participants declared that they were worried about the Coronavirus infection with a median score of 3 (IQR 2-3). 16% reported having been infected with SARS-CoV-2, 56.96% of HCWs were worried about "The risk of infection for the surrounding people". 63.43% of the sample reported having sleep disturbances; at the beginning of the pandemic, 59.19% reported perceiving a high risk of being infected. About psychological aspects, 83.85% of HCWs perceived need for psychological support but only 9.38% received it.

Conclusion: the results concerning the high degree of worries and the presence of sleep disturbances firstly indicate that institutions need to be better prepared to deal with contingency plans, especially in the areas of mental health, workload and resource access. These fields in turn contain specific problems that cover other areas and affect HCWs. Our findings highlight the importance of psychological and psychiatric support services during the COVID-19 pandemic scenario. These services may be useful for health authorities and policy makers to ensure the psychological well-being of healthcare workers and to promote precautionary behaviors among them.

Chapter 1

Background

1.1 Emerging Infectious Diseases and Coronavirus: SARS-CoV, MERS-CoV and SARS-CoV-2

An emerging infectious disease (EID) is an infection that either first appeared in a population, or was already present but rapidly increased in incidence, or spread in a new geographical area [1,2]. Many EIDs are zoonotic.A zoonotic disease (i.e. zoonosis) can be transmitted naturally from animals to humans and vice versa [3]. Literature data show that ~60% of human infections are due to zoonosis in nature and - among these - more than 70% of pathogens derived from wildlife species [3,4]. Although contact with animals represents a direct exposure source, several indirect exposure routes can influence the transmission of pathogens.

The origin of EIDs is therefore significantly associated to environmental and sociocultural factors and can even be accelerated by human development (e.g. demographic changes)[5,6]; climate changes such as global warming can also modify the distribution of vectors allowing them to thrive in previously inhospitable areas [7]. Globalization and travels mainly play a key role in the spread of emerging and re-emerging infectious diseases (REIDs) by facilitating the presence of infection clusters which in turn favor virus transmission [8,9]. In this regard, it should be noted that less than twenty years ago the first epidemic outbreak of the 21st century due to SARS-CoV virus, known as Severe Acute Respiratory Syndrome disease (SARS) outbreak, occurred [10,11].

Unlike other diseases, EIDs are difficult to predict and they have the potential to lead to global outbreaks with disastrous consequences. For this reason, the World Health

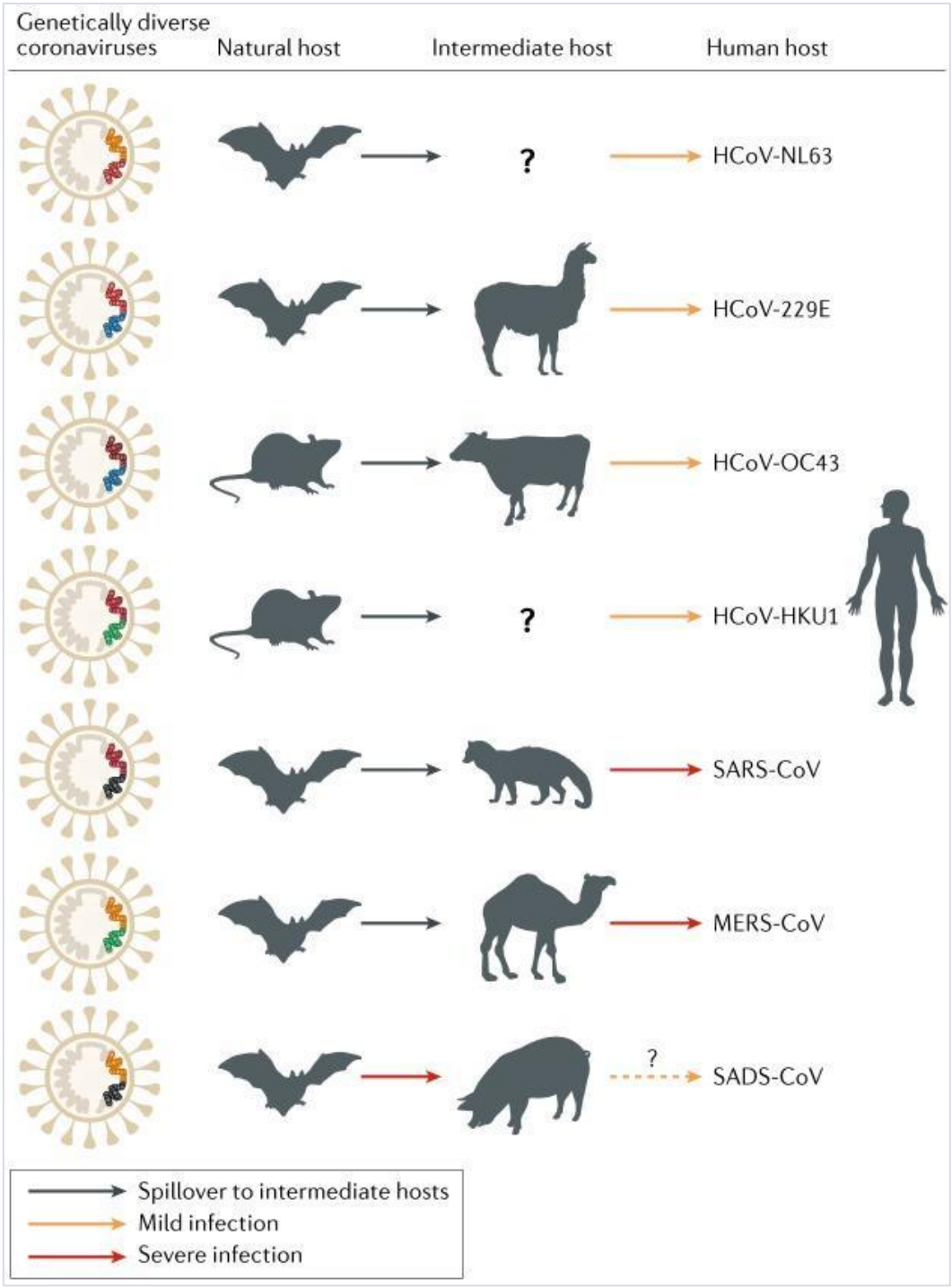
Organization (WHO) and other organizations have focused their attention on EIDs, especially recognizing the importance of surveillance systems, risk assessment and identification of these diseases.

Centers for Disease Control and Prevention (CDC) currently distinguish over 50 different emerging and re-emerging pathogens or diseases [9]. SARS, Ebola, HIV/AIDS, the Nipah virus encephalitis, avian and H1N1 influenza, the Middle East respiratory syndrome (MERS) coronavirus and the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are among the best-known EIDs [12,13]. Below there is a description of coronaviruses characteristics, as pathogens responsible for diseases that have had and are still having a significant impact worldwide.

Coronaviruses (CoVs) are the largest group of viruses belonging to the *Nidovirales* order. They are enveloped, non-segmented positive-sense RNA viruses [14]. Common characteristics of the *Nidovirales* order include genomic organization, high mutation rate, mechanisms of protein and RNA synthesis, virus-specific accessory genes and composition of the replicas machinery and virus particles [15]. According to CoVs' genomic structures and phylogenetic relationships it is possible to classify the four following genera: *Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus* [16].

Of these ones, the first couple of genera only infect mammals (they usually cause enteric disease in animals and respiratory illness in humans), while the other two infect birds but some of them can also infect mammals [17]. Until 2018, some recognized human CoVs all originated by animals (bats or rodents, Figure 1) were known [17,18], some of these causing minor infections while others being particularly serious or even lethal to humans, even though prior to the SARS outbreak their dangerousness was not fully evident [16].

Figure 1. *Animal origins of human coronaviruses. Retrieved from"Origin and evolution of pathogenic coronaviruses", 2019, Nature, by Cui J, Li F, Shi ZL.*



In the last decades, coronaviruses have represented a source of concern for global public health, since they have been the responsible agents for three worldwide large-scale outbreaks: SARS, Middle East respiratory syndrome (MERS) and, recently, COVID-19 (from SARS-CoV-2 agent) [19,20].

SARS-CoV (or SARS-CoV-1) was the first coronavirus known to cause SARS and it was isolated in a wildlife market in China (where bats and raccoon dogs were exposed for sale) in 2003 [21]. In regard to SARS, its outbreak was associated with atypical pneumonia originated in China in 2002 [17]. One year later it rapidly spread through international air traffic from China to South-East Asia, Europe and North America with a total of 8422 cases and 916 deaths and with a ~15% case fatality rate (CFR)[14,22–24]. The main clinical symptoms of SARS include fever, shortness of breath, headache, myalgia, chills, nausea, dry cough, dizziness, rhinorrhea, diarrhea and respiratory distress as a late symptom [21]. In most patients, pharmacological treatment included the use of antiviral drugs in combination with anti-inflammatory ones [25].

Ten years after SARS another highly pathogenic coronavirus emerged in Middle Eastern countries causing highly pathogenic respiratory infections, the MERS-CoV virus, which is phylogenetically related to bats and other animals such as camels (intermediate hosts in the virus transmission to humans) [17]. The major cases of MERS were reported by Saudi Arabia, even if the outbreak affected 27 countries of Middle East, Northeast Asia, North Africa, North America and Europe with 2562 confirmed cases and 881 deaths [26], the CFR being higher than SARS with a ~30% rate [14,21,26]. The outbreak was associated with cases of acute respiratory distress and acute kidney injury [27].

Clinical symptoms of SARS and MERS are similar and include fever, nausea, dry cough, chills, headache, runny nose, sore throat, abdominal pain etc.; however, disease manifestation can vary in severity degree from a lack of symptoms to a severe respiratory illness with rapid evolution to respiratory failure [21,28]. In regard to treatment, there are no effective antiviral drugs against MERS, which has contributed to the grave mortality rate [20]. For both SARS and MERS, there is still no effective understanding of the viral

pathogenesis. As a result, it is difficult to define a treatment that is usually based on the patients' clinical status, thus in these cases an early diagnosis is important [29].

Lastly, more recently a novel coronavirus, SARS-CoV-2, has caused the spread of the severe acute respiratory syndrome coronavirus (COVID-19) evolving in a pandemic outbreak of unprecedented scale. As the two coronaviruses mentioned above, Sars-CoV-2 is a member of *Betacoronavirus* and its genome sequence shares a ~50% identity with MERS-CoV and a ~80% identity with SARS-CoV [30]. Generally speaking, transmission of all human CoVs principally occurs through droplets, but transmission dynamics also include other sources such as aerosols, fecal-oral transmission and direct contact with contaminated surfaces [31].

SARS, MERS, and COVID-19 share many similarities in terms of transmission, clinical manifestation and management. Mainly, their challenge (and the EIDs' one) regards their impact on humans and their possible evolution into epidemics and pandemics, which represent a global threat.

Further information about COVID-19 epidemiology, transmission and features will be provided in more detail in the following paragraph.

1.2 COVID-19 outbreak and epidemiology

At the end of 2019, Sars-CoV-2 emerged in Wuhan (China) causing the outbreak of an epidemic associated with unusual pneumonia of unknown etiology. The first cluster of patients showed symptoms of viral pneumonia. Most of these cases were epidemiologically linked to a wildlife and seafood market in the center of Wuhan [32].

On December 31st 2019, the Wuhan Municipal Health Commission informed the WHO and publicly notified the unknown pneumonia outbreak. In January 2020, an independent team of Chinese scientists identified a *Betacoronavirus* - previously found in bats - as the causative agent of this emerging disease [33]. Later, further patients not linked to Wuhan were identified and within a month the virus spread all over the country with thousands of cases reported every day until mid-January. It must be remembered that the outbreak period coincided with the Chinese Lunar New Year, therefore intercity travelling favored the spread of the disease by providing clear evidence of human-to-human transmission [30].

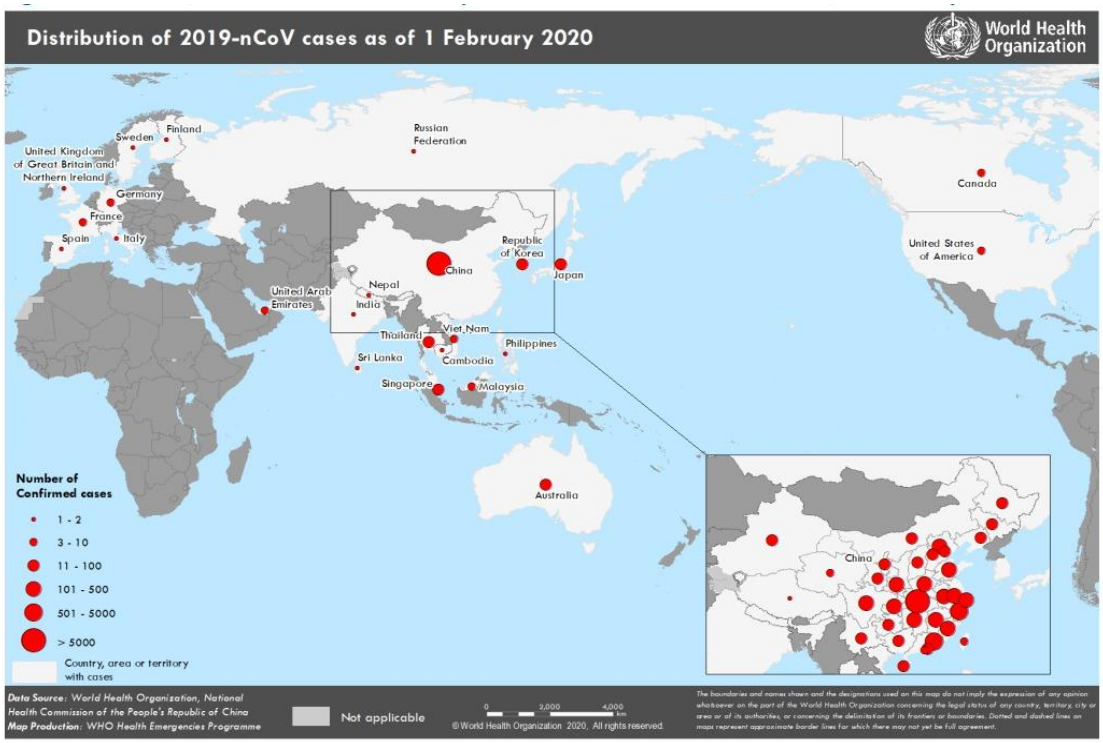
On January 30th 2020, the WHO declared the novel coronavirus outbreak as a public health emergency of international concern. In February it reached epidemic proportions with a rate of more than 3000 newly confirmed cases per day [21].

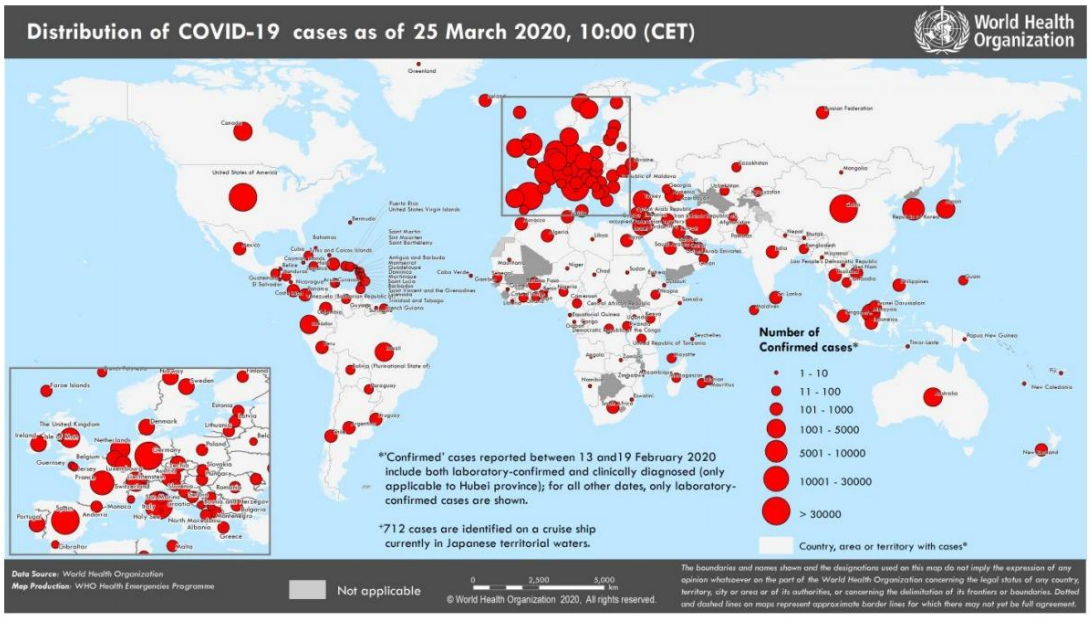
To cope with the epidemic, China implemented unprecedented public health measures, first sealing Wuhan off, which was therefore inaccessible. Over the next two weeks, all outdoor activities and gatherings were limited and public facilities were shut down in most cities. As a result of these measures, the daily number of new cases in China steadily declined. However, since late February, international travels allowed the virus to spread worldwide, so on March 11th 2020, with more than 118000 cases in 114 countries and 4291 deaths, the WHO officially declared the COVID-19 outbreak a pandemic [30,34]. During the following 10 months, more than 30 million cases were confirmed worldwide [30]. Figure 2 shows the timeline of the key events of the pandemic since December 2020.

Figure 2. *Timeline of the key events of the COVID-19 outbreak. Retrieved from "Characteristics of SARS-CoV-2 and COVID-19", 2020, Nature, by Ben Hu, Hua Guo, Peng Zhou & Zheng-Li Shi.*

In Europe, the first few cases have been detected in Spain, France, Germany and in Italy, which was one of the most affected countries with the first European outbreak occurring on February 22nd 2020 [35]. In Italy, the first two cases were identified when a couple of tourists from Wuhan arrived in Milan (on January 23rd) and thereafter traveled to Rome, where they were admitted to the Spallanzani Hospital with Coronavirus symptoms. After these two confirmed cases, Italy declared the state of emergency [36]. On February 20th in Lombardy there was a hospitalization case for atypical pneumonia later confirmed as COVID-19 (Patient 1 from Codogno). The next day, thirty-six cases occurred in the same region, thus initiating one of the largest COVID-19 clusters, the Italian one [37]. In order to better understand the rapid spread of the virus, it must be highlighted that on February 1st there were 11953 global confirmed cases of which 132 outside China (in Italy there were still 2 cases); while on March 25th the confirmed cases were 413467; of these, 69176 occurred in Italy, and deaths were 18433 [38,39]. This case increase is clearly visible in Figure 3.

Figure 3.*Distribution of COVID-19 cases as of February 1st, 2020 and as of March 25th, 2020. Retrieved from "Novel Coronavirus (2019-nCoV) Situation Report – 12 and Coronavirus disease 2019 (COVID-19) Situation Report – 65" Data Source WHO.*





On May 6th 2020 (immediately after the date of the gradual easing of Italy's lockdown), according to the official data reported by the Istituto Superiore di Sanità (ISS), the confirmed cases in Italy were 212532 with 27402 deaths and 23718 confirmed cases referred to healthcare workers[1] (HCWs) (which clearly indicates the high risk of infection in hospitals and healthcare facilities)[40].

In the initial period, in accordance with the data from Wuhan the CFR ranged from 4% to 11%. In April 2020, the CFR in Italy was 12.73 higher than in China (CFR 4.01) and in other countries and lower only if compared to the CFR in France (CFR 15.23). Although highly contagious, the COVID-19 CFR appears to be lower compared to other previous Coronaviruses outbreaks (SARS and MERS) but higher compared to influenza [41,42]. In the early phase of the pandemic, in China the basic reproduction number (R_0) for COVID-19 ranged from 2.2 to 2.7 while in Italy it was 3.10 [41,43].

It must be remembered that R_0 is an epidemiological measure widely used to assess the contagiousness of infectious agents and it refers to the number of secondary infections resulting from a single primary one. An R_0 value less than one means that an infected subject can infect less than one person [43]. The CFR and the R_0 can be both calculated by means of different methods, so they may differ according to regions and countries.

Focusing on Italy, data about the epidemic curve showed that the plateau phase began on March 22nd (one month after the epidemic onset) and ended on April 8th with a duration of 17 days and an increasing period of 29 days (it must be remembered that in a plateau phase the incidence is stable) [41]. Epi curve information is important as it allows to visualize over the time the disease progression during an outbreak. As better described below, the epidemiological measures indicated above may also vary according to clinical factors and prevention/restrictive actions, especially in cases of mortality.

[1]https://www.epicentro.iss.it/en/coronavirus/bollettino/Infografica_6maggio%20ENG.pdf, last accessed August 30th, 2021.

