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Medical Masks Versus N95 Respirators for Preventing COVID-19 Among Health Care Workers

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A Randomized Trial

Mark Loeb, MD, Amy Bartholomew, MScN, Madiha Hashmi, MD, ... View all authors +

Author, Article, and Disclosure Information

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Eligible for CME Point-of-Care

Visual Abstract. Medical Masks Versus N95 Respirators for COVID-19.

It is uncertain if medical masks offer similar protection against COVID-19 compared with N95 respirators. This randomized trial, which enrolled participants in Canada, Israel, Pakistan, and Egypt, aimed to determine whether medical masks are noninferior to N95 respirators to prevent COVID-19 in health care workers providing routine care.

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Abstract

Background:

It is uncertain if medical masks offer similar protection against COVID-19 compared with N95 respirators.

Objective:

To determine whether medical masks are noninferior to N95 respirators to prevent COVID-19 in health care workers providing routine care.

Design:

Multicenter, randomized, noninferiority trial. (ClinicalTrials.gov: NCT04296643).

Setting:

29 health care facilities in Canada, Israel, Pakistan, and Egypt from 4 May 2020 to 29 March 2022.

Participants:

1009 health care workers who provided direct care to patients with suspected or confirmed COVID-19.

Intervention:

Use of medical masks versus fit-tested N95 respirators for 10 weeks, plus universal masking, which was the policy implemented at each site.

Measurements:

The primary outcome was confirmed COVID-19 on reverse transcriptase polymerase chain reaction (RT-PCR) test.

Results:

In the intention-to-treat analysis, RT-PCR–confirmed COVID-19 occurred in 52 of 497 (10.46%) participants in the medical mask group versus 47 of 507 (9.27%) in the N95 respirator group (hazard ratio [HR], 1.14 [95% CI, 0.77 to 1.69]). An unplanned subgroup analysis by country found that in the medical mask group versus the N95 respirator group RT-PCR–confirmed COVID-19 occurred in 8 of 131 (6.11%) versus 3 of 135 (2.22%) in Canada (HR, 2.83 [CI, 0.75 to 10.72]), 6 of 17 (35.29%) versus 4 of 17 (23.53%) in Israel (HR, 1.54 [CI, 0.43 to 5.49]), 3 of 92 (3.26%) versus 2 of 94 (2.13%) in Pakistan (HR, 1.50 [CI, 0.25 to 8.98]), and 35 of 257 (13.62%) versus 38 of 261 (14.56%) in Egypt (HR, 0.95 [CI, 0.60 to 1.50]). There were 47 (10.8%) adverse events related to the intervention reported in the medical mask group and 59 (13.6%) in the N95 respirator group.

Limitation:

Potential acquisition of SARS-CoV-2 through household and community exposure, heterogeneity between countries, uncertainty in the estimates of effect, differences in self-reported adherence, differences in baseline antibodies, and between-country differences in circulating variants and vaccination.

Conclusion:

Among health care workers who provided routine care to patients with COVID-19, the overall estimates rule out a doubling in hazard of RT-PCR–confirmed COVID-19 for medical masks when compared with HRs of RT-PCR–confirmed COVID-19 for N95 respirators. The subgroup results varied

by country, and the overall estimates may not be applicable to individual countries because of treatment effect heterogeneity.

Primary Funding Source:

Canadian Institutes of Health Research, World Health Organization, and Juravinski Research Institute.

Health care workers use either medical masks, also called surgical masks, or N95 respirators for the routine care of patients with COVID-19 as a component of their personal protective equipment. Medical masks are recommended by the World Health Organization for routine care (1, 2), whereas N95 respirators are recommended by the Centers for Disease Control and Prevention for the routine care of patients with COVID-19 (3–5).

It is uncertain if medical masks offer similar protection against COVID-19 compared with N95 respirators (6). Observational studies report varied findings and are limited by self-reported outcomes, potential recall bias, and ecological analyses (7–14). Systematic reviews of randomized trials and observational studies of other respiratory viruses suggest similar protection (15, 16).

There is concern that medical masks offer less protection because of their looser fit and that they do not filter as effectively, whereas N95 respirators are fit tested and provide greater filtration (17). There were insufficient supplies of N95 respirators globally during the pandemic, and currently there is a lack of access in low- and middle-income countries because of the high costs (18).

One randomized controlled trial set in the community reported a reduction of SARS-CoV-2 with medical masks (19). It is important to determine the relative protection of medical masks compared with N95 respirators.

We conducted an international pragmatic randomized controlled trial where health care workers were randomly assigned to either medical masks or N95 respirators when providing routine care to patients with suspected or confirmed COVID-19. We hypothesized that medical masks would be noninferior to N95 respirators.

Methods

Trial Design and Oversight

This pragmatic, randomized, open-label, multicenter trial initially aimed to assess whether medical masks were noninferior to N95 respirators for protection against COVID-19 among unvaccinated nurses providing routine care to patients with suspected or confirmed COVID-19 (see the study protocol and statistical analysis plan). The evolution of the pandemic led to protocol changes (Supplement). Before trial commencement, in addition to nurses, other health care workers were made eligible to increase enrollment, and follow-up was reduced from 12 to 10 weeks to minimize loss to follow-up. As circulation of SARS-CoV-2 increased, health care workers known to have a previous laboratory-confirmed clinical diagnosis of COVID-19 at the time of enrollment were excluded. As vaccine rollout began, participants with receipt of 1 or more doses of a COVID-19 vaccine with greater than 50%

efficacy for the circulating strain (for example, messenger RNA [mRNA] or vector-based COVID-19 vaccine against the original SARS-CoV-2 strain) were excluded, and sites in Israel, Pakistan, and Egypt were added to increase enrollment. Participants that received a single dose of an mRNA or vector-based COVID-19 vaccine after enrollment (with an estimated >50% efficacy against the circulating strain) were followed until 2 weeks after their first dose and then censored. The variable follow-up time led to a change to a time-to-event analysis, and a hazard ratio (HR) was used for the noninferiority margin.

