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Protecting hospitals from SARS-CoV-2 infection: A review-based comprehensive strategy for COVID-19 prevention and control

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ABSTRACT. SARS-CoV-2-related infection can determine hospital-acquired infections among patients and healthcare workers. Aim of this paper was to review the literature for developing a strategy for protecting healthcare workers, patients, and visitors by COVID-19 hospital infection. A critical and rapid revision of the literature and international standards and Regulations on this topic allowed us to propose an evidence-based strategy in the framework of the workplace risk assessment for preventing nosocomial COVID-19 outbreaks. The virus' high transmissibility, the high prevalence of asymptomatic carriers and false-negative Covid-19 rates on naso- and oropharingeal swabs, put hospitals at high-risk of COVID-19 outbreaks. A comprehensive strategy based on standard precautions, administrative, environmental, and engineering controls, a screening protocol for patients on their admission to hospital, and a testing-based strategy for HCWs within health surveillance programs may prevent the onset of hospital outbreaks, which are a threat to community, patients and HCWs, compromising the sustainability of healthcare facilities.

Key words: *hospital infection, healthcare associated infection, occupational injury, SARS-CoV-2 prevention, COVID 19 pandemic.*

RIASSUNTO. SARS-CoV-2 può determinare infezioni acquisite in ospedale tra pazienti e operatori sanitari. Lo scopo di questo studio è rivedere la letteratura per lo sviluppo di una strategia per la protezione di operatori sanitari, pazienti e visitatori dall'infezione ospedaliera da COVID-19. Una revisione critica e rapida della letteratura e degli standard e regolamenti internazionali su questo argomento, ci ha permesso di proporre una strategia basata sull'evidenza nel quadro della valutazione del rischio sul posto di lavoro per prevenire le epidemie nosocomiali da COVID-19. L'elevata trasmissibilità del virus, l'elevata prevalenza di portatori asintomatici e di tamponi naso e orofaringei falsi negativi, mettono gli ospedali ad alto rischio per lo sviluppo di focolai da COVID-19. Una strategia globale, basata su precauzioni standard, controlli amministrativi, ambientali e tecnici, su un protocollo di screening per i pazienti al momento del ricovero in ospedale, insieme ad una strategia operativa basata sui test di screening per gli operatori sanitari all'interno dei programmi di sorveglianza sanitaria, possono prevenire l'insorgenza di epidemie ospedaliere che rappresentano una minaccia per la comunità, per i pazienti e per gli operatori sanitari, compromettendo la sostenibilità delle stesse strutture sanitarie.

Parole chiave: infezione ospedaliera, infezione associata all'assistenza sanitaria, infortunio sul lavoro, prevenzione SARS-CoV-2, pandemia COVID 19.

Introduction

Since first being reported in December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly spread worldwide. Thus, as of December, 30, 2020, 80,316,555 cases of COVID-19 were globally reported, including 1,770,695 deaths (1). Current scientific consensus suggests that SARS-CoV-2 is transmitted primarily from direct contact via the mouth, nose, or eyes with infected person through respiratory droplets (> 5 μm in diameter). However, transmission may also occur indirectly via fomite contaminated by respiratory secretions or droplets (2) and via droplets less than 5 μm in diameter ("droplet nuclei" or "microdroplets"), the so-called "airborne transmission" (3). These modality of viral transmission places health workers (HWs) at a high risk of infection (4), citing them as a possible source of nosocomial transmission clusters (5). Early available evidence suggested that HCWs are being increasingly infected with the novel infection ranging from 15% to 18% and in some cases up to 20% of the infected population (6). HCWs are more susceptible to COVID-19 due to several risk factors like long duty hours, lack or inadequate use of Personal Protective Equipments (PPEs), uncertain diagnostic criteria, unavailability of diagnostic criteria, stressful and high-risk working environments with concentration of infected patients and high viral loads, lack of measures to prevent the spread in hospitals (6-12).

All these risk factors coupled with the role of asymptomatic or presymptomatic who can act as potential "superspreaders" may contribute to the onset of COVID-19 hospital outbreaks (13, 14). COVID-19 infection is an occupational injury for HCWs (15). At the same time, HCWs can be source of COVID-19 hospital-acquired infections (16), which are nosocomially-acquired infections that are typically not present or might be incubating at the time of admission (17). Healthcare infected can be source of COVID-19 nosocomial outbreaks spreading to the entire community (5). The implementation of effective containment measures is, therefore, particularly important in hos-

pitals and homecare facilities, where the risk of contagion is higher and the magnitude of consequences is amplified by the presence of "frailty" among patients and home care clients, who are often elderly and immune-depressed patients with co-morbidities (18-20). Furthermore, depletion of healthcare workforce may affect the quality of care delivered by overwhelmed healthcare systems, especially for diseases other than COVID-19 (21-23). Hospital outbreaks can be crucial in the sustainment of the viral community transmission. For all these reasons, hospital administrators and managers have to implement effective Infection Preventive Control (IPC) measures. Aim of this paper was to develop a review-based strategy for protecting hospitals from COVID-19 infection outbreaks.

Methods

A literature review focusing on the main preventive and protective measures in healthcare facilities against COVID-19 and including administrative engineering, environmental, and individual measures was carried out. SARS-CoV-2 infection characteristics and some challenging diagnostic aspects of COVID-19 infection, were also analyzed. The literature review was the starting point for developing a screening pathway for patients on their hospital admission, and a targeted workplace health surveillance programme for screening hospital workers. Due to the current health emergency, a rapid review design, which is a "type of knowledge in which components of the systematic reviews process are simplified or omitted to produce information in a short period of time" (24), by limiting inclusion by date or language and reporting results narratively, was used (25). Rapid reviews have been described as a "streamlined alternative to standard systematic reviews" and a key use of this type of review is to provide summary evidence in an environment where health service delivery decisions need to be made quickly and not within the time frames of traditional reviews (25). They also provide a format that makes evidence accessible for decision makers and are a valuable way of supporting evidenced-based decision making (26). Relevant terms relating to the following themes: "healthcare outbreaks"; "health surveillance"; "preventive measures" were combined. Searches were initially limited to May 25, 2020 and were updated to December 31, 2020 to ensure that current findings are included in the analysis and that results are relevant to current services. A combination of free-text and medical subject headings (MeSH) search terms, as well as appropriate subheadings, was used. Key words such as "Infection control", "Hospital", "diagnosis", "Hospital transmission", "SARS-CoV-2", "2019-nCoV", and "COVID-19" were used in several combinations. Two authors (FC and AS) independently conducted targeted database searches using the following databases: Medline, PMC, and Google Scholar. COVID-19 resources center by Lancet, New England Journal of Medicine, JAMA, Nature, Cell, BMJ, Science, the most important publishers (Elsevier, Oxford, Wiley), and non-peer reviewed papers from medRxiv and Google Scholar were consulted, as well as Italian and international guidelines, including those published by the US-Centers for Disease Control and Prevention (CDC), the European Centre for Disease Control and Prevention (ECDC) and the WHO. Only papers written in english and Italian languages were considered. The articles included were analyzed qualitatively.