1.2.1 Clinical features and treatment

The COVID-19 incubation period was ~5 days, although most people showed disease signs after a period of 1-14 days. Dyspnea and pneumonia developed within a median time of 8 days after the onset, while critical disease and death occurred at ~16 days [30]. In survivors, the longest median viral shedding was 37 days and the median duration was 20 days [41].

Infection severity varied from asymptomatic infection to critical disease. Classification of clinical severity included five groups ranging from "asymptomatic" to "critical infection". The asymptomatic infection occurs when the PCR test is positive but there are no clinical symptoms; asymptomatic subjects (more frequently young people) had a significant role in the transmission mechanisms since they could cause family clusters, especially in the case of pediatric patients. Other levels of infections are: mild (absence of pneumonia and presence of symptoms of acute upper respiratory tract infection); moderate (presence of pneumonia, fever and cough); severe (hypoxemia, oxygen saturation <92%, cyanosis and dyspnea within around one week) and critical (presence of acute respiratory distress syndrome or respiratory failure, multiple organ dysfunction and shock) [41].

Median age of infection was ~50 years; symptoms included fever, myalgia, cough, dyspnea, fatigue, sore throat, runny nose, sneezing and other symptoms related to viral pneumonia and upper respiratory tract infection. Although all age groups were susceptible to be infected, clinical manifestation differs according to age. Most children and young subjects showed only mild disease without pneumonia, while in advanced age patients the evolution of the disease can be quick and the median survival time can be as little as five days. Generally speaking, men over sixty years of age with co-morbidities are more likely to require hospitalization, have multiple organ failure or even die [30,41,44].

Risk factors associated with COVID-19 death were age >65 years and co-morbidities such as diabetes, cardiovascular and respiratory diseases, hypertension, cancer and chronic renal failure; moreover, the risk was lower in pregnant women without evidence of vertical

transmission, even though in the minority of cases literature data show that infected mothers can transmit severe acute respiratory syndrome [21,30,45]. In addition to this, during the first pandemic wave there were more hospitalized patients with a high viral load (source of nosocomial transmission) and the availability of personal protective equipment (PPE) was scarce. These factors have certainly facilitated the virus transmission. In order to make a diagnosis, the gold standard is represented by the detection of SARS-CoV-2 nucleic acid by means of throat and nasopharyngeal swabs and serological test. In some cases, these were associated with a chest-computed tomography (CT) to confirm the diagnosis (CT on positive patients showed common features). In the initial period a specific vaccine or treatment against SARS-CoV-2 was not available, so adopted therapies were mainly based on the use of antiviral drugs and primarily aimed at treating symptoms [30].

1.3 Implications for the Health Care System and Healthcare workers

The novel coronavirus pandemic has generated global health crises, straining the resources of health systems and revealing their vulnerabilities with profound implications for health. Implementation of restriction measures and fear of being infected in health facilities have therefore caused a reduction in the use of health services and have unfavorably affected clinical decision-making, not only in the current pandemic but also in other previous outbreaks [46–48].

During the first COVID-19 wave, global healthcare systems were overwhelmed with potentially infectious patients. As a result, services such as physical exams, elective and preventive visits, outpatient services, non-urgent patient visits were limited or even cancelled in order to allow a reallocation of resources for urgent care of COVID-19 patients [44]. In the first pandemic phase all the affected countries had a critical shortage of resources, PPE and ventilators, the last ones being essential given the severity of the respiratory disease at the time of the outbreak, when infected patients showed respiratory complications requiring hospitalization in ICU [49–51].

In this regard, at the beginning of the Italian plateau phase on March 22nd, in Italy 18454 patients were weekly admitted in hospital for COVID-19 (Figure 4). In addition, at the same time Italy was the country with the highest number of patients in ICU (n=3009) (Figure 5).

It should also be noted that at the beginning of the pandemic not all the healthcare settings were prepared to manage infectious diseases; this, together with the lack of epidemiological knowledge about COVID-19 and the unexpected incidence of the disease, did not allow to implement effective and timely interventions. Therefore, the magnitude of the pandemic's impact on the healthcare system varied significantly according to place, type of healthcare facility and service, thus intensifying existing inequalities in health systems [47].

Figure 4. *Number of COVID-19 patient weekly admitted in hospital as of March22nd 2020 in the world. Retrieved from "Our world in data".*

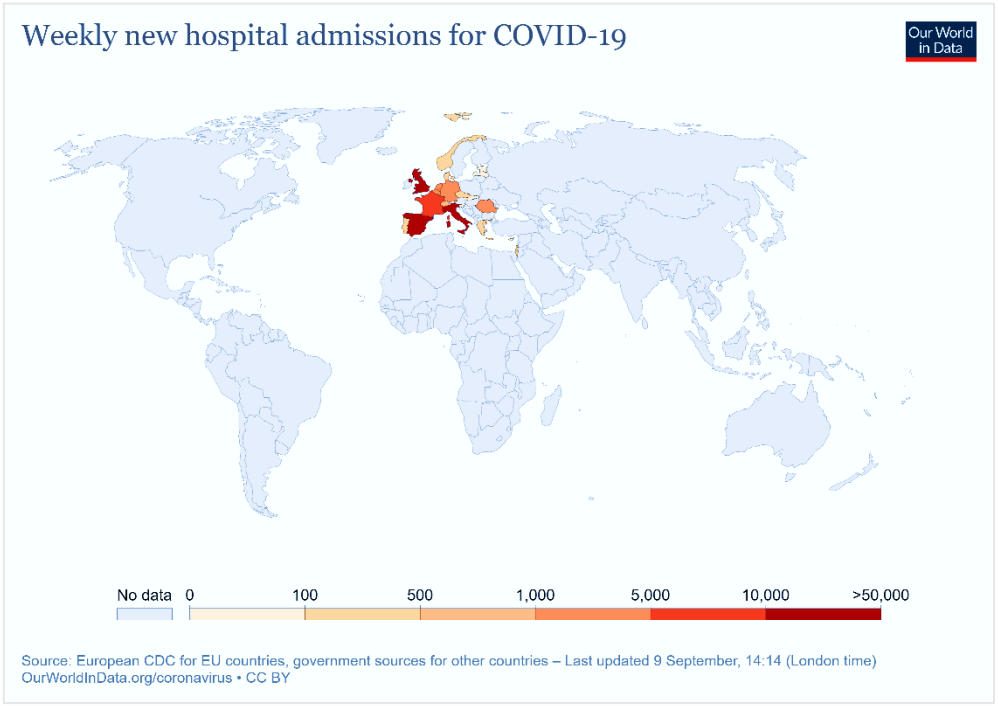
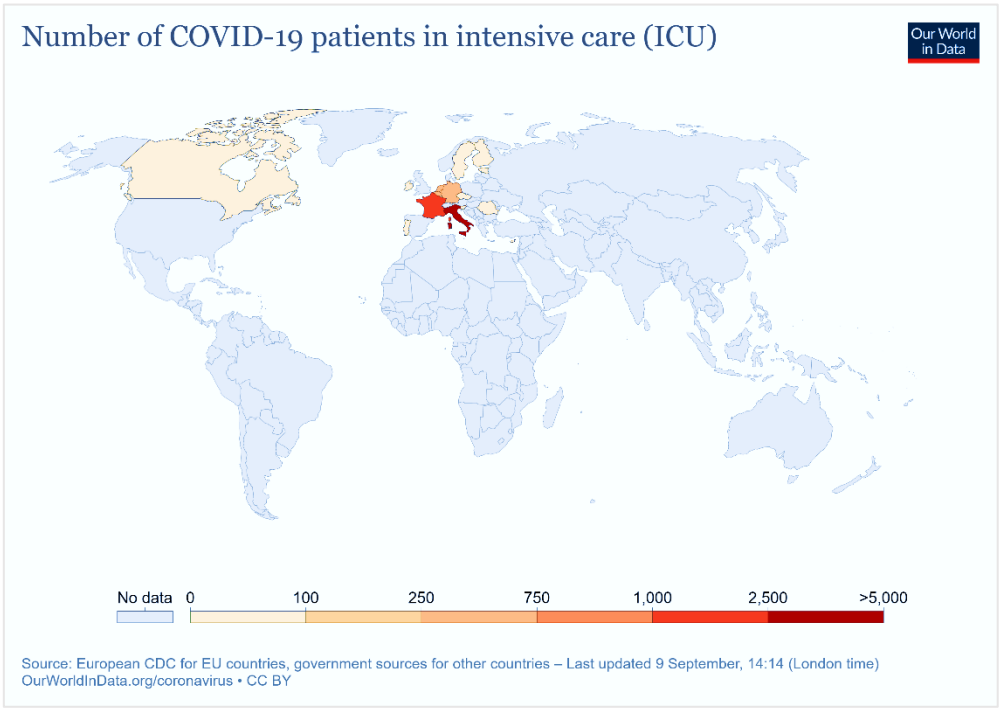


Figure 5. *Number of COVID-19 patient in ICU as of March22nd 2020in the world. Retrieved from "Our world in data".*



In this climate of persistent challenges, in order to mitigate the COVID-19 spread health systems worldwide considered alternative channels to provide services. Among these, telemedicine certainly had the potential to control disease and clinical case management [52]. In a pandemic scenario, several benefits may result from the use of telemedicine; the most evident is clearly the minimization of the risk of direct infection transmission [53]. Telemedicine is also useful in services without direct interaction between patient and health professional (i.e. psychological services); other benefits are related to the reduction of resources in health centers, direct access to caregivers, etc. [54]. Although patients are willing to use telemedicine, physicians highlighted the existence of some barriers to its use due to issues connected with privacy, safety, technical and clinical quality [52,55].

Even if the pandemic effect on medical care for conditions other than COVID-19 has been difficult to quantify, as described below, it has affected several medical practice areas. In the case of primary care, centers worldwide switched to remote consultations with *ad hoc* in-person medical visits. Primary care acts as a health system gateway and through management, monitoring and follow-up promotes the achievement of health outcomes for people with chronic conditions. These changes have caused for chronic conditions a ~60% decrease in in-person outpatient visits and an increase ranging from 60% to 100% in telephone and video consultations [44].

In regard to radiology practice, in the first pandemic wave there was a decline up to ~70% in imaging services demand [56]. A decrease was also observed in stroke imaging, which suggests a reduction in the number of patients evaluated [57], and in screening programs [58].

In some Chinese cities, as imposed by health authorities, dental centers have had to suspend elective care and to provide urgent treatment only[59].

In psychiatric settings, much of the outpatient care has been virtually provided, and many associations have prepared guidelines in order to allow verbal prescription for some drugs (methadone and Suboxone) by phone without the need for a medical visit [60].

In the case of emergency conditions such as acute myocardial infarction, a decrease in the number of patients presenting to hospitals has been observed: in relation to the pre-COVID-19 era, the first pandemic wave (from March 4th through April 14th 2020) showed lower prevalence of hospital admissions for percutaneous coronary intervention, coronary artery disease and acute myocardial infarction [61]. Similar results were observed in France, USA, Brazil, Spain and Italy with a decrease from 18% to 80% [62–65]. Fear of contagion caused a reduction in hospitalizations [66]. Nevertheless, in some countries an increase in mortality from heart diseases has been observed to be concurrent with the decrease in hospitalizations [62,65]. Furthermore, clinical research has found out an important pandemic impact: in the oncology field there has been a decrease of patients enrolled in clinical trials (~70%) and many cancer centers have reduced their service provision [67].

With regard to financial impact, this has been severe. Hospitals and health facilities in fact have carried enormous costs for patient care, PPE purchase, hospital supplies and equipment. A 202.6 billion dollars financial impact in lost revenue has been estimated for American hospitals and health systems, while for low- and middle-income countries estimation has been ~52 billion dollars. The United Nations predicted that the pandemic will cost the global economy around 2 trillion dollars this year, while the World Bank expects global growth to decrease by approximately 8% with the poorest countries suffering most [68].

To put it simply, the COVID-19 pandemic has shown that health systems vulnerabilities can have profound implications not only for health, but also for economic development.

In this context, it is evident that the pandemic has serious effects on HCWs as they are directly linked to health systems. Thus, their exposure to COVID-19 involves biological and psychophysical risks, which, together with inadequate working conditions, expose them to greater risk and greater vulnerability.

The following paragraph explains the reasons why HCWs are so vulnerable especially in terms of the pandemic impact on their mental health.

1.3.1 Mental health and emotional distress among HCWs: concern and sleep disturbances

As for other infectious disease outbreaks, exposure to COVID-19 is associated with psychological distress and symptoms of mental illness that may affect the general population. Also, there are some vulnerable groups at risk such as healthcare professionals [69,70].

Namely, HCWs (especially frontline workers) are vulnerable firstly because of the high risk of infection, but there are several reasons why they can be classified as at risk and vulnerable to mental health problems. During the pandemic, they may experience fear of contagion for their families, colleagues and friends. Isolation from their close families, quarantine and stressful workplace (and workload), may arouse depression, anxiety and a sense of frustration [70,71]. Other factors involved in such adverse psychological outcomes are the lack of PPE, the feeling of poor or inadequate support, the over enthusiastic information provided by media and the infection rate among colleagues. Moreover, in case of infection, the healthcare worker becomes a patient, and this change of status may lead to problems of adaptation, fear of discrimination by the medical staff, frustration and social stigma [72].

Recent studies have assumed that the conflicting thoughts about balancing of roles and family duties may further compromise HCWs' resilience causing them to feel a sense of guilt. Additionally, coping with the mortality of patients who had been in isolation, and having to subsequently communicate their death to the family members, can be traumatizing and lead to burnout and extreme stress for the HCWs [73,74]. Literature data show that in China and Italy during the first wave of pandemic there was a decrease in medical staff due to infection and to the consequences of acute stress and frustration [75].

A recent review of the psychological sequelae in HCWs has showed there were various emotional outcomes associated with quarantine, that is, depression, sleep disturbances, fear, frustration, and stigma, some of which persisted after the quarantine period [76]. Other

factors associated with mental health problems were rapidity of spread, speculation about transmission and lack of either vaccines or definitive treatment protocols [72].

Some studies showed that nurses experienced a higher level of anxiety and depression than physicians; other evidences showed that in cases of disastrous events, HCWs working in infectious diseases departments, emergency and intensive care units are at greater risk of developing a negative psychiatric impact. As pointed out in recent reviews, risk factors of psychiatric problems were lack of training, communication and social support [72,77].

At the beginning of the pandemic, the Chinese government was the first one to implement guidelines and policies to address the mental health problems in general population and in HCWs. For the latter, strategies to mitigate mental problems have included the creation of psychological and psychosocial intervention teams and online counseling. Generally speaking, during infectious disease outbreaks authorities keep their attention focused on the biological and physical domains, thus neglecting unmet psychological needs. In fact, in the case of COVID-19, only few countries published specific psychological protocols for HCWs, whereas the majority of them opted for online services [72,73,78]. Literature data identified published programs in Malaysia, North America, France and Italy. The Italians did not promote immediate interventions for everyone but they waited for individual workers' requests in order to implement targeted and personalized interventions. The Italian protocol aimed to monitor workers directly involved in the health emergency as well as those ones who had already suffered from psychiatric and psychological problems before the pandemic. All programs mentioned above were developed by University Hospitals and recognized the importance of collaboration within a multidisciplinary team [73].

A Japanese study conducted in the first wave of the pandemic found that poor information and insufficient PPE were source of major concern for HCWs. Lack of information was associated with psychological distress, with no differences in degree of worry between frontline and non-frontline HCWs [79]. As the pandemic evolved, different concerns about the cultural and institutional context emerged. Indeed, in the second wave, HCWs showed concerns about how they were evaluated by the Institution and about the transparency of

the evaluation process [80]. Recent studies have highlighted a higher level of concern about COVID-19 than about previous outbreaks (the SARS and MERS pandemics) [79,81].

Moreover, if we take into account factors indicating emotional distress and occurring in the event of disasters and pandemics, we have certainly to refer to sleep disturbances.

During the pandemic, sleep disturbances have affected millions of people from both the general population and the HCWs category, representing a growing issue of public health concern because they are associated with psychological distress and mental illness. Persistent sleep disturbances were detected in subjects who were under isolation or hospitalized for COVID-19. Furthermore, in the case of hospitalizations longer than seven days insomnia was more prevalent than depression and anxiety [82,83]. Other factors that could reduce sleep quality were the risk of being infected and the financial distress due to job insecurity; however, these factors can vary according to personal experience and individual characteristics [84].

As stated by Becker (2021), HCWs showed significantly higher incidence of insomnia, anxiety and depression compared to other professionals. Although the need to manage sleep disturbances was quickly recognized, interventions were not timely. The most used strategies to deal with these disorders were mostly self-help (through consultation of information brochures) and only few HCWs required counseling or psychotherapy [82].

In summary, the nature of healthcare work, characterized by high risk of infection, contact with suffering patients and irregular and exhausting shifts, may explain the high prevalence of sleep disorders found in HCWs [85].

1.3.2 Risk perception and behavior

The term "perception of risk" refers to the individual's perception and understanding of objective risks in the external world [86]. The concept of risk has been developed in

different theoretical frameworks; however, the predominant paradigm in psychological research is the psychometric one, according to which risk is divided into: "*unknown risk*" (consistent with the cognitive dimension and therefore the understanding) and "*dread risk*" (consistent with the emotional dimension)[87]. The former is related to new, non-observable events with delayed effect, while the latter is connected with uncontrollable catastrophic events with fatal consequences. Unknown risk may influence dread risk and both influence risk perception [87–89].

With reference to the pandemic, although there is still no empirical evidence, it is possible to hypothesize that both types of risk may characterize the perception of disease and that they may change according to the phases of the pandemic. For example, during an initial phase in which there is no clear understanding of the phenomena and there are delayed visible effects, perception can be probably modulated by an unknown risk. In other phases, instead, in which infection clearly appears to be lethal, such as in a catastrophic event, the perceived risk is more shaped as a dread [88].

Risk perception is very important, because it influences decision-making and people's behaviors. Perception also plays a main role in driving economic impact, as it can cause a decrease or even a fall in demand, especially in the case of services related to tourism, transport and recreational activities (individuals' choice is mitigated by their perception) [90].

A realistic risk perception allows to implement and promote voluntary preventive behaviors. Consequently, its assessment plays a key role in the management of crisis events such as an epidemic/pandemic, when in most of the cases in the early phase neither treatments nor vaccines are available [90,91]. A realistic perception is based on having correct information (which is usually scarce in the case of EIDs). In this regard an effective risk communication is essential, as it conveys scientific knowledge [91]. However, as highlighted by Brug et al. (2009), the perception of risk is not lacking in bias; for example, an idealistic optimism about health risks can result in a lack of precautions and unfounded sense of safety. On the other hand, a pessimistic perception can lead to unjustified mass alarms [92].

Since the SARS outbreak occurred, scientific research has been focusing on risk perception. As a result, there are studies documenting risk perception in previous epidemic/pandemics.

Vartti et al (2009) conducted a research in Finland and in the Netherlands aimed at investigating perception of risk, worries and precautionary behaviors at the time of the SARS outbreak. Their findings showed that the Finns were more likely than the Dutch to have low perceived SARS risk, and to be more well informed and worried about SARS. According to the authors, these differences rested upon a dissimilar communication in the two countries. At the time of the outbreak a Finnish high-level official died in Asia from SARS, and this news probably influenced the media information coverage and consequently the public perception [93].

Similar results emerged from the study of Brug et al. (2004), who stated that the SARS outbreak did not fuel fears among Dutch people, who were not more concerned than usual about the risk and had a good knowledge about the SARS epidemic [94].

A study conducted among the Chinese community in UK and Netherlands [92] reported that the perception of risk was influenced by information and by the cultural and spiritual background. Namely, the study participants reported a difference in the type of information provided by European and Asian media. European media were focused on travel warnings, alarmist forecasts about the global spread and blaming the Chinese government's handling of the epidemic, while Asian ones caused panic among communities, as they were associated with a regularly updated bulletin of deaths [92].

A Korean study aimed at evaluating risk perception during the MERS outbreak showed that knowledge, communication, trust and vulnerability were major factors influencing perception. Specifically, the trust in experts and in the government was crucial in allaying the public's fears of the pandemic disease, while less vulnerability was associated with increased perceived risk (a higher risk perception was observed in vulnerable groups such as subjects with a disability or the elderly) [95]. Other findings revealed that a greater exposure to social media was associated with a greater risk perception. Furthermore, in the first phase of the outbreak, people notably used social media as an alternative source of information, as traditional media (television and newspapers) did not provide enough

information (for example in China the government controlled the information). In addition, it is important to remember that social media give people the opportunity of sharing information in a public space; consequently, it is easier for people to disseminate information (including the one that can be omitted from traditional media) [96].