The trial enrolled participants in 29 health care facilities: 17 acute care hospitals in Canada, 4 acute care hospitals in Pakistan, 2 long-term care facilities in Israel (facilities where trained medical staff are always available to assist residents and where high-flow oxygen and medication via inhalation could be administered), and 6 acute care hospitals in Egypt. The study was done from 4 May 2020 to 29 March 2022.

The trial was approved by the Hamilton Integrated Research Ethics Board and the institutional review boards at all participating institutions. All participants provided written informed consent. The trial was restricted to health care settings where the policy was to use medical masks while providing routine care to patients with confirmed or suspected COVID-19. A data monitoring committee provided oversight of safety considerations in the trial.

Participants

Health care workers who provided direct care to patients with suspected or confirmed COVID-19 in specialized COVID-19 units and in emergency departments, medical units, pediatric units, and long-term care facilities were enrolled; intensive care units were not included in the study. Health care workers were required to spend 60% or more of their time doing clinical work when enrolled.

Health care workers were excluded if they did not have a valid fit test within the past 24 months or could not pass a fit test, had 1 or more high-risk comorbidities for COVID-19 (hypertension, cardiac disease, pulmonary disease, chronic kidney disease, diabetes, chronic liver disease, actively treated cancer, or immunosuppression due to illness or medications), had a previous laboratory-confirmed clinical diagnosis of COVID-19 at the time of enrollment, or had received 1 or more doses of a COVID-19 vaccine with greater than 50% efficacy for the circulating strain (for example, mRNA or vector-based COVID-19 vaccine against the original SARS-CoV-2 strain).

Randomization and Blinding

Trial participants were randomly assigned (1:1) to either medical masks or N95 respirators. Participants were randomly assigned centrally by a study statistician who generated the sequence using a computerized random number generator. Randomization was stratified by site in permuted blocks of 4. The randomization scheme was provided by an interactive web response system and performed centrally. Investigators were blinded to the

group assignment, but it was not possible to conceal the identity of the medical mask or N95 respirator assignment to the study staff or participants.

Interventions

Health care workers randomly assigned to the medical mask group were instructed to use the medical mask when providing routine care to patients with COVID-19 or suspected COVID-19, which aligned with the current policy in their setting. The ASTM International certified masks were provided to the health care workers either by their health care facility or by the study (Supplement Table 1). As part of the trial protocol, health care workers could also use the N95 respirator at any time based on a point-of-care risk assessment.

Health care workers randomly assigned to the N95 respirator group were instructed to use a fit-tested National Institute for Occupational Safety and Health–approved N95 respirator when providing routine care to patients with COVID-19 or suspected COVID-19. Participants were required to use the type of device they were allocated to, either a medical mask or an N95 respirator, for 10 weeks.

The intervention included universal masking, which was the policy implemented at each site. This refers to the use of a mask when in the health care facility for all activities, whether patient related or not, including in workrooms, meetings, and treating persons that were not suspected or known to be positive for COVID-19. Participants were asked to report the extent to which they used the mask that they were assigned to on a weekly

basis—that is, “During your last work shift, to what extent did you wear the mask you were assigned,” where the possible responses were “Always,” “Sometimes,” “Never,” or “Do not recall.” In both study groups, health care workers were required to use the N95 respirator for aerosol-generating medical procedures, as this was in keeping with their institutional policies. In keeping with local policies, eye protection, gowns, and gloves were worn when caring for patients with suspected or confirmed COVID-19. Participants were asked to discard the medical mask or N95 respirator if it became soiled or damaged or if breathing through the device became difficult. If the institutional policy was for extended use and masks were not typically removed after a patient encounter, the extended use procedure was to be followed.

Outcomes

The primary outcome was time to reverse transcriptase polymerase chain reaction (RT-PCR)–confirmed COVID-19. This was measured from the date of randomization until the date of procurement of a specimen that was positive by RT-PCR. Follow-up continued until the end of 10 weeks, until 2 weeks (1 incubation period) after receipt of an mRNA vaccine, or until the date of a participant withdrawal from the trial. Laboratory personnel doing COVID-19 testing were blind to treatment allocation. Testing was done at the health care facility laboratory using health care–administered nasopharyngeal swabs. Sera from participants was obtained at baseline and at the end of follow-up and then tested for spike IgG antibodies and for nucleocapsid IgG antibodies using EUROIMMUN assays.

Secondary outcomes included serologic evidence of infection (done in participants who were seronegative at baseline and defined as a change from negative EUROIMMUN spike IgG and nucleocapsid IgG antibodies at baseline to positive nucleocapsid IgG antibody), acute respiratory illness (defined by fever and cough), work-related absenteeism, lower respiratory tract infection or pneumonia, intensive care admission, mechanical ventilation, or death. Laboratory-confirmed infection was defined as COVID-19 confirmed by RT-PCR in symptomatic participants or seroconversion.