Results and Discussion

Proposal of a strategy for the prevention of COVID-19 hospital outbreak/ COVID-19 Hospital-Acquired Infection

The risk of COVID-19 hospital-acquired infections and hospital outbreaks stems from several SARS-CoV-2 characteristics: the high transmissibility of the SARS-CoV-2; the high and unknown prevalence of asymptomatic carriers of the virus (27); the plurality of modalities of transmission (i.e., by fomites, droplet contacts and airborne transmission) (2, 3), and the high probability that patients, hospital visitors and healthcare staff who are infected can transmit the infection when asymptomatic, paucisymptomatic or presymptomatic (before 48 hours the onset of symptoms) (28). The fact that neither epidemiological nor clinical criteria permit to identify and isolate patients, visitors or carriers of infection, is the major determinant of COVID-19 infection in terms of either hospital-acquired infection and hospital-associated outbreaks. We developed a tailored strategy for preventing them (Figures 1a, 1b, and 2), which is based on early recognition and source control of COVID-19 in HCWs, hospital workers, visitors and patients, and the application of standard precautions for all patients, regardless of suspected or known infection. The implementation of additional precautions for COVID-19 infected patients, as well as administrative, environmental and engineering control measures were also included, in the framework of the workplace risk assessment (WRA), which is the "core" process of health and safety practices at workplace, aimed to identify, control and eliminate all the hazards for workers and third parties (29).

Administrative, environmental, and engineering controls

Administrative control measures are as the following: 1) routinely refreshing training to all the hospital staff on the IPC measures; 2) primary screening of workers, visitors and patients at all the entrances of the hospital (temperature and symptom screening; 3) different pathway for patients with suspected COVID-19 infection; 4) person-to-person distance of at least 1,5 mt (e.g., waiting area); 5) universal masking of visitors; 6) implementation of online consultation system; 7) primary screening and testing and temporary isolation for patients waiting for confirmation ("isolation room" within both emergency rooms and wards), and when single rooms are not available, people suspected of having COVID-19 should be cohorted together; 8) different treatment sites for COVID-19 patients on the basis of the illness severity (29, 30).

The main environmental preventive measure is ensuring environmental cleaning and disinfection procedures with commonly used hospital-level disinfectants (e.g., sodium hypochlorite).

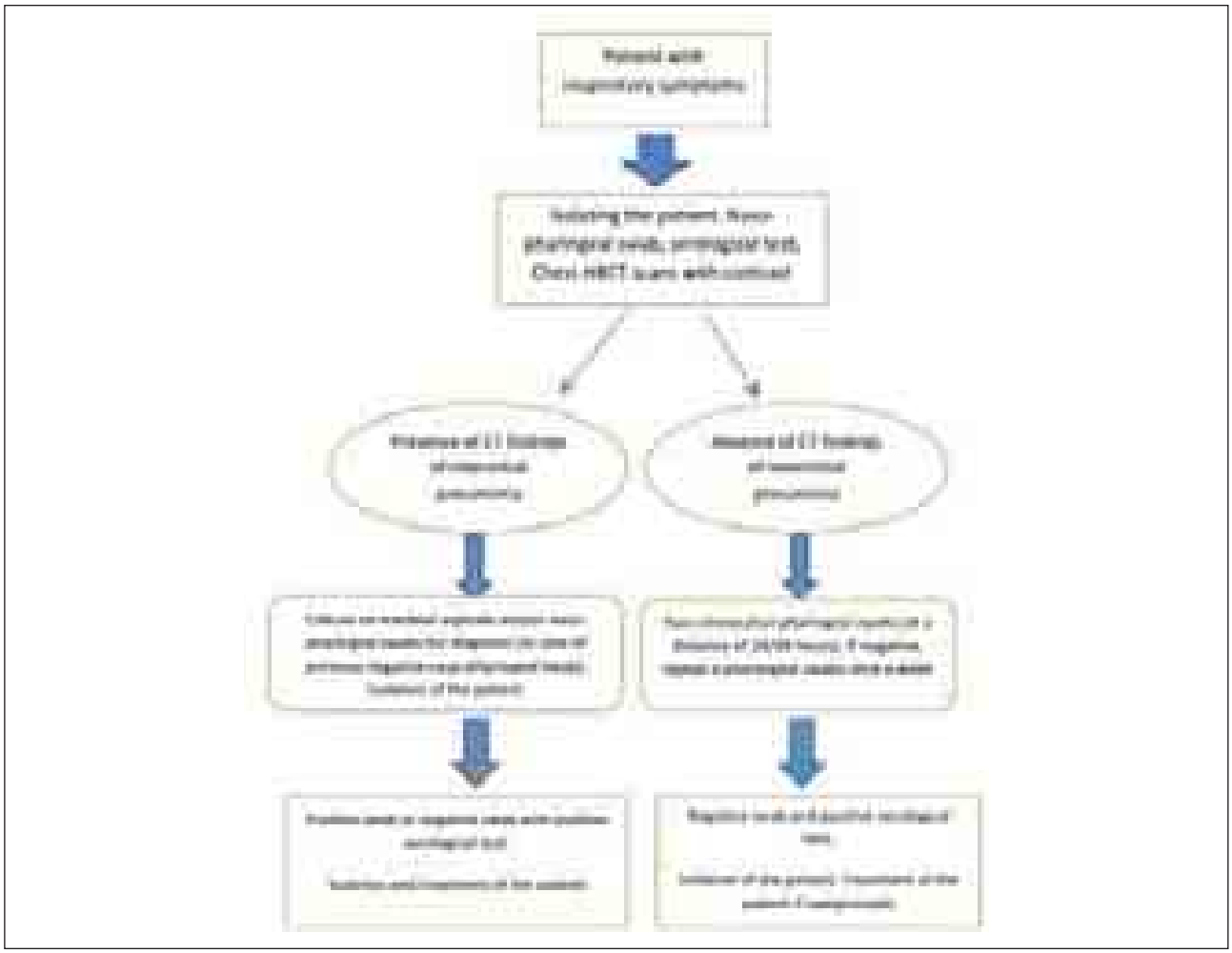

Figure 1a. *Procedure for monitoring patients with COVID-19 suspected symptoms admitted to hospital*