In literature there are several studies about risk perception also in relation to the recent COVID-19 pandemic. Their findings are consistent with evidence found in previous outbreaks. They show a high risk perception and recognize that factors such as knowledge, education, cognitive skills, communication, confidence in government or physicians play a key role in modulating it, which in turn is related to the implementation of protective behaviors [97–99].

To recapitulate, many studies agree that risk perception changes during the different phases of crisis events. The studies above mentioned show variability among different countries (cultural background) and explain more clearly how risk perception is influenced by and in turn influences many factors. Therefore, although necessary, the assessment of risk perception alone is not sufficient to explain certain behaviors.

1.4 Italian responses to COVID-19 emergency: public management and public health perspectives

On January 31st 2020, the Italian government declared the state of emergency. Later on, following the example of other countries, it adopted unprecedented and progressively restrictive measures in order to cope with the health emergency due to the novel Coronavirus.

Below a description can be found of the most important actions the Government took in accordance with the Ministry of Health in the first pandemic wave to limit virus transmission [100].

The first measure, introduced on January 30th, concerned the interruption of air traffic to and from China. Meanwhile, the Risk Assessment Document was updated. Firstly, from February 21st to 23rd (Decree-Law February 23rd2020), containment measures were taken for those who had been in the areas at risk or had come into close contact with infected people: mandatory isolation and quarantine, mandatory communication to the Health Department followed by active surveillance (contact tracing was implemented also in healthcare settings). A"red zone" was defined for Lombardy and Veneto regions. Citizens from the red zone could not leave their municipality, and, where possible, remote working was activated. Furthermore, all social events (i.e. religious, sport events, etc.), together with commercial (for non-essential goods) and educational activities were suspended (schools were closed). In March, these measures were extended to the whole country with prohibition of any form of gathering of people (in private as well as in public places); so on March 9th the first national lockdown came into force (namely phase 1 from March 9th to May 4th 2020).

Later, on November 3rd 2020, according to the regional risk level, three areas - yellow, orange and red - were identified, each one with specific measures (the red area considered to be at high risk was characterized by the most severe restrictions) [101]. Since these measures have had a dramatic impact on the country's economy, in order to support the population strained by the financial crisis economic bonuses were given and taxes were reduced or suspended. Significant efforts have also been made in the field of prevention and treatment, mainly through health monitoring and the search for adequate treatments. The definition of the strategies and the intervention plan synergistically involved many institutions, such as the Ministry of health, universities, the WHO, the ISS, the Department of Civil Protection, the Regional Emergency Agency, etc. In January 2020, in compliance with the WHO guidelines, the Ministry of Health created a task force aimed at enabling airport controls, alerting health facilities, issuing operational prevention guidelines, managing confirmed cases in collaboration with local and regional health services, repatriating nationals from risky areas and verifying implementation of response actions.

In February, the Technical Scientific Committee(CTS) was promptly created to support coordination activities and preparedness studies were carried out to classify risk level. Moreover, the ISS designated the National Reference Laboratory for confirming and reporting all the infected cases to the WHO. At the same time, a network of 31 laboratories with diagnostic capabilities was built up as recommended by the WHO guidelines [102].

On March 19th 2020, a medical task force was created for recruiting 300 volunteer physicians to support the most critical Italian regions [100]. Furthermore biologists, physicists, chemists, military doctors, doctors and nurses were recruited by means of an extraordinary procedure. In addition, there was an empowerment in military health facilities and in PPE production. Finally, as a means to provide new healthcare personnel, the exams customarily required to be taken in order for students of the medical and healthcare professions to gain their qualifications were either waived or modified such that their recruitment was facilitated (law Decree no. 18 of March 17th 2020, also named *Cura Italia* decree) [103]. Since the beginning of the pandemic, to limit the spread, there have been constant communication actions aiming to raise public awareness about the adoption of preventive behaviors, in terms of use of PPE (surgical masks in particular), hand washing, social distancing (> 1 m) and indoor natural ventilation.

Anyway, in Italy all the response actions were implemented in line with the WHO strategic indications. The WHO has defined the following eight pillars of response and preparedness to the health emergency: 1) country-level coordination, planning, and monitoring; 2) risk communication and community engagement; 3) surveillance, rapid response teams and case investigation; 4) points of entry; 5) national laboratories; 6) infection prevention and control 7) case management; 8) operational support and logistics [104]. Table 1 describes some of the most important Italian activities undertaken in relation to the eight pillars indicated by the WHO [102]. Even if it excludes the prevention field, it is worth remembering the immense efforts made by physicians, nurses and all other health professionals involved in the management of health emergency, especially in the first wave, when the pandemic was of catastrophic proportions. As a matter of fact, as highlighted by

a systematic review (December 2020), up to May 8th 2020, among HCWs worldwide infection cases were 152888 and the number of reported deaths was 1413 [105].

Table 1. Italian public health emergency preparedness and response to COVID-19 in the autumn-winter 2020 season.

Italian activities according to WHO strategic pillars	
Pillar 1	Implementation of regulations and guidelines; risk classification weekly monitoring system; strengthening of the endowments and organization of hospital and territorial assistance; each region prepared a regular report in compliance with the health regional system representative (in accordance with Ministry of health and ISS). **Country-level coordination, planning, and monitoring**
Pillar 2	Countering fake news; supporting the dissemination of surveillance and epidemiological data; promoting stakeholder training supporting the prevention of fragile subjects; constant monitoring of population sentiment through research; timely information on diagnosis. Activities implemented by use of official media, press and social media. **Risk communication and community engagement**
Pillar 3.	Data collection by integrated epidemiological and microbiological surveillance system; reporting to the regional authorities for the activation of surveillance; control of passengers list; contact tracking application (immune app). **Surveillance, rapid response teams and case investigation**
Pillar 4	Travelers temperature monitoring was for all departures and destinations; training workers in sanitization of travel environments. **Points of entry**
Pillar 5	Laboratories protocols development to differentiate and identify SARS-CoV-2; measures to ensure national accurate comparable diagnostic capacity. **National laboratories**
Pillar 6	Technical protocols updating, continuous training of HCW, regulations of schools reopening; provision of PPE. Infection prevention and control
Pillar 7	Clinical manifestation classification and symptomatology, ARDS treatment; clinical management treatment recommendations based on the scientific evidence found. **Case management**
Pillar 8	Implementation of the "*Rilancio*" decree. Strengthening hospital facilities; provision of swabs, tests and PPE; actions to contrast drug shortages (streamlining of EU import procedures). **Operational support and logistics**

The peak of the ascending epi curve was observed on March 21st, and from that date onward the number of daily cases started to decrease with a slight increase in April, then cases stably decreased from May/June 2020 [106]. The joint implementation of public health preventive measures and governmental restrictions allowed the improvement of the epidemiological trend. It should be noted that at the time of the Italian outbreak, there were neither vaccines nor specific treatments, so early diagnosis and the adoption of the measures mentioned above were the only resources to limit the virus spread and contagion.

However, early research focused on vaccine development and later, on December 21st and 22nd 2020, the European Commission and the Italian Drug Agency respectively authorized the first vaccine against COVID-19, that is, the mRNA BNT162b2 vaccine, produced by Pfizer and BioNTech [107]. As of June 3rd 2021, six vaccines against COVID-19 met the WHO criteria for safety and efficacy; they were the AstraZeneca/Oxford, Johnson and Johnson, Moderna, Pfizer/BionTech, Sinopharm and Sinovac vaccines [108][2].

In conclusion, the COVID-19 health emergency has shown that public health interventions had a central role in social and economic development.

With a view of perspectives on future, the Italian National Prevention Plan (NPP) 2020-2025 is certainly the essential tool in defining interventions aimed at prevention and health promotion. Taking account of the pandemic scenario, the NPP recognizes the need for a multidisciplinary, cross-sectoral and coordinated approach to cope with current and potential risks. This approach emphasizes the centrality of the individual, in a perspective of interconnection with animals and environment, and takes into account social, economic and environmental factors to ensure fairness among population. As extensively discussed before, individual behaviors can make the difference especially in the prevention field.

Principles that inspire the NPP vision are the empowerment of healthcare structures and their integration with the territory, the communication actions and the availability of updated data. In regard to communication, especially in the advanced pandemic phases, it may represent a vaccine education strategy, as well as it may prove essential to create public

[2]Data available at https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines/advice, last updated on 14 July 2021, last accessed 2021/09/09.

trust in institutions. Furthermore, it may be useful in minimizing social stigma. Other principles are health promotion and the strengthening of health literacy, registers and the surveillance system. The measures are still strongly oriented to the surveillance system (with the empowerment of mapping systems and tracking cases), as it is crucial for EIDs management. However, the surveillance issue is, in turn, strongly linked to other ethically relevant issues such as personal data protection and consent, equity (especially among Regions) and no stigmatization (mostly of vulnerable groups). Continuous training represents the basis of all health strategies, especially for HCWs.

To improve the health system's ability to promote prevention, 13 central support lines have been identified. Among these, the most important ones concern the activation of technical tables (to strengthen the above mentioned strategies); the promotion of environmental interventions; a national plan for indoor air quality; the development of the One Health and Planetary Health approach for the post COVID-19 governance (implementation of guidelines); the primary prevention and the preparation of a national plan to respond to an influenza pandemic.

Furthermore, in terms of prevention, the Essential Levels of Assistance (LEA) of the National Health Service were revised and defined as "Collective prevention and public health" which includes epidemiological surveillance programs for infectious and diffusive diseases [109–111].

In conclusion, it is worth highlighting that, in order to fully achieve public health purposes, health institutions cannot disregard a close collaboration with government and other institutions involved in the management of the emergency.

Chapter 2

Aims

The general aim of this thesis project was to investigate the factors related to the mental health of Italian HCWs in relation to COVID-19 during the first pandemic wave.

Specifics aims were:

- To describe the degree of worry.
- To explore the level of risk perception of being infected among HCWs.
- To define the prevalence of sleep disturbances.

Addressing HCWs' emotional distress is important to preserve their individual optimal health. Healthcare professionals who are not in good mental and physical health may experience difficulties with caring for others. Identifying these issues may enable healthcare professionals to provide the best possible care for their patients and perceive the need for the necessary support.

Chapter 3

Methods

3.1 Study Protocol

In the first phase, a research protocol was prepared in order to be submitted to the reference Ethical committee. Firstly, a literature review was conducted in order to know: 1) the worries that can affect HCWs in epidemics/pandemics; 2) the tools used to identify them. The literature review revealed the existence of well-structured validated tools (questionnaires) that were long and required availability of time to be filled in, so we decided not to use them. Since this research was carried out in the first wave of the pandemic (when HCWs were overworked) we considered more appropriate to design an *ad hoc questionnaire* which was quicker to fill in by taking our cue from those existing in literature. Then, the research protocol reported the aim and the methods (data collection, statistical analysis, privacy etc.) of the study. The protocol has been prepared in accordance with the guidelines for observational studies (STROBE guidelines)[112].

The research protocol was developed by a multidisciplinary team including biostatisticians, psychiatrists and prevention technicians. The presence of these experts with different skills has certainly made it possible to grasp further aspects of the topic under study within a perspective of greater completeness. Finally, the protocol was presented and accepted by the Institutional Ethical committee of Pavia.

3.2 Study Design and Participants

A cross-sectional study was designed in order to assess the prevalence of worries in Italian HCWs.

Cross-sectional studies analyze data from a population at a single point in time and are often used to measure the prevalence of health outcomes and to describe the characteristics of a population. They are often performed by means of either questionnaires or interviews [113].We implemented an *ad hoc* questionnaire that was administered online (web-based open survey).

Cross-sectional studies are primarily descriptive but also analytics, thus their main effect measure is the prevalence, although it is also possible to estimate odds ratios (ORs).

The main strength of these studies is that they are relatively fast and inexpensive to conduct. Furthermore, participants are neither deliberately exposed nor treated (so, ethical problems are not frequent). In addition, these study designs may be useful for public health planning, evaluation and monitoring; in fact they are often used in community surveillance systems (or among high-risk subject groups: cross-sectional sentinel surveys)[113,114].

Eligibility criteria were to be physicians, nurses, medical staff (radiologic technologists, rehabilitation technicians, physiotherapists and midwives), healthcare support and administrative personnel working in hospitals, nursing homes and therapeutic communities in Italy during the first wave of the pandemic period (February - May 2020). Trainee students, who had not obtained the qualification at the time of the interview yet, were excluded.

3.3 Recruitment, ethics and sample size

All participants, who had been recruited by using a "snow-ball" sampling, by email, newsletters and social media (Facebook and LinkedIn), were required to provide an informed consent before taking part in the web survey and to agree to data collection and storage for analysis and publication. Participants were aware of the voluntary nature of their participation and confidentiality of information was assured. The survey was completely anonymous. The final sample size was equal to the number of HCWs who completed the online questionnaire and met the inclusion criteria (that were being a health professional with the necessary qualifications and providing informed consent). The study received the approval for investigation from the Ethics Committee.

Assuming 50% of the subjects are very worried about COVID-19, the sample size needed to estimate this prevalence with an error of 2.5% is 1553 subjects. Assuming a drop-out rate of 20%, being a survey, the final sample size will be at least 1841 subjects.

3.4 Data Collection and questionnaire

An online questionnaire using the online Google platform "Form" was drawn up. It was available online from May 5th to June 6th.

The following information was collected: age, sex, marital status, region of residence (recoded in geographical area: North, Centre and South), work experience (expressed in years), educational level, occupational category and hospital ward/department, perceived risk of infection (high, medium, or low), worries and knowledge about the pandemic. Items about worries over COVID-19 had a score that ranged between 0 to 4, where 4 represents the highest degree of concern (questionnaire is available in Appendix 1).

Before starting the research, a pilot study was performed to assess the questionnaire's clarity and suitability. Students attending either the final year of the Medicine course or health professions courses (30 subjects) filled in the questionnaire and expressed a positive feedback about its feasibility.

3.5 Statistical Analysis

Data quality assessment was ensured by evaluation of the completeness and consistency of the collected data, which were stored in an *ad hoc* database.

Descriptive statistics were used to describe the collected data. Thus, quantitative variables were summarized as mean values, standard deviations (sd), median and interquartile range (IQR) as appropriate, whereas qualitative variables were summarized as frequencies and percentage.

Normality of data was assessed by Shapiro-Wilk test and graphical methods. In order to compare qualitative variables, either the Pearson Chi-square or the Fisher exact test were applied. Differences for quantitative variables among groups were instead evaluated by Student *t* for unpaired samples or Mann-Whitney *U* for comparison between two groups, and by the Kruskal-Wallis nonparametric test in case of three or more groups.

Multivariable logistic regression was implemented to identify factors associated with sleep disturbances. In addition, to explore factors associated with risk perception of being infected (classified as low, medium and very high), a multinomial logistic regression was performed using "very high" risk perception as the reference category in the model. Results were reported as Relative Risk Ratios (RRRs) and corresponding 95% Confidence Intervals (95% CI).

For all regression models, candidate variables were selected if they were significant at univariate test or for their clinical relevance. Then, the likelihood ratio (LR) test was used to evaluate the difference between nested models (i.e. to assess the significant contribution of variables to the model). Homer-Lemeshow (HL) test of goodness of fit was performed.

Statistical significance was set at 5% ($\alpha = 0.05$). In case of multiple testing, the significance level was adjusted by using the Bonferroni method, by dividing the probability of a Type-I error for the k comparisons ($\alpha' = \alpha / k$). The Bonferroni correction was used for the comparison of variables among five groups of HCWs (physicians, nurses, medical, healthcare support and administrative staff). The software used for data analysis was STATA/SE for Window, version 15 (StataCorp., College Station, TX, USA).

Chapter 4

Results

4.1 Survey respondents characteristics

Survey respondents were 2103; among these, 2078 met the inclusion criteria. Females were 78.8%, mean age was 42.17±10.98 years with no sex differences (females 42.13±10.93 years and males 42±11.15 years; p=0.7370).

The most represented geographical area was the northern one, with 70% of participants. In regard to the type of healthcare structure, the majority of respondents worked in hospitals (88.6%), followed by nursing homes (7%) and therapeutic communities (4.4%).

As to occupational category, about two-thirds of the sample was made up of physicians (40.75%) and nurses (32.15%), followed by medical (18%), healthcare support (4.5%) and administrative staff (4.6%). The overall mean in terms of years of work experience was 15.99±10.94 years, with no differences among professional groups (physicians mean years of work experience 17±11, nurses 16±11 years, medical staff 17±11 years, healthcare support staff 10±10 years and administrative staff 15±12 years) (p=0.384).

Educational level within the sample was high: 43.2% of participants had a postgraduate qualification and 45% an undergraduate degree; the remaining 11.8% had a high school diploma. Table 2 shows participants' characteristics. Some parts of the following results have already been published in Puci et al. (2020) (doi.org/10.3390/healthcare8040535).

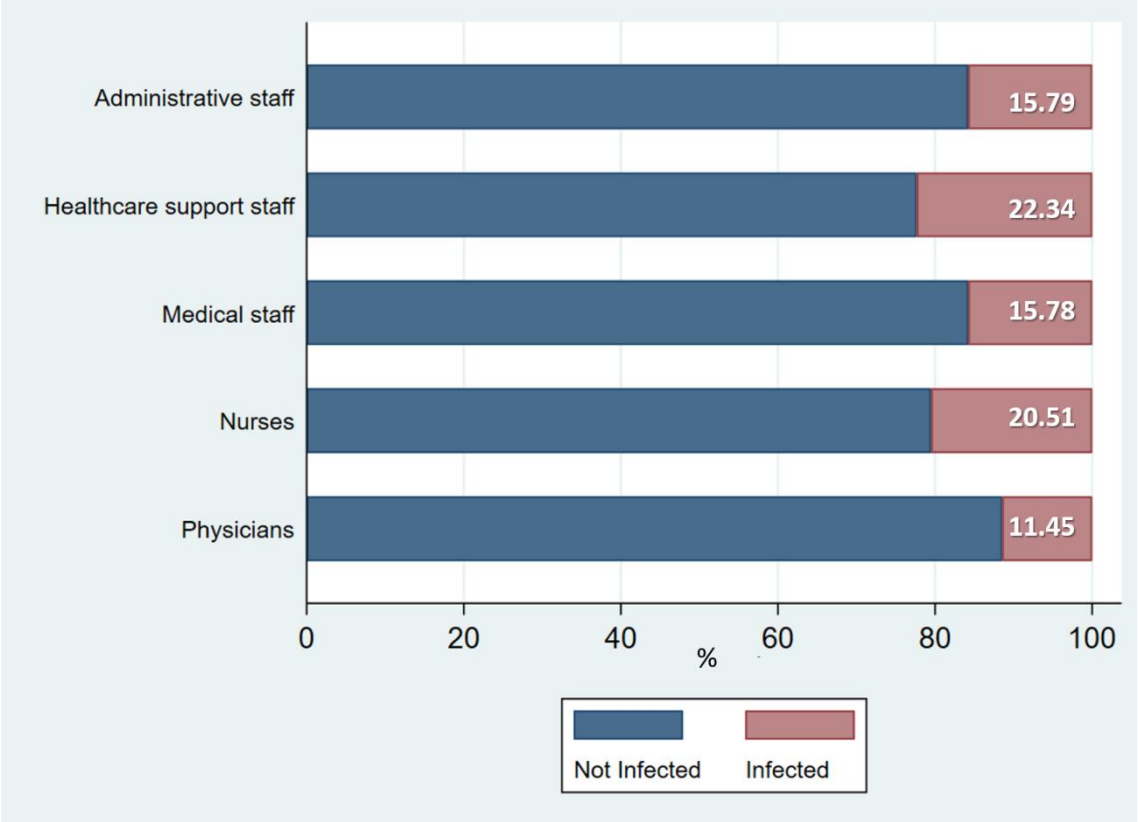
Table 2. *Participants' characteristics (n=2078).*

Participants characteristics	**All sample N=2078**
Age(years), mean(sd)	42.17 (10.98)
Years of work experience, mean(sd)	15.99 (10.94)
Sex, n(%)	
Female	1637 (78.80)
Marital status, n(%)	
Single	519 (24.96)
Divorced	139 (6.70)
Widowed	11 (0.53)
Married	1409 (67.81)
Geographical area, n(%)	
North	1454 (70.00)
Center	254 (12.20)
South	370 (17.80)
Education, n(%)	
High School Diploma	246 (11.80)
Undergraduate Degree	935 (45.00)
Postgraduate Education	897 (43.20)
Type of Health Structure, n(%)	
Therapeutic Community	91 (4.40)
Nursing home	145 (7.00)
Hospital	1842 (88.60)
Occupational category, n(%)	
Physicians	847 (40.75)
Nurses	668 (32.15)
Medical staff	374 (18.00)
Healthcaresupport staff	94 (4.50)
Administrative staff	95 (4.60)

4.2 Worries and concerns about the COVID-19 pandemic

About 16% of HCWs reported having been infected with SARS-CoV-2, with significant differences among groups. Precisely, a higher prevalence of infection was observed in healthcare support staff (22.34%) and a lower one in physicians (X^2=26.145; p<0.001) (Figure 6).