Participants were assessed for signs and symptoms of COVID-19 through twice-weekly automated text messages. A nasopharyngeal swab was obtained if any one the following symptoms or signs was present: fever (≥38 °C), cough, or shortness of breath, or if 2 of the following were present: fatigue, myalgia, headache, dizziness, expectoration, sore throat, diarrhea, nausea, vomiting, abdominal pain, runny nose, altered taste or smell, conjunctivitis, or painful swallowing.

Adherence to the assigned medical mask or N95 respirator for routine care and to hand hygiene was measured using weekly self-reporting for all participants and external monitoring wherever feasible. Audits were done once at 3 hospitals in Pakistan and were repeated once at 2 of these hospitals within a 2-week period. They were done at 6 hospitals in Egypt where they were repeated twice at 2 hospitals and repeated once at 4 hospitals over a 4-week period. To conduct the audits of adherence to the intervention (medical mask or N95 respirator), the coordinating center randomly selected 20% of shifts at a health care facility, and during these shifts, trial

participants were observed. Wearing an N95 respirator for aerosol-generating procedures was not considered during the observed audits. Reported exposures and potential exposures to COVID-19, including community and home exposure, hospital exposures, participation in aerosol-generating procedures, and hospital outbreaks (as defined by the health care facility) were measured. Participants were asked to keep diaries of signs and symptoms of respiratory illness and exposure to household and community members with respiratory illness. Cycle threshold values from patients with COVID-19, obtained while participants were on the same study units as the patients, were used to estimate viral load as a surrogate for exposure risk.

Statistical Analysis

The study was powered based on the primary outcome of RT-PCR–confirmed COVID-19. For a noninferiority HR of 2, a sample size of 875 participants provided 90% power at a 0.025 significance level for event rates of 10% and an actual HR of 1. The original design estimated an event rate of 5% with a noninferiority margin of 5 percentage points (that is, up to a 10% event rate would be considered noninferior). On changing the outcome from 10-week occurrence of RT-PCR–confirmed COVID-19 to time to RT-PCR–confirmed COVID-19 so as to allow for censoring due to vaccination, the original margin on the absolute effect size corresponds to a relative effect size (HR) of 2 (see the Supplement for earlier trial design sample size calculations). A final sample size of 1010 accounted for participants who could not complete 10 weeks of follow-up because of administration of mRNA vaccine as well as for withdrawals. Hazard ratios and corresponding 2-sided 95% CIs were

estimated using a Cox proportional hazards model stratifying by health care facility. The analysis fulfilled the Schoenfeld residual test for the assumption of proportional hazards in Cox analysis. The cumulative incidence of RT-PCR–confirmed COVID-19 was estimated using Kaplan–Meier methods.

Outcomes were analyzed on an intention-to-treat basis, defined by medical mask or N95 respirator assignment and follow-up until 10 weeks or 2 weeks after the first mRNA vaccine dose. Participants did not have to complete 10 weeks of follow-up to be included in the intention-to-treat analysis. Censoring was assumed independent of the randomized group assignment. No attempt was made to impute missing postrandomization values, and only observed values were used in the analysis. A post hoc analysis of the primary outcome with participants restricted to those seronegative at baseline was done using a Cox proportional hazards model stratifying by health care facility.

For serology and overall laboratory-confirmed infection, we conducted a logistic regression analysis adjusting for site to obtain odds ratios and 95% CIs. Although subgroup analyses based on pre-Omicron variant versus Omicron variant and by universal masking were planned a priori, these analyses are not reported because of potential confounding of Omicron by country and because of the mandatory policy of universal masking for all health care facilities in the trial.

A post hoc subgroup analysis was done to compare the effect of medical masks versus N95 respirators in participants with no reported exposure to household or community members with respiratory illness to those that

reported at least 1 such exposure. We also conducted an unplanned subgroup analysis of the primary outcome by country. For the safety analyses, the number and percentage of participants with an adverse event according to study group are reported. For participant exposure to patients with COVID-19 or exposure to patients with suspected COVID-19, the number of exposures per week for up to 10 weeks were counted and categorized (0, 1 to 5, 6 to 10, or ≥11 exposures). The number of exposure categories per 1000 participant-days was then calculated by country and study group. Statistical analyses were done using R, version 4.2.0 (R Foundation for Statistical Computing).

Role of the Funding Source

The study was funded by the Canadian Institutes of Health Research, World Health Organization, and Juravinski Research Institute. The external funders of the study had no role in study design, data collection, data analysis, or data interpretation, or in writing this report.

Results

Between 4 May 2020 and 12 January 2022, a total of 1191 health care workers were assessed for eligibility, and 1009 were enrolled. There were 500 randomly assigned to medical masks and 509 to the N95 respirator (Figure 1). There were 268 participants from Canada, 34 from Israel, 187 from Pakistan, and 520 from Egypt. The baseline characteristics were well balanced overall and were similar within each country (Table). However, seropositivity at

baseline varied by country, with few seropositive participants in Canada (2%) and a majority (81%) seropositive in Egypt (Table). Overall, there were 185 (37.5%) participants in the medical group versus 185 (37.2%) in the N95 respirator group who were seronegative at baseline—that is, had no SARS-CoV-2 spike IgG or nucleocapsid IgG antibodies at baseline.