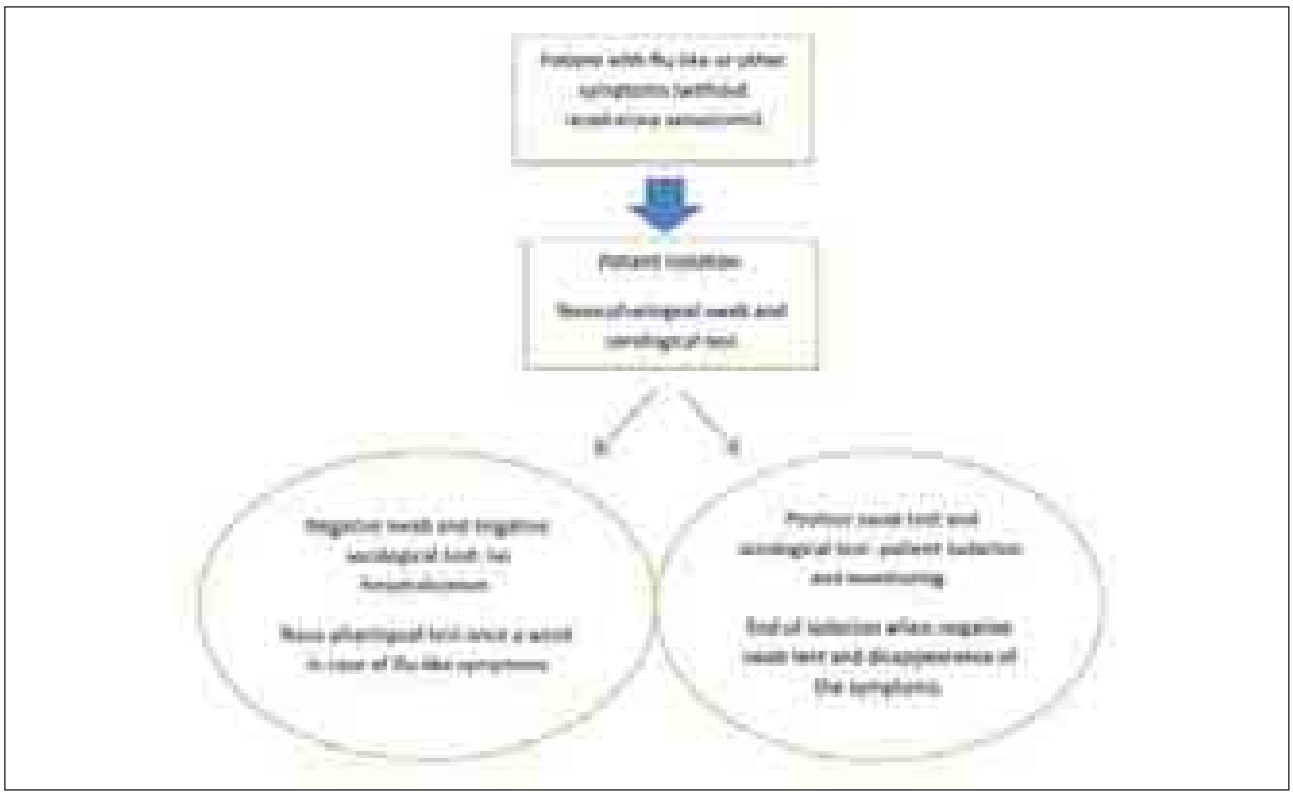

Figure 1b. *Procedure for monitoring patients without respiratory symptoms admitted to hospital*

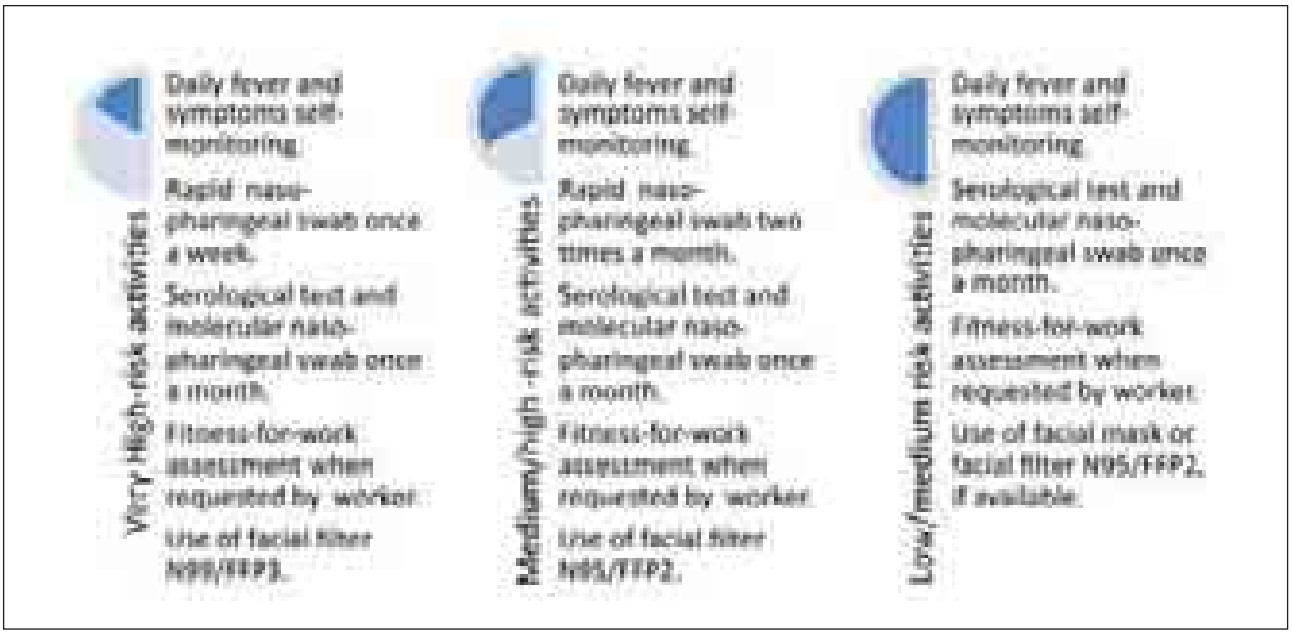

Figure 2. ***Health surveillance protocol for hospital healthcare workers***

With regard to engineering control measures, natural ventilation can be used in airborne precaution rooms, whereas a mechanically ventilated room with special features in air handling and airflow direction should be used for infection isolation rooms (29, 31). Heat Ventilation Air Conditioning systems need that air from the room can be exhausted directly to the outdoors, where the droplet nuclei will be diluted in the outdoor air, or alternatively passed through a special HEPA filter that removes most (99.97%) of the droplet nuclei before it is returned to the general circulation (3, 29), especially if aerosol-generating procedures are performed (29).

