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Effectiveness of prevention of SARS-CoV-2 transmission among unvaccinated Italian healthcare workers

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Abstract

Background: *We aimed to investigate the association between personal protective equipment (PPE) use and SARS-CoV-2 infection among healthcare workers (HCWs).* **Methods:** *We analyzed occupational surveillance contact forms followed by a PCR test notified between March and September 2020 by Italian HCWs. The odds ratios (ORs) and 95% Confidence Intervals (CIs) for positive PCR based on HCWs and contacts characteristics were calculated through multivariable logistic regression models. When multiple contacts were potentially effective for a PCR test, they were weighted by the inverse of their number.* **Results:** *Overall, 4,883 contacts reported by 2,952 HCWs were analyzed, and 224 contacts among 144 HCWs had positive PCR. No difference was found according to sex, age, employment, or job title, except for an OR of 0.30 (95%CI 0.11-0.78) for resident physicians, compared to administrative staff. The ORs for use of surgical mask were 0.59 (95%CI=0.40-0.86) for use only by HCW, 0.49 (95%CI=0.22-1.07) only by the infected person, and 0.40 (95%CI=0.27-0.60) by both, compared to use by neither. Use of other PPEs was not associated with infection, while the OR for hand sanitation was 0.61 (95%CI=0.40-0.93). HCWs reporting fever, cough, and asthenia had a higher risk of infection.* **Conclusions:** *Use of surgical masks was associated with a 40-60% lower risk of infection, especially when both HCWs and infected individuals used them. Our results quantify the role played by mask use and hand sanitation in preventing SARS-CoV-2 transmission in high-risk circumstances.*

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1. Introduction

To date, increasing evidence on the epidemiology of SARS-CoV-2 infection has risen worldwide. Particular attention has been given to health-care workers (HCWs) due to their higher probability of exposure. Before the introduction of vaccines, the use of personal protection equipment (PPE) has represented an important means to decrease the risk of transmission of the virus.

Available studies [1] provide evidence of efficacy against infection for masks, gowns, eye protection, and handwashing, including a dose-response relationship between adequate use of PPE and risk REDUCTION. Despite its ascertained benefit in preventing SARS-CoV-2 transmission, the effectiveness of the use of masks has not been precisely characterized, as it depends on idiosyncratic circumstances which may be difficult to take into account [2]. Besides this, reuse of PPE is common, and additionally the prolonged wearing of PPE has been associated with adverse effects like heat, thirst, and pressure areas up to exhaustion [3].

When infection started to spread in Italian hospitals, surveillance systems were set up to monitor its diffusion, with occupational medicine units involved in its control among the HCWs. We previously reported the results of a pooled analysis of data from occupational surveillance from six different Italian centers, including a subset of the present study population (843 infections diagnosed between March and May 2020) [4]. In that study, infection was more common among men, and mask used by the infected contact was an independent protective factor, while we found no difference based on job title or working department. Another large cohort study conducted in China described a higher risk of SARS-CoV-2 transmission for severe index cases, and reported a ten-fold higher risk for acquired infection in the household compared to the hospital setting, which may be explained by more frequent and longer unprotected exposure in the former and by mandatory use of mask and the high perceived risk within in the latter [5]. Since transmission can occur before symptoms' onset, a single infection can lead to multiple unprotected contacts before being diagnosed [6].

At the beginning of the pandemic, the Occupational Medicine Unit of Turin's University Hospital, set up a health surveillance program to identify infected HCWs, and to isolate and monitor them according to the public health regulations of the time. All HCWs were asked to notify each contact with a COVID-19 case. Risk assessment was performed to individuate those contacts possibly at risk and needing a diagnostic test.

This study aims to investigate the association between PPE use and SARS-CoV-2 infection among HCWs during the first wave of the SARS-CoV-2 pandemic, when vaccines were not available, and knowledge about the infection as well as guidelines for handling potential occupational contacts were rapidly developing.