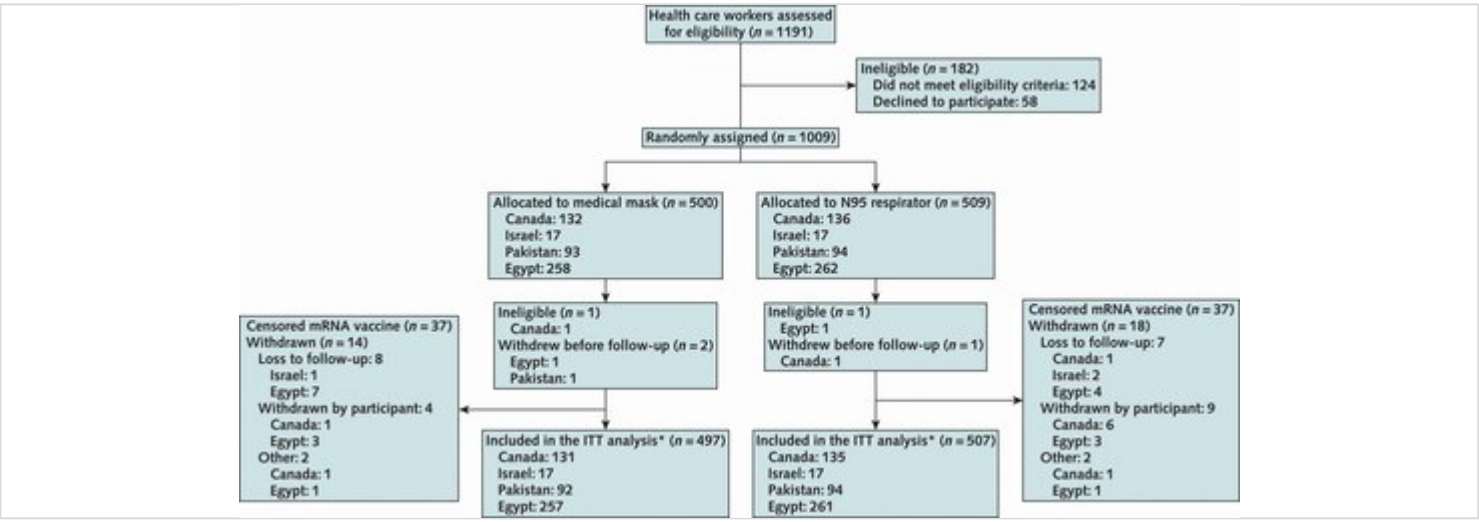

Figure 1. Trial flow diagram.

ITT = intention-to-treat; mRNA = messenger RNA.

* Dates of follow-up: Canada (May 2020 to May 2021), Israel (November 2020 to January 2021), Pakistan (June 2021 to December 2021), and Egypt (December 2021 to March 2022).

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Table. Participant Characteristics

Table. Participant Characteristics

Characteristic	Medical Mask (n = 497)	N95 Respirator (n = 507)
Mean age (SD) [range], y		
Canada	35.5 (10.0) [22-61]	36.5 (10.1) [20-69]
Israel	29.5 (8.7) [23-58]	31.5 (8.9) [20-51]
Pakistan	27.5 (5.7) [20-54]	26.8 (5.2) [20-45]
Egypt	36.9 (10.4) [19-59]	37.3 (11.5) [18-78]
All sites	34.6 (10.2) [19-61]	34.9 (10.9) [18-78]
Female, n (%)		
Canada	109 (83.2)	105 (77.8)
Israel	13 (76.5)	9 (52.9)
Pakistan	47 (51.1)	47 (50.0)
Egypt	192 (74.7)	177 (67.8)
All sites	361 (72.6)	338 (66.7)
Distribution by job type, n (%)		
Canada		
Nurse	96 (73.3)	111 (82.2)
Physician	25 (19.1)	17 (12.6)
Personal support worker	6 (4.6)	4 (3.0)
Allied health	4 (3.1)	3 (2.2)
Israel		
Nurse	13 (76.5)	7 (41.2)
Physician	0 (0)	1 (5.9)
Personal support worker	0 (0)	0 (0)
Allied health	4 (23.5)	9 (52.9)
Pakistan		
Nurse	84 (91.3)	84 (89.4)
Physician	3 (3.3)	5 (5.3)
Personal support worker	0 (0)	0 (0)
Allied health	5 (5.4)	5 (5.3)
Egypt		
Nurse	86 (33.5)	87 (33.3)
Physician	10 (3.9)	9 (3.5)
Personal support worker	119 (46.3)	122 (46.7)
Allied health	42 (16.3)	43 (16.5)
All sites		
Nurse	279 (56.1)	289 (57.0)
Physician	38 (7.7)	32 (6.3)
Personal support worker	125 (25.2)	126 (24.9)
Allied health	55 (11.1)	60 (11.8)
Distribution by unit type, n (%)		
Canada		
Acute care	97 (74.1)	107 (79.3)
Emergency department	34 (26.0)	28 (20.7)
Long-term care	0 (0)	0 (0)
Israel		
Acute care	0 (0)	0 (0)
Emergency department	0 (0)	0 (0)
Long-term care	17 (100)	17 (100)
Pakistan		
Acute care	71 (77.2)	69 (73.4)
Emergency department	21 (22.8)	25 (26.6)
Long-term care	0 (0)	0 (0)
Egypt		
Acute care	239 (93.0)	243 (93.1)
Emergency department	18 (7.0)	18 (6.9)
Long-term care	0 (0)	0 (0)
All sites		
Acute care	407 (81.9)	419 (82.6)
Emergency department	73 (14.7)	71 (14.0)
Long-term care	17 (3.4)	17 (3.4)
Distribution by region, n (%)		
Canada	131 (26.4)	135 (26.6)
Israel	17 (3.4)	17 (3.4)
Pakistan	92 (18.5)	94 (18.5)
Egypt	257 (51.7)	261 (51.5)
Received vaccine with efficacy ≤50%, n (%)*		
Canada	0 (0)	0 (0)
Israel	0 (0)	0 (0)
Pakistan	70 (76.1)	74 (78.7)
Egypt	127 (49.4)	137 (52.5)
All sites	197 (39.6)	211 (41.6)
Seropositivity at baseline, n/N (%)†		
Canada	3/129 (2.3)	2/128 (1.6)
Israel	2/16 (12.5)	2/15 (13.3)
Pakistan	72/92 (78.3)	82/94 (87.2)
Egypt	209/254 (81.6)	210/261 (80.5)
All sites	286/491 (58.0)	296/498 (59.4)