Current challenges for COVID-19 identification and diagnosis in HCWs and patients

Currently, there are two main tests available for COVID-19: direct tests (i.e., molecular tests) that are designed for diagnosing a current infection, and indirect tests (i.e., serological tests) that are designed to ascertain seroconversion upon a previous (IgG) or an early (IgM) infection. A combination of these tests may inform crucial decisions by healthcare providers and policy makers (32). The COVID real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test is considered to be the gold standard test for the qualitative and quantitative detection of viral nucleic acids. Several point-of-care tests (POCTs), which are rapid antigen tests were developed for rapid diagnosis of infected patients. However, these tests tend to have lower sensitivity than RT-PCR. Therefore, even if they may be useful during an ongoing outbreak, when timely access to sensitive molecular testing is unavailable, a negative result should be interpreted by a healthcare professional with caution and based on clinical judgement (33). In the event of suspected symptoms, the molecular swabs should be immediately performed to confirm diagnosis, isolate the positive subject and trace his/her contacts (34, 35). RT-PCR is the frontline diagnostic test for COVID-19 that is capable of analyzing thousands of specimens in a single day and shows a testing sensitivity of 95% (36). It can be carried out on different types of samples (i.e., nasopharyngeal swab, oropharyngeal swab, bronchoalveolar lavage, tracheal aspirates, and saliva). At present the US-CDC recommend collecting and testing a nasopharyngeal specimen as the preferred choice for swab-based SARS-CoV-2 testing. For individuals having invasive procedures, lower respiratory tract specimens are recommended, if available (37). The RT-PCR technique shows, however, some analytical problems, such as inadequate procedures for collection, handling, transport and storage of the swabs, manual errors, testing outside the diagnostic window, active viral recombination, use of inadequately validated assays, that contribute to jeopardize the diagnostic accuracy (38). In literature, authors have reported several cases of COVID-19 patients with false negative swabs (39-49). Since the risk for recurrent infection with SARS-CoV-2 is not known for COVID-19, detection of one or two antibodies (IgM and/or IgG) does not necessarily guarantee immunity against reinfection. Furthermore, negative results do not rule out SARS-CoV-2 infection, particularly in those who have been in contact with the virus and positive results may be due to past or present infection with SARS-CoV (50). The Italian National Institute of Health recommends using CLIA and ELISA serological tests, with a specificity of at least 95% and sensitivity of at least 90% (51), only for epidemiological surveys on communities such as occupational cohorts, but not for clinical diagnosis as a substitute of swab tests (52, 53). Due to the shortage of kits and false negative rate of RT-PCR, the Hubei Province, China temporarily used CT scans as a clinical diagnosis for COVID-19 (54). CT systems are expensive, require technical expertise, and cannot specifically diagnose COVID-19 (55), yet they can be highly useful for early diagnosis and follow-up (42, 56-58), having a higher sensitivity in

patients with positive RT-PCR (59), and lower in patients with only non-respiratory symptoms (60). Conventional chest X-ray sensitivity is at around 59% (61). Ultrasounds show an estimated sensitivity of 75%, with a low specificity and high variability depending on factors such as disease severity, patient weight and operator skills. Therefore, they could be useful as a screening tool in combination with clinical finings and molecular testing for early diagnosis, for monitoring the progression of the disease (62), and distinguishing COVID-19 by community-acquired pneumonia (CAP) (63).

Testing strategies on HCWs and patients

To identify and isolate asymptomatic patients admitted to hospital, it is insufficient a single oro-nasopharyngeal swab tests before the admission. The critical point concerns the quality of the samples. In case of suspected infection, operators should collect swabs by multiple sites, taking into consideration both the symptoms and the stage of the clinical course. In presence of radiological signs (bilateral interstitial pneumonia) of COVID-19, swabs should be taken by lower airways. For diagnosis, chest High Resolution Computed tomography (HR-CT) manifestations can supplement parts of limitations of real-time reverse transcription polymerase chain reaction (RT-PCR) assay. Serological tests can contribute to diagnosis, where they are complemented with naso-pharingeal swab tests (52, 53). In case of patient with respiratory symptoms (breathing difficulty, cough, chest pain), all the containment measures should be activated in any case.

One of the most known strategies to control the spread of COVID-19 infection among hospital staff is the 3T (testing, tracing, and treating) strategy (11, 62). In Indonesia polymerase chain reaction (PCR) swabs tests, implementation of contact tracing and isolation of infected operators were effective for controlling the spread of COVID-19 and reducing the risk of spreading infection (11). In Korea, the robust control of a COVID-19 healthcare-associated outbreak minimized the transmission of SARS-CoV-2 within hospitals and local communities. However, there was also much debate over the appropriate period of hospital shutdown and testing of all hospital staff and patients (62). In one of the largest international survey studies in the field of surgery, significant rates of centers had experienced in-hospital COVID-19 infection (31.5%) worldwide, confirming a wide prevalence of the initial symptom-based preoperative testing policies, which may have missed the asymptomatic case (63). International and local surgical guidelines recommend preoperative testing when available and practical, considering that SARS-Cov-2 make asymptomatic patients more likely to transmit the disease than in the previous epidemics (63). A study from China reported a higher prevalence of asymptomatic COVID-19 infection in hospitalized patients (5.8%) compared to the community (1.2%) (64), and asymptomatic hospitalized patients were frequently reported as a source of in-hospital outbreaks (65).

Occupational health surveillance of HCWs and hospital workers can be decisive for protecting hospital from COVID-19 infection (66). HCWs may be "dangerous" for patients and family members. Trough mandatory health surveillance, "vulnerable" workers (i.e., those affected by cardiovascular diseases, chronic obstructive pulmonary diseases, diabetes mellitus, conditions of immunosuppression, or other conditions associated with higher risk of COVID-19 related complications and mortality) can be monitored. There are currently no widely available reliable antibody testing to demonstrate both current and previous COVID-19 infection, thus their usage could raise technical and ethical concerns (67). On the contrary, all HCWs, including those asymptomatic, should be routinely tested with Reverse Transcription Polymerase Chain Reaction (RT-PCR) testing on nasopharingeal swabs for early diagnosis of SARS-CoV-2 (66). Viral test are the best available tools to diagnose current infection with SARS-CoV-2 and point-of-care tests, meaning results may be available at the testing site in less than an hour, could be particularly useful.

Standard precautions and individual IPC measures for preventing COVID-19 hospital infections

Standard precautions include hand and respiratory hygiene, appropriate PPEs, injection safety practices, safe waste management, proper linens management, environmental cleaning, and sterilization of patient care equipment. All individuals, including family members, visitors and health-care workers, should apply contact and droplet precautions (67, 68). WHO has developed the WHO COVID-19 risk assessment tool (69). HCWs are classified as "high" or "low" risk to COVID-19 infection, if they follow or not, respectively the IPC measures while performing medical activities and aerosol-generating procedures on COVID-19 patient in health care facilities. IPC measures on COVID-19 patients include wearing of single-use gloves, medical masks, face shield or goggles/protective glasses, disposable gown, removing and replacing PPEs according to protocol, performing hand hygiene (before and after touching a COVID-19 patient, before and after any clean or aseptic procedure, after exposure to body fluids, after touching patient surroundings) and decontaminating high touch surfaces at least 3 times daily. The IPC measures during aerosol-generating procedures include wearing of single-use gloves, N95 mask (or equivalent operator), face shield or goggles/protective glasses, disposable gown, waterproof apron, removing and replacing PPE according to protocol, performing hand hygiene (before and after touching a COVID-19 patient, before and after any clean or aseptic procedure, after exposure to body fluids, after touching patient surroundings), decontaminating high touch surfaces at least 3 times daily, whether the healthcare worker had any type of accident with body fluid/respiratory secretions of a COVID-19 patient (67-69).