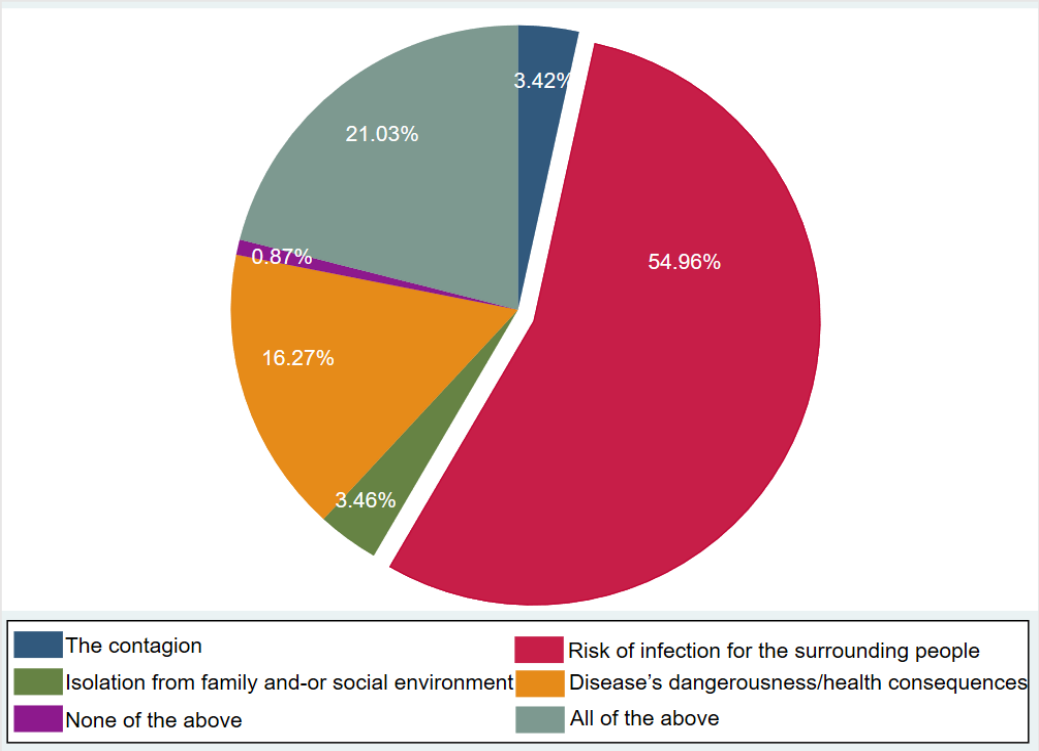
Figure 6. *Distribution of SARS-CoV-2 infection - comparison among HCWs groups.*



Overall, the median degree of worry was 3(IQR 2-3) to indicate a high worry experience (score ranging from 0 to 4, the last value corresponding to a higher worry degree) with similar results among HCWs groups: a median score of 3(2-3) was observed in all groups, while among healthcare support staff the median score was 3(2-4).

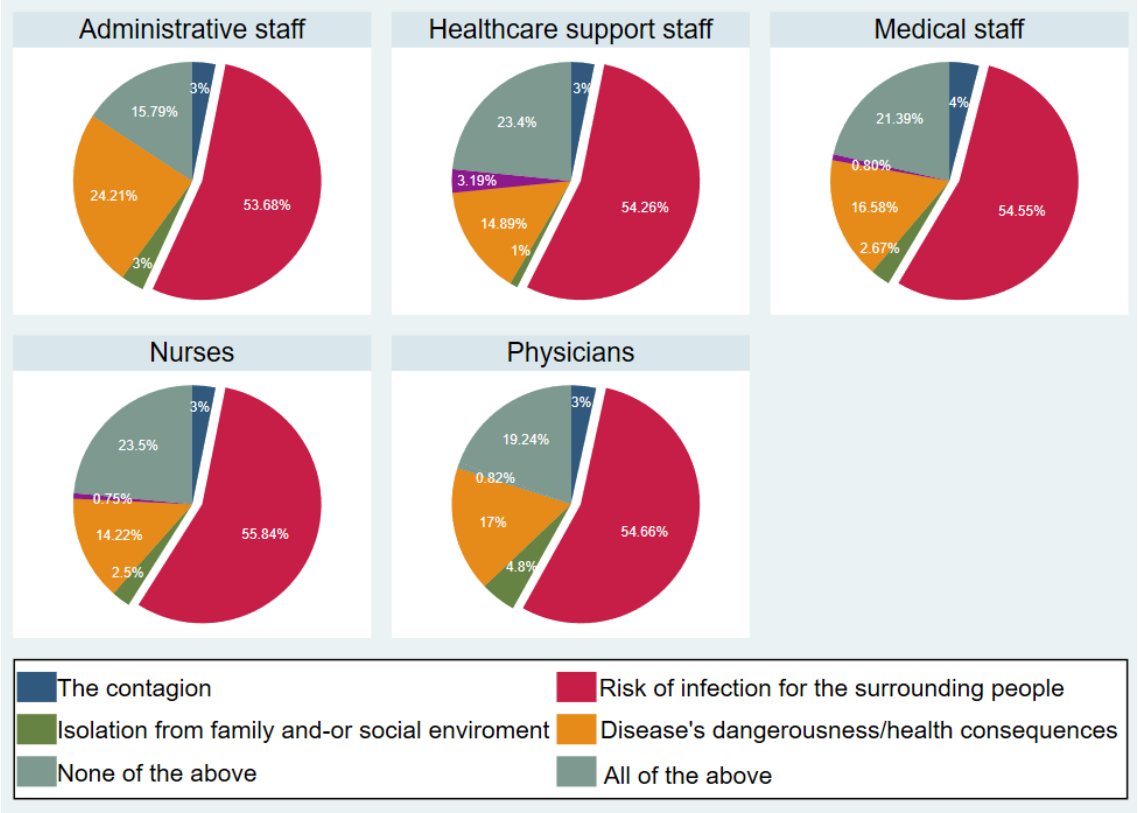
With regard to the type of worry, for the majority of HCWs the most frequent worry was about "*The risk of infection for the surrounding people*" (54.96%), followed by "*The disease's dangerousness/health consequences"* (16.27%), "*The isolation from family and/or social environment"* (3.46%) and *"The contagion"* (3.42%) (Figure 7).

Figure 7. *Distribution of the types of worry (n=2078).*



Similar results were observed stratified by HCWs groups, whose prevalent worry was "*The risk of infection for the surrounding people*", with no differences among groups (p=0.148) (Figure 8).

Figure 8. *Distribution of the types of worry among HCW's groups.*



However, as reported in Table 3, significant differences were observed only for *"Isolation from family and-or social environment"*, since physicians, nurses and healthcare support staff appeared to be more worried than medical and administrative staff with higher prevalence of "very worry" (p=0.037) (Table 3). As to the information provided by the Department, about two-thirds of the sample (70.21%) was quite or very worried about *"Insufficient information about infection"* and *"Insufficient staff"*, while 67% were not worried about *"Intentional absenteeism in the workplace"*. In relation to *Insufficient information about infection",* the proportion of subjects who reported not being worried was significantly higher among administrative staff (44.21%), compared to other groups (p<0.001). Worry about *"Insufficient staff"* was significantly higher among nurses and healthcare support staff compared to other groups (p<0.001). Finally, the majority of the sample (~70%) was quite worried about *"Lack of recognition about my work"*. Table 3 also shows prevalence of these factors among HCWs groups.

Table 3. *Healthcare workers' worries and concerns about COVID-19 pandemic.*

Worries	All N=2078	1.Physicians N=847	2.Nurses N=668	3.Medical staff N=374	4.Healthcare support staff N=94	5.Administrative staff N=95	P-value
How much are you worry about, n(%):							
The contagion							0.198#
Very worried	566(27.24)	220(25.97)	193(28.89)	102(27.27)	27(28.72)	24(25.26)	
Quite worried	1292(62.18)	526(62.10)	425(63.62)	227(60.70)	56(59.57)	58(61.05)	
Not worried	220(10.59)	101(11.92)	50(7.49)	45(12.03)	11(11.70)	13(13.68)	
The disease's dangerousness/health consequences							0.592#
Very worried	648(31.18)	261(30.81)	206(30.84)	125(33.42)	29(30.85)	27(28.42)	
Quite worried	1247(60.01)	500(59.03)	414(61.98)	220(58.82)	55(58.51)	58(61.05)	
Not worried	183(8.81)	86(10.15)	48(7.19)	29(7.75)	10(10.64)	10(10.53)	
The risk of infection for the surrounding people							0.683#
Very worried	1268(61.02)	516(60.92)	408(61.08)	228(60.96)	55(58.51)	61(64.21)	
Quite worried	724(34.84)	295(34.83)	237(35.48)	132(35.29)	32(34.04)	28(29.47)	
Not worried	86(4.14)	36(4.25)	23(3.44)	14(3.74)	7(7.45)	6(6.32)	
The isolation from family and/or social environment							0.037#
Very worried	586(28.20)	258(30.46)	201(30.09)	80(21.39)	25(26.60)	22(23.16)	
Quite worried	1018(48.99)	394(46.52)	322(48.20)	201(53.74)	53(56.38)	48(50.53)	
Not worried	474(22.81)	195(23.02)	145(21.71)	93(24.87)	16(17.02)	25(26.32)	
How would you score your degree of job satisfaction? Score 0-4							<0.001§
I'm not satisfied-I'm very satisfied, mean±sd	2.8±1.0	2.6±1.1	3.0±1.0	2.8±1.1	3.4±0.8	3.0±1.1	
Median (Iqr)	3(2-4)	3(2-3)[5]	3(2-4)[3,5]	3(2-4)[4]	4(3-4)[5]	3(2-4)	
What worries you most about your ward/department? n(%)							
Insufficient information about infection							<0.001#
Very worried	421 (20.26)	158(18.65)	146(21.86)	80(21.39)	24(25.53)	13(13.68)	
Quite worried	1038(49.95)	405(47.82)	350(52.40)	188(50.27)	55(58.51)	40(42.11)	
Not worried	619(29.79)	284(33.53)	172(25.75)	106(28.34)	15(15.96)	42(44.21)	
Insufficient personal protective equipment							0.274#
Very worried	688(33.11)	285(33.65)	223(33.38)	120(32.09)	38(40.43)	22(23.16)	
Quite worried	872(41.96)	359(42.38)	278(41.62)	149(39.84)	38(40.43)	48(50.53)	
Not worried	518(24.93)	203(23.97)	167(25.00)	105(28.07)	18(19.15)	25(26.32)	
Insufficient staff							<0.001#
Very worried	558(26.85)	207(24.44)	216(32.34)	78(20.86)	37(39.36)	20(21.05)	
Quite worried	841(40.47)	331(39.08)	280(41.92)	160(42.78)	34(36.17)	36(37.89)	
Not worried	679(32.68)	309(36.48)	172(25.75)	136(36.36)	23(24.47)	39(41.05)	
Intentional absenteeism in the workplace							<0.001#
Very worried	212(10.20)	54(6.38)	81(12.13)	48(12.83)	16(17.02)	13(13.68)	
Quite worried	476(22.91)	138(16.29)	183(27.40)	99(26.47)	32(34.04)	24(25.26)	
Not worried	1390(66.89)	655(77.33)	404(60.48)	227(60.70)	46(48.94)	58(61.05)	
Lack of recognition of my work							<0.001#
Very worried	118(5.68)	33(3.90)	42(6.29)	32(8.56)	4(4.26)	7(7.37)	
Quite worried	1475(70.98)	687(81.11)	442(66.17)	224(59.89)	62(65.96)	60(63.16)	
Not worried	485(23.34)	127(14.99)	184(27.54)	118(31.55)	28(29.79)	28(29.47)	

#Chi-square or Fisher Exact-Test; §Kruskal-Wallis Test; [n]Significant differences between the group and the one mentioned by numbers (correction Bonferroni post-hoc tests).

4.3 Perceived Risk of Infection and Information about the COVID-19 Pandemic

Table 4 shows results about the perceived risk of being infected and the related information. At the beginning of the pandemic, 59.19% of HCWs reported perceiving a high risk of being infected; similar results were observed at the time of the questionnaire administration (May/June 2020): the risk of being infected was high for 58.85% of the sample.

The highest proportion of "high risk" perception was observed in nurses (62.87%), followed by physicians (60.92%), healthcare support staff (59.57), medical (52.14) and administrative staff (45.26%) ($p<0.001$).

In regard to environment, the workplace was the place at highest risk of being infected for 71% of the sample. The degree of perceived sufficiency of information about contamination routes, preventive measures, symptoms, treatment, prognosis and risk factors may be considered moderately high (median score ranged from 4 to 5). However, the general tendency showed that among administrative staff a slightly lower median value was observed for treatment and prognosis (3, IQR 2–4 for both) compared to other professionals ($p=0.029$ and $p=0.150$, respectively).

In addition, administrative staff had higher median values of agreement on the Department's preparedness to deal with the emergency and its ability to provide clear and complete information than other groups (last two items in Table 4).

Table 4. *Healthcare workers' perceived risk of infection and perceived information about COVID-19 pandemic*

Perceived risk of infection and perceived information	**All N=2078**	**1.Physicians N=847**	**2.Nurses N=668**	**3.Medical staff N=374**	**4.Healthcare support staff N=94**	**5.Administrative staff N=95**	**P-value**
At the beginning of the pandemic, you thought that your risk of being infected was: n(%)							0.001#
low	367(17.66)	153(18.06)	114(17.07)	69(18.45)	13(13.83)	18(18.95)	
medium	481(23.15)	178(21.02)	134(20.06)	110(29.41)	25(26.60)	34(35.79)	
high	1230(59.19)	516(60.92)	420(62.87)	195(52.14)	56(59.57)	43(45.26)	
At the beginning of the pandemic, you thought that your risk of being infected was higher: n(%)							<0.001#
in the workplace	1475(70.98)	687(81.11)	442(66.17)	224(59.89)	62(65.96)	60(63.16)	
outside the workplace	118(5.68)	33(3.90)	42(6.29)	32(8.56)	4(4.26)	7(7.37)	
the same in both environments	485(23.34)	127(14.99)	184(27.54)	118(31.55)	28(29.79)	28(29.47)	
Currently, you think that your risk of being infected is: n(%)							<0.001#
low	527(25.36)	224(26.45)	189(28.29)	67(17.91)	31(32.98)	16(16.84)	
medium	328(15.78)	112(13.22)	104(15.57)	75(20.05)	13(13.83)	24(25.26)	
high	1223(58.85)	511(60.33)	375(56.14)	232(62.03)	50(53.19)	55(57.89)	
Currently, you think that your risk of being infected is higher: n(%)							<0.001#
in the workplace	1000(48.12)	495(58.44)	275(41.17)	155(41.44)	39(41.49)	36(37.89)	
outside the workplace	373(17.95)	125(14.76)	133(19.91)	82(21.93)	18(19.15)	15(15.79)	
the same in both environments	705 (33.93)	227(26.80)	260(38.92)	137(36.63)	37(39.36)	44(46.32)	
Have people close to you contracted the infection? n(%)							<0.001
friends	137(6.58)	43(5.06)	32(4.79)	48(12.80)	5(5.32)	9(9.47)	
colleagues	749(35.98)	309(36.35)	252(37.72)	113(30.13)	36(38.30)	39(41.05)	
family	134(6.44)	44(5.18)	41(6.14)	31(8.27)	11(11.70)	7(7.37)	
at least two of the above	409(19.64)	169(19.88)	160(23.95)	55(14.67)	11(11.70)	14(14.74)	
none of the above	653(31.36)	285(33.53)	183(27.40)	128(34.13)	31(32.98)	26(27.37)	

#Chi-square or Fisher Exact-Test; ∫Kruskal-Wallis Test; nSignificant differences between the group and the one mentioned by numbers (correction Bonferroni post-hoc tests).

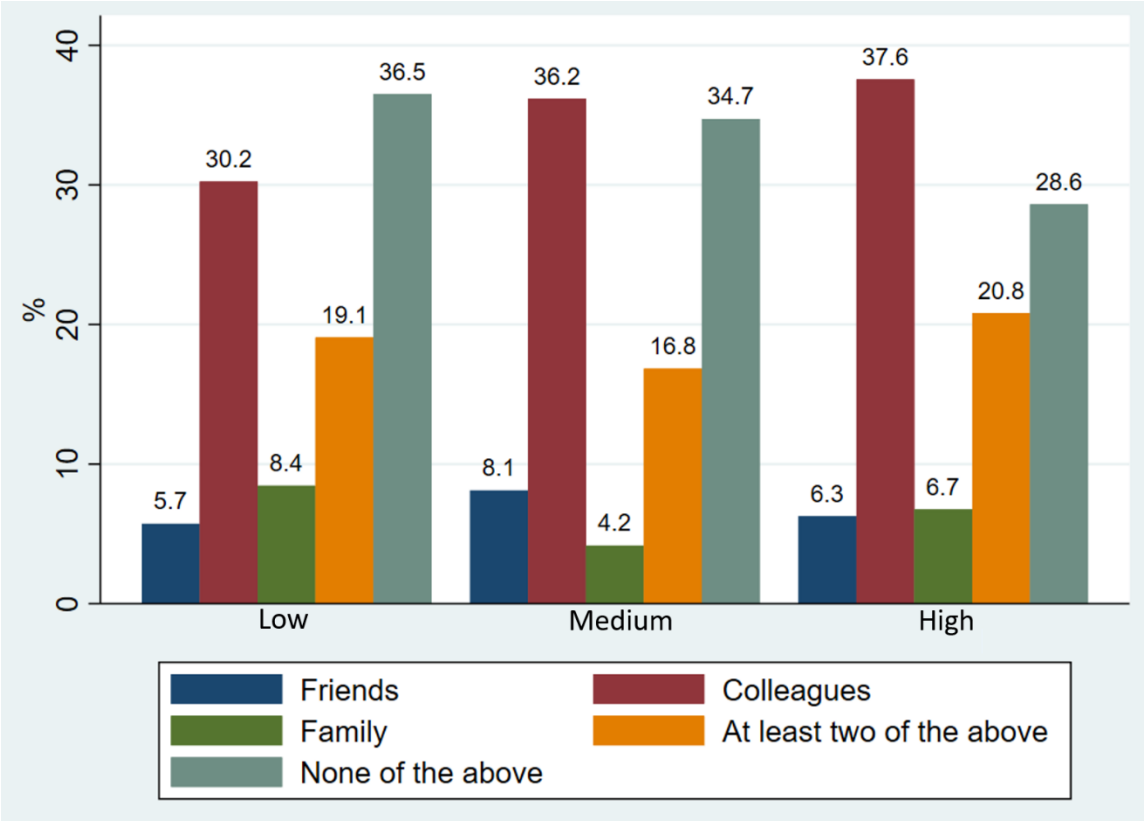
Table 4. *Cont.*

Perceived risk of infection and perceived information	All N=2078	1.Physicians N=847	2.Nurses N=668	3.Medical staff N=374	4.Healthcare support staff N=94	5.Administrative staff N=95	P-value
I believe I have sufficient information about: score 1-5							
I strongly disagree - I strongly agree							
contamination routes, mean±nsd	4.12±1.14	4.24 ± 1.09	4.03±1.17	4.16±1.11	3.73±1.38	4.02±1.16	<0.001
median(Iqr)	5 (4-5)	5(4-5)[2,4]	4(4-5)	5(4-5)[4]	4(2-5)	4(4-5)	
preventive measures, mean±nsd	3.95±1.22	4.14±1.18	3.86±1.26	4.02±1.14	3.73±1.42	3.81±1.28	0.095§
median(Iqr)	4 (4-5)	4(4-5)	4(3-5)	4(4-5)	4(2-5)	4(3-5)	
symptoms, mean±nsd	3.97±1.15	4.14±1.09	3.84±1.19	3.95±1.13	3.61±1.31	3.78±1.19	<0.001§
median(Iqr)	4 (4-5)	4(4-5)[2,3,4,5]	4(3-5)	4(4-5)	4(3-5)	4(3-5)	
treatment, mean±nsd	3.31±1.20	3.38±1.18	3.29±1.22	3.25±1.17	3.37±1.28	2.98±1.30	0.029§
median(Iqr)	4 (2-4)	4(2-4)[5]	4(2-4)	3(2-4)	4(2-4)	3(2-4)	
prognosis, mean±nsd	3.35±1.19	3.39±1.17	3.32±1.20	3.31±1.17	3.53±1.26	3.15±1.32	0.150§
median(Iqr)	4 (2-4)	4(2-4)	4(2-4)	4(2-4)	4(3-5)	3(2-4)	
risk factors, mean±nsd	3.62±1.21	3.64±1.19	3.58±1.23	3.67±1.17	3.68±1.35	3.46±1.30	0.532§
median(Iqr)	4 (3-5)	4(3-5)	4(3-5)	4(3-5)	4(3-5)	4(2-5)	
Do you believe that your department is adequately prepared to cope with the emergency due to the infection? Score 0-4							<0.001§
I strongly disagree - I strongly agree							
mean±nsd	3.14±1.12	2.98±1.13	3.23±1.09	3.28±1.09	3.27±1.16	3.36±1.09	
median(Iqr)	3 (2-4)	3(2-4)[2,3,5]	3(3-4)	3(3-4)	3(3-4)	4(3-4)	
Do you believe that your department provides complete and clear information about the management of the infection? Score 0-4							<0.001§
I strongly disagree - I strongly agree							
mean±nsd	3.10±1.15	2.93±1.13	3.14±1.15	3.29±1.14	3.23±1.14	3.55±1.18	
median(Iqr)	3 (2-4)	3(2-4)[2,3,5]	3(2-4)[5]	3(3-4)	3(3-4)	4(3-4)	

#Chi-square or Fisher Exact-Test; §Kruskal-Wallis Test; [n]Significant differences between the group and the one mentioned by numbers (correction Bonferroni post-hoc tests).