* Sinopharm (China National Pharmaceutical Group) or Sinovac (Sinovac Biotech).
† Seropositivity was defined by a positive SARS-CoV-2 spike IgG antibody or nucleocapsid IgG antibody. Data were missing for 4 participants in the medical mask group and 9 in the N95 respirator group.

Follow-up began on 4 May 2020 and ended on 29 March 2022. Participants were enrolled from 4 May 2020 to 22 May 2021 in Canada, from 11 November 2020 to 27 January 2021 in Israel, from 24 June 2021 to 18 December 2021 in Pakistan, and from 19 December 2021 to 29 March 2022 in Egypt. The mean duration of follow-up was similar between the 2 study groups—9.06 weeks in the medical mask group and 9.03 weeks in the N95 respirator group. Five participants who were randomly assigned but never followed were excluded from analysis—3 in the medical mask group (1 was previously positive for COVID-19 on RT-PCR and 2 withdrew) and 2 in the N95 respirator group (1 was previously positive for COVID-19 on RT-PCR and 1 withdrew) (Figure 1). Of the resulting 1004, follow-up was complete (that is, full 10 weeks or 14

days after first vaccination) in 483 (97.1%) in the medical mask group and 489 (96.4%) in the N95 respirator group.

The primary outcome in the intention-to-treat analysis, RT-PCR–confirmed COVID-19, occurred in 52 of 497 (10.46%) in the medial mask group versus 47 of 507 (9.27%) in the N95 respirator group (HR, 1.14 [95% CI, 0.77 to 1.69]). The proportional hazards assumption was tested for the primary outcome and was plausible. In an unplanned subgroup analysis by country, we found that in the medical mask group versus N95 respirator group, RT-PCR–confirmed COVID-19 occurred in 8 of 131 (6.11%) versus 3 of 135 (2.22%) in Canada (HR, 2.83 [CI, 0.75 to 10.72]), 6 of 17 (35.29%) versus 4 of 17 (23.53%) in Israel (HR, 1.54 [CI, 0.43 to 5.49]), 3 of 92 (3.26%) versus 2 of 94 (2.13%) in Pakistan (HR, 1.50 [CI, 0.25 to 8.98]), and 35 of 257 (13.62%) versus 38 of 261 (14.56%) in Egypt (HR, 0.95 [CI, 0.60 to 1.50]) (Figure 2). The overall cumulative incidence is shown in Figure 3 and that by country in Figure 4.

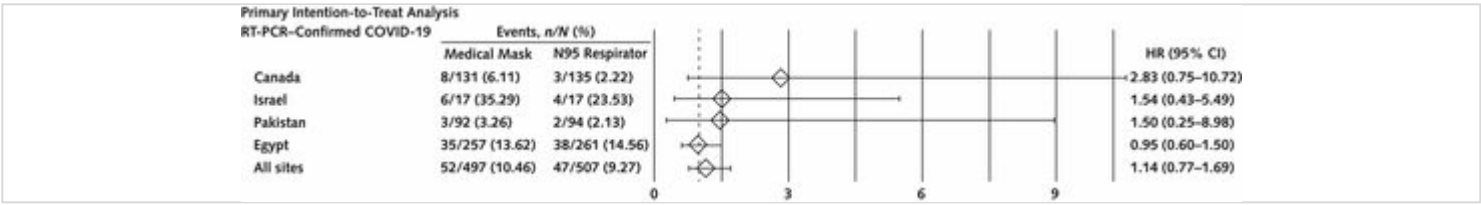

Figure 2. Forest plot of the primary intention-to-treat analysis of RT-PCR–confirmed COVID-19.

There were 86 of 8338 (1%) weekly surveys missing in the medical mask group and 65 of 8468 (0.8%) missing in the N95 respirator group. The subgroup analysis by country was added to show the heterogeneity of treatment effect. HR = hazard ratio; RT-PCR = reverse transcriptase polymerase chain reaction.

