

### American Journal of Emergency & Critical Care Medicine

**Review Article** 

# Prevention of COVID-19 Outbreak: Measures for Controlling the Spread of Covid-19 - @

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### Submitted: 09 September 2020; Approved: 12 October 2020; Published: 20 October 2020

**Citation this article:** Perrone FNS, Schino S, Russo D, Beggio E, Romeo F, et al. Prevention of COVID-19 Outbreak: Measures for Controlling the Spread of Covid-19. American J Emerg Crit Care Med. 2020;3(2): 054-058.

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#### ABSTRACT

From the first days of December, 2019 a severe form of pneumonia, caused by a novel coronavirus called 2019-nCoV, started affecting people in China and rapidly it spread worldwide.

The first phase of the pandemic was characterized by increased number of deaths and symptomatic people, first of all because the virus was highly contagious and then because of the lack of information about physiopathology of the disease and so of an adequate therapy.

Since WHO declaration of the pandemic state, several states developed spreading preventive measures in order to avoid personto-person transmission of the virus that seems to occur through respiratory droplets and close contacts; these measures included public health interventions like social distancing and school closures, and the use of preventive personal equipment as barrier devices like facemasks and goggles. Increasing environmental hygiene with surface disinfectants and regular hands hygiene were other measures that contributed to reduce virus dissemination. Quarantine measures for exposed people prevented 44% to 81% of incident cases and 31% to 63% of deaths; social distancing seems to reduce the absolute risk of infection by 12, 8%. The use of a face mask significantly reduced the risk of infection by 80% among healthcare workers and by 56% in non-healthcare workers.

Thanks to these actions, after an initial period of high spread, we observed in a second phase a slow reduction in spread and Intensive Care Unit (ICU) recovering. So far, few studies have been realized about the real efficacy of these methods.

In this review, we summarize the best available evidence and recommendations about the preventive intervention efforts.

Keywords: 2019 novel coronavirus; Severe acute respiratory syndrome coronavirus 2; Prevention; COVID-19

#### **ABBREVIATIONS**

SARS-Cov-2: Severe Acute Respiratory Syndrome coronavirus 2; Intensive Care Unit (ICU); COVs: Coronaviruses; CDC: Centers for Disease Control and Prevention; SARS: Severe Acute Respiratory Syndrome; SARS-CoV: Severe Acute Coronary Syndrome Coronavirus; MERS-CoV: Middle East Respiratory Syndrome-Related Coronavirus; 2019-nCoV: 2019 Novel Coronavirus; SARS-CoV: Severe Acute Respiratory Syndrome Coronavirus; WHO: World Health Organization; IPC: Infection Prevent and Control; PPE: Personal Protection Equipment

#### **INTRODUCTION**

Coronaviruses (COVs) are single stranded enveloped RNA viruses; so called because of the crown-like spikes on their surface. There are four genera: alpha, beta, gamma and delta. The first two families can infect humans, presenting with upper and lower respiratory tract symptoms. According to the Centers for Disease Control and prevention (CDC), the most common human coronaviruses are 229E (alpha coronavirus), NL63 (alpha coronavirus), OC43 (beta coronavirus), HKU1 (beta coronavirus), all responsible for upper mild respiratory tract symptoms. Two coronaviruses were responsible for relevant endemic infections: Severe Acute Respiratory Syndrome (SARS) coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome-Related Coronavirus (MERS-CoV).

On December 8<sup>th</sup> 2019, in Wuhan, capital of Hubei province, China, people started suffering of a severe form of pneumonia, caused by a new form of coronavirus, called 2019 novel coronavirus (2019-nCoV) and the disease was termed Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) or COVID-19 [1,2]. It is a novel single stranded enveloped RNA virus, the 7th known human coronavirus. Its structure and genes are similar to the zoonotic Severe Acute Respiratory Syndrome (SARS) coronavirus (SARS-CoV) 2002 [3] and the Middle East Respiratory Syndrome-Related Coronavirus (MERS-CoV) 2012 [4].