A significant association was observed between risk perception of being infected and having infected people in close contact. Namely, Figure 9 shows the distribution of infected people close to HCWs by different levels of risk perception. Infected colleagues were higher in medium and high perception than in the low one (X^2=23.49; p=0.003).

Figure 9. *Distribution of infected people close to HCWs by risk perception level (n=2078).*



In order to explore factors associated to risk perception of being infected, a multinomial logistic regression was implemented, using "low" risk perception (this variable as codified as "low, medium and high") as the reference category.

Table 5 summarizes the results of the model, where RRRs of estimated coefficient indicate how the outcome risk falling into the comparison category (i.e. group) compared to the one falling into the referent category changes with the variable under consideration. In other words, it refers to the probability of being in the comparison category, compared with the reference outcome (category).

According to the results of the multinomial analysis, none of the variables was statistically significant in the comparison between medium and low risk categories. The comparison of the high-to-low risk perception categories suggests instead some interesting results. Therefore, significant associations were found for sleep disturbances, environment and worry about the infection risk for the surrounding people. Specifically, these variables increase the relative risk of having high-risk perception of being infected compared to low one, given that the other variables in the model are held constant.

As reported in table 5, the relative risk ratio for having sleep disturbances, workplace and being worried about the infection risk for the surrounding people was: RRR=1.641; 95%CI:1.278-2.107, RRR=3.981; 95%CI:2.480-6.390, RRR=2.576; 95%CI:1.500-4.423 for very worried and RRR=2.891; 95%CI:1.672-5.001 for quite worried, respectively. The model results were adjusted for each variable shown in the table. The Hosmer-Lemeshow goodness of fit test indicated a good model fitting (p=0.239).

Table 5.*Risk perception of being infected: relative risk ratios from multinomial logistic regression (n=2078).*

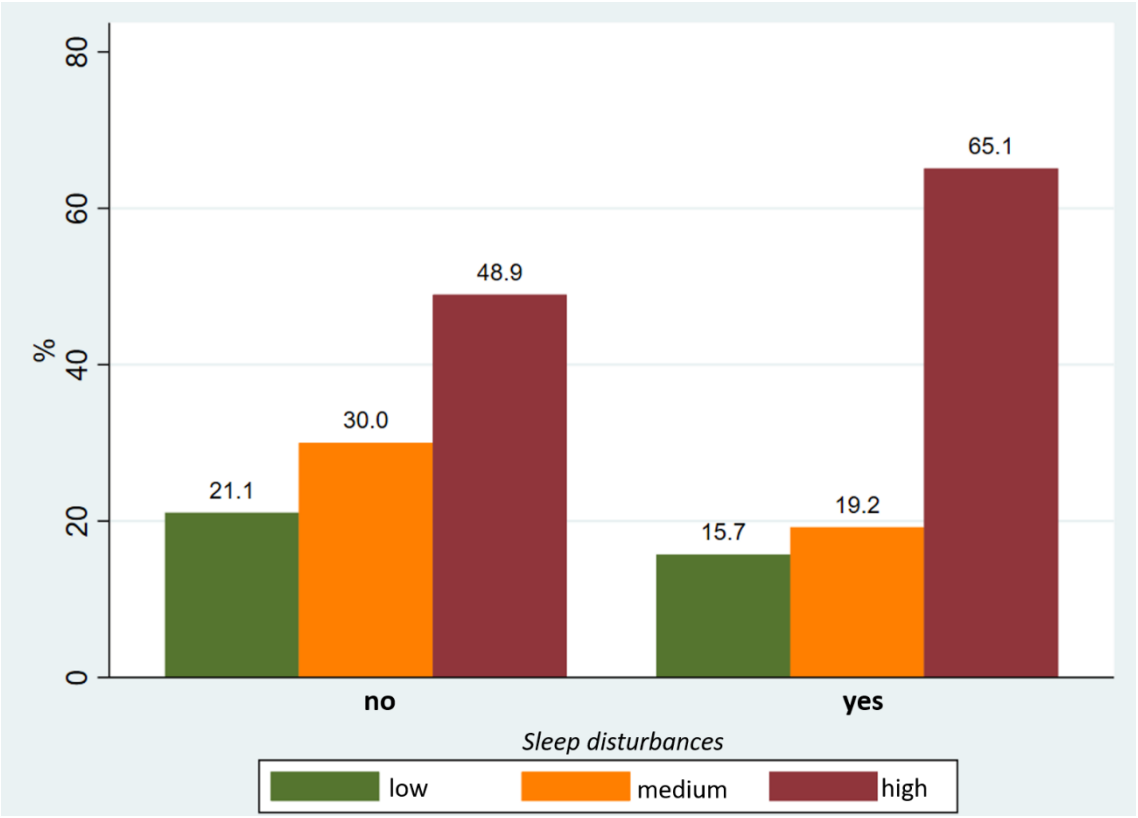
	Risk perception of being infected							
	Medium vs Low				***High vs Low***			
	RRRs	**95%CI**		**P-value**	**RRRs**	**95%CI**		**P-value**
Age (years)	1.001	0.994	1.020	0.320	1.002	0.991	1.013	0.747
Sex - Male vs female	0.845	0.607	1.176	0.318	0.853	0.640	1.137	0.279
Occupational category - vs admin. staff								
Healthcare support staff	0.959	0.392	2.346	0.927	1.578	0.682	3.652	0.287
Medical staff	0.803	0.418	1.543	0.511	1.130	0.601	2.125	0.703
Nurses	0.618	0.327	1.166	0.137	1.376	0.750	2.257	0.303
Physicians	0.608	0.324	1.143	0.122	1.236	0.676	2.261	0.492
At the beginning of the pandemic, environment with higher risk of being infected - vs outside the workplace								
Workplace	1.406	0.866	2.283	0.169	3.981	2.480	6.390	<0.001
The same in both environments	1.547	0.917	2.609	0.102	2.663	1.560	4.434	<0.001
Geographical area – vs South								
Center	0.870	0.520	1.456	0.596	1.214	0.786	1.876	0.383
North	1.012	0.704	1.464	0.936	1.253	0.910	1.723	0.167
Worry about insufficient information about infection provided by ward/department - vs not worried								
Very worried	1.062	0.696	1.617	0.780	1.272	0.889	1.812	0.188
Quite worried	1.556	.839	1.591	0.376	1.015	0.767	1.342	0.918
Worry about the risk of infection for the surrounding people - vs not worried								
Very worried	2.169	1.162	4.045	0.015	2.576	1.500	4.423	0.001
Quite worried	2.776	1.482	5.201	0.001	2.891	1.672	5.001	<0.001
Sleep disturbances - yes vs no	0.824	0.621	1.093	0.180	1.641	1.278	2.107	<0.001

4.4 Sleep disturbances and psychological aspects

Among HCWs 63.43% reported having sleep disturbances, with significant differences among HCW groups (Table 5). Specifically, the proportion of subjects with sleep disturbances was the highest among nurses (70.36%) and the lowest among administrative staff (51.58%) ($p<0.001$).

Moreover, "high" risk perception was significantly higher in HCWs with sleep disturbances than in those without (Figure 10. $X^{2=}53.537$; $p<0.001$).

Figure 10. *Risk perception by sleep disturbances – beginning of the pandemic.*



No significant association was found instead for environments and sleep disturbances ($X^{2=}5.141$; $p=0.007$).

Table 6 shows items describing sleep disturbances and psychological aspects. In regard to the question: "*Do you believe that your department/ward is paying adequate attention to employees' mental health in this emergency period?",* HCWs reported a median value of 3 (IQR 1-3); only for physicians the median value was 2 (IQR 1-3) ($p<0.001$) (score ranging from 0 to 4 where 4 represents strong agreement).

Although 83.35% of HCWs acknowledged the usefulness of getting psychological support during the pandemic scenario, only 9.38% received it. The highest proportion was represented by physicians (10.63%) and nurses (10.18%). The highest percentage (29.47%) of subjects who declared that psychological support was not useful was observed among administrative staff ($p=0.016$); 38.16% of the sample stated that their department/ward did not provide any psychological support service.

As to the use of drugs, 11.07% of participants declared to take them (5.15% anxiolytics, 4.14% sleeping pills and 1.78% antidepressants)[3]. Drug use was proportionally high among physicians (13.70%) followed by nurses (11.23%), administrative (8.45%), healthcare support (7.45%) and medical staff (6.42%) ($X^2=16.105$; $p=0.003$).

[3] Data about type of drugs are not shown in the table.

Table 6. *Cont. Healthcare workers' psychological aspects and sleep disturbances.*

Psychological profile	All N=2078	1.Physicians N=847	2.Nurses N=668	3.Medical staff N=374	4.Healthcare support staff N=94	5.Administrative staff N=95	P-value
Have you suffered from sleep disturbances in the last two months? n(%)							<0.001 #
no	760(36.57)	320(37.78)	198(29.64)	163(43.58)	33(35.11)	46(48.42)	
yes	1318(63.43)	527(62.22)	470(70.36)	211(56.42)	61(64.89)	49(51.58)	
Do you believe that your department/ward is paying adequate attention to the employees' mental health in this emergency period? Score 0-4							<0.001§
I strongly disagree -I strongly agree							
mean±nsd	2.57±1.25	2.38±1.21	2.69±1.26	2.68±1.20	2.59±1.35	2.95±1.33	
median(Iqr)	3 (1-3)	2(1-3)[2,3,5]	3(2-4)	3(2-4)	3(1-4)	3(2-4)	
Do you believe psychological support is useful in the current situation? n(%)							0.016#
no	346(16.65)	137(16.17)	99(14.82)	67(17.91)	15(15.96)	28(29.47)	
yes	1732(83.35)	710(83.83)	569(85.18)	307(82.09)	79(84.04)	67(70.53)	
Have you received psychological support in the last two months? n(%)							0.092#
no	1883(90.62)	757(89.37)	600(89.82)	347(92.78)	88(93.62)	91(95.79)	
yes	195(9.38)	90(10.63)	68(10.18)	27(7.22)	6(6.38)	4(4.21)	
Does your department/ward provide a psychological support service? n(%)							<0.001 #
no	793(38.16)	358(42.27)	193(28.89)	171(45.72)	49(52.13)	22(23.16)	
yes	1285(61.84)	489(57.73)	475(71.11)	203(54.28)	45(47.87)	73(76.84)	
Have you taken psychopharmacological drugs?							0.003#
no	1848(88.93)	731(86.30)	593(88.77)	350(93.58)	87(92.55)	87(91.58)	
yes	230(11.07)	116(13.70)	75(11.23)	24(6.42)	7(7.45)	8(8.42)	

#Chi-square or Fisher Exact-Test; §Kruskal-Wallis Test; [n]Significant differences between the group and the one mentioned by numbers (correction Bonferroni post-hoc tests).

Finally, a multivariable logistic regression model was implemented in order to explore factors related to sleep disturbances. The model showed that being a female (OR=1.565; 95%CI:1.240-1.975), having a high risk perception of being infected (OR=1.603; 95%CI:1.156-2.221), being a nurse (OR=1.664; 95%CI:1.290-2.146) and having a high score of worry (OR=1.680; 95%CI:1.476-1.913) were significantly associated with the presence of sleep disturbances (HL test p=0.5086) (Table 7). ORs were adjusted for each variable shown in the table.

Table 7. *Factors associated with the presence of sleep disturbances: results from multivariable logistic regression model (n=2078).*

	OR	95% CI		P-value
		Lower	Upper	
Age (years)	0.999	0.990	1.008	0.862
Sex				
Female vs Male	1.565	1.240	1.975	<0.001
Perception of risk of being infected				
Medium vs low	1.250	0.957	1.633	0.103
High vs low	1.603	1.156	2.221	0.005
Occupational category				
Nurses vs medical/healthcare support/administrative staff	1.664	1.290	2.146	<0.001
Physicians vs medical /healthcare support /administrative staff	1.202	0.951	1.518	0.124
Degree of worry (score)	1.680	1.476	1.913	<0.001

Firstly, we implemented the model considering the variable "occupational category" with five levels corresponding to HCWs. As the different models demonstrated that nurses were always the only group showing a statistically significant OR, for sake of clarity we decided to fit the model by using a dichotomous variable: nurses and physicians (frontline) versus all the other health professionals.

4.5 Further results

This paragraph illustrates results that go beyond the scope of this research, but that are nevertheless important for a better understanding of the field under study. Literature data showed a lack of evidence about studies conducted in healthcare contexts such as TCs; therefore, analysis results for this subcategory are presented below. According to the peculiarities of the TCs and the number of respondents (n=91), HCWs were stratified into two groups: physicians and medical staff (all professionals other than physicians). Moreover, we reported results according to Italian geographical areas, healthcare structures and sex.

4.5.1 Therapeutic communities

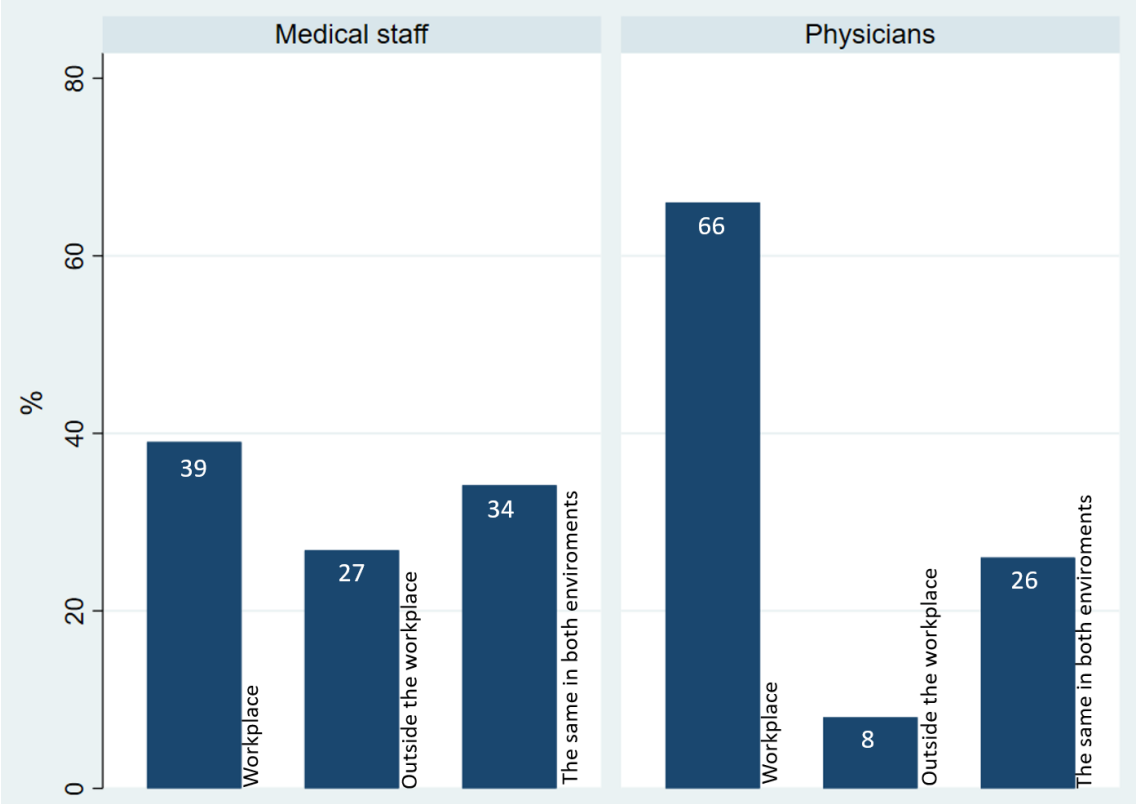
Among 91 HCWs working in Therapeutic communities, 10% reported having been infected with SARS-CoV-2, with a similar proportion among physicians and medical staff (10% vs 9.8%; p=0.626).

In regard to worries, as observed for the entire sample, the general median score was 3(IQR 2-3). For all professionals, the median degree of worry was high but not significantly different between subgroups: median score among physicians was 3(IQR 2-4) and among medical staff was 3(IQR 2-3) (p=0.489).

Two-thirds of the sample was worried for *"The risk of infection for the surrounding people"* (52%) and *"The disease's dangerousness/health consequences"* (21%). Minor percentages referred to *"The isolation from family and/or social environment"* (5%) and *"The contagion"* (4%). Only 1% stated that they had no worries and 17% declared to be worried about all of the above. For both groups *"The risk of infection for the surrounding people"* still remains the most frequent type of worry (percentages ranged from 51% to 52%). Instead, for 47% of the sample the risk perception at the beginning of the pandemic was high, for 29% it was medium and for 24% low. At the time of the questionnaire administration, workplace was the environment where HCWs perceived the highest risk of being

infected, with significant differences between physicians and medical staff (X^2=8.394; p=0.015) (Figure 11).

Figure 11. *Risk perception and environment - comparison between physicians and medical staff.*



Among HCWs, different perception about adequacy of departments/wards to cope with the emergency was observed: medical staff with a median score of 3(IQR 2-4) reported a greater agreement than physicians with a median score of 2(IQR 1-3) (p<0.001). Finally, 55% of the sample reported having sleep disturbances, with no significant differences among medical staff (54%) and physicians (46%) (p=0.058). Additionally, 6.59% of participants declared that they use drugs: no statistical difference was found between the two subgroups (medical staff vs physicians: 5% vs 8%; p=0.687).

4.5.2 Geographical areas

SARS-CoV-2 was significantly prevalent in northern Italy with 18.84% of infected HCWs, followed by the southern (9.19%) and the central area of the country (8.27%) (X^2=33.061; p<0.001). In each area, the major source of concern was about "*The risk of infection for the surrounding people"* (Table 8). Median degree of worry was similar in all areas: North 3(2-3), Center 3-(2-3) and South 3(2-4) (p=0.0001). Post hoc analysis revealed slight differences between northern and southern Italy (Bonferroni post hoc test: p<0.0001). In all geographical areas risk perception was high (percentages ranging from 56.49% to 62.60%) and more identified in the workplace (in both cases differences were not significant) (Table 8).

Table 8*. Degree and type of worry among Italian geographical areas.*

	Italian geographical area			
	North (n=1454)	Center (n=254)	South (n=370)	
	n(%)	n(%)	n(%)	**P-value**
What worries you most about				
The contagion	45(3.09)	11(4.33)	15(4.05)	0.304#
The risk of infection for the surrounding people	792(54.47)	132(51.97)	218(58.92)	
The isolation from family and/or social environment	47(3.23)	14(5.51)	11(2.97)	
The disease's dangerousness/health consequences	249(17.13)	41(16.14)	48(12.97)	
None of the above	15(1.03)	2(0.79)	1(0.27)	
All of the above	306(21.05)	54(21.26)	77(20.81)	
At the beginning of the pandemic, you thought that your risk of being infected was:				
Low	249(17.13)	46(18.11)	72(19.46)	0.436*
Medium	343(23.59)	49(19.29)	89(24.05)	
High	862(59.28)	159(62.60)	209(56.49)	
At the beginning of the pandemic, you thought that your risk of being infected was higher:				
In the workplace	674(46.35)	125(49.21)	201(54.32)	0.047*
Outside the workplace	277(19.05)	46(18.11)	50(13.51)	
The same in the both environments	503(34.59)	83(32.68)	119(32.16)	

#Fisher Excat test; *Pearson Chi Square test.