According to the WHO, strategies to protect HCWs from hospital-acquired COVID-19 infection should include training of HCWs to recognize respiratory diseases, an increased access to PPEs, support for HCWs to reduce their high workload, a strong hospital surveillance system filling the existing gaps of the healthcare system to protect HCWs and their patients.

As suggested by Ashinyo et al (70), HCWs should adhere to WHO and national IPC protocols through constant

training on IPC protocols coupled with a regular supply of appropriate PPEs and supportive supervision of HCWs exposed to the COVID-19 virus.

PPEs in healthcare facilities

The PPEs needed to protect HCWs are masks (face masks and shields), respirators, gloves, body covers and googles. A systematic review of observational studies on Severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and COVID-19 found that the use of N95 or similar respirators might be associated with greater reduction in risk than medical masks. However, very few studies included in the review evaluated the transmission risk of COVID-19. Despite the WHO's call for increased production of PPEs (71), and WHO, CDC, and FDA have suggested their rational use (72-74), there are still shortages of PPEs (4, 75, 76) for healthcare personnel.

There are two types of mask for medical use in healthcare facilities: 1) medical masks that are defined as surgical or procedure masks; and 2) Filtering facepiece respirators (FFR), or respirators, offer a balance of filtration and breathability. European FFP2/FFP3 guarantees a filtration of at least 94%/99% solid NaCl particles and oil droplets and corresponds to US N95, filtering at least 95%/99% NaCl particles (77). Policies on wearing a mask for HCWs have been much debated (4, 77, 78). The WHO guidelines recommend that health care workers should wear a medical mask when entering a room where patients with suspected or confirmed COVID-19 are admitted (79). This WHO's document published on 5 June 2020 and updated on 1 December 2020, recommend for HCWs the use of medical mask in the absence of aerosol generating procedures (AGPs), and the use of FFP2/FFP3 only when AGPs are performed, or in other care settings if they are widely available and if costs is not an issue. In areas of known or suspected community or cluster SARS-CoV-2 transmission, universal masking for all persons (staff, patients, visitors, service providers and others) within the health facility (including primary, secondary and tertiary care levels; outpatient care; and long-term care facilities) is advisable. WHO recommends, furthermore, adherence to correct mask management practices (79).

Bellato et al. (63) in their study on surgeons argue that local testing capability and PPEs availability are the best protective measures under the current risk of asymptomatic COVID-19 patients. Saran et al (80) showed technical issues concerning design and materials of PPEs. In their systematic review, Tian et al. (81) showed that community mask use could be beneficial, but higher-level specification of masks and respirators could provide better protection for HCWs (78, 79). WHO (82), CDC (83) and ECDC (84) released strategies to tackle SARS-CoV, MERS-CoV and SARS-CoV-2 infections. They include a risk assessment, which is based on type of activity performed by HCWs (Table I).

Conclusion

Preventing COVID-19 hospital infections has a positive impact on healthcare systems and community. A review-based comprehensive strategy integrating occupational health practice and public health activities, can promote their respective preventive strategies (85-87). The proposed protocol, finally, could be useful for the current COVID-19 pandemic and for future epidemic driven by new and old airborne-transmitted biological hazards.

CRediT authorship contribution statement

Francesco Chirico: Conceptualization, Methodology, Literature search, Writing – original draft, editing, Supervision. Gabriella Nucera: Conceptualization, Writing – review & editing. Angelo Sacco: Literature search, review. Giuseppe Taino: Review & editing. Marcello Imbriani: Review & editing.

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Conflicts of interest

None declared.

Table I. ***Coronavirus infection prevention strategies***

Biological hazard	WHO		CDC		ECDC	
	Low risk profile	*High-risk profile*[1]	*Low risk profile*	*High risk profile*	*Low risk profile*	*High risk profile*
SARS-CoV	FFP2/FFP3 respirator[2]	FFP2/FFP3 respirator	FFP2/FFP3 respirator	FFP2/FFP3 respirator	–	–
MERS-CoV	Surgical mask	FFP2/FFP3 respirator	FFP2/FFP3 respirator	FFP2/FFP3 respirator	Surgical mask/ FFP2/FFP3 respirator	FFP2/FFP3 respirator
SARS-CoV-2	Surgical mask	FFP2/FFP3 respirator	Surgical mask	FFP2/FFP3 respirator	Surgical mask/ FFP2/FFP3 respirator	FFP2/FFP3 respirator

Note: CDC, Centers for Disease Control and Prevention; ECDC, European Centre for Disease Control and Prevention; WHO, World Health Organization. 1: Aerosol-generating procedures; 2: FFP2 / FFP3 respirators; 3: Based on the risk assessment; 4: surgical mask and, if available, FFP2 / FFP3 respirators.

