

Review

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Review

# Prevention of COVID-19. Part 1: Non-Pharmacological Strategies and Interventions for Effective Disease Control

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**Abstract:** (1) Background: The COVID-19 pandemic had a devastating impact on the world, causing widespread illness and death. It is essential to focus on prevention strategies to limit the spread of the disease. Despite the advent of vaccines, maintaining a vigilant approach to prevention remains paramount. While vaccines are essential, they do not guarantee absolute immunity, and their protective effect may diminish over time; (2) Methods: We reviewed effective strategies to prevent COVID-19 transmission. We focused on meta-analyses (MA), literature reviews (LR) and the health care context. Various prevention measures and interventions were reviewed. Both established practices and unresolved issues were considered; (3) Results: Standard precautions (SP) as the cornerstone of infection control, with hand hygiene and mask use as key components. Debate about the relative importance of droplet versus aerosol transmission led to differences in recommendations between agencies at the onset of the pandemic. We have clarified the role of personal protective equipment (PPE), including eye protection. The effectiveness of masks in preventing transmission is reviewed. The use of surgical masks is recommended to prevent droplet transmission, while eye protection is recommended in combination with masks. Although data show some risk reduction, the clear superiority of N95/FFP2 over surgical masks remains unproven. In terms of room occupancy, ventilation is critical in reducing the risk of transmission in poorly ventilated environments. The use of negative pressure isolation rooms (NPIRs) is being investigated. The presence of viral RNA on surfaces does not necessarily indicate infectivity, and the risk of transmission by surface contact is low if surfaces are properly maintained and hand hygiene is practised regularly. Testing for SARS-CoV-2 in asymptomatic persons in healthcare settings may help prevent transmission; (4) Conclusions: Prevention of SARS-CoV-2 transmission requires a multifaceted approach, including reducing particle emissions from infected persons by wearing masks, eliminating aerosols by ventilation, ensuring physical separation, and protecting exposed persons with masks and eye protection.

**Keywords:** COVID-19; SARS-CoV-2; prevention; non-pharmacological interventions; standard precautions; airborne and droplet transmission; personal protective equipment; mask; ventilation; room occupancy; testing for SARS-CoV-2

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## 1. Introduction

The COVID-19 pandemic has had an immense global health, social and economic impact. As the world grapples with the challenges posed by the SARS-CoV-2 virus, it is critical to focus on prevention strategies to limit the spread of the disease, even in the presence of vaccines.

The aim of this review is to present effective prevention strategies for Covid-19, focusing primarily on meta-analyses (MA) and literature reviews (LR). In addition, interventions that have generated debate within the scientific community will be discussed.

Effective prevention measures not only protect individuals from infection, but also contribute to the collective effort to reduce transmission within communities and the burden on healthcare systems.

In general, prevention can be linked to the natural history of the disease.

The classification of the natural history of a disease can be divided into five stages: underlying, susceptible, subclinical, clinical and recovery/disability/death.

The corresponding preventive health measures can be grouped into primordial prevention, primary prevention, secondary prevention and tertiary prevention [1].

Primordial prevention aims to address the underlying social and environmental conditions that promote the onset of disease. In the case of COVID-19, examples of primordial prevention may include:

- Promoting health education campaigns that focus on hygiene practices, such as hand washing and respiratory etiquette, to prevent the spread of COVID-19.

Primary prevention aims to prevent the disease from occurring in healthy individuals. For COVID-19, primary prevention measures may include:

- Vaccination campaigns to provide immunity to COVID-19, thereby reducing the risk of infection and severe illness.
- Promoting measures such as wearing masks, maintaining physical distance and practicing good hand hygiene to prevent transmission of the virus.

Secondary prevention focuses on early detection and intervention in people with subclinical forms of the disease. For COVID-19, examples of secondary prevention may include:

- Implementation of regular COVID-19 testing and screening programmes in high-risk settings to identify asymptomatic or pre-symptomatic individuals.
- Contact tracing efforts to identify and isolate individuals who have been in close contact with confirmed COVID-19 cases.