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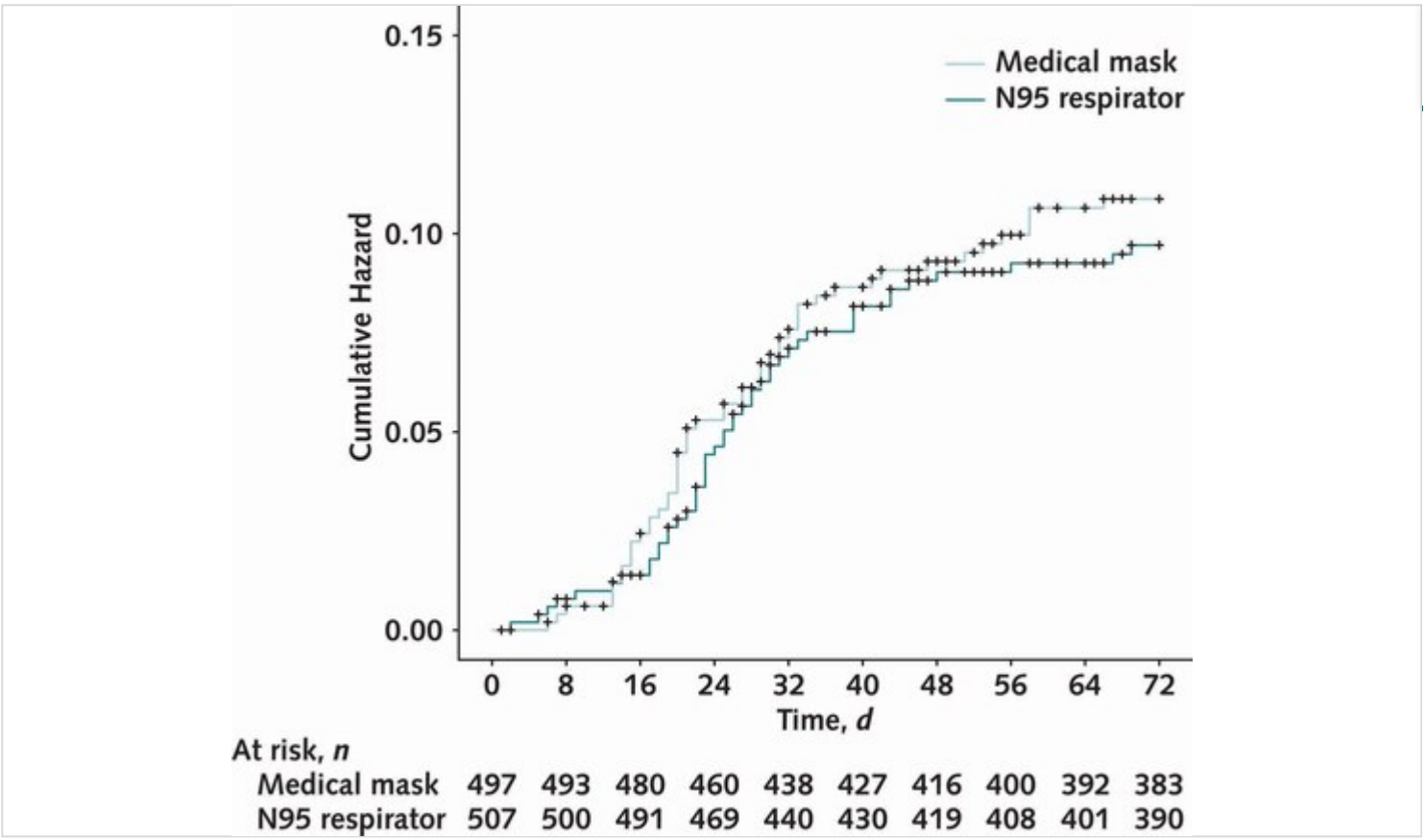

Figure 3. Cumulative incidence of primary analysis of RT-PCR–confirmed COVID-19.

RT-PCR = reverse transcriptase polymerase chain reaction.