References

1) European Centre for Disease Prevention and Control. COVID-19 situation update worldwide, as of 3 June 2020. Stockholm: ECDC; 2020
2) Zisook RE, Monnot A, Parker J, Gaffney S, Dotson S, Unice K. Assessing and managing the risks of COVID-19 in the workplace: Applying industrial hygiene (IH)/occupational and environmental health and safety (OEHS) frameworks. Toxicol Ind Health 2020 Sep;36(9):607-18. doi: 10.1177/0748233720967522.
3) Chirico F, Sacco A, Bragazzi NL, Magnavita N. Can Air-Conditioning Systems Contribute to the Spread of SARS/MERS/COVID-19 infection? Insights from a Rapid Review of the Literature. Int J Environ Res Public Health 2020;17(17):6052. doi: https://doi.org/10.3390/ijerph17176052.
4) Chirico F, Nucera G, Magnavita N. COVID-19: Protecting healthcare workers is a priority. Infect Control Hosp Epidemiol 2020 (epub 17 April 2020). https://doi.org/10.1017/ice.2020.148.
5) Calò F, Russo A, Camaioni C, De Pascalis S, Coppola N. Burden, risk assessment, surveillance and management of SARS-CoV-2 infection in health workers: a scoping review. Infect Dis Poverty 2020 Oct 7;9(1):139. doi: 10.1186/s40249-020-00756-6.
6) Ali S, Noreen S, Farooq I, Bugshan A, Vohra F. Risk Assessment of Healthcare Workers at the Frontline against COVID-19. Pak J Med Sci 2020 May;36(COVID19-S4):S99-S103. doi: 10.12669/pjms.36.COVID19-S4.2790.
7) Chirico F, Nucera G. Tribute to healthcare operators threatened by COVID-19 pandemic. J Health Soc Sci 2020;5(2):165-8. doi: 10.19204/2020/trbt1.
8) Chirico F, Nucera G, Magnavita N. Protecting the mental health of healthcare workers during the COVID-19 emergency. BJ Psych International 2020:1-6. doi: 10.1192/bji.2020.39.
9) Chirico F, Nucera G. An Italian Experience of Spirituality from the Coronavirus Pandemic. J Relig Health 2020. doi: https://doi.org/10.1007/s10943-020-01036-1.
10) Gaspar-Hernández J, Araiza-Garaygordobil D, Gopar-Nieto R, Martínez-Amezcua P, Arias-Mendoza A. Impact of the Coronavirus Disease-19 Pandemic on Acute Cardiovascular Emergencies in a Third Level Cardiology Hospital: A Call for Action. Rev Invest Clin 2020 May 7;72(5). doi: 10.24875/RIC.20000349.
11) Hidayat R, Aini N, Ilmi AFN, Azzahroh F, Giantini A. Test, Trace, and Treatment Strategy to Control COVID-19 Infection Among Hospital Staff in a COVID-19 Referral Hospital in Indonesia. Acta Med Indones 2020 Jul;52(3):206-13.
12) World Economic Forum. What's needed now to protect health workers: WHO COVID-19 briefing. Available at: How to protect health workers now: WHO COVID-19 briefing | World Economic Forum (weforum.org) [last accessed January 2021].
13) Kim SW, Jo SJ, Lee H, Oh JH, Lim J, Lee SH, et al. Containment of a healthcare-associated COVID-19 outbreak in a university hospital in Seoul, Korea: A single-center experience. PLoS One 2020 Aug 14;15(8):e0237692. doi: 10.1371/journal.pone.0237692.
14) Hu LQ, Wang J, Huang A, Wang D, Wang J. COVID-19 and improved prevention of hospital-acquired infection. Br J Anaesth 2020 Sep; 125(3):e318-e319. doi: 10.1016/j.bja.2020.05.037. Epub 2020 May 31.
15) Chirico F, Magnavita N.COVID-19 infection in Italy: An occupational injury. S Afr Med J 2020;110(6). doi: https://doi.org/10.7196/SAMJ.2020. v110i6.14855.
16) Monegro AF, Muppidi V, Regunath H. Hospital Acquired Infections. 2020 Sep 3. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan.
17) Kucharski AJ, Klepac P, Conlan A, et al. Effectiveness of isolation, testing, contact tracing and physical distancing on reducing transmission of SARS-CoV-2 in different settings. medrxiv.doi. https://doi.org/10.1101/2020.04.23.20077024. Available at: https://www.medrxiv.org/content/medrxiv/early/2020/04/29/2020.04.23.20077024.full.pdf [last accessed January 2021].
18) Webforum. Available at: https://www.weforum.org/agenda/2020/03/testing-tracing-backbone-who-coronavirus-wednesdays-briefing/ [last accessed January 2021].
19) Istituto Superiore di Sanità. Survey nazionale sul contagio COVID-19 nelle strutture residenziali e sociosanitarie. Terzo Report. Aggiornamento 14 aprile ore 20.00. Available at https://www.epicentro.iss.it/coronavirus/pdf/sars-cov-2-survey-rsa-rapporto-3.pdf. [last accessed May 2020].
20) Magnavita N, Di Prinzio RR, Chirico F, Sacco A, Quintavalle G. COVID-19 and staff mental health: is there an evidence? An Italian field study. Eur J Public Health. 2020;30(5 Suppl):ckaa165.565. doi: https://doi.org/10.1093/eurpub/ckaa165.565.
21) Magnavita N, Sacco A, Chirico F. Covid-19 pandemic in Italy: Pros and cons. Zdrowie Publiczne i Zarządzanie 2018;16(4):32-5.
22) Chirico F, Nucera G, Magnavita N. Estimating case fatality ratio during COVID-19 epidemics: Pitfalls and alternatives. J Infect Dev Ctries 2020;14(5):438-39. Published 2020 May 31. doi:10.3855/jidc.12787.
23) Gaspar-Hernández J, Araiza-Garaygordobil D, Gopar-Nieto R, Martínez-Amezcua P, Arias-Mendoza A. Impact of the Coronavirus Disease-19 Pandemic on Acute Cardiovascular Emergencies in a Third Level Cardiology Hospital: A Call for Action. Rev Invest Clin 2020 May 7;72(5). doi: 10.24875/RIC.20000349.
24) Khangura S, Konnyu K, Cushman R, Grimshaw J, Moher D. Evidence summaries: the evolution of a rapid review approach. Syst Rev 2012;1:10.
25) Tricco AC, Antony J, Zarin W, Strifler L, Ghassemi M, Ivory J, et al. A scoping review of rapid review methods. BMC Med 2015 Sep 16;13:224. doi: 10.1186/s12916-015-0465-6.
26) Peterson K, Floyd N. Ferguson L, Christensen V, Helfand M. User survey finds rapid evidence reviews increase uptake of evidence by Veterans Health Administration leadership to inform fast-paced health-system decision-making. Syst Rev 2016;5:132.
27) Furukawa NW, Brooks JT, Sobel J. Evidence supporting transmission of severe acute respiratory syndrome coronavirus 2 while presymptomatic or asymptomatic. Emerg Infect Dis 2020 Jul. Available at: https://doi.org/10.3201/eid2607.201595 [last accessed January 2021].
28) WHO. Severe acute respiratory infections treatment centre: practical manual to set up and manage a SARI treatment centre and SARI screening facility in health care facilities. Geneva: World Health Organization; 2020 (WHO/2019-nCoV/SARI_treatment_center/2020.1). Licence: CC BY-NC-SA 3.0 IGO.
29) Agarwal A, Nagi N, Chatterjee P, Sarkar S, Mourya D, Sahay RR, et al. Guidance for building a dedicated health facility to contain the spread of the 2019 novel coronavirus outbreak. Indian J Med Res 2020 Feb & Mar;151(2 & 3):177-83. doi: 10.4103/ijmr.IJMR_518_20.
30) Ventilation: engineering controls for TB. Lansing, MI: Michigan Occupational Safety and Health; 2017.
31) WHO. Coronavirus disease 2019 (COVID-19). Situation Report-73. Published on 2 April 2020. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports [last accessed May 2020].
32) Kucharski AJ, Klepac P, Conlan A, Kissler SM, Mmath MLT, Fry H, et al. Effectiveness of isolation, testing, contact tracing and physical distancing on reducing transmission of SARS-CoV-2 in different settings. medrxiv. https://doi.org/10.1101/2020.04.23.20077024.
33) Woelfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Muller MA, et al. Clinical presentation and virological assessment of hospitalized cases of coronavirus disease 2019 in a travel-associated transmission cluster. medRxiv 2020 Mar 8. doi: 10.1101/2020.03.05.20030502.
34) Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving sepsis campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). Intensive Care Med 2020 May;46(5):854-87. doi: 10.1007/s00134-020-06022-5. Epub 2020 Mar 28.
35) D'Cruz RJ, Currier AW, Sampson VB. Laboratory Testing Methods for Novel Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2). Front Cell Dev Biol 2020 Jun 4;8:468. doi: 10.3389/fcell.2020.00468.
36) La Marca A, Capuzzo M, Paglia T, Roli L, Trenti T, Nelson SM. Testing for SARS-CoV-2 (COVID-19): a systematic review and clinical guide to molecular and serological in-vitro diagnostic assays. Reprod Biomed Online 2020 Sep;41(3):483-99. doi: 10.1016/j.rbmo.2020.06.001.