Tertiary prevention aims to reduce the severity of the disease and associated complications in people who already have the disease. Examples of tertiary prevention for COVID-19 may include

- Providing medical care and treatments such as antiviral therapies, oxygen therapy and supportive care to individuals with severe COVID-19 to improve outcomes and minimise complications.
- Implementation of rehabilitation programmes to support the recovery of individuals who have experienced long-term effects or disabilities due to COVID-19.

Quaternary prevention aims to protect individuals from unnecessary or potentially harmful medical interventions. In the context of COVID-19, examples of quaternary prevention may include:

- Avoiding unnecessary use of certain medications or treatments that have not been shown to be effective in the treatment of COVID-19.

We have chosen to focus on the prevention of Covid-19 in the hospital, with a presentation that is relatively consistent with the practices of health care facilities. Consequently, certain types of prevention, such as primordial prevention, will not be discussed in this article.

We review a comprehensive range of preventive measures and strategies used to control COVID-19.

We address the importance of non-pharmaceutical interventions in preventing the spread of COVID-19. These measures include standard precautions (e.g. hand hygiene) and other precautions, personal protective equipment (e.g. masks), maintaining physical distance and ensuring proper ventilation in enclosed spaces.

We review the scientific evidence supporting these interventions and highlight their role in reducing the risk of transmission.

Alongside non-pharmaceutical interventions, we emphasise the fundamental role of vaccination in preventing severe illness, hospitalisation and death.

We consider the importance of testing as a preventive measure. We examine the use of diagnostic tests to identify and isolate infected individuals, with a particular focus on asymptomatic cases.

Finally, we have shown that a multifaceted approach to prevention is essential.

## 2. Materials and Methods

We conducted a comprehensive search using electronic scientific resources such as PubMed, Science Direct, Google Scholar and MedRxiv between 2020 and July 2023. Our aim was to identify relevant English-language articles using terms such as prevention, "standard precaution", "contact precaution", droplet, airborne, "surgical mask", "N95 mask", "FFP2 mask", ventilation, surface, "non-pharmacological" (or "non-pharmaceutical"), "preventive measure" (or "preventive intervention"), etc., in relation to "COVID-19", "SARS-CoV-2" or "severe acute respiratory syndrome".

In addition to LR and MA, we also looked for relevant original articles on the topic.

To supplement our search, we manually identified and included references to recent research, and we also thoroughly checked the reference lists of selected literature.

The following eligibility criteria were used to select articles for inclusion in this review: articles were published in English; articles were either reviews (narrative or MA) or original research articles.

## 3. Results

### 3.1. Standard precautions

Standard precautions (SP) [2] prevent the spread of infections in healthcare settings. SP have been adopted worldwide and are regularly updated. Hand hygiene is a key component of SP, with the use of hydro-alcoholic solutions in hospitals. Hospitals have been under pressure to produce their own products, some of which are based on WHO formulations (the original and modified). Published tests have shown that these formulations are active against SARS-CoV-2 [3].

### 3.2. Airborne and droplet precautions

Uncertainties about the relative importance of droplet and aerosol transmission mean that there may be discrepancies in recommendations between different agencies. For example, for MERS-CoV, the WHO has historically advocated "contact + droplet" precautions versus "contact + air" precautions for the CDC [4].

See Personal protective equipment section for details.

### 3.3. Personal protective equipment

#### 3.3.1. Masks

In order to prevent droplet transmission, wearing a surgical mask is recommended [5]. This recommendation is based on an abundant literature related to respiratory viruses including influenza and several RCT on masks, alone [6,7], or associated with hand hygiene [8]. RCT did not show any significant difference, in term of reduction in the incidence of infection, between surgical mask and FFP2/N95 mask (more precisely non-inferiority for one of the studies [6] and no difference for another [7]).

For coronavirus, low-level evidence data suggest that surgical masks and FFP2/N95 masks provide similar protection in HCW during AGP [9].