2. Methods

We conducted a cross-sectional study on SARS-CoV-2 infection focusing on the use of PPEs and other characteristics among HCWs. Data were collected by the occupational medicine unit of the University Hospital of Turin, Northern Italy, from late February to September 2020. Surveillance systems, including contact tracing and monitoring of infected subjects, were established within the hospital in order to monitor HCWs for possible infection with SARS-CoV-2. Testing for infection was set up with rhino-pharyngeal swabs to detect SARS-CoV-2 RNA by RT-PCR, in a reference laboratory, and databases were established to monitor and follow subjects. SARS-CoV-2 RNA was studied by a molecular test, AptimaTM SARS-CoV-2 Assay with the PantherTM Fusion System (Hologic, Rome, Italy) [7]. The assay combines the technologies of target capture, Transcription Mediated Amplification, and Dual Kinetic Assay and detects two conserved regions of the ORF1ab gene. Qualitative results were determined by a cut-off based on the total Relative Light Units and the kinetic curve type. No information on viral load was available. Samples were analyzed according to the guidelines proposed by the World Health Organization. Risk assessment was performed for each contact reported by HCWs, and additional PCR tests were prescribed based on it.

The first risk management protocol was established on March 6th, 2020, four days after the first index case in Turin. Before standardizing the procedure, when epidemiological criteria were poorly defined (i.e., emphasis was on return from endemic areas), information on suspected cases was collected from wards and transmitted in different ways to the occupational medicine unit. With the exponential increase of cases, the risk management protocols evolved, and with them, the forms used to notify the contacts. On April 10th, reporting procedures were shifted into a dedicated platform; this reduced significantly missing data, filling errors, accelerated risk assessment, and further communication to the HCW [8].

Risk management protocol indications for PCR test included: (i) suspected symptoms (fever defined as a temperature higher than 37.5 °C, dry cough of recent onset, dyspnea or minimum two symptoms among sore throat, severe asthenia, ageusia/hypogeusia, anosmia/hyposmia, headache, diarrhea/nausea/vomit, bilateral conjunctivitis, rhinorrhea), or (ii) at-risk contact, defined as not fully protected contact (surgical mask or facial respirator if aerosol exposed, glasses or visor, gloves or hand sanitization and gown) with a confirmed COVID-19 case for more than 15 minutes or at a distance of less than 2 meters.

The time schedules for PCR testing changed over time, but usually tests were performed at least 3 days after the contact at risk. A contact was considered at risk if it happened at least 48 hours before, and at maximum 14 days after the assessment of the infection.

Negative results were communicated by email, while positive results were communicated by phone call and an email containing information about self-isolation and return to work procedures. Quarantine of positive subjects ended when two consecutive negative tests were obtained.

The form used to collect surveillance data included: basic demographic information, job title, department of employment, self-reported circumstances of contact with a COVID-19 case, self-reported use of PPEs, and selected self-reported symptoms. Also, data were available for use of a surgical mask by the source of infection (patient or colleague). Contact forms were matched with the results of the PCR tests. Details on the timing of the contacts were derived from the date of contact notification.

The original dataset included more than 10,000 reporting forms. Contacts that filled the following conditions were considered potentially effective and retained in the analysis: (i) complete information on date of contact or date of infection of the source of contact, and date of PCR test; (ii) contact declared from 2 days before to 14 days after the date of a positive PCR test performed by the source of contact; (iii) PCR test performed by the HCW 2-14 days after the contact.

For HCW with at least one positive PCR test, only contacts potentially effective for the first positive PCR test were retained in the analysis; for HCW with only negative PCR tests, contacts potentially effective for all tests were included. When multiple contacts were potentially effective for a PCR test, they were weighted by the inverse of their number. For example, if a HCW reported two contacts qualifying to be effective (e.g., one 6 days and one 10 days before a PCR test), both contacts were retained in the analysis, each of them being weighted 0.5. For this reason, descriptive statistics of the contacts are presented only as percentages since the absolute numbers no longer correspond to individual contacts.