37) Lippi G, Simundic AM, Plebani M. Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19). Clin Chem Lab Med 2020 Jun 25;58(7):1070-6. doi: 10.1515/cclm-2020-0285.
38) Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for Typical Coronavirus Disease 2019 (COVID-19) Pneumonia: Relationship to Negative RT-PCR Testing. Radiology 2020 Aug;296(2):E41-E45. doi: 10.1148/radiol.2020200343. Epub 2020 Feb 12.
39) Cao G, Tang S, Yang D, Shi W, Wang X, Wang H, et al. The potential transmission of SARS-CoV-2 from patients with negative RT-PCR swab tests to others: two related clusters of COVID-19 outbreak. Jpn J Infect Dis 2020;73(6). 10.7883/yoken.jjid.2020.165.
40) Winichakoon P, Chaiwarith R, Liwsrisakun C, Salee P, Goonna A, Limsukon A, et al. Negative Nasopharyngeal and Oropharyngeal Swabs Do Not Rule Out COVID-19. J Clin Microbiol 2020 Apr 23;58(5):e00297-20. doi: 10.1128/JCM.00297-20.
41) Kumar DS, O'Neill SB, Johnston JC, Grant JM, Sweet DD. SARS-CoV-2 infection in a 76-year-old man with negative results for nasopharyngeal swabs and possible nosocomial transmission. CMAJ 2020;192(20):E546-E549. doi: https://doi.org/10.1503/cmaj.200641.
42) Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology 2020 Aug;296(2):E32-E40. doi: 10.1148/radiol.2020200642. Epub 2020 Feb 26.
43) Chirico F, Nucera G, Magnavita N. Hospital infection and COVID-19: Do not put all your eggs on the "swab" tests [published online ahead of print, 2020 May 27]. Infect Control Hosp Epidemiol 2020;1-2. doi:10.1017/ice.2020.254.
44) Pan Y, Zhang D, Yang P, Poon LLM, Wang Q. Viral load of SARS-CoV-2 in clinical samples. Lancet Infect Dis 2020 Apr;20(4):411-12. doi: 10.1016/S1473-3099(20)30113-4. Epub 2020 Feb 24.
45) Yang Y, Yang M, Shen C, Wang F, Yuan J, Li J, et al. Laboratory Diagnosis and Monitoring the Viral Shedding of 2019-nCoV Infections. medRxiv February 17, 2020. doi: 10.1101/2020.02.11.20021493.
46) To KK, Tsang OT, Leung WS, Tam AR, Wu TC, Lung DC, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis 2020 May;20(5):565-74. doi: 10.1016/S1473-3099(20)30196-1.
47) Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. N Engl J Med 2020 Mar 19;382(12):1177-9. doi: 10.1056/NEJMc2001737.
48) He X, Lau EHY, Wu P, Deng X, Wang J, Hao X. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med 2020 May;26(5):672-5. doi: 10.1038/s41591-020-0869-5. Epub 2020 Apr 15.
49) Guo L, Ren L, Yang S, Xiao M, Chang D, Yang F, et al. Profiling Early Humoral Response to Diagnose Novel Coronavirus Disease (COVID-19). Clin Infect Dis 2020 Jul 28;71(15):778-85. doi: 10.1093/cid/ciaa310.
50) Ministero della Salute. Direzione Generale della Prevenzione Sanitaria. COVID-19: test di screening e diagnostici. Circolare del 09 Maggio 2020 n. 0016106-09/05/2020-DGPRE-DGPRE-P.
51) European Center for Disease Center and Control. Diagnostic testing and screening for SARS-CoV-2. Available from: https://www.ecdc.europa.eu/en/covid-19/latest-evidence/diagnostic-testing [last accessed January 2021].
52) Lisboa Bastos M, Tavaziva G, Abidi SK, Campbell JR, Haraoui LP, Johnston JC, et al. Diagnostic accuracy of serological tests for covid-19: systematic review and meta-analysis. BMJ 2020 Jul 1;370:m2516. doi: 10.1136/bmj.m2516.
53) Long QX, Liu BZ, Deng HJ, Wu GC, Deng K, Chen YK, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med 2020 Jun;26(6):845-8. doi: 10.1038/s41591-020-0897-1.
54) Udugama B, Kadhiresan P, Kozlowski HN, Malekjahani A, Osborne M, Li VYC, et al. Diagnosing COVID-19: The Disease and Tools for Detection. ACS Nano 2020 Apr 28;14(4):3822-35. doi: 10.1021/acsnano.0c02624. Epub 2020 Mar 30.
55) Yang W, Yan F. Patients with RT-PCR Confirmed COVID-19 and Normal Chest CT. Radiology 2020:200702. doi: 10.1148/radiol.2020200702.
56) Yam WC, Chan KH, Poon LL, Guan Y, Yuen KY, Seto WH, et al. Evaluation of reverse transcription-PCR assays for rapid diagnosis of severe acute respiratory syndrome associated with a novel coronavirus. J Clin Microbiol. 2003 Oct;41(10):4521-4. doi: 10.1128/jcm.41.10.4521-4524.2003
57) Feng H, Liu Y, Lv M, Zhong J. A case report of COVID-19 with false negative RT-PCR test: necessity of chest CT. Jpn J Radiol 2020 May;38(5):409-10. doi: 10.1007/s11604-020-00967-9.
58) Kanne JP, Little BP, Chung JH, Elicker BM, Ketai LH. Essentials for radiologists on COVID-19: an update—radiology scientific expert panel. Radiology 2020:200527.
59) Bernheim A, Mei X, Huang M, Yang Y, Fayad ZA, Zhang N, et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. Radiology 2020;295:685-91. doi: https://doi.org/10.1148/radiol.2020200463.
60) Pascarella G, Strumia A, Piliego C, Bruno F, Del Buono R, Costa F, et al. COVID-19 diagnosis and management: a comprehensive review. J Intern Med 2020 Aug;288(2):192-206. doi: 10.1111/joim.13091. Epub 2020 May 13.
61) Tan G, Lian X, Zhu Z, Wang Z, Huang F, Zhang Y, et al. Use of Lung Ultrasound to Differentiate Coronavirus Disease 2019 (COVID-19) Pneumonia From Community-Acquired Pneumonia. Ultrasound Med Biol 2020 Oct;46(10):2651-8. doi: 10.1016/j.ultrasmedbio.2020.05.006. Epub 2020 Jun 5.
62) Kim SW, Jo SJ, Lee H, Oh JH, Lim J, Lee SH, et al. Containment of a healthcare-associated COVID-19 outbreak in a university hospital in Seoul, Korea: A single-center experience. PLoS One 2020 Aug 14;15(8):e0237692. doi: 10.1371/journal.pone.0237692.
63) Bellato V, Konishi T, Pellino G, An Y, Piciocchi A, Sensi B, et al. on behalf of S-COVID Collaborative Group. Screening policies, preventive measures and in-hospital infection of COVID-19 in global surgical practices. J Glob Health 2020;10:020507.
64) He G, Sun W, Fang P, Huang J, Gamber M, Cai J, et al. The clinical feature of silent infections of novel coronavirus infection (COVID-19) in Wenzhou. J Med Virol 2020. doi:10.1002/jmv.25861.
65) Pang KH, Osman NI. Asymptomatic COVID-19 infection in a patient evaluated for ureteric colic: Radiological findings and impact on management. Urology 2020;S0090-4295:30440-4.
66) Chirico F, Magnavita N. The Crucial Role of Occupational Health Surveillance for Health-care Workers During the COVID-19 Pandemic. Workplace Health Saf. 2021;69(1):5-6. doi:10.1177/2165079920950161.
67) Center for Diseases Prevention and Control. (2020, July 21). Interim Guidance on Testing Healthcare Personnel for SARS-CoV-2. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-healthcare-personnel.html [last accessed January 2021].
68) Severe acute respiratory infections treatment centre: practical manual to set up and manage a SARI treatment centre and SARI screening facility in health care facilities. Geneva: World Health Organization; 2020 (WHO/2019-nCoV/SARI_treatment_center/2020.1). Licence: CC BY-NC-SA 3.0 IGO.
69) World Health Organization. Risk Assessment and Management of Exposure of Health Care Workers in the Context of COVID-19: Interim Guidance. March 19, 2020. World Health Organization; 2020). WHO-2019-nCov-HCW_risk_assessment-2020.2-eng.pdf
70) Ashinyo ME, Dubik SD, Duti V, Amegah KE, Ashinyo A, Larsen-Reindorf R, et al. Healthcare Workers Exposure Risk Assessment: A Survey among Frontline Workers in Designated COVID-19 Treatment Centers in Ghana. J Prim Care Community Health 2020 Jan-Dec:11:2150132720969483. doi: 10.1177/2150132720969483.
71) WHO Shortage of Personal Protective Equipment Endangering Health Workers Worldwide. 2020, March 3Available at: https://www.who.int/news-room/detail/03-03-2020-shortage-of-personal-protective-equipment-endangering-health-workers-worldwide.
72) WHO. Advice on the Use of Masks in the Context of COVID-19. 2020 May. Available at: http://www.who.int/publications-detail/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak. [last accessed January 2021].
73) NIOSH. Brosseau L. N95 Respirators and Surgical Masks. 2020 May. Available at: http://blogs.cdc.gov/niosh-science-blog/2009/10/14/n95/. [last accessed January 2021].