4.5.3 Healthcare structures

With regard to the type of healthcare structures, prevalence of SARS-CoV-2 infection was significantly higher in nursing homes (23.45%) compared to hospitals (15.53%) and TCs (9.89%) (X^2=8.852; p=0.012).

Median degree of worry was 3(2-3) in all structures (p=0.0746). There were not significant differences in type of worry; however, in each structure, "*The risk of infection for the surrounding people"* was prevalent with percentages ranging from 52% to 55%. At the beginning of the pandemic, although the risk perception of being infected was highly transversal to all structures, high perception of risk was prevalent in hospitals (60.31%) compared to nursing homes (52.41%) and TCs (47.25%) (X^2=11.737; p=0.019).

Prevalence of sleep disturbances was higher in hospitals (64.06%) followed by nursing homes (60.69%) and TCs (54.95%) (X^2=3.610; p=0.0165).

4.5.4 Sex differences

SARS-CoV-2 prevalence was 15.46% among females and 17.39% among males (X^2=0.969; p=0.325). Table 9 shows the main results about worries and risk perception stratified by sex. For both sexes, in half of the sample the greatest worry was about "*The risk of infection for the surrounding people*". A slight difference was observed in the distribution of "*The disease's dangerousness/health consequences*"; among males it appeared slightly more prevalent than among females (21.05% vs 15.03%; p=0.036). No differences were observed for environment and level of risk perception of being infected. Median degree of worry was 2(2-3) in both groups (n.s.).

***Table 9**. Degree and type of worry among males and females.*

	Female (n=1637)	Male (n=254)	
	n(%)	n(%)	**P-value**
What worries you most about			
The contagion	53(3.24)	18(4.12)	0.036#
The risk of infection for the surrounding people	915(55.89)	225(51.49)	
The isolation from family and/or social environment	56(3.42)	16(3.66)	
The disease's dangerousness/health consequences	246(15.03)	92(21.05)	
None of the above	13(0.79)	5(1.14)	
All of the above	354(21.62)	81(18.54)	
At the beginning of the pandemic, you thought that your risk of being infected was:			
Low	279(17.04	88(20.14)	0.283*
Medium	378(23.09	102(23.34)	
High	980(59.87	247(56.52)	
At the beginning of the pandemic, you thought that your risk of being infected was higher:			
In the workplace	1157(70.68)	317(72.54)	0.703*
Outside the workplace	93(5.68)	25(5.72)	
The same in the both environments	387(23.64)	95(21.74)	

#Fisher Exact test; *Pearson Chi Square test

Sleep disturbances were significantly higher among females than among males: 66.46% vs 52.17%, respectively (X^2=30.369; p<0.001).

Chapter 5

Discussion

5.1 Key findings

The purpose of this thesis project was to explore factors related to mental health in Italian healthcare workers in the first wave of the pandemic, specifically aiming at describing their worries, risk perceptions of being infected and sleep disturbances.

This research yielded the following main findings:

- *Worries and concerns.* All HCWs reported experiencing high levels of worry, identifying *"The risk of infection for the surrounding people*" as the greatest source of concern. These results were common to all occupational category, type of healthcare facilities and geographical areas. SARS-CoV-2 infection was significantly high in nursing homes and among healthcare support staff. Additionally, it was higher in the North compared to central and southern area.

- *Risk perception of being infected.* It was high among all HCWs, even if in this case the distribution of the risk levels appeared to be different among groups: physicians, nurses and healthcare support staff seemed to perceive a higher risk whereas administrative staff seemed to perceive a lower risk, as it was "high level"; furthermore, it was higher in hospitals than in other facilities. Environment plays a key role in modulating risk perception; therefore, the workplace was identified as the place with the highest risk. Generally speaking, physicians showed a lower degree of agreement than other groups on the adequacy of the Department / ward to cope with the emergency. The same tendency was observed in regard to the information the department provided about infection: a lower degree of agreement was noticed for both physicians and nurses. This last result

was observed also in TCs. However, at the multivariable analysis risk perception was significantly associated with worry about *"The risk of infection for the surrounding people*", presence of sleep disturbances and workplace, in terms of increased probability of having a high level of risk perception rather than a low one.

- *Sleep disturbances*. They affected all HCWs groups and they were higher in hospitals than in nursing homes and TCs. Furthermore, multivariable analysis showed that their presence was associated with a higher degree of worry, and a high perception of risk. Females and nurses were more likely to have sleep disturbances than males and other HCW groups.

5.2 Relevant findings and comparison with previously published evidence

The study results describe the extent of HCWs' concerns about the health emergency and offer noticeable insights on rising concerns about the management of the international health crisis among the occupational categories involved - albeit to a different extent. In our sample, which is consistent with previous studies, participants were mostly females [115,116]; they reported higher sleep disturbances than males but no significant differences in worries and risk perception.

With regard to concerns, more than half of the HCWs reported being highly worried about the COVID-19 pandemic, and the most frequent worry was about *"The risk of infection for the surrounding people"*. This aspect is strongly linked to their human and health professional nature. HCWs, especially those working in hospitals, take care of infected patients; this close contact may be a source of vulnerability and fear for the virus transmission to their family, friends or colleagues [117].

As regards the type of worries, there were no differences in their distribution among the HCWs groups[4]. These results are in line with what reported by Sahashi et al. (2021), who found the same concerns [118]and with the study by Riguzzi and Gashi (2021), which showed that HCWs were more concerned about infecting their family/friends than being infected themselves [119].

[4]See Figure 9.

Reported prevalence of Sars-Cov-2 infection (15.80%) was higher compared to results of some study conducted in Germany and U.S.A (where self-report prevalence was 6% and 7% respectively) [120,121]. Nevertheless, results from meta-analysis showed that prevalence (detected by RT-PCR) ranged from 0.4% to 57.06% [122]. The highest prevalence in the current study was observed in nursing homes. Two studies showed that infection prevalence in nursing homes was lower than our result, with a range from 3.7% to 9.5%; the former reported higher prevalence in nursing homes than in primary care centers (9.5% vs 5.9%) while the latter showed opposite results, according to which prevalence was lower than in hospital settings (3.7% vs 8.4%) [123,124]. These heterogeneous results can be ascribed to the different methods of detection and identification of the virus that can lead to estimation bias. In addition, many of the studies cited only referred to hospitals or dissimilar settings. As expected, SARS-CoV-2 infection was significantly more prevalent in the North than in the Center and South. As extensively discussed in the first chapter, this result finds its explanation in the fact that at the beginning of the pandemic northern Italy was the first and most affected area. Furthermore, probably due to the direct biological exposition to the virus associated with bedside activity, infection was higher among healthcare support staff (22.34%). Nurses, who are second with 22.34% of infected personnel, confirm literature results being one of the groups with a high SARS-CoV-2 prevalence [122,123,125,126]. Finally, as reported by Perez et al (2021), physicians had a lower prevalence of infection [127].

Risk perception of being infected was higher in hospitals than in nursing homes and TCs. The type of services offered by the diverse facilities mainly explains this result: essentially, as places of care hospitals are the structures used for the treatment of COVID-19 patients, especially during the first wave when patients required hospitalization for severe respiratory problems. The type of treatment and contact with patients substantially differentiate the healthcare structures. In addition, as reasonably expected, univariate analysis showed that the perceived risk was significantly higher for physicians, nurses and healthcare support staff than for other healthcare professionals. This result is consistent with the direct exposition to SARS-CoV-2 associated with their bedside activity. Dryhurst at al. (2020), in their study aimed at mapping risk perception worldwide, underlined that risk perception about COVID-19 was high in all countries, stating that subjects who experienced a personal contact with the virus had a different perception in

terms of more accurate and higher perception [128]. Results of an Italian study showed a greater perception of risk in northern Italy, compared to central and southern areas [129]; current findings do not confirm this result, as risk perception was high in all geographical areas without significant differences. In our sample, at the time of the questionnaire administration (Italian reopening phase), risk perception still was high as at the beginning of the pandemic. This result may be explained by the high intensity of mass media communication, which may have amplified the information on the risk and, probably, on its perception [91].

As to environment, in line with other studies results showed that workplace had an important impact on risk perception as it was identified as the highest top-score degree of infection risk [130–132]. Although direct contact and care of infected patients characterize the work environment as a high-risk place, to further support these results, in this study the majority of HCWs reported to have infected colleagues. This explains not only the high perceived risk in the workplace, but also the concern about the virus transmission to the surrounding people. Moreover, in the workplace, other factors such as information or concern about insufficient PPE can influence risk perception. As regards the shortage of PPE, this was not a reason of concern in our study.

The degree of perceived sufficiency of information about contamination routes, preventive measures, symptoms, treatment, prognosis and risk factors was moderately high. However, administrative staff showed lower levels of high-risk perception and reported a slightly lower median value in relation to perceived information about treatment and prognosis compared to other groups. One of the possible reasons probably may be the educational and training background that is different among health professional categories. This difference may in turn lead to a different perception of risk. Several studies showed that greater knowledge and awareness in individuals were associated with greater perception of risk and higher level of involvement in precautionary behaviors [133–135]. A study conducted in Wuhan reported conflicting results, since risk perception was negative correlated to knowledge, even though the relationship reported in the study was very poor [136].

Finally, multivariable analysis results showed that workplace, concern about the risk of infecting the surrounding people and having sleep disturbances increased the probability of having a higher

perception (compared to a lower one). In the data analysis phase, many variables were evaluated including geographical areas and healthcare structures, but they did not give significant contribution to the model.

Finally, more than a half of the sample reported sleep disturbances, with higher risk for females, higher prevalence among nurses and healthcare support staff and lower among administrative staff. Moreover, a significantly higher perception of risk was prevalent in HCWs with sleep disturbances than among other groups; a high-risk level was indeed a risk factor for developing sleep disturbances. These results are consistent with other studies: namely, a systematic review showed that incidence of insomnia was higher either in nurses (especially females) or in frontline HCWs compared to non-frontline ones [28,69,137–140]. In addition, a meta-analysis revealed that nurses were more nervous, anxious and stressed than other health professionals [72]. Although information about anxiety and stress was not collected in this study, it would be plausible to think that also these factors, like worries, affected our HCWs and may have influenced their sleep quality [85]. However, it is reasonable to think that the catastrophic pandemic scenario has greatly increased the frequency of sleep disturbances in individuals. This especially refers to the first wave when, in addition to worries related to the virus and its consequences, the enormous workload caused changes in the work routine with dysregulated sleep-wake cycles that may have led to alterations of circadian rhythms and of the sleep quality.

Other findings revealed that there was more agreement among administrative staff than among other groups on the adequacy of the Department/ward to cope with the emergency and on the information about infection provided by the department, whereas a lower level of agreement was observed in physicians and nurses. This is probably due to the different role of professionals, their needs and involvement in the health emergency that may have influenced perceptions about the Department management. Similar results were observed among HCWs working in TCs. The initial lack of PPE, protocols, beds and devices to manage clinical complications (it must be remembered that there were no respirators) certainly affected the department management as it was not prepared to deal with an emergency of disastrous proportions.

Literature data about TCs were, moreover, scarce. Especially in the first wave, studies focused their attention on the evaluation of mental health disorders among HCWs directly exposed to the

virus and in hospitals as care settings for COVID-19 patients. However, the results shown here indicate that HCWs working in TCs experienced the same concern as in other healthcare settings.

Some important findings emerged from this study on the evident divergence between the perceived need for psychological support and the relative lack of this service among healthcare providers. Lack of psychological support may play a key role in forming a spiral of chronicity in the previously cited mental health issues (i.e., insomnia). As explained in the introduction, in the initial phase there was a lack of centers for psychological support because treating patients was the priority and there was no immediate counseling support. Furthermore, recognizing the need for psychological help may still represent a taboo; the stigma associated with mental illness still pervades the health sector with a strong impact on the psychological well-being of healthcare professionals, who can perceive a double barrier due to the traumatic experience and to the stigma of the working entourage [141,142]. These results, in line with other studies, suggest that early mental health support should be available to HCWs in any healthcare settings [79,143].

In summary, the main findings showed a high prevalence of insomnia and worries among all healthcare workers. These findings need attention, since the sleeping problems may be of greater concern as they are associated with anxiety, burnout and mental health disorders.

5.3 Strengths and Limitations

The results of this research refer to a large sample of Italian healthcare professionals. This response indicates their great participation and confirms their involvement especially in a period that was critical and exhausting from a professional viewpoint. In this regard, during the questionnaire administration some professionals contacted the research team to express their enthusiasm for participating. These data highlight both their willingness and their need to express themselves and to make their voices heard.

Despite its limitations, as described below, the questionnaire was easy to use and this, together with the online administration, motivated healthcare professionals to participate. These characteristics made it possible to conduct this research during a very challenging period in which HCWs were exposed to arduous work shifts and did not have time for matters not related to their priority at that juncture, namely the management of the health emergency.

Finally, to the best of our knowledge, these results fill the gap in our understanding of the issues faced by HCWs in TCs, illustrating the concerns of the practitioners in these facilities.

Nevertheless, this project has some limitations, mainly due to its design, i.e., a cross-sectional survey where information and answers were self-reported. Other limitations are related to the use of a non-representative sample of the overall Italian healthcare workers (based on different geographical areas) and of non-validated questionnaires. In this regard, the validated questionnaires found in literature were very long. This choice was weighed up and based on priorities related to healthcare workers, as they were overworked at the time of the questionnaire administration. Finally, we cannot rule out the possibility that health professionals in deep distress were underrepresented, as these individuals may have been either on leave due to their concerns about the pandemic or extremely busy working in the Intensive Care Unit and consequently unable to join the study.

5.4 Implications

The implications of this thesis project firstly indicate that institutions need to be better prepared to deal with contingency plans, especially in the areas of mental health, workload and resource access. These fields in turn contain specific problems that cover other areas and affect HCWs.

To be practical, a sudden change in the workplace may increase their stress level, which in turn may compromise their mental health and work ability. It follows that contingency plans drawn up around these areas may assist institutions to adapt to atypical circumstances.

Furthermore, a reflection is needed even under the best conditions, in order to be able to cope with changes brought about by the pandemic. Institutional programs should include actions aiming at monitoring such changes and continuing employee training. Protection of healthcare professionals is fundamental, thus policy should be focused on risk assessment.

Chapter 6

Conclusion

This thesis has given a small contribution to the literature about HCWs' mental health by documenting a variety of effects of the COVID-19 pandemic during the Italian first wave. In addition, it points to an important issue related to the impact that the pandemic has had on HCWs' psychological and physical well-being.

Our findings cast light on a concept of well-being that appears to be complex and related to a synergy of multiple factors. This dense texture clearly reveals the impact of social and work environment on mental health.

Additionally, it is reasonable to think that the pandemic scenario has led HCWs to define their priorities in a moment of general instability characterized by the precariousness of life itself, arousing their vulnerability.

This, together with the concerns previously discussed, highlights HCWs' emotional and human frailty. It is necessary to be aware of these factors in order to implement intervention plans focused on the crisis and on specific HCWs' needs.

All these aspects occupy a crucial role in fostering psychological and physical well-being which, if compromised, may lead to negative consequences that also affect work behaviors and therefore the quality of the health services provided. It is a well-known fact that untreated psychic distress leads to even severe health issues, involving both psychiatric and organic diseases, thus compromising work quality and proficiency together with life quality.

Finally, such results suggest the importance of psychological and psychiatric support services in an infectious disease emergency scenario. They also point to the institutions' lack of attention to these issues. Therefore, it is essential to increase psychosocial support by rendering it easily accessible to HCWs, and to ensure that healthcare staff is aware of the possibility of having benefit from these services, with either direct or remote access, in order to deal with the needs of hospital work shifts.

Managers and team leaders play a leading role in ensuring the psychological well-being of their employees, and should take into account the factors mentioned above in the development of target actions.

It is important to remember that assessment of risk perception is central in the EIDs control because a realistic risk perception allows to implement and promote voluntary preventive behaviors that are often the only defense in the early phase. Thus, risk communication in the workplace may represent an effective strategy for achieving success in the promotion of precautionary behaviors among health professionals.

A mentally healthy workplace is achievable in all organizational contexts; however, in order for this to happen, an authentic and continuous commitment is required at all levels. Finally, managers and stakeholders play a key role in risk communication in the workplace, and they can promote precautionary behaviors among health care professionals.

6.1 Future research perspectives

This research provides a significant overview of concerns of HCWs in the first pandemic wave. Therefore, future research should investigate the medium- and long-term psychological implications, as HCWs may have suffered from significant deterioration, both psychologically and physically. It follows that follow-up studies may be useful, also to evaluate the possible benefits that implementation of therapeutic interventions and recourse to them in the following phases may bring.

Other perspectives concern data collection by validated tools. Further information on anxiety, burnout and the use of PPE may be useful in understanding the mechanisms of modulation of risk perception. In addition, it would be interesting to design studies aimed at identifying and evaluating the HCWs coping strategies during the pandemic.

Finally, it would be useful to describe the protocols developed to cope with mental health problems, and to evaluate the effectiveness of surveillance and risk assessment programs.

How many protocols have been developed? What are their contents? What results have they shown in terms of improving the professionals well-being and in terms of public health? Have there been any changes in the access to health care services? Answering these questions is fundamental to evaluate the impact of measures implemented in order to ensure safety and well-being of employees.

References

1. Mukherjee, S. Emerging Infectious Diseases: Epidemiological Perspective. *Indian J. Dermatol.***2017**, *62*, 459, doi:10.4103/IJD.IJD_379_17.

2. McArthur, D.B. Emerging Infectious Diseases. *Nurs. Clin. North Am.***2019**, *54*, 297, doi:10.1016/J.CNUR.2019.02.006.

3. Rahman, M.T.; Sobur, M.A.; Islam, M.S.; Ievy, S.; Hossain, M.J.; Zowalaty, M.E. El; Rahman, A.T.; Ashour, H.M. Zoonotic Diseases: Etiology, Impact, and Control. *Microorganisms***2020**, *8*, 1–34, doi:10.3390/MICROORGANISMS8091405.

4. 2010 AsiA PAcific strAtegy for emerging DiseAses South-East Asia Region Western Pacific Region.

5. Watkins, K. Emerging Infectious Diseases: a Review. *Curr. Emerg. Hosp. Med. Rep.***2018**, *6*, 86, doi:10.1007/S40138-018-0162-9.

6. Jones, K.E.; Patel, N.G.; Levy, M.A.; Storeygard, A.; Balk, D.; Gittleman, J.L.; Daszak, P. Global trends in emerging infectious diseases. *Nat. 2008 4517181***2008**, *451*, 990–993, doi:10.1038/nature06536.

7. Organization, W.H. SEA-CD-139 Distribution: General Combating Emerging Infectious Diseases in the South-East Asia Region. **2005**.

8. Lim, P.L. Travel and the globalization of emerging infections. *Trans. R. Soc. Trop. Med. Hyg.***2014**, *108*, 309, doi:10.1093/TRSTMH/TRU051.

9. Mackey, T.K.; Liang, B.A.; Cuomo, R.; Hafen, R.; Brouwer, K.C.; Lee, D.E. Emerging and reemerging neglected tropical diseases: a review of key characteristics, risk factors, and the policy and innovation environment. *Clin. Microbiol. Rev.***2014**, *27*, 949–79, doi:10.1128/CMR.00045-14.

10. Heymann, D.L.; Mackenzie, J.S.; Peiris, M. SARS legacy: outbreak reporting is expected and respected. *Lancet (London, England)***2013**, *381*, 779, doi:10.1016/S0140-6736(13)60185-3.

11. Cherry, J.D.; Krogstad, P. SARS: The First Pandemic of the 21st Century. *Pediatr. Res.***2004**, *56*, 1, doi:10.1203/01.PDR.0000129184.87042.FC.

12. A brief guide to emerging infectious diseases and zoonoses. **2014**.

13. Brachman, P.S. Infectious diseases—past, present, and future. *Int. J. Epidemiol.***2003**, *32*, 684–686, doi:10.1093/IJE/DYG282.

14. Mohammadi, M.; Meskini, M.; Pinto, A.L. do N. 2019 Novel coronavirus (COVID-19) overview. *J. Public Heal. 2020***2020**, 1–9, doi:10.1007/S10389-020-01258-3.

15. Gorbalenya, A.E.; Enjuanes, L.; Ziebuhr, J.; Snijder, E.J. Nidovirales: Evolving the largest RNA virus genome. *Virus Res.***2006**, *117*, 17, doi:10.1016/J.VIRUSRES.2006.01.017.