Multivariable weighted logistic regression models were employed to estimate the odds ratio (OR) and 95% Confidence Interval (CI) of effective contact for different predictors, which can be distinguished into subject-related and contact-related characteristics. The former group included sex, age, job title and department of employment; the latter group included use of PPEs, symptoms, and period and type of exposure related to the specific contact.

The main regression model included sex, age group, and job title as predictors. A sub-analysis using the same model was performed excluding the first 2 weeks of March. More complex models were estimated for variables regarding use of PPEs, symptoms, and period and type of exposure by adding a group of covariates, in turn, to this core set, based on backward selection.

The statistical package, STATA, Version 16, was used for the analysis [9].

3. Results

A total of 4,883 total contacts, reported by 2,952 different HCWs (average of 1.64 contacts per HCW) were retained in the analysis. Among these, we observed 224 (4.6%) effective individual contacts, i.e., contacts followed by a positive PCR test 2-14 days after COVID-19 contact occurrence, and 4,659 (95.4%) ineffective COVID-19 contacts, i.e., contacts reported by HCWs without any positive PCR test. A total of 144 (4.9%) individuals tested positive. Table 1 summarizes the main characteristics of the study population while the characteristics of the contacts are presented in Table 2.

Women represented 70.5% of HCWs included in the analysis, and the average age was 45.9 (range 23-70). The largest number of COVID-19 contacts were reported in the second half of March 2020 (n=1,832, 35%), corresponding also to the higher number of positive tests (n. 107), while the highest proportion of positive tests was reported between 1 and 15 March (13.5%).

Table 1. Main characteristics of the study population of health care workers*.

Characteristic	Number	%
Sex		
Male	866	29.5
Female	2,071	70.5
Age group		
20-35	654	22.1
36-50	1,107	37.5
51-70	1,191	40.4
Job title		
Physician	553	18.8
Resident physician	318	10.8
Nurse	1,190	40.4
Health assistant	461	15.6
Healthcare professional	270	9.2
Administrative staff/Other	151	5.1
Department		
Inpatients	1,956	67.9
Emergency room	328	11.2
Intensive care unit	165	5.6
COVID-19 unit	207	7.1
Total	2,952	100

**Numbers might not add to the total because of missing values.*

Overall, most HCWs reported wearing a mask during the contact (72.2%), while the source of infection did not (55.4%). Between 1 and 15 March 15, 41.4% of HCWs reported wearing a mask, against 76.9% in the second half of March 2020 and 79.3.0-85.6% during the following months. The source of infection was reported to wear the mask in 45.7% of the contacts; this proportion was 17.8% before 15 March, and between 37.6% and 61.9% in the following weeks. Most contacts occurred when the HCW was not wearing gloves (56.1%) or a face shield (83.1%). Additionally, we assessed the use of a mask by both the HCW and the source of infection for 4,807 contacts. In 22.6% of those, none was wearing a mask, 32.7% occurred with only the HCW wearing a mask, 5.1% with only the infected wearing a mask, and 39.6% with both wearing a mask. Despite the reported use of a mask by both subject and infected, 3.2% of these contacts resulted in a positive test. We observed no association between number of contacts notified and risk of infection. Among the symptoms declared by the HCWs, the most frequent were cough (10%), sore throat (6.5%), and fever (2.3%).

Table 3 shows the ORs of effective contact for sex, age, job title, PPE use, symptoms, and type of contact.

No associations were observed according to sex and age. When considering job title, resident physicians were less likely to report an effective contact (OR 0.30, 95%CI 0.11, 0.78, p=0.014) compared to administrative staff. Use of a mask by either the HCW (OR 0.63, 95%CI 0.45-0.87, p=0.006) and the source of infection (OR 0.63, 95%CI 0.45-0.89, p=0.008) was negatively associated with an effective contact.