Initially it looked like a viral pneumonia limited to the Hubai region but in the first months of the 2020, it spread all over the world, and on January 30th 2020 the World Health Organization (WHO)

declared the Public Health Emergency of International Concern and, on March 11th, the Pandemic state. WHO called the syndrome Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2) because the first and most dramatic manifestation of the virus was of pulmonary nature [5]. However, with the spread of the virus, new clinical manifestations of this infection has been described and several questions are still opened about the possible role of this virus in systems different from the lungs.

Since the beginning, several antiviral and immunosuppressive drugs have been used in order to fight against this virus, with few benefits. At the same time, several states have operated spreading preventive measures, as social distancing and the use of facemasks. Thanks to these actions, after an initial period of high spread, we observed in a second phase a slow reduction in spread and Intensive Care Unit (ICU) recovering.

So far, no effective pharmacological intervention or vaccine is available in clinical practice; hence, preventing the virus transmission and reducing the rate of infection (flattening the curve of contagion) should be the priority. 2019-nCoV is transmitted person-to-person through respiratory droplets generated by breathing, sneezing, coughing, etc., as well as close contact (direct contact with an infected subject or indirect contact, trough hand-mediated transfer of the virus from contaminated fomites to the mouth, nose, or eyes) [6]. Several measures of preventive care, based on social or physical distancing, the use of facemasks and periodic cleaning of hands and environments, have been proposed. In this review, we summarize the best available evidence and recommendations about the preventive intervention efforts.

#### DISCUSSION

#### Quarantine

According to the WHO guidelines, quarantine is one of the best option to guarantee an optimal disease control. Quarantine means to separate potentially affected people from healthy one. At the same time WHO recommends isolation for people with symptoms of CoVID-19 and physical distance for healthy people [7].

Some studies showed how quarantine is efficient in reducing

the spread of the disease; in fact quarantine measures for exposed people prevented 44% to 81% of incident cases and 31% to 63% of deaths, compared with no measures. In this contest, early quarantine measures could allow a significant cost reduction [8].

Another measure of spread prevention, especially in combination with the quarantine measure, was represented by school closures. If this measure was effective in reducing the dissemination of the virus is debated, because scientific evidence is contradictory and it varies in different places. A population-based observational study conducted between March 9, 2020, and May 7, 2020, in US showed a reduction of CoVID-19 incidence and mortality in association with school closure [9]; instead, a time-series analysis of daily data of the COVID-19 and coronavirus infection incidence in Japan until March 31, 2020 revealed that the intervention of school closure did not appear to decrease the incidence of coronavirus infection [10].

#### Make-shift hospitals

Initially in Wuhan, then in various cities worldwide, in order to face the emergency and the increasing number of patients, several sports stadium and convention centers have been converted into mobile cabin hospitals, generally divided in contamination, semicontamination, and clean areas. The aim of these structures was to admit asymptomatic or mild symptomatic patients and to examine them periodically in order to identify any deteriorating cases and transfer them to regular hospitals [11].

In some circumstances, as the number of patients increased, the facilities were ramped up and some of these structures had almost all medical facilities and ventilators.

#### Social distancing

Considering the lack of a specific antiviral therapy and the clinical impact of this infection, based on previous pandemics as the Spanish Flu in 1918-1920, the first strategy to prevent the virus transmission is physical and social distancing, being ascertained that the SARS-CoV-2 is spread through close contact. In fact, several studies showed how human-to-human transmission is based on respiratory droplets and airborne transmission. According to the WHO guidelines, Infection Prevent and Control (IPC) is the first approach to act because it can result in a reduction > 30% of infection [12].

A recent meta-analysis analyzed 172 observational studies across 16 countries and 6 continents, in order to establish the physical distance associated with reduced risk of acquiring the virus, when getting in touch with an infected person, both in health-care and non-health care settings [13]. The meta-analysis found a strong association between proximity of the exposed individual and the risk of infection (Absolute Risk [AR] 12,8% with shorter distance vs 2,6% with further distance); the strength of association was higher at increasing distance. Transmission of the virus was lower with a physical distance of 1 meter (3 feet) or more, compared with a shorter distance (pooled Adjusted Odds Ratio [aOR] 0.18, 95% CI 0,19-0,38). The study concluded recommending a physical distance of at least 1 meter, even if distances of 2 meters might be more effective in preventing the infection.