16. Fehr, A.R.; Perlman, S. Coronaviruses: An Overview of Their Replication and Pathogenesis. *Coronaviruses***2015**, *1282*, 1, doi:10.1007/978-1-4939-2438-7_1.

17. Cui, J.; Li, F.; Shi, Z.-L. Origin and evolution of pathogenic coronaviruses. *Nat. Rev. Microbiol.***2019**, *17*, 181, doi:10.1038/S41579-018-0118-9.

18. Zhu, Z.; Lian, X.; Su, X.; Wu, W.; Marraro, G.A.; Zeng, Y. From SARS and MERS to COVID-19: a brief summary and comparison of severe acute respiratory infections caused by three highly pathogenic human coronaviruses. *Respir. Res.***2020**, *21*, doi:10.1186/S12931-020-01479-W.

19. Lauxmann, M.A.; Santucci, N.E.; Autrán-Gómez, A.M. The SARS-CoV-2 Coronavirus and the COVID-19 Outbreak. *Int. braz j urol***2020**, *46*, 6–18, doi:10.1590/S1677-5538.IBJU.2020.S101.

20. House, N.N.C.; Palissery, S.; Sebastian, H. Corona Viruses: A Review on SARS, MERS and COVID-19: *https://doi.org/10.1177/117863612110024*81**2021**, *14*, 117863612110024, doi:10.1177/11786361211002481.

21. Mann, R.; Perisetti, A.; Gajendran, M.; Gandhi, Z.; Umapathy, C.; Goyal, H. Clinical Characteristics, Diagnosis, and Treatment of Major Coronavirus Outbreaks. *Front. Med.***2020**, *0*, 766, doi:10.3389/FMED.2020.581521.

22. Zhong, N.; Zheng, B.; Li, Y.; Poon, L.; Xie, Z.; Chan, K.; Li, P.; Tan, S.; Chang, Q.; Xie, J.; et al. Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong, People's Republic of China, in February, 2003. *Lancet (London, England)***2003**, *362*, 1353, doi:10.1016/S0140-6736(03)14630-2.

23. CHAN-YEUNG, M.; XU, R. SARS: epidemiology. *Respirology***2003**, *8*, S9, doi:10.1046/J.1440-1843.2003.00518.X.

24. World Health Organization *Consensus document on the epidemiology of severe acute respiratory syndrome (SARS)*; 2003;

25. Hilgenfeld, R.; Peiris, M. From SARS to MERS: 10 years of research on highly pathogenic human coronaviruses. *Antiviral Res.***2013**, *100*, 286, doi:10.1016/J.ANTIVIRAL.2013.08.015.

26. Zhang, A.-R.; Shi, W.-Q.; Liu, K.; Li, X.-L.; Liu, M.-J.; Zhang, W.-H.; Zhao, G.-P.; Chen, J.-J.; Zhang, X.-A.; Miao, D.; et al. Epidemiology and evolution of Middle East respiratory syndrome coronavirus, 2012–2020. *Infect. Dis. Poverty***2021**, *10*, 66, doi:10.1186/s40249-021-00853-0.

27. Al-Omari, A.; Rabaan, A.A.; Salih, S.; Al-Tawfiq, J.A.; Memish, Z.A. MERS coronavirus outbreak: Implications for emerging viral infections. *Diagn. Microbiol. Infect. Dis.***2019**, *93*, 265–285, doi:10.1016/j.diagmicrobio.2018.10.011.

28. Soriano, J.B.; Kendrick, P.J.; Paulson, K.R.; Gupta, V.; Abrams, E.M.; Adedoyin, R.A.; Adhikari, T.B.; Advani, S.M.; Agrawal, A.; Ahmadian, E.; et al. Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: a systematic analysis for the

Global Burden of Disease Study 2017. *Lancet Respir. Med.***2020**, *8*, 585–596, doi:10.1016/S2213-2600(20)30105-3.

29. Junior, J.A.C.N.; Santos, A.M.; Quintans-Júnior, L.J.; Walker, C.I.B.; Borges, L.P.; Serafini, M.R. SARS, MERS and SARS-CoV-2 (COVID-19) treatment: a patent review. *https://doi.org/10.1080/13543776.2020.1772231***2020**, *30*, 567–579, doi:10.1080/13543776.2020.1772231.

30. Hu, B.; Guo, H.; Zhou, P.; Shi, Z.-L. Characteristics of SARS-CoV-2 and COVID-19. *Nat. Rev. Microbiol. 2020 193***2020**, *19*, 141–154, doi:10.1038/s41579-020-00459-7.

31. Harrison, A.G.; Lin, T.; Wang, P. Mechanisms of SARS-CoV-2 Transmission and Pathogenesis. *Trends Immunol.***2020**, *41*, 1100–1115, doi:10.1016/J.IT.2020.10.004.

32. Jiang, S.; Du, L.; Shi, Z. An emerging coronavirus causing pneumonia outbreak in Wuhan, China: calling for developing therapeutic and prophylactic strategies. *https://doi.org/10.1080/22221751.2020.1723441***2020**, *9*, 275–277, doi:10.1080/22221751.2020.1723441.

33. Wu, F.; Zhao, S.; Yu, B.; Chen, Y.-M.; Wang, W.; Song, Z.-G.; Hu, Y.; Tao, Z.-W.; Tian, J.-H.; Pei, Y.-Y.; et al. A new coronavirus associated with human respiratory disease in China. *Nat. 2020 5797798***2020**, *579*, 265–269, doi:10.1038/s41586-020-2008-3.

34. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020 Available online: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020 (accessed on Sep 5, 2021).

35. E, G.; I, P.; G, L.; AŞ, A.; C, L.; P, B.; D, A.; D, G. Excess of all-cause mortality is only partially explained by COVID-19 in Veneto (Italy) during spring outbreak. *BMC Public Health***2021**, *21*, doi:10.1186/S12889-021-10832-7.

36. Giovanetti, M.; Benvenuto, D.; Angeletti, S.; Ciccozzi, M. The first two cases of 2019-nCoV in Italy: Where they come from? *J. Med. Virol.***2020**, *92*, 518, doi:10.1002/JMV.25699.

37. Livingston, E.; Bucher, K. Coronavirus Disease 2019 (COVID-19) in Italy. *JAMA***2020**, *323*, 1335–1335, doi:10.1001/JAMA.2020.4344.

38. Situation Report-65 HIGHLIGHTS.

39. Situation Report-12 SITUATION IN NUMBERS total and new cases in last 24 hours.

40. ISS Integrated surveillance of COVID - 19 in Italy. **2020**, *157*, 943.

41. Med Sci, T.J.; Bulut, C.; Kato, Y. Turkish Journal of Medical Sciences Epidemiology of COVID-19., doi:10.3906/sag-2004-172.

42. Rajgor, D.D.; Lee, M.H.; Archuleta, S.; Bagdasarian, N.; Quek, S.C. The many estimates of the COVID-19 case fatality rate. *Lancet. Infect. Dis.***2020**, *20*, 776, doi:10.1016/S1473-3099(20)30244-9.

43. D'Arienzo, M.; Coniglio, A. Assessment of the SARS-CoV-2 basic reproduction number, R0, based on the early phase of COVID-19 outbreak in Italy. *Biosaf. Heal.***2020**, *2*, 57, doi:10.1016/J.BSHEAL.2020.03.004.

44. Kendzerska, T.; Zhu, D.T.; Gershon, A.S.; Edwards, J.D.; Peixoto, C.; Robillard, R.; Kendall, C.E. The Effects of the Health System Response to the COVID-19 Pandemic on Chronic Disease Management: A Narrative Review. *Risk Manag. Healthc. Policy***2021**, *14*, 575, doi:10.2147/RMHP.S293471.

45. AM, K.; O, G.; A, C.; S, P.; A, G.; O, T.; HS, T.; R, T. Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis. *Am. J. Obstet. Gynecol.***2021**, *224*, 35-53.e3, doi:10.1016/J.AJOG.2020.07.049.

46. Chang, H.-J.; Huang, N.; Lee, C.-H.; Hsu, Y.-J.; Hsieh, C.-J.; Chou, Y.-J. The Impact of the SARS Epidemic on the Utilization of Medical Services: SARS and the Fear of SARS. *https://doi.org/10.2105/AJPH.94.4.562***2011**, *94*, 562–564, doi:10.2105/AJPH.94.4.562.

47. Xiao, H.; Dai, X.; Wagenaar, B.H.; Liu, F.; Augusto, O.; Guo, Y.; Unger, J.M. The impact of the COVID-19 pandemic on health services utilization in China: Time-series analyses for 2016-2020. *Lancet Reg. Heal. Pacific***2021**, *9*, 100122, doi:10.1016/j.lanwpc.2021.100122.

48. Lu, T.H.; Chou, Y.J.; Liou, C.S. Impact of SARS on healthcare utilization by disease categories: Implications for delivery of healthcare services. *Health Policy (New. York).***2007**, *83*, 375–381, doi:10.1016/J.HEALTHPOL.2007.03.001.

49. McMahon, D.E.; Peters, G.A.; Ivers, L.C.; Freeman, E.E. Global resource shortages during COVID-19: Bad news for low-income countries. *PLoS Negl. Trop. Dis.***2020**, *14*, 1–3, doi:10.1371/JOURNAL.PNTD.0008412.

50. Ranney, M.L.; Griffeth, V.; Jha, A.K. Critical Supply Shortages — The Need for Ventilators and Personal Protective Equipment during the Covid-19 Pandemic. *https://doi.org/10.1056/NEJMp2006141***2020**, *382*, e41, doi:10.1056/NEJMP2006141.

51. Livingston, E.; Desai, A.; Berkwits, M. Sourcing Personal Protective Equipment During the COVID-19 Pandemic. *JAMA***2020**, *323*, 1912–1914, doi:10.1001/JAMA.2020.5317.

52. Monaghesh, E.; Hajizadeh, A. The role of telehealth during COVID-19 outbreak: a systematic review based on current evidence. *BMC Public Health***2020**, *20*, doi:10.1186/S12889-020-09301-4.

53. BL, C. Telemedicine can lower costs and improve access. *Healthc. Financ. Manage.***2000**, *54*, 66–69.

54. Chauhan, V.; Galwankar, S.; Arquilla, B.; Garg, M.; Somma, S. Di; El-Menyar, A.; Krishnan, V.; Gerber, J.; Holland, R.; Stawicki, S.P. Novel Coronavirus (COVID-19): Leveraging Telemedicine to Optimize Care While Minimizing Exposures and Viral Transmission. *J. Emerg. Trauma. Shock***2020**, *13*, 20, doi:10.4103/JETS.JETS_32_20.

55. Portnoy, J.; Waller, M.; Elliott, T. Telemedicine in the Era of COVID-19. *J. Allergy Clin. Immunol. Pract.***2020**, *8*, 1489, doi:10.1016/J.JAIP.2020.03.008.

56. Parikh, K.D.; Ramaiya, N.H.; Kikano, E.G.; Tirumani, S.H.; Pandya, H.; Stovicek, B.; Sunshine, J.L.; Plecha, D.M. COVID-19 Pandemic Impact on Decreased Imaging Utilization: A Single Institutional Experience. *Acad. Radiol.***2020**, *27*, 1204–1213, doi:10.1016/J.ACRA.2020.06.024.

57. Kansagra, A.P.; Goyal, M.S.; Hamilton, S.; Albers, G.W. Collateral Effect of Covid-19 on Stroke Evaluation in the United States. *https://doi.org/10.1056/NEJMc2014816***2020**, *383*, 400–401, doi:10.1056/NEJMC2014816.

58. RC, A.; JR, M. The impact of COVID-19 on national screening programmes in England. *Public Health***2021**, *198*, 174–176, doi:10.1016/J.PUHE.2021.07.022.

59. Guo, H.; Zhou, Y.; Liu, X.; Tan, J. The impact of the COVID-19 epidemic on the utilization of emergency dental services. *J. Dent. Sci.***2020**, *15*, 564–567, doi:10.1016/J.JDS.2020.02.002.

60. Bojdani, E.; Rajagopalan, A.; Chen, A.; Gearin, P.; Olcott, W.; Shankar, V.; Cloutier, A.; Solomon, H.; Naqvi, N.Z.; Batty, N.; et al. COVID-19 Pandemic: Impact on psychiatric care in the United States. *Psychiatry Res.***2020**, *289*, 113069, doi:10.1016/J.PSYCHRES.2020.113069.

61. Solomon, M.D.; McNulty, E.J.; Rana, J.S.; Leong, T.K.; Lee, C.; Sung, S.-H.; Ambrosy, A.P.; Sidney, S.; Go, A.S. The Covid-19 Pandemic and the Incidence of Acute Myocardial Infarction. *https://doi.org/10.1056/NEJMc2015630***2020**, *383*, 691–693, doi:10.1056/NEJMC2015630.

62. De Rosa, S.; Spaccarotella, C.; Basso, C.; Calabrò, M.P.; Curcio, A.; Filardi, P.P.; Mancone, M.; Mercuro, G.; Muscoli, S.; Nodari, S.; et al. Reduction of hospitalizations for myocardial infarction in Italy in the COVID-19 era. *Eur. Heart J.***2020**, *41*, 2083–2088, doi:10.1093/eurheartj/ehaa409.

63. Mesnier, J.; Cottin, Y.; Coste, P.; Ferrari, E.; Schiele, F.; Lemesle, G.; Thuaire, C.; Angoulvant, D.; Cayla, G.; Bouleti, C.; et al. Hospital admissions for acute myocardial infarction before and after lockdown according to regional prevalence of COVID-19 and patient profile in France: a registry study. *Lancet Public Heal.***2020**, *5*, e536–e542, doi:10.1016/S2468-2667(20)30188-2.

64. Garcia, S.; Albaghdadi, M.S.; Meraj, P.M.; Schmidt, C.; Garberich, R.; Jaffer, F.A.; Dixon, S.; Rade, J.J.; Tannenbaum, M.; Chambers, J.; et al. Reduction in ST-Segment Elevation Cardiac Catheterization Laboratory Activations in the United States During COVID-19 Pandemic. *J. Am. Coll. Cardiol.***2020**, *75*, 2871–2872, doi:10.1016/j.jacc.2020.04.011.

65. Normando, P.G.; Araujo-Filho, J. de A.; Fonseca, G. de A.; Rodrigues, R.E.F.; Oliveira, V.A.; Hajjar, L.A.; Almeida, A.L.C.; Bocchi, E.A.; Salemi, V.M.C.; Melo, M. Redução na Hospitalização e Aumento na Mortalidade por Doenças Cardiovasculares durante a Pandemia da COVID-19 no Brasil. *Arq. Bras. Cardiol.***2021**, *116*, 371, doi:10.36660/ABC.20200821.

66. D'Ascenzi, F.; Cameli, M.; Forni, S.; Gemmi, F.; Szasz, C.; Fabrizio, V. Di; Mechi, M.T.;

Nocci, M.; Mondillo, S.; Valente, S. Reduction of Emergency Calls and Hospitalizations for Cardiac Causes: Effects of Covid-19 Pandemic and Lockdown in Tuscany Region. *Front. Cardiovasc. Med.***2021**, *8*, 625569, doi:10.3389/fcvm.2021.625569.

67. Bianchi, F.; Dama, E.; Nicolantonio, F. Di; Baldassarre, G.; Guerriero, I.; Torchiaro, E.; Bruno, A.; Blandino, G.; Allavena, P.; Chiarugi, P.; et al. COVID-19 epidemic strongly affected cancer research in Italy: a survey of the Italian Cancer Society (SIC). *ESMO Open***2021**, *6*, 100165, doi:10.1016/J.ESMOOP.2021.100165.

68. Kaye, A.D.; Chancellor of Academic Affairs, V.; Okeagu, C.N.; Professor, A.; Pham, A.D.; Physician, R.; Silva, R.A.; Student, M.; Hurley, J.J.; Arron, B.L.; et al. Economic impact of COVID-19 pandemic on healthcare facilities and systems: International perspectives., doi:10.1016/j.bpa.2020.11.009.

69. Cabarkapa, S.; Nadjidai, S.E.; Murgier, J.; Ng, C.H. The psychological impact of COVID-19 and other viral epidemics on frontline healthcare workers and ways to address it: A rapid systematic review. *Brain, Behav. Immun. - Heal.***2020**, *8*, 100144, doi:10.1016/J.BBIH.2020.100144.

70. Xiang, Y.-T.; Yang, Y.; Li, W.; Zhang, L.; Zhang, Q.; Cheung, T.; Ng, C.H. Timely mental health care for the 2019 novel coronavirus outbreak is urgently needed. *The Lancet. Psychiatry***2020**, *7*, 228, doi:10.1016/S2215-0366(20)30046-8.

71. Khajuria, A.; Tomaszewski, W.; Liu, Z.; Chen, J.; Mehdian, R.; Fleming, S.; Vig, S.; Crawford, M.J. Workplace factors associated with mental health of healthcare workers during the COVID-19 pandemic: an international cross-sectional study. *BMC Heal. Serv. Res. 2021 211***2021**, *21*, 1–11, doi:10.1186/S12913-021-06279-6.

72. Spoorthy, M.S.; Pratapa, S.K.; Mahant, S. Mental health problems faced by healthcare workers due to the COVID-19 pandemic–A review. *Asian J. Psychiatr.***2020**, *51*, 102119, doi:10.1016/J.AJP.2020.102119.

73. Buselli, R.; Corsi, M.; Veltri, A.; Baldanzi, S.; Chiumiento, M.; Lupo, E. Del; Marino, R.; Necciari, G.; Caldi, F.; Foddis, R.; et al. Mental health of Health Care Workers (HCWs): a review of organizational interventions put in place by local institutions to cope with new psychosocial challenges resulting from COVID-19. *Psychiatry Res.***2021**, *299*, 113847, doi:10.1016/J.PSYCHRES.2021.113847.

74. Buselli, R.; Baldanzi, S.; Corsi, M.; Chiumiento, M.; Lupo, E. Del; Carmassi, C.; Dell'Osso, L.; Cristaudo, A. Psychological Care of Health Workers during the COVID-19 Outbreak in Italy: Preliminary Report of an Occupational Health Department (AOUP) Responsible for Monitoring Hospital Staff Condition. *Sustain. 2020, Vol. 12, Page 5039***2020**, *12*, 5039, doi:10.3390/SU12125039.

75. Godderis, L.; Boone, A.; Bakusic, J. COVID-19: a new work-related disease threatening healthcare workers. *Occup. Med. (Lond).***2020**, *70*, 315–316, doi:10.1093/OCCMED/KQAA056.

76. Pfefferbaum, B.; North, C.S. Mental Health and the Covid-19 Pandemic.

*https://doi.org/10.1056/NEJMp2008017***2020**, *383*, 510–512, doi:10.1056/NEJMP2008017.

77. Naushad, V.A.; Bierens, J.J.; Nishan, K.P.; Firjeeth, C.P.; Mohammad, O.H.; Maliyakkal, A.M.; ChaliHadan, S.; Schreiber, M.D. A Systematic Review of the Impact of Disaster on the Mental Health of Medical Responders. *Prehosp. Disaster Med.***2019**, *34*, 632–643, doi:10.1017/S1049023X19004874.

78. Kang, L.; Li, Y.; Hu, S.; Chen, M.; Yang, C.; Yang, B.X.; Wang, Y.; Hu, J.; Lai, J.; Ma, X.; et al. The mental health of medical workers in Wuhan, China dealing with the 2019 novel coronavirus. *The Lancet Psychiatry***2020**, *7*, e14, doi:10.1016/S2215-0366(20)30047-X.

79. Sahashi, Y.; Endo, H.; Sugimoto, T.; Nabeta, T.; Nishizaki, K.; Kikuchi, A.; Matsumoto, S.; Sato, H.; Goto, T.; Hasegawa, K.; et al. Worries and concerns among healthcare workers during the coronavirus 2019 pandemic: A web-based cross-sectional survey. *Humanit. Soc. Sci. Commun. 2021 81***2021**, *8*, 1–8, doi:10.1057/s41599-021-00716-x.

80. Berkhout, S.G.; Sheehan, K.A.; Abbey, S.E. Individual- and Institutional-level Concerns of Health Care Workers in Canada During the COVID-19 Pandemic: A Qualitative Analysis. *JAMA Netw. Open***2021**, *4*, e2118425–e2118425, doi:10.1001/JAMANETWORKOPEN.2021.18425.

81. Abolfotouh, M.; Almutairi, A.; BaniMustafa, A.; Hussein, M. Worries and Concerns of Healthcare Workers About COVID-19 Pandemic in a Tertiary Care Setting With a Previous MERS-COV Outbreak Experience. **2020**, doi:10.21203/RS.3.RS-35022/V1.