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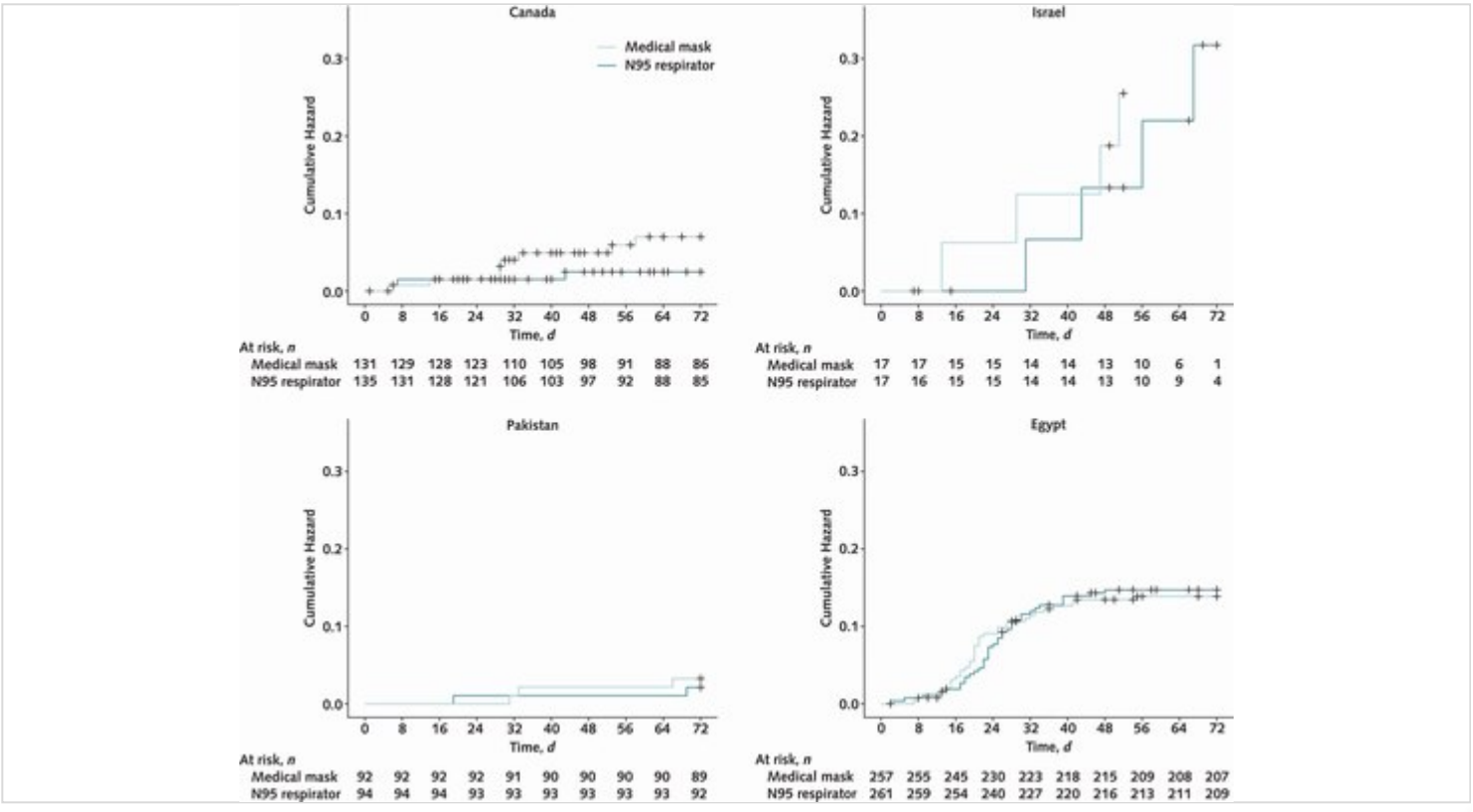

Figure 4. Cumulative incidence of primary analysis of RT-PCR–confirmed COVID-19 by country.

RT-PCR = reverse transcriptase polymerase chain reaction.

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The secondary outcomes, which varied substantially by country, are shown in Supplement Table 2. The sensitivity analysis for RT-PCR–confirmed COVID-19 in participants who were seronegative at baseline showed within-country between-group HRs similar to those that include all participants (Supplement Figure).

Pre-Omicron exposure occurred in Canada, Israel, and Pakistan, whereas Omicron exposure occurred in Egypt. This is based on dates of SARS-CoV-2 circulation given that enrollment in Egypt began on 19 December 2021, whereas enrollment from other countries ended earlier in the pandemic, with follow-up in Pakistan ending on 28 December 2021. The post hoc intention-to-treat subgroup analysis of no reported household or community exposure to respiratory illness (HR, 1.06 [CI, 0.53 to 2.11]) versus 1 or more reported household or community exposure to respiratory illness (HR, 1.08 [CI, 0.66 to 1.78]) did not show heterogeneity of treatment effect based on a test of interaction ($P = 0.96$) (Supplement Table 3).

There were 2 participants who had serious adverse events in the medical mask group (both hospitalizations for COVID-19, where 1 had confirmed pneumonia) and 1 participant in the N95 respirator group (hospitalization for COVID-19 pneumonia). In addition, there were 3 participants (2 in the medical mask group and 1 in the N95 respirator group) who could not be safely isolated at home and were hospitalized for isolation. There were no

intensive care admissions and no deaths. There were 47 (10.8%) adverse events related to the intervention reported in the medical mask group and 59 (13.6%) in the N95 respirator group (Supplement Table 4). There was 1 participant in the medical mask group and 3 in the N95 respirator group who withdrew because of discomfort or adverse events related to the device they were assigned.

Exposure to patients with confirmed or suspected COVID-19, minutes of exposure to patients with COVID-19, aerosol-generating procedures, and community exposures were similar between study groups (Supplement Tables 5 to 9). Mean cycle threshold values of patients positive for COVID-19 were less than 30 in 84% of the 25 study units where these data were collected (Supplement Table 10). Ventilation in the study varied by location (Supplement Table 11). Outbreaks of COVD-19 were reported in 5 of 29 (17%) study units in Canada, in both long-term care facilities in Israel, and in all 6 acute care hospitals in Egypt (Supplement Table 12).

Adherence with the assigned medical mask or N95 respirator was self-reported as “always” in 91.2% in the medical mask group versus 80.7% in the N95 respirator group and as “always” or “sometimes” in 97.7% in the medical mask group versus 94.4% in the N95 respirator group (Supplement Table 13). Of 118 participants observed in the medical mask group, 116 (98.3%) were reported by monitors to be adherent to their assigned mask—14 (100%) in Pakistan and 102 (98%) in Egypt. Of 117 observed in the N95 respirator group, 113 (96.6%) were reported to be adherent—8 (80%) in Pakistan and 105 (98%) in Egypt (Supplement Table 14). Self-reported rates of adherence to

hand hygiene, eye protection, use of gowns, and use of gloves were similar between study groups (Supplement Table 13).

Discussion

Among health care workers who took care of patients with suspected or confirmed COVID-19, although the upper limit of the CIs of the pooled estimate for medical masks when compared with N95 respirators for preventing RT-PCR–confirmed COVID-19 was within the noninferiority margin of 2, this margin was wide, and firm conclusions about noninferiority may not be applicable given the between-country heterogeneity.