Compared to contacts in which neither the HCW nor the source of infection wore a mask, the OR of positivity for contacts in which both wore a mask was 0.40 (95%CI 0.27-0.60). The use of a filtering facepiece 2 or 3 (FFP2/FFP3) mask was not common and resulted in an OR equal to 0.48, (95%CI 0.21-1.09). Women were 16% more likely

Table 2. Characteristics of contacts (Total number of contacts=4,883, 100%).

	Effective contacts* (%)	Ineffective contacts* (%)	Percentage of contacts over the total for each category
Time period of contact			
1 March - 15 March 2020	13.5	86.4	15.7
16 March - 31 March 2020	5.3	94.7	35.0
1 April - 15 April 2020	2.0	98.0	23.6
16 April - 30 April 2020	2.4	97.6	11.5
1 May - 30 September 2020	0.9	99.1	14.2
Use of PPEs (HCW)			
Surgical mask	4.0	96.0	72.2
FFP2/FFP3 mask	3.4	96.6	7.5
Face shield	3.8	96.2	16.9
Gloves	4.9	95.1	43.9
Hand sanitation (HCW)	3.2	96.8	29.7
Use of any mask			
HCW	4.0	96.0	72.2
Contact	3.4	96.6	44.6
Combined use of mask			
None	7.9	92.1	22.6
HCW alone	4.8	95.2	32.7
Contact alone	4.2	95.8	5.1
Both HCW and contact	3.2	96.7	39.6
Symptoms (HCW)			
Fever	29.7	70.3	2.3
Cough	15.1	84.9	10.0
Sore throat	4.0	96.0	6.5
Asthenia	13.8	86.2	0.9
Dyspnea	12.1	87.9	1.0
Anosmia/hyposmia	22.9	77.1	0.4
Ageusia/hypogeusia	12.7	87.3	0.5
Migraine	7.6	92.4	1.5
Total	4.9	95.1	100.0

**Effective contacts: contacts followed by a positive PCR test; ineffective contacts: contact not followed by a positive PCR test.*
Note: Of the 2,952 HCWs included, 1,891 (38.7%) reported 1 contact; 1,222 (25.0%) reported 2 contacts; 747 (15.3%) reported three contacts; 436 (8.93%) reported 4 contacts; 195 (4.00%) reported 5 contacts; 322 (6.60%) reported 6-10 contacts; 70 (1.40%) reported >10 contacts.

to use masks compared to men (p=0.056). With reference to job title, administrative staff was less likely to wear masks compared to the other professionals (p<0.001). The OR for hand sanitation was 0.61 (95%CI 0.40-0.93). The use of gloves or of a face shield was not associated with effective contact.

When excluding the first 2 weeks of March, results for the associations between PPE use and risk

Table 3. Odds ratio of infection among HCWs according to sex, age and job title, use of mask, use of other PPEs, symptoms, type of exposure and period of exposure.