Several aspects can affect and modify the virus spread. For example, the wind speed can modify the travel distance of airborne droplets. When wind speed increases from 4 km/h to 15 km/h, the saliva droplet can travel up to 6 m with a corresponding decrease of its concentrations and liquid droplet size. Instead, small particles may cover a distance of up to 10 m in an indoor environment. For this reason, even if a social distancing of at least one meter is always necessary, the optimum distance is related to the single circumstance and it should be conformed to the environment [14].

The limitations of the meta-analysis were that no randomized clinical trial was available, as all the studies published so far were observational; also, the study did not consider the effect of duration of exposure on risk for virus transmission.

#### Face masks

As previously described, CoVID-19 is an airborne infection and droplet transmission occurs within a short distance of 1 meter. Droplets > 5-10 micron in diameter are the way the virus spreads from a person to another one, invading into the epithelial layer of the upper respiratory tract [7]. For this reason, a physical barrier may reduce the droplet mediated transmission; therefore, the use of face masks and similar Personal Protection Equipment (PPE) has been advocated as a preventive measure. Different masks are now available, as paper mask, dust mask, face mask, surgical mask, laser mask and respirator. USA center for disease control and WHO recommend N95/P100 respirators with three level of protection (FFP1, FFP2 and FFP3). It seems that they can provide a high protection against CoVID-19, filtering out 99.9% of 0.3 micron particles [15]. There are different types of medical mask on the basis of their bacterial filtration efficiency: the type I, generally for the patients with the aim of controlling the source, type II used by the healthcare workers in operatory room. In the second group we can involve the medical mask, loose-fitting, that does not need any fit-test (id est a test which confirms the filtering ability of the PPE); it protects from droplets, but it has a variable filter performance thus it is not protective for inhalation. The FFP1, FFP2 (N95 in the United States), FFP3 need an appropriate fit-test, they all protect from droplets and airbone particles with different filter performance (> 80%, > 94%, > 99% respectively) and progressively reduced inward leakage (< 22%, <8%, <2%). Moreover, the filtering performance strongly depends on their fitting, since they are not devices intended to be one-sizefits-all. Shaving is required since it can alter the sealing [16]. All the FFP devices are also available with the expiratory valve, which open in the expiratory phase and reduces the goggles fogging [17]. The "respirators" are intended to as filtering media in the form of half or full-facemasks; they have interchangeable filters with different performance, they are reusable and very expensive. Unfortunately they are not wide spread in the healthcare settings.

This protective measure is debated by medias and public health authorities: in particular, the use of face masks for general population and the type of PPE optimal in the health-care setting, having to face the challenge of PPE shortages [18]. In a meta-analysis, the use of face masks resulted in a large reduction of the risk of infection (aOR 0,15, 95% CI 0,07-0,34). The protection from infection was more effective with N95 or similar respirators compared with other masks (aOR 0,04, CI 95% 0,004-0,30 vs aOR 0,33 95% CI 0,17-0,61), especially in health-care contest [12].

Being the use of facemasks protective both for health-care workers and general population, the use of facemasks is supported irrespective of the setting. In the health-care contest, the higher protective role of respirators compared to surgical masks may be due to the aerosolization of the virus during in-hospital procedures [19]. Nevertheless, it is likely that respirators are more effective than masks even in the absence of aerosolized SARS-CoV-2. These results are inconsistent with those from a review of four randomized trials

which did not suggest a better protective role of N95 or similar masks compared with surgical masks and 12-16-layer cotton masks [20]. On the other hand, the meta-analysis results accorded with a randomized clinical trial demonstrating a potential benefit of N95 respirator use over medical masks in preventing transmission of seasonal viral infections [21]. Two trials are ongoing to better analyze the optimal use of face masks against SARS-CoV-19.

Liang et al. in a recent metanalysis described how the use of face masks can significantly reduce virus spread. According to their analysis, wearing masks significantly reduced by 80% the risk of infection among healthcare workers. At the same time, using masks reduces the risk of virus infection by 56% in non-healthcare workers, indicating the potential benefits of wearing masks for the general public. According to their analysis, there is no doubt about the use of the masks in every social interaction [22].