Kunstler et al. [10] performed a MA to compare N95/FFP2 vs surgical mask, in order to prevent SARS-CoV-2 infection. Twenty-one studies were included, with most having high risk of bias. OR between N95/FFP2 and surgical mask was 0.85 (95%CI: 0.72-1.01). HCW experienced significantly more adverse events (headaches, respiratory distress, facial irritation and pressure-related injuries) when wearing N95/FFP2 compared to surgical mask.

For the prevention of Covid-19, whether in the community settings or in health care settings, recently published observational studies provided insufficient evidence for N95/FFP2 vs surgical masks [11].

In late 2022, Loeb et al. [12] published a RCT comparing the effectiveness of medical masks versus N95 respirators in preventing COVID-19 among health care workers providing routine care. The trial took place from May 2020 to March 2022 in 29 healthcare facilities in Canada, Israel, Pakistan

and Egypt. A total of 1009 healthcare workers participated. The primary outcome measure was confirmed COVID-19 by reverse transcriptase polymerase chain reaction (RT-PCR). The results showed that in the intention-to-treat analysis, the incidence of RT-PCR-confirmed COVID-19 was similar in the medical mask group (10.46%) compared with the N95 respirator group (9.27%) (hazard ratio [HR], 1.14 [95% CI: 0.77-1.69]). However, an unplanned subgroup analysis by country showed variability in the results. There were adverse events in both groups. There were 47 (10.8%) intervention-related adverse events in the medical mask group and 59 (13.6%) in the N95 respirator group. The study concludes that among health care workers providing routine care to patients with COVID-19, the overall estimates exclude a doubling of hazard with RT-PCR-confirmed COVID-19 for medical masks compared with the HRs of RT-PCR-confirmed COVID-19 for N95 respirators. Limitations include potential acquisition of SARS-CoV-2 through household and community exposure, heterogeneity between countries, uncertainty in effect estimates, differences in self-reported adherence, differences in baseline antibodies, and between-country differences in circulating variants and vaccination.

Chou et al. [13] recently published (June 2023) a MA to update the understanding of the effectiveness of masks in preventing SARS-CoV-2 infection in both community and healthcare settings. They analysed RCT and observational studies of N95 respirators, surgical masks and cloth masks. The results showed that mask use in community settings may be associated with a small reduction in the risk of SARS-CoV-2 infection, based on the results of two RCT and seven observational studies. In routine patient care settings, surgical masks and N95 respirators were similarly effective in preventing SARS-CoV-2 infection, according to one new RCT and four observational studies. However, limitations in the available evidence prevented a comprehensive evaluation of other mask types and comparisons.

In conclusion, according to Chou et al. [13], masks may provide a modest reduction in the risk of SARS-CoV-2 infection in community settings, while the effectiveness of N95 respirators in hospital settings cannot be definitively determined.

### 3.3.2. Eye protection

There is evidence that SARS-CoV-2 can either infect ocular surface cells directly or be transported by tears through the nasolacrimal duct to infect the nasal or gastrointestinal epithelium [14,15] Goggles and visors, which are anti-projection devices and therefore have no filtering capacity, should be combined with mask use [16].

According to the nationwide matched case-control study by Belan et al. [17], eye protection (OR: 0.57; 95% CI: 0.37-0.87) and also wearing a gown (0.58; 0.34-0.97) were protective when caring for COVID-19 patients.

In conclusion, the implementation of eye protection measures is proving to be an effective strategy in reducing the transmission of Covid-19, particularly in the care of patients affected by the virus.

### 3.4. Ventilation

The risk of transmission of the virus from an asymptomatic carrier can vary depending on several parameters: distance, room ventilation and case activity. Jones et al. [18] propose a risk assessment table that takes these parameters into account (Figure 3 of their article).

"High-density environments are most at risk. This is the case when HCW occupy poorly ventilated spaces: rest rooms, meeting rooms or changing rooms... "High density" implies the presence of a large number of people in a small space. It can also refer to the presence of "superspreaders" in a volume that appears ad hoc given the number of people [18].

Negative pressure isolation rooms (NPIR) have been proposed for COVID-19 patients [19]. They are designed to maintain a lower air pressure than the surrounding area, preventing contaminated air from escaping and potentially infecting others.