Characteristic	OR	95%CI
Sex[1]		
Male	ref	-
Female	0.94	(0.68-1.31)
Age group[2]		
20 - 35	ref	-
36 - 50	1.30	(0.87-1.94)
51 - 70	0.99	(0.65-1.50)
Job title[3]		
Administrative staff / Other	ref	
Physician	1.01	(0.50-2.04)
Resident physician	0.30	(0.11-0.78)
Nurse	0.66	(0.34-1.29)
Health assistant	0.92	(0.44-1.90)
Healthcare professional	0.60	(0.25-1.43)
Use of mask		
Healthcare worker[4]	0.63	(0.45-0.87)
Source[5]	0.63	(0.45-0.89)
Combined use of mask[6]		
None	ref	-
HCW alone	0.59	(0.40-0.86)
Contact alone	0.49	(0.22-1.07)
Both HCW and contact	0.40	(0.27-0.60)
Use of other PPEs[*]		
FFP2 / FFP3[7]	0.48	(0.21-1.09)
Gloves[7]	1.32	(0.85-2.04)
Glasses / Visor[7]	0.82	(0.51-1.31)
Hand sanitization[7]	0.61	(0.40-0.93)
Symptoms[8*]		
Fever	7.25	(3.49-15.08)
Cough	2.75	(1.57-4.84)
Sore throat	0.79	(0.32-1.95)
Asthenia	4.25	(1.38-13.08)
Dyspnea	1.54	(0.48-4.91)
Hyposmia / Anosmia	3.69	(0.32-41.80)
Hypogeusia / Ageusia	0.70	(0.05-9.17)
Migraine	1.15	(0.28-4.65)
Period of exposure[9]		
01.03.2020 - 15.03.2020	ref	-
16.03.2020 - 30.03.2020	0.35	(0.25-0.52)
01.04.2020 - 15.04.2020	0.13	(0.07-0.24)
16.04.2020 - 30.04.2020	0.16	(0.08-0.31)
after 01.05.2020	0.07	(0.02-0.17)
Type of exposure[10]		
Meals, meetings	ref	-
Patient assistance and handling, patient hygiene	1.52	(0.90-2.56)
Medical examination, therapy administration, parameters measurement	0.81	(0.41-1.59)
Room sharing	1.30	(0.76-2.23)
Aerosol generating manipulations, surgery, invasive procedures	0.41	(0.11-1.55)

Notes: OR, odds ratio; CI, Confidence Interval; ref, reference category.
[1] OR adjusted for age group.
[2] OR adjusted for sex. [3] OR adjusted for sex and age group.
[4] OR adjusted for sex, age group, job title and use of mask by source.
[5] OR adjusted for sex, age group, job title and use of mask by HCW.
[6] OR adjusted for sex, age group and job title.
[7] OR adjusted for sex, age group, job title, use of mask, use of other PPEs.
[8] All the ORs are adjusted for sex, age group and other symptoms.
[9] OR adjusted for sex, age group, job title and use of mask.
[10] OR adjusted for sex, age group, period of exposure.
**OR of use of each PPE (reference category: no use of that PPE).*
***OR of presence of each symptom (reference category: absence of that symptom).*

of infection were weaker, with only hand sanitation remaining significantly protective.

ORs for reported fever, cough, asthenia, anosmia/hyposmia, dyspnea, and migraine were all elevated, although the association was not significant for the last three symptoms.

In terms of period and type of exposure, the first half of March 2020 was the period with the highest risk of infection. We found no association between the reported type of exposure and infection. Finally, employment in a COVID-19 designated department was not associated with the risk of infection.

In order to address possible bias from the fact that unprotected contacts might preferentially lead to a test, we repeated the analysis restricted to 579 HCWs who were tested because they reported symptoms. The OR of positive PCR result for use of a mask by both the HCW and the contact compared to use by neither was 0.69 (95%CI 0.34-1.43).

4. Discussion

We reported findings from more than 4,800 detailed COVID-19 contact-reporting forms compiled by over 2,900 HCWs and collected in one of the largest hospitals in Italy. Our analysis suggests that proper mask use (both by the contact and the source of infection) is highly effective for reducing transmission of SARS-CoV-2, with an increasing degree of protection from no use, use by one between HCW or source of infection, and use by both. This latter corresponds to an OR of 0.40 (95%CI=0.27-0.60) for infection compared to no use of a mask.

Evidence that an appropriate PPE use is highly effective in preventing infection among HCWs is well established [10-13]. However, despite several studies supporting their role in controlling SARS-CoV-2 transmission, potential sources of bias commonly affect analyses on PPE use, including misclassification of mask use as well as heterogeneous COVID-19 testing. Also, several previous studies were based on convenience sampling, resulting in possible selection bias [10, 11].