74) FDA. N95 Respirators and Surgical Masks (Face Masks). 2020 May. Available at: http://www.fda.gov/medical-devices/personal-protective-equipment-infection-control/n95-respirators-and-surgical-masks-face-masks. [last accessed January 2021].
75) Priyadarshini R, Jafrin L, Aravinthan A, Sivagnanam G. Rationing PPEs during a pandemic: The COVID-19 scenario. Res Social Adm Pharm 2021 Jan;17(1):2044-5. doi: 10.1016/j.sapharm.2020.06.008.
76) Chu DK, Akl EA, Duda S, Solo K, Yaacoub S, Schunemann HJ, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. Lancet 2020;395(10242):1973-87.
77) Magnavita N, Sacco A, Nucera G, Chirico F. First aid during the COVID-19 pandemic. Occup Med (Oxford Med) 2020 Oct 1;70(7):458-460. doi:10.1093/occmed/kqaa148.
78) Magnavita N, Chirico F. Headaches, Personal Protective Equipment, and Psychosocial Factors Associated With COVID-19 Pandemic. Headache The Journal of Head and Face Pain 60(7):1444-5. doi: 10.1111/head.13882.
79) World Health Organization. Advice on the use of masks in the community during home care and in the healthcare settings in the context of the novel coronavirus outbreak. Available at: https://www.who.int/publications-detail/advice-on-the-use-of-masks-in-the-community-during-home-careand-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak. [last accessed April 2020].
80) Saran S, Gurjar M, Baronia AK, Lohiya A, Azim A, Poddar B, et al. Personal protective equipment during COVID-19 pandemic: a narrative review on technical aspects. Expert Rev Med Devices 2020 Dec 31:1-12. doi: 10.1080/17434440.2020.1852079.
81) Tian Z, Stedman M, Whyte M, Anderson SG, Thomson G, Heald A. Personal protective equipment (PPE) and infection among healthcare workers - What is the evidence? Int J Clin Pract 2020 Nov;74(11):e13617. doi: 10.1111/ijcp.13617.
82) World Health Organization. (2020). Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases: interim guidance, 2 March 2020. World Health Organization. Available at: https://apps.who.int/iris/handle/10665/331329. [last accessed May 2020].
83) Centers for Disease Control and Prevention. Evaluating and Testing Persons for Coronavirus Disease 2019 (COVID-19). Last updated: May 05,2020. Available at: https://doi.org/10.3201/eid2607.201595. [last accessed April 2020].
84) European Center for Disease Prevention and Control. Strategies for the surveillance of Covid-19. 9 April 2020. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/COVID-19-surveillance-strategy-9-Apr-2020.pdf. [last accessed April 2020].
85) Chirico F, Magnavita N. West Nile virus infection in Europe: need for an integration of occupational health practice and public health activities. Ann Ist Super Sanità 2019;55(1):3-5.
86) Chirico F, Magnavita N. The West Nile Virus epidemic-occupational insight. Lancet 2019 Mar 30;393(10178):1298.
87) Magnavita N, Chirico F**.** New and emerging risk factors in Occupational Health. Applied Sciences. 2020;10(4):8906. doi: 10.3390/app10248906.

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