When an infected person is placed in a NPIR, air is continuously drawn into the room and then filtered and exhausted to the outside. This helps to minimise the concentration of viral particles in the air, reducing the risk of transmission to healthcare workers and other patients in the facility.

It's important to note that NPIR alone are not a foolproof solution and should be used in conjunction with other preventive measures such as personal protective equipment (PPE) and appropriate hygiene practices. In addition, the effectiveness of NPIR in preventing COVID-19 transmission depends on a number of factors, including proper design, construction and adherence to established guidelines and protocols.

Overall, NPIRs are an essential tool in the management of COVID-19 cases by reducing the risk of airborne transmission and protecting healthcare workers and others from exposure to the virus.

Chung-Yen Chen et al [20] compared international guidelines and recommendations for ventilation in modified NPIRs for COVID-19 patients.

Modified "quasi-negative pressure" isolation wards were found to be a feasible, inexpensive, safe and effective measure to control nosocomial outbreaks.

Preventive measures such as CO2 monitoring, mechanical ventilation, and air purification should be carefully considered [21].

In conclusion, the minimum ventilation volume required for an isolation unit should be determined based on the severity of COVID-19 patients. Mechanical ventilation remains the mainstay for achieving this requirement, although support from recirculation may also be helpful.

In addition to adequate tidal volumes, "clean to less clean" directional airflow remains the golden rule for indoor ventilation solutions. This means that air should flow from clean areas to less clean areas, such as from the corridor to the isolation unit.

Virus-laden exhaust air should be treated with HEPA/UV equipment. HEPA filters can capture particles as small as 0.3 microns, while UV light can kill viruses and bacteria.

In essence, infection control strategies involving room ventilation are highly dependent on the specific characteristics and use of each room. In order to implement effective infection control measures, a thorough analysis of individual rooms is essential. The selection of the most appropriate and feasible ventilation system should be based on a number of factors, including available vents, room height, volume, use, economic and energy requirements, and structural considerations [22].

### 3.5. Room occupancy

Bertuzzi et al. [23] conducted a systematic review (SR) to assess the impact of single rooms versus shared accommodation on inpatient outcomes not specific to Covid-19 (clinical, humanistic and economic outcomes). While the overall benefit of single rooms was inconclusive, they did show a small clinical advantage for critically ill patients, particularly neonates in intensive care. However, methodological problems and a lack of adjustment for confounding factors limited the overall quality of the included studies.

Hospitalisation in a double room, compared to a single room, increases the risk of nosocomial infections such as influenza [24]. We can therefore assume that the same is true for Covid-19.

Karan et al. [25] assessed SARS-CoV-2 transmission between patients in shared rooms in an academic hospital (during the first wave). 11 290 patients were admitted to shared rooms, of whom 25 tested positive. Of 31 exposed roommates, 12 (39%) tested positive within 14 days. Transmission was associated with PCR-CT (cycle thresholds)  $\leq 21$ .

Hyun et al. [26] randomised 666 patients with Covid-19 to shared room occupancy (group A) and single room occupancy (group B). Outcome measures were: microbiological cure rates, time to clinical symptom improvement, time to defervescence, and negative-to-positive conversion rates of PCR results during hospitalisation. No statistically significant differences were observed between the two groups. These results suggest that shared accommodation for patients with mild symptoms could be an alternative to single room occupancy during the COVID-19 pandemic.

Trannel et al. [27] assessed the incidence following exposure in shared patient rooms in a tertiary care centre.

There were 38,142 patient days in shared rooms between July 2020 and May 2021. We identified 53 COVID-19 inpatients who had a roommate during the infectious period, for a total of 70 exposed roommates. The incidence of SARS-CoV-2 exposure in a shared room was 1.8 per 1,000 patient days in a shared room. A total of 37 (52.9%) exposed roommates completed follow-up testing. Of these, 8 (21.6%) converted. This secondary attack rate was comparable to that reported in household exposures.