82. Becker, P.M. Overview of sleep management during COVID-19. *Sleep Med.***2021**, doi:10.1016/J.SLEEP.2021.04.024.

83. Shi, L.; Lu, Z.-A.; Que, J.-Y.; Huang, X.-L.; Liu, L.; Ran, M.-S.; Gong, Y.-M.; Yuan, K.; Yan, W.; Sun, Y.-K.; et al. Prevalence of and Risk Factors Associated With Mental Health Symptoms Among the General Population in China During the Coronavirus Disease 2019 Pandemic. *JAMA Netw. Open***2020**, *3*, e2014053–e2014053, doi:10.1001/JAMANETWORKOPEN.2020.14053.

84. Varma, P.; Burge, M.; Meaklim, H.; Junge, M.; Jackson, M.L. Poor sleep quality and its relationship with individual characteristics, personal experiences and mental health during the covid-19 pandemic. *Int. J. Environ. Res. Public Health***2021**, *18*, doi:10.3390/ijerph18116030.

85. Alimoradi, Z.; Brostr, A.; Om, €; Tsang, H.W.H.; Griffiths, M.D.; Haghayegh, S.; Ohayon, M.M.; Lin, C.-Y.; Pakpour, A.H. Sleep problems during COVID-19 pandemic and its' association to psychological distress: A systematic review and meta-analysis. **2021**, doi:10.1016/j.eclinm.2021.100916.

86. Sjöberg, L. Factors in Risk Perception. *Risk Anal.***2000**, *20*, 1–12, doi:10.1111/0272-4332.00001.

87. Xu, L.; Qiu, J.; Gu, W.; Ge, Y. The Dynamic Effects of Perceptions of Dread Risk and Unknown Risk on SNS Sharing Behavior During Emerging Infectious Disease Events:

Do Crisis Stages Matter? *J. Assoc. Inf. Syst.***2020**, *21*, 8, doi:10.17705/1jais.00612.

88. Leppin, A.; Aro, A.R. Risk Perceptions Related to SARS and Avian Influenza: Theoretical Foundations of Current Empirical Research., doi:10.1007/s12529-008-9002-8.

89. Slovic, P. Perception of risk. *Science (80-.).***1987**, *236*, 280–285, doi:10.1126/SCIENCE.3563507.

90. Smith, R.D. Responding to global infectious disease outbreaks: Lessons from SARS on the role of risk perception, communication and management. *Soc. Sci. Med.***2006**, *63*, 3113–3123, doi:10.1016/j.socscimed.2006.08.004.

91. Brug, J.; Aro, A.R.; Richardus, J.H. Risk Perceptions and Behaviour: Towards Pandemic Control of Emerging Infectious Diseases International Research on Risk Perception in the Control of Emerging Infectious Diseases., doi:10.1007/s12529-008-9000-x.

92. Jiang, X.; Elam, G.; Yuen, C.; Voeten, H.; De Zwart, O.; Veldhuijzen, I.; Brug, J. The Perceived Threat of SARS and its Impact on Precautionary Actions and Adverse Consequences: A Qualitative Study Among Chinese Communities in the United Kingdom and the Netherlands. **2009**, doi:10.1007/s12529-008-9005-5.

93. Vartti, A.-M.; Oenema, A.; Schreck, M.; Uutela, A.; De Zwart, O.; Brug, J.; Aro, A.R. SARS Knowledge, Perceptions, and Behaviors: a Comparison between Finns and the Dutch during the SARS Outbreak in 2003., doi:10.1007/s12529-008-9004-6.

94. Brug, J.; Aro, A.R.; Oenema, A.; Zwart, O. de; Richardus, J.H.; Bishop, G.D. SARS Risk Perception, Knowledge, Precautions, and Information Sources, the Netherlands. *Emerg. Infect. Dis.***2004**, *10*, 1486, doi:10.3201/EID1008.040283.

95. Kim, S.; Kim, S. Exploring the Determinants of Perceived Risk of Middle East Respiratory Syndrome (MERS) in Korea. *Int. J. Environ. Res. Public Health***2018**, *15*, doi:10.3390/IJERPH15061168.

96. Choi, D.H.; Yoo, W.; Noh, G.Y.; Park, K. The impact of social media on risk perceptions during the MERS outbreak in South Korea. *Comput. Human Behav.***2017**, *72*, 422–431, doi:10.1016/J.CHB.2017.03.004.

97. Schneider, C.R.; Dryhurst, S.; Kerr, J.; Freeman, A.L.J.; Recchia, G.; Spiegelhalter, D.; Linden, S. van der COVID-19 risk perception: a longitudinal analysis of its predictors and associations with health protective behaviours in the United Kingdom. *https://doi.org/10.1080/13669877.2021.1890637***2021**, *24*, 294–313, doi:10.1080/13669877.2021.1890637.

98. Birhanu, Z.; Ambelu, A.; Fufa, D.; Mecha, M.; Zeynudin, A.; Abafita, J.; Belay, A.; Doyore, F.; Oljira, L.; Bacha, E.; et al. Risk perceptions and attitudinal responses to COVID-19 pandemic: an online survey in Ethiopia. *BMC Public Heal. 2021 211***2021**, *21*, 1–17, doi:10.1186/S12889-021-10939-X.

99. Attema, A.E.; L'Haridon, O.; Raude, J.; Seror, V.; Group, T.C.; Peretti-Watel, P.; Seror, V.; Cortaredona, S.; Launay, O.; Raude, J.; et al. Beliefs and Risk Perceptions About COVID-

19: Evidence From Two Successive French Representative Surveys During Lockdown. *Front. Psychol.***2021**, *0*, 72, doi:10.3389/FPSYG.2021.619145.

100. Coronavirus, le misure adottate dal Governo | www.governo.it Available online: https://www.governo.it/it/coronavirus-misure-del-governo (accessed on Sep 8, 2021).

101. Gazzetta Ufficiale Available online: https://www.gazzettaufficiale.it/eli/id/2020/02/23/20A01228/sg (accessed on Sep 8, 2021).

102. Prevention and response to COVID-19: evolution of strategy and planning in the transition phase for the autumn-winter season. English version - ISS (EN) - ISS Available online: https://www.iss.it/web/iss-en/monographs/-/asset_publisher/yZRmELq8dkmf/content/prevention-and-response-to-covid-19-evolution-of-strategy-and-planning-in-the-transition-phase-for-the-autumn-winter-season.-english-version (accessed on Sep 9, 2021).

103. GAZZETTA UFFICIALE DELLA REPUBBLICA ITALIANA PARTE PRIMA SI PUBBLICA TUTTI I GIORNI NON FESTIVI DIREZIONE E REDAZIONE PRESSO IL MINISTERO DELLA GIUSTIZIA-UFFICIO PUBBLICAZIONE LEGGI E DECRETI-VIA ARENULA 70-00186 ROMA AMMINISTRAZIONE PRESSO L'ISTITUTO POLIGRAFICO E ZECCA DELLO STATO-LIBRERIA DELLO STATO-PIAZZA G.

104. OPERATIONAL PLANNING GUIDELINES TO SUPPORT COUNTRY PREPAREDNESS AND RESPONSE. **2020**.

105. Bandyopadhyay, S.; Baticulon, R.E.; Kadhum, M.; Alser, M.; Ojuka, D.K.; Badereddin, Y.; Kamath, A.; Parepalli, S.A.; Brown, G.; Iharchane, S.; et al. Infection and mortality of healthcare workers worldwide from COVID-19: a systematic review. *BMJ Glob. Heal.***2020**, *5*, doi:10.1136/BMJGH-2020-003097.

106. Flora, S. De; Maestra, S. La Growth and decline of the COVID-19 epidemic wave in Italy from March to June 2020. *J. Med. Virol.***2021**, *93*, 1613–1619, doi:10.1002/JMV.26499.

107. Comirnaty (BNT162b2), il primo vaccino contro il COVID-19 approvato in Europa e in Italia Available online: https://www.epicentro.iss.it/vaccini/covid-19-vaccino-pfizer-biontech (accessed on Sep 8, 2021).

108. COVID-19 Vaccines Advice Available online: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines/advice (accessed on Sep 9, 2021).

109. Generale, D.; Sanitaria, D.P. Ministero della Salute.

110. Berardi, C.; Antonini, M.; Genie, M.G.; Cotugno, G.; Lanteri, A.; Melia, A.; Paolucci, F. The COVID-19 pandemic in Italy: Policy and technology impact on health and non-health outcomes. *Heal. Policy Technol.***2020**, *9*, 454, doi:10.1016/J.HLPT.2020.08.019.

111. Prevenzione collettiva e sanità pubblica Available online:

https://www.salute.gov.it/portale/lea/dettaglioContenutiLea.jsp?lingua=italiano&id=4695&area=Lea&menu=prevLea (accessed on Sep 10, 2021).

112. Pocock, S.J.; Vandenbroucke, J.P. Strengthening the reporting of observational studies in epidemiology (StroBE) statement: guidelines for reporting observational studies.

113. Wang, X.; Cheng, Z. Cross-Sectional Studies: Strengths, Weaknesses, and Recommendations. *Chest***2020**, *158*, S65–S71, doi:10.1016/J.CHEST.2020.03.012.

114. Setia, M.S. Methodology Series Module 3: Cross-sectional Studies. *Indian J. Dermatol.***2016**, *61*, 261, doi:10.4103/0019-5154.182410.

115. Lai, J.; Ma, S.; Wang, Y.; Cai, Z.; Hu, J.; Wei, N.; Wu, J.; Du, H.; Chen, T.; Li, R.; et al. Factors Associated With Mental Health Outcomes Among Health Care Workers Exposed to Coronavirus Disease 2019. *JAMA Netw. Open***2020**, *3*, e203976–e203976, doi:10.1001/JAMANETWORKOPEN.2020.3976.

116. Lai, X.; Wang, M.; Qin, C.; Tan, L.; Ran, L.; Chen, D.; Zhang, H.; Shang, K.; Xia, C.; Wang, S.; et al. Coronavirus Disease 2019 (COVID-2019) Infection Among Health Care Workers and Implications for Prevention Measures in a Tertiary Hospital in Wuhan, China. *JAMA Netw. Open***2020**, *3*, e209666–e209666, doi:10.1001/JAMANETWORKOPEN.2020.9666.

117. Xiang, Y.-T.; Yang, Y.; Li, W.; Zhang, L.; Zhang, Q.; Cheung, T.; Ng, C.H. Timely mental health care for the 2019 novel coronavirus outbreak is urgently needed. **2020**, doi:10.1016/S2215-0366(20)30046-8.

118. Sahashi, Y.; Endo, H.; Sugimoto, T.; Nabeta, T.; Nishizaki, K.; Kikuchi, A.; Matsumoto, S.; Sato, H.; Goto, T.; Hasegawa, K.; et al. Worries and concerns among healthcare workers during the coronavirus 2019 pandemic: A web-based cross-sectional survey. *Humanit. Soc. Sci. Commun.***2021**, *8*, doi:10.1057/S41599-021-00716-X.

119. Riguzzi, M.; Gashi, S. Lessons From the First Wave of COVID-19: Work-Related Consequences, Clinical Knowledge, Emotional Distress, and Safety-Conscious Behavior in Healthcare Workers in Switzerland. *Front. Psychol.***2021**, *0*, 44, doi:10.3389/FPSYG.2021.628033.

120. Bergh, M.F.Q.K. den; Buiting, A.G.M.; Pas, S.D.; Bentvelsen, R.G.; Bijllaardt, W. van den; Oudheusden, A.J.G. van; Rijen, M.M.L. van; Verweij, J.J.; Koopmans, M.P.G.; Kluytmans, J.A.J.W. Prevalence and Clinical Presentation of Health Care Workers With Symptoms of Coronavirus Disease 2019 in 2 Dutch Hospitals During an Early Phase of the Pandemic. *JAMA Netw. Open***2020**, *3*, e209673–e209673, doi:10.1001/JAMANETWORKOPEN.2020.9673.

121. Barrett, E.S.; Horton, D.B.; Roy, J.; Gennaro, M.L.; Brooks, A.; Tischfield, J.; Greenberg, P.; Andrews, T.; Jagpal, S.; Reilly, N.; et al. Prevalence of SARS-CoV-2 infection in previously undiagnosed health care workers in New Jersey, at the onset of the U.S. COVID-19 pandemic. *BMC Infect. Dis. 2020 201***2020**, *20*, 1–10, doi:10.1186/S12879-020-05587-2.

122. Gómez-Ochoa, S.A.; Franco, O.H.; Rojas, L.Z.; Raguindin, P.F.; Roa-Díaz, Z.M.; Wyssmann, B.M.; Guevara, S.L.R.; Echeverría, L.E.; Glisic, M.; Muka, T. COVID-19 in Health-Care Workers: A Living Systematic Review and Meta-Analysis of Prevalence, Risk Factors, Clinical Characteristics, and Outcomes. *Am. J. Epidemiol.***2021**, *190*, 161–175, doi:10.1093/AJE/KWAA191.

123. Martín, V.; Fernández-Villa, T.; Lamuedra Gil de Gomez, M.; Mencía-Ares, O.; Rivero Rodríguez, A.; Reguero Celada, S.; Montoro Gómez, M.; Nuevo Guisado, M.T.; Villa Aller, C.; Díez Flecha, C.; et al. Prevalence of SARS-CoV-2 infection in general practitioners and nurses in primary care and nursing homes in the Healthcare Area of León and associated factors. *Semergen***2020**, *46*, 35–39, doi:10.1016/J.SEMERG.2020.05.014.

124. Ocias, L.F.; Skogstam, A.; Kjerstadius, T.; Lundin, F.; Tevell, S. Higher rate of SARS-CoV-2 IgG seropositivity in hospital-based healthcare workers compared to elderly care staff in a Swedish low-prevalence region: a cross-sectional study. *https://doi.org/10.1080/23744235.2021.1959949***2021**, doi:10.1080/23744235.2021.1959949.

125. Sabetian, G.; Moghadami, M.; Hashemizadeh Fard Haghighi, L.; Shahriarirad, R.; Fallahi, M.J.; Asmarian, N.; Moeini, Y.S. COVID-19 infection among healthcare workers: a cross-sectional study in southwest Iran. *Virol. J. 2021 181***2021**, *18*, 1–8, doi:10.1186/S12985-021-01532-0.

126. Zheng, L.; Wang, X.; Zhou, C.; Liu, Q.; Li, S.; Sun, Q.; Wang, M.; Zhou, Q.; Wang, W. Analysis of the Infection Status of Healthcare Workers in Wuhan During the COVID-19 Outbreak: A Cross-sectional Study. *Clin. Infect. Dis.***2020**, *71*, 2109–2113, doi:10.1093/cid/ciaa588.

127. Robles-Pérez, E.; González-Díaz, B.; Miranda-García, M.; Borja-Aburto, V.H. Infection and death by COVID-19 in a cohort of healthcare workers in Mexico. *Scand. J. Work. Environ. Health***2021**, *47*, 349–355, doi:10.5271/sjweh.3970.

128. Dryhurst, S.; Schneider, C.R.; Kerr, J.; Freeman, A.L.J.; Recchia, G.; Bles, A.M. van der; Spiegelhalter, D.; Linden, S. van der Risk perceptions of COVID-19 around the world. *https://doi.org/10.1080/13669877.2020.1758193***2020**, *23*, 994–1006, doi:10.1080/13669877.2020.1758193.

129. Simione, L.; Gnagnarella, C. Differences Between Health Workers and General Population in Risk Perception, Behaviors, and Psychological Distress Related to COVID-19 Spread in Italy. *Front. Psychol.***2020**, *0*, 2166, doi:10.3389/FPSYG.2020.02166.

130. Aranaz-Andrés, J.M.; McGee-Laso, A.; Galán, J.C.; Cantón, R.; Mira, J.; COVID-19, on behalf of the T. of W. Activities and Perceived Risk of Transmission and Spread of SARS-CoV-2 among Specialists and Residents in a Third Level University Hospital in Spain. *Int. J. Environ. Res. Public Heal. 2021, Vol. 18, Page 2838***2021**, *18*, 2838, doi:10.3390/IJERPH18062838.

131. Gross, J.V.; Mohren, J.; Erren, T.C. Original research: COVID-19 and healthcare workers:

a rapid systematic review into risks and preventive measures. *BMJ Open***2021**, *11*, doi:10.1136/BMJOPEN-2020-042270.

132. Lee, J.; Lee, H.J.; Hong, Y.; Shin, Y.-W.; Chung, S.; Park, J. Risk Perception, Unhealthy Behavior, and Anxiety Due to Viral Epidemic Among Healthcare Workers: The Relationships With Depressive and Insomnia Symptoms During COVID-19. *Front. Psychiatry***2021**, *0*, 358, doi:10.3389/FPSYT.2021.615387.

133. Iorfa, S.K.; Ottu, I.F.A.; Oguntayo, R.; Ayandele, O.; Kolawole, S.O.; Gandi, J.C.; Dangiwa, A.L.; Olapegba, P.O. COVID-19 Knowledge, Risk Perception, and Precautionary Behavior Among Nigerians: A Moderated Mediation Approach. *Front. Psychol.***2020**, *0*, 3292, doi:10.3389/FPSYG.2020.566773.

134. Lanciano, T.; Graziano, G.; Curci, A.; Costadura, S.; Monaco, A. Risk Perceptions and Psychological Effects During the Italian COVID-19 Emergency. *Front. Psychol.***2020**, *0*, 2434, doi:10.3389/FPSYG.2020.580053.

135. Shahin, M.A.H.; Hussien, R.M. Risk perception regarding the COVID-19 outbreak among the general population: a comparative Middle East survey. *Middle East Curr. Psychiatry 2020 271***2020**, *27*, 1–19, doi:10.1186/S43045-020-00080-7.

136. Zhong, Y.; Liu, W.; Lee, T.-Y.; Zhao, H.; Ji, J. Risk perception, knowledge, information sources and emotional states among COVID-19 patients in Wuhan, China. *Nurs. Outlook***2021**, *69*, 13, doi:10.1016/J.OUTLOOK.2020.08.005.

137. Wańkowicz, P.; Szylińska, A.; Rotter, I. Assessment of Mental Health Factors among Health Professionals Depending on Their Contact with COVID-19 Patients. *Int. J. Environ. Res. Public Heal. 2020, Vol. 17, Page 5849***2020**, *17*, 5849, doi:10.3390/IJERPH17165849.

138. Collantoni, E.; Saieva, A.M.; Meregalli, V.; Girotto, C.; Carretta, G.; Boemo, D.G.; Bordignon, G.; Capizzi, A.; Contessa, C.; Nesoti, M.V.; et al. Psychological Distress, Fear of COVID-19, and Resilient Coping Abilities among Healthcare Workers in a Tertiary First-Line Hospital during the Coronavirus Pandemic. *J. Clin. Med. 2021, Vol. 10, Page 1465***2021**, *10*, 1465, doi:10.3390/JCM10071465.

139. Salari, N.; Khazaie, H.; Hosseinian-Far, A.; Ghasemi, H.; Mohammadi, M.; Shohaimi, S.; Daneshkhah, A.; Khaledi-Paveh, B.; Hosseinian-Far, M. The prevalence of sleep disturbances among physicians and nurses facing the COVID-19 patients: a systematic review and meta-analysis. *Global. Health***2020**, *16*, doi:10.1186/S12992-020-00620-0.

140. Gupta, B.; Sharma, V.; Kumar, N.; Mahajan, A. Anxiety and Sleep Disturbances Among Health Care Workers During the COVID-19 Pandemic in India: Cross-Sectional Online Survey. *JMIR Public Heal. Surveill.***2020**, *6*, doi:10.2196/24206.

141. Knaak, S.; Mantler, E.; Szeto, A. Mental illness-related stigma in healthcare: Barriers to access and care and evidence-based solutions. *http://dx.doi.org/10.1177/0840470416679413***2017**, *30*, 111–116, doi:10.1177/0840470416679413.

142. Nyblade, L.; Stockton, M.A.; Giger, K.; Bond, V.; Ekstrand, M.L.; Lean, R.M.; Mitchell, E.M.H.; Nelson, L.R.E.; Sapag, J.C.; Siraprapasiri, T.; et al. Stigma in health facilities: why it matters and how we can change it. *BMC Med. 2019 171***2019**, *17*, 1–15, doi:10.1186/S12916-019-1256-2.

143. Greenberg, N.; Docherty, M.; Gnanapragasam, S.; Wessely, S. Managing mental health challenges faced by healthcare workers during covid-19 pandemic. *BMJ***2020**, *368*, doi:10.1136/BMJ.M1211.

Appendix 1

Questionnaire for assessing general hospital staff's worries, risk perception and perceived information on the COVID-19 pandemic