A unique aspect of our study was the ability to integrate information on exposure characteristics and symptoms across multiple potentially effective contacts. This approach increased the chances to match the result of each PCR test with information on the relevant circumstances of exposure to SARS-CoV-2. Our analysis provides useful insight to better understand the prevalence and the spreading of infection in the hospital setting. Weighting each PCR test by the number of potentially effective contacts for which it was prescribed increased the validity of the analysis by avoiding overcounting potentially effective contacts, as well as the arbitrary selection of one of the contacts. This reduced the opportunity for bias in the analysis and represented an improvement over previous analyses on SARS-CoV-2 infections among HCWs, including those done by our group [4].

A key point during contact tracing was risk assessment [14]. Contacts, if not PPE fully protected, entailing prolonged (>15 minutes) sharing of a room, short distance and talking activity, or medical procedures directly on the body and face of a positive subject were considered at risk, and consequently investigated through PCR testing. Among the risk criteria, the correct use of PPE, in which mask was the principal discriminant between appropriate or inappropriate protection, was of importance.

When the strategies to address the pandemic took shape, an increasing number of tests was implemented in the hospital setting [15]. This could have led to the over-testing of HCWs compared to the general population. Anyway, the database analyzed included tests performed based on risk assessment derived from contact tracing, thus the high proportion of HCWs with multiple testing in our study population can be mainly explained by either repeated contacts or by the request of two negative tests for return to work. To enhance both the specificity and the sensitivity of our analysis, we considered all possible contacts – after weighting them – to identify the profile of risk of infection.

Results on mask effectiveness in preventing SARS-CoV-2 infections are not fully consistent between studies among general population and HCWs, with the first group showing lower protective ability than the second one [2]. This can be explained by several factors, including differences in age range, health status, and types and characteristics of PPEs. In fact, community- and hospital-based studies can contribute complementary evidence on the effectiveness of PPE use in preventing SARS-CoV-2 infection, with the latter being particularly accurate in assessing the effectiveness of PPEs in well-controlled circumstances of use by trained individuals. Regarding the use of FFP2/3 masks, we confirmed previous findings about their high effectiveness in preventing-SARS-CoV-2 infection [10, 14].

In our study, wearing gloves was associated with an increased risk of infection while the opposite effect was shown for hand sanitization. While the use of gloves avoids pathogen dissemination, it may provide a false sense of security and may increase virus spread [16], and published studies have led to contradictory results [1]. HCWs should therefore be informed that gloves do not provide complete protection against hand contamination: exposure to pathogens may occur because of defects in gloves or more commonly during glove removal, leading to self-contamination [17]. The recommendation to wear gloves during an entire episode of care of a patient undergoing isolation precautions could actually lead to HCWs missing hand hygiene. This supports the importance of HCWs' training in the sequence of procedures, limiting the use of gloves, and maximizing non-touch techniques during patients' care.

Among this study population gender and age were not associated with the risk of infection. In literature, those findings often disagree [4]. While a sex disparity of COVID-19-related morbidity and mortality have been observed in several studies, with 50% more hospitalized men than women based on data from 6 different European countries-Italy included, no significant difference emerges for SARS-CoV-2 transmission [18]. Also, in a study conducted on HCWs from Veneto, Northern Italy, no difference in SARS-CoV2 antibodies seroprevalence was detected by gender [19]. While an excess risk of infection has been described in men older than 60 [18], our population includes mainly individuals below that age.

We described different risks of effective contact and the prevalence of PPE use in the different health care professionals, including the administrative staff. The timeframe considered in our analysis (March-September 2020) corresponds to the very first wave of the pandemic when the management of daily hospital activities was particularly delicate and went through a progressive reconfiguration. Indeed, in order to limit overcrowding in the hospital, many professionals were assigned to smart working. This not only regarded administrative staff, but also several physicians and nurses (e.g., from department of neurology and surgery). The administrative staff who worked in presence in Turin hospital were assigned to activities of patient acceptance, secretary and back-office. They were provided with hand sanitation gel, surgical masks (or FFP2/3) and protective barriers, with the recommendation to strictly follow social distancing rules. Our analysis showed that administrative staff were less likely to wear mask, while they were not more likely to get infection.