Another element to consider is the deterioration of the surgical mask, due to saliva, biofluid or moisture that can reduce its protective role and at the same time can provide an environment for other microbes.

#### Goggles and eye protection

The eyes are another way for virus entering as well as a source of transmission, in fact its presence has been detected in tears and ocular fluids [23]. Even if the scientific evidence concerning ophthalmological transmission of the virus is limited and, in many cases, contradictory [24,25], WHO recommends well-fitting, protective glass. A meta-analysis confirmed the role of the eye protection in reducing infection (aOR 0,22, 95% CI 0,12-0,39); it was based on 13 unadjusted studies and 2 adjusted studies, suggesting that it might be used to achieve additional benefit [12].

#### Gowns

Gowns are the best gadget health professionals have in order to reduce the risk of infection. They provide a complete protection thanks to their design. Some evidence showed that people with long aprons had less contamination than those with coveralls, and that the coveralls were more challenging to wear [8].

#### Surface disinfectant

Even if droplets are the most frequent way of transmission, the virus can survive on surfaces from one to nine days, in relation to the type, pH, temperature and humidity of the surface [26]. So the highly risk exposed, surfaces need to be disinfected frequently with alcohol or alcohol-like compounds. A single study conducted in Zhijiang Campus, China, showed that routine disinfection procedures could reduce the risk of healthcare SARS-CoV-19 infection [27].

#### Hand hygiene and elbow contact

CoVID-19, like other viruses, can survive and be transmitted by the hands; so, the human-to-human transmission can be reduced by frequent washing hands with water and soap or an alcohol-based sanitizer. WHO reported a reduction in transmission of about 50% thanks to this preventive care [7]. The main risk of a wide use of alcohol-based sanitizer is in the reduction of the oils layer of the skin, resulting in dehydrated skin and cracked cuticles that can be a way for microbial infection.

Another issue is the etiquette maneuver of coughing and sneezing into the flexed elbow, covering both mouth and nose, instead of the hand as recommended by the World Health Organization (WHO). Unfortunately, a study based on 31 healthy nonsmokers found out that this maneuver is not as safe as it was thought. Since SARS-Cov-2 remains viable on many different surfaces for variable hours to days, this elbow contact may be an additional potential risk factor for the transmission of the virus. In addition, at the beginning of the pandemic it was advisable to meet and greet by elbow contact to prevent contact through hand-shaking. It sounds unreasonable since touching each other elbow forces people at approaching closer than 1 meter and no precautions are available for disinfecting the elbow that might have been used previously for sneezing and coughing. In conclusion, this cannot be advised any more and more etiquette maneuver need to be established to reduce viral infection [28].

#### CONCLUSION

COVID-19 is a novel pandemic disease that spread all over the world in few months, it is highly contagious and it is provoking the death of millions of people. For this reason, it is very important to provide a strategy to destroy this novel coronavirus. So far, no specific pharmacological treatment or vaccine are available, so the best strategy to fight this battle is to adopt common measures to limit the transmission of the virus among people.

At present, according to the most recent literature, quarantine of infected people, school closure, physical distancing of at least 1 meter are protective, with increasing safety at higher distance. Even if strong evidence is lacking, the spreading use of personal protective equipment like facemasks, in particular respirators in the health-care setting and 12-16-layer cotton or surgical mask in general population, seems to be an effective strategy; eye protection with goggles may also provide an additional safety for prevention virus transmission via conjunctiva; gowns and gloves can be useful to limit the direct contact between healthcare people and potential source of transmission like human fluids and infective surface. Finally, but not less important, regular hands hygiene and surface disinfection in healthcare places and at home could favorite elimination of the virus.

In conclusion, in our opinion three specific precautions have to be guaranteed by everyone in order to reduce the risk of infection: a social distancing of at least one meter, the use of face mask everywhere, periodically washing hands, avoiding every physical unsecure maneuver as elbow contact.

Globally collaborative studies, including randomized trials, are needed to enrich the acknowledgment about correct and completely prevention of the infection. Nowadays old methods to limit virus diffusion are the only way we can follow.

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