The median time to conversion was 5 days (range: 2-11). The incidence of conversion after exposure was 0.4 per 1,000 patient days in a shared room. None of the conversions were related to an AGP. There were no statistically significant differences in age, sex, or presence of infectious patient symptoms (source) between those who converted and those who did not.

The median exposure time was 1.9 days (range, 0.1-3 days) for converters and 0.6 days (range, 0.04-3.1) for non-converters (odds ratio, 1.05; 95% confidence interval, 1.05-5.38). Of the patients who converted, 3 were discharged before testing positive and 1 of these had documented household exposure prior to conversion. In addition, 2 patients were in a psychiatric ward during an outbreak and may have been exposed to other infectious patients. Of those who converted, 2 were asymptomatic, 5 had mild to moderate symptoms and 1 had severe symptoms.

Williams et al. [28] conducted a study to assess the effectiveness of universal admission testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in preventing transmission in shared patient rooms. The study was conducted at a large academic medical centre in the United States and included a total of 28,603 patients.

Universal admission testing was effective in preventing transmission, especially since the emergence of the SARS-CoV-2 omicron variant.

The yield of identifying infectious asymptomatic cases more than doubled during the omicron era.

Of the asymptomatic patients identified as infectious, 67% were directly admitted to a private room and 33% were temporarily admitted to a shared room.

Among contacts of asymptomatic patients, 4.1% developed SARS-CoV-2 infection.

Williams et al. [28] concluded that universal admission testing is an effective way to prevent transmission of SARS-CoV-2 in shared patient rooms.

In any case, hospitalisation in a double room does not impede the provision of appropriate care, even in the context of Covid-19. In fact, the implementation of testing alongside other infection prevention and control (IPC) measures has facilitated the safe provision of patient care in a hospital where shared patient rooms predominate [29].

In conclusion, hospitals should implement measures to reduce exposure in shared rooms in light of these findings from the literature.

### 3.6. Other: surfaces

The role of surfaces in SARS-CoV-2 contamination has been debated since the beginning of the CoV-19 pandemic.

If the virus survives on surfaces, what are the conditions for its survival? Can surface transmission be quantified? Can surface disinfection reduce the risk of SARS-CoV-2 infection?

Several articles have highlighted the presence of SARS-CoV-2 viral RNA on surfaces (and in the air). One of the best known is that of Van Doremalen et al. [30]. The main limitation of this paper is that the experimental conditions of the study do not reflect reality (transposition to emissions produced by an individual, e.g. spontaneous breathing in a room). The survival of the virus in the environment and its transmission to a susceptible host depends on many factors specific to the virus, the host and the environmental conditions (temperature, humidity, etc.) [31].

Furthermore, the presence of viral RNA does not imply infectivity [32]. For example, in the study by Zhou et al. [33], viral RNA was detected in 53% (114/218) of surface samples and 38.7% (14/31) of air samples. Detection of this RNA was more frequent in areas directly occupied by COVID-19 patients than in other areas. The authors mention that "the high Ct PCR value for all samples (>30) indicated that the virus would not be culturable".

In conclusion, detection of viral RNA by PCR on surfaces can take several hours or even days. Nevertheless, the viral load decreases rapidly. The risk of transmission by contact therefore appears to be low and easily manageable with regular surface maintenance and frequent hand hygiene.

However, the stability of SARS-CoV-2 on various inanimate surfaces and its potential for surface transmission remain a concern. A LR by Xu et al. [34] considered three variables: temperature, relative humidity (RH) and initial virus titer. These factors were examined in various experimental studies to understand their effect on virus stability.

The stability of SARS-CoV-2 on six different contact materials was investigated: plastic, metal, glass, protective equipment, paper and fabric. The factors influencing the half-life of the virus on these surfaces were also investigated.

The half-life of SARS-CoV-2 on different contact materials ranged from 2 to 10 hours, up to 5 days and as low as 30 minutes at a temperature of 22°C. In contrast, the half-life of SARS-CoV-2 on non-porous surfaces was generally 5 to 9 hours, up to 3 days and as low as 4 minutes at the same temperature. On porous surfaces, the half-life was typically 1 to 5 hours, up to 2 days and as short as 13 minutes at 22°C. Thus, the half-life of SARS-CoV-2 on non-porous surfaces was longer than that on porous surfaces. In addition, the half-life of the virus decreased with increasing temperature, while RH had a stable negative inhibitory effect only within a certain humidity range.