The heterogeneity in the RT-PCR positivity rate, as well as the heterogeneity in baseline seropositivity by country, may be explained by many factors. Enrollment in Canada occurred early in the pandemic in acute health care facilities. In contrast, in Israel, the study was done in long-term care facilities that had substantial outbreaks. Later in the pandemic, enrollment occurred in Pakistan and Egypt, countries with a high population density, where seropositivity in participants due to previous exposure to SARS CoV-2 and receipt of vaccine was more common. Circulation of Omicron may have been a contributing factor to the high rates of RT-PCR–confirmed COVID-19 in Egypt.

The observed results are consistent with a range of protection, from a 23% reduction in the HR with medical masks to a 69% risk increase. The relative protection of medical masks compared with N95 respirators varied by

country. However, this finding does not seem to be explained by differences in baseline seropositivity given that a post hoc analysis of the effect of medical masks versus N95 respirators on RT-PCR–confirmed COVID-19 that was restricted to participants seronegative at baseline led to similar within-country point estimates compared with analyses that included the seropositive participants.

Point estimates of the HRs for medical masks versus N95 respirators for both Israel and Pakistan were similar (HRs of 1.54 and 1.50). For Canada, the point estimate of 2.83 is suggestive of an increased risk with the medical mask, however, the absolute number of events is small. It is unclear whether lower COVID-19 rates in that setting, reducing the possibility of participants acquiring COVID-19 in the community, made such an effect more apparent. However, a post hoc subgroup analysis that compared participants with no reported household or community illness exposures to those that reported at least 1 exposure showed no heterogeneity in treatment effect and very similar effect sizes for both subgroups.

It is notable that there was a close to null effect of medical masks compared with N95 respirators in Egypt, where Omicron was circulating, and from where over half of our participants were enrolled. It is possible that a higher rate of community transmission could have obscured a higher rate of infection with the medical mask versus the N95 respirator, in contrast to what was seen in Canada. It is also possible that given the high rate of exposure to patients with COVID-19 reported by health care workers in Egypt with the more transmissible Omicron, the results reflect no difference

between the groups in health care acquisition of RT-PCR–confirmed COVID-19. The latter is supported by the post hoc subgroup analysis comparing participants with and without exposures to household or community illness. Differences in preexisting antibodies are another possible explanation for the difference between Canada and Egypt, although the post hoc analysis that was restricted to participants seronegative at baseline, where point estimates did not change, argues against preexisting antibodies as an explanation for differences between Canada and Egypt. These findings and those of other country-specific data should be tempered by the pitfalls of overinterpreting subgroup effects (20).

Although self-reported adherence was lower in the N95 respirator group, the randomly conducted audited adherence was similar in both groups—98.3% in the medical mask group versus 96.6% in the N95 respirator group. It should be noted that the intervention included the mask policy at each site and not only the type of mask to which participants were randomly assigned. It is possible that the type of mask influenced adherence, which would be intrinsic to the pragmatic nature of the trial. We acknowledge concerns of suboptimal filtering capacity of medical masks, but the trial was done strictly in settings where the policy was use of medical masks for routine care, and no participants who were using N95 respirators were asked to use medical masks. In Pakistan and Egypt, the trial offered superior-quality medical masks and N95 respirators to participants who would otherwise not have access. High-risk participants were excluded from the study, and the data were routinely monitored by the Data Safety Committee. Furthermore,

participants who believed they were at high risk during a particular exposure were allowed to use the N95 respirator if assigned to a medical mask.

Some of the challenges experienced when conducting this trial included lengthy delays for ethics approvals and the establishment of contracts with sites. Implementation challenges included shipping supplies internationally and delays at customs of some of these sites, long regulatory approval delays, difficulty with procurement of N95 respirators because of supply chain issues, and delays due to the need to establish research contracts with sites. Some of the lessons learned include early onboarding of new study sites, identification of new sites through national and international public health agencies, the need for expedited ethics review and streamlined contractual processes, and early planning for design adaptation due to rollout of vaccines and new emerging variants.

In conclusion, among health care workers who provided routine care to patients with COVID-19, the overall estimates rule out a doubling in hazard of RT-PCR–confirmed COVID-19 for medical masks when compared with HRs of RT-PCR–confirmed COVID-19 for N95 respirators. The subgrou results varied by country, and the overall estimates may not be applica individual countries because of treatment effect heterogeneity.

Comments

1 Comment

Lisa M Brosseau • University of Minnesota • 1 December 2022

Unethical Study Without A Control

I request that the journal rescind this study. It was unethical to perform this type of study during the pandemic, when the data clearly support transmission of SARS-CoV- by aerosol inhalation, not droplets. Surgical masks are not designed to protect the wearer from inhalation of small infectious particles and will not prevent person-to-person transmission from patients or co-workers. Respirators must be worn during all exposures - with all patients and co-workers - to ensure user protection. It is clear from the data provided in the supplementary files that this was not the case. Without a control (no mask), it is impossible to conclude that surgical masks or respirators were effective. It is likely they were equally ineffective - for different reasons. There are many studies - in laboratories, clinical settings, etc. - that clearly demonstrate the efficacy of fit-tested respirators for protecting workers from hazardous aerosol exposures. But only if they are worn for every exposure. This paper does a significant disservice to healthcare workers, who have given their jobs and lives caring for patients throughout this pandemic.

PREVIOUS ARTICLE

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