Garzaro et al. carried out a survey based on the first 3,000 contact forms from our center [8] and reported that administrative staff was at higher risk of infection while physicians were the main source of infection. A large review found that nurses were the most commonly infected group of HCWs, despite no evidence of a higher infection rate for those involved in high-risk tasks [20]. These data suggest that factors other than direct contact with infected persons are involved, underlying the role played by PPEs and sanitation, which have been introduced very soon in COVID-19-designated departments for HCWs' protection.

The lack of statistical significance in the sub-analysis excluding the first 2 weeks of March are mainly due to the high prevalence of use of PPE after the very first weeks of Sars-CoV-2 pandemic, while in early March the paucity of PPE use led to the evidence of the differences made by PPE between effective and ineffective contacts.

Our study showed that all HCWs were at comparable risk of infection, with the minor exception of resident physicians. This could be explained by the increased use of PPEs over time. As suggested by Boffetta et al. in a previous study also including a subset of the current population [4], the lack of a job-related pattern of risk indicates that all HCWs share similar risk levels of infection, including those who worked in COVID-19 departments. Further confirmation comes from our results on the type of exposure, which did not identify differences among HCWs reporting high-risk procedures like those generating aerosol compared to common situations like sharing a room or attending a meeting in presence of a positive case. However, this aspect can suffer from reporting bias, since HCWs may have been prone to declare that one of the parties did not correctly wear a mask, because of excessive caution and willingness to be screened. This bias is likely to be non-differential with respect to infection since it was collected before the HCWs knew about their status.

The findings of an early survey conducted among some of the subjects included in this study led to the inclusion of hyposmia/anosmia as major symptoms in the COVID-19 reporting form; this extended analysis further confirms this finding [8]. In addition, accordingly to our risk-assessment protocol, as well as with the literature [21], we found strong associations between infection and fever, cough, and asthenia.

Our study showed a higher risk between 1 March and 15 March, 2020. These data reflect the pandemic situation of that time, when in addition to the novelty of the situation, Italy suffered from a scarcity of PPEs, lack of scientific knowledge, and reduced attention to between-person distancing, enhancing the likelihood of infection transmission both inside and outside the hospital setting. This agrees with the results reported by Wang et al. at the time of the first wave of the pandemic and following the introduction of restrictions and PPE use [13]. In addition, these findings may be associated also with the hospital setting of this study, as SARS-CoV-2 infection heavily affected Italy's healthcare system in the very first phase of the pandemic.

One of the main strengths of this study is the availability of detailed information, particularly on PPE use, including data on the use of facial masks by the source of infection at the time of the contact. These data allowed a quantitative assessment of the effectiveness of wearing surgical mask to prevent SARS-CoV-2 infection. The systematic collection of this information during contact tracing provided the early identification of the typical symptoms of COVID-19 such as hyposmia/anosmia and hypogeusia/ageusia. An additional strength is the large number of HCWs included in the study and the detailed contact-tracing forms based on a standardized procedure. High compliance was demonstrated by HCWs, who fully adhered to the monitoring system set up in the hospital. This is an advantage compared to population-based surveys, in which many people may not be contacted or declined to cooperate [22, 23]. Moreover, multiple tests in the same subject were based on the same assay, enabling a valid comparison of the results. Finally, we were able to identify a set of contacts likely to include the one responsible for the infection. This allowed us to combine the use of masks by the HCW and the case index and to analyze different exposure circumstances, where none using a mask identified the highest likelihood of SARS-CoV-2 transmission and both using a mask the lowest. Given the personal concern of HCWs for their own health as well as that of their patients and families, and the lack of negative consequences in case of incorrect use of PPEs, it is likely that mask reporting was more sensitive than specific. This misclassification was likely non-differential with respect to the infection status, leading to an underestimate of the effectiveness of surgical masks. The reliability of this information is likely to be good because the forms were used as part of a standardized contact tracing procedure and most of them were completed within 10 days from the contact.