Considering the stability of SARS-CoV-2 on different surfaces, it is possible to implement specific disinfection measures in daily life to interrupt virus transmission, prevent COVID-19 infections and avoid excessive disinfection. However, Xu et al. [34] concluded that due to the controlled conditions of laboratory studies and the lack of evidence on surface transmission in the real world, it is difficult to provide strong evidence on the effectiveness of surface-to-human transmission of the virus.

If surfaces play a role in the transmission of COVID-19, can we assess the role of contaminated surfaces through studies evaluating the effectiveness of surface disinfection in preventing the occurrence of COVID-19?

A review of randomised controlled trials (RCTs) by Thomas et al. [35] found that only five of the 14 RCTs reviewed showed a reduction in the risk of infection. The review focused on multidrug-resistant organisms (MDROs) and *Clostridioides difficile* (CD), but the findings may not be relevant to COVID-19.

Ray et al. [36] focused on CD and found that an environmental disinfection intervention improved the thoroughness and effectiveness of cleaning, but did not reduce the incidence of healthcare-associated CD infections.

We did not find any RCTs evaluating the effectiveness of surface disinfection in preventing the occurrence of Covid-19. Therefore, the evidence for the effectiveness of surface disinfection in preventing the occurrence of COVID-19 is limited.

In conclusion, surfaces may play a role in the transmission of COVID-19, but the evidence is limited.

### *3.7. Testing for SARS-CoV-2 in asymptomatic patients*

Direct testing for SARS-CoV-2 in asymptomatic persons in healthcare settings is intended to prevent SARS-CoV-2 transmission in these settings. ESCMID has developed guidelines using the GRADE approach [37].

Indications for direct testing for SARS-CoV-2 in asymptomatic individuals in health care settings, with the aim of preventing SARS-CoV-2 transmission in these settings, have been formulated in ESCMID-approved guidelines developed using the GRADE approach [37].

For example, one question: "Does systematic testing of asymptomatic patients before elective surgical procedures reduce transmission of SARS-CoV-2?".

Answer: "The Panel recommends preoperative testing of asymptomatic patients 48-72 hours before elective surgery requiring anaesthesia to reduce the exposure of HCWs in settings with a high transmission rate and/or low vaccination coverage and/or limited access to PPE (conditional recommendation, QoE: very low).

The benefits of "asymptomatic screening" are unclear when added to other infection prevention measures. In line with ESCMID's position, the Society for Healthcare Epidemiology of America (SHEA) advises against routine universal use of asymptomatic screening in healthcare settings [38]. SHEA states "Admission screening may be beneficial during times of increased virus transmission in some settings where other layers of controls are limited (eg, behavioral health, congregate care, or shared patient rooms), but widespread routine use of admission asymptomatic screening is not recommended over strengthening other infection prevention controls.

In their Viewpoint article, Brust et al. [39] state that no increase in hospital-acquired COVID-19 has been documented since the discontinuation of admission testing. This statement is based on an analysis of the few published experiences with cessation of testing for SARS-CoV-2 in asymptomatic patients. Most of the studies were retrospective observational analyses; Brust et al. [39] could not find any prospective evaluations involving control units or hospitals.

In conclusion, evidence on the effectiveness of direct testing for SARS-CoV-2 in asymptomatic persons in healthcare settings is limited. ESCMID guidelines recommend preoperative testing of asymptomatic patients in some settings, but the benefit of this testing is unclear. SHEA advises against routine universal use of asymptomatic screening in healthcare settings.

#### 4. Discussion

We conducted this LR to report effective prevention strategies for Covid-19, focusing primarily on MA and LR. Interventions that have generated debate were also discussed.