This study suffers from some limitations. First, we did not have information on SARS-CoV-2 variants, as our data refer to the first phase of the epidemic. In addition, we did not consider super-spreading events, and we could only partially characterize the type of exposure to infection, as the information on extra-occupational exposure circumstances was self-reported and was not based on a standardized questionnaire. Furthermore, we could not investigate the difference between sources of infections (i.e., patients, colleagues, relatives, or friends). Similarly, the information on symptoms was self-reported and therefore subject to some degree of misclassification, which, as in the case of PPE use discussed above, was likely to be non-differential. Finally, we did not have information on chronic conditions of HCWs, which might have increased the risk of SARS-CoV-2 infection, although it is not certain that these conditions would be associated with a higher probability of an effective contact, thus exerting a confounding effect.

The unit of the statistical analysis was the contact. During the timeframe considered, the same HCW could have notified to Occupational Medicine Unit several contacts. Moreover, multiple contacts could have been reported by the same HCW in a very short time, because of the spreading of outbreaks of infection in the hospital, leading to one single PCR test. For these reasons, the number of subjects reporting contacts does not correspond to the number of tests. This does not apply only to this specific population but reflectshe circumstances of COVID-19 pandemic, and particularly its first wave.

We tried to address this problem by focusing on the number of contacts, which was an intermediate measure among subjects and PCR tests performed, and because our aim was to determine which factors were associated to effective contacts, namely notified contacts which ended up with COVID-19 transmission assessed by PCR test. The limitation of this approach is that when the same subject declared different contacts, the personal characteristics of the subject were taken into account multiple times (namely, sex, age, and job title), which we addressed by includinh weights. Conversely, the different contacts by the same subject may differ according to use of PPE, type of contacts and other characteristics independent from the subject.

The results obtained are useful to clarify the predictors of SARS-CoV-2 transmission, whose understanding is of primary interest to reduce the likelihood of infection even in the global vaccination era and for emergency phases of future pandemics. Characterization of risk based on mask use helps in the risk assessment and corroborates the fact that mask use must be required in the hospital setting to guarantee the safety of both HCWs and patients. Indeed, PPEs remain a fundamental set of tools even among vaccinated, thus their correct use should be encouraged. This is especially important in worksites at high exposure to public, where contact with unvaccinated or even positive subjects, whether symptomatic or not, is frequent. The study is based on data collected during the first phase of the pandemic, when knowledge about virus spreading was limited and hospitals had to deal with an increasing number of potentially infected patients, that challenged both the clinical infrastructure and the occupational surveillance. Further studies on the combined use of PPEs analyzed with respect to different hypothetical conditions of SARS-CoV-2 transmission are worthwhile. Models on the potential public health interventions which should have been successful in avoiding the pandemic, and the prompt recommendation of using surgical masks, would be of high value for the future. It should also be considered that the frequency of SARS-CoV-2 infection is dependent on the geographical exposure to the virus and primarily to family rather than hospital exposure [24].

5. Conclusions

This study provided evidence of masks' protective effect during SARS-CoV-2 exposure. The study refers to the first pandemic wave when the virus spreading knowledge was limited and hospitals had to deal with increased number of patients without renouncing security procedures. PPEs shortage was an issue worldwide and many questions on their suitability were risen, in particular, whether surgical masks could provide an adequate standard of protection compared to FFP2/3 masks. This study demonstrates that surgical masks (especially if worn by both the HCW and the contact) offer a similar protection compared to FFP2/3.

Institutional review board statement: The study was approved by the Institutional Review Board of the University Hospital of Turin. The Review Board waived the request for informed consent from study participants. All methods were performed in accordance with the relevant guidelines and regulations.

Declaration of interest: The authors declare no conflict of interest.

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