- Established points

According to several guidelines, in particular the French guidelines [40], the prevention of transmission of SARS-CoV-2, whatever the variant, is based on a series of complementary and simultaneous measures aimed at

Reducing the particle emission of the infected person: wearing a mask by the infected person;

Elimination of aerosols by dispersal and dilution: by ventilating or aerating the premises;

Ensure physical distance: at least 2 metres if the mask cannot be worn;

Protect the exposed person:

Oropharyngeal mucous membranes: Wear a mask (surgical mask or FFP2/N95 mask) during AGP;

Ocular mucous membranes, in the context of projection or aerosolization of a biological product, splash or aerosolization: wear protective goggles, visor or face shield.

This multifaceted approach to prevention is essential.

Overall, the evidence from the literature suggests that non-pharmacological preventive measures are effective in preventing the spread of COVID-19. These measures should be used in combination with vaccination to protect individuals from the virus.

For vaccination, see Part 2 of this article, which discusses pharmacological interventions to prevent COVID-19.

- Contrast with existing literature

Several LR or MA have been published on the prevention of Covid-19. They concern global public health measures such as quarantine, social distancing, etc. [41–43] or are specific to one type of measure such as mask use (see). For example, the MA by Chou et al. [44], published at the beginning of the pandemic, addresses mask and eye protection as a means to prevent the occurrence of Covid-19. Chou et al. [13] conducted an updated MA of the effectiveness of mask wearing in preventing SARS-CoV-2.

The MA by Alkhalaf et al. [45] focused on dentistry.

The study by Utzet et al. [46] focused specifically on HCWs. It evaluated the effectiveness of non-pharmacological preventive measures for COVID-19 in HCWs before the vaccination era. A dynamic cohort of 5543 HCWs employed for at least one week in a Spanish hospital in 2020 was used. Negative binomial regression models were used to assess the incidence rate and rate ratio (RR) during two different waves (15 March to 21 June and 22 June to 31 December), adjusting for natural

immunity from the first wave and contextual factors. Socio-occupational variables were adjusted for in stratified analyses.

There was a significant reduction in the average COVID-19 incidence rate per 1000 working days between the two waves, from 0.82 (CI95%: 0.73-0.91) to 0.39 (0.35-0.44). After adjustment for natural immunity and contextual factors, the adjusted RR was 0.54 (0.48-0.87). The authors concluded that the remarkable decrease in COVID-19 incidence was largely due to improvements in non-pharmacological preventive measures.

As the authors point out, their study considered non-pharmacological preventive measures as a whole, which calls for a more specific evaluation of the effectiveness of selected non-pharmacological preventive measures.

- **Strengths and limitations**

The strength of our review is a detailed report of several non-pharmacological preventive measures for Covid-19, considering their effectiveness one by one.

Our review had tried to address all types of measures together and updated them with the latest articles published in 2023. Some of the recently published MA, by including more articles, allow a more precise estimation of the effect measure, such as odds ratio (or relative risk, or hazard ratio, etc.).

We have also tried to summarise a large and dynamic field of research.

One of the limitations of our review is that we only considered issues related to the non-pharmacological prevention of Covid-19. The pharmacological aspects of prevention, vaccination and prophylactic drugs (such as monoclonal antibodies used to prevent infection and disease progression) will be discussed in the second part of our article.

Another limitation of this review is that it is a narrative review of the literature. Our work is therefore essentially subjective. However, it is difficult to carry out such a review of the entire field of Covid 19 prevention because of the thousands of articles published on the subject.

- **Unresolved issues**

Despite the publication of numerous MA and literature reviews, there are still unanswered questions.

With regard to masks in particular, the superiority of N95/FFP2 over surgical masks in the prevention of Covid-19 has not yet been demonstrated. The same applies to the modalities of mask wear in the hospital, continuous or intermittent wear, etc.

See Fang et al. [47] and related letters to the editor.

Compared to the surgical mask, the effectiveness of the N95 respirator in the patient care area cannot be definitively determined.

## 5. Conclusions

Our review provides updated available information on several non-pharmacological measures, e.g. precautions and air and droplet precautions, mask wearing, adequate room ventilation, which are effective in preventing the occurrence of Covid-19.

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