

## MASK REFERENCES

### **Natural Disasters and Severe Weather | Wildfire Smoke and COVID-19**

[https://www.cdc.gov/disasters/covid-19/wildfire\\_smoke\\_covid-19.html](https://www.cdc.gov/disasters/covid-19/wildfire_smoke_covid-19.html)



Wildfire smoke can irritate your lungs, cause inflammation, affect your immune system, and make you more prone to lung infections, including SARS-CoV-2, the virus that cause COVID-19. Because of the COVID-19 pandemic, preparing for wildfires might be a little different this year. Know how wildfire smoke can affect you and your loved ones during the COVID-19 pandemic and what you can do to protect yourselves.

#### **Prepare for wildfires.**

Prepare for the wildfire smoke season [PDF-205 KB] as you would in any other summer.

Give yourself more time than usual to prepare for wildfire events. Home delivery is the safest choice for buying disaster supplies; however, that may not be an option for everyone. If in-person shopping is your only option, take steps to protect your and others' health when running essential errands.

Talk with a healthcare provider. Plan how you will protect yourself against wildfire smoke.

Stock up on medicines routinely taken. Store a 7 to 10-day supply of prescription medicines in a waterproof, childproof container to take with you if you evacuate.

As part of your planning for a potential evacuation, consider developing a family disaster plan.

### **Cloth masks will not protect you from wildfire smoke.**

Cloth masks that are used to slow the spread of COVID-19 by blocking respiratory droplets offer little protection against wildfire smoke. They do not catch small, harmful particles in smoke that can harm your health.

Although N95 respirators do provide protection from wildfire smoke, they might be in short supply as frontline healthcare workers use them during the pandemic.

### **Take actions to protect yourself from wildfire smoke during the COVID-19 pandemic.**

The best way to protect against the potentially harmful effects of wildfire smoke is to reduce your exposure to wildfire smoke, for example, by seeking cleaner air shelters and cleaner air spaces.

Limit your outdoor exercise when it is smoky outside or choose lower-intensity activities to reduce your smoke exposure.

Keep in mind that while social distancing guidelines are in place, finding cleaner air might be harder if public facilities such as libraries, community centers, and shopping malls are closed or have limited their capacity.

### **Create a cleaner air space at home to protect yourself from wildfire smoke during the COVID-19 pandemic.**

Use a portable air cleaner in one or more rooms. Portable air cleaners work best when run continuously with doors and windows closed.

If you use a do-it-yourself box fan filtration unit, never leave it unattended.

During periods of extreme heat, pay attention to temperature forecasts and know how to stay safe in the heat.

Whenever you can, use air conditioners, heat pumps, fans, and window shades to keep your cleaner air space comfortably cool on hot days.

If you have a forced air system in your home, you may need to speak with a qualified heating, ventilation, and air conditioning (HVAC) professional about different filters (HEPA or MERV-13 or higher) and settings (“Recirculate” and “On” rather than “Auto”) you can use to reduce indoor smoke.

Avoid activities that create more indoor and outdoor air pollution, such as frying foods, sweeping, vacuuming, and " using gas-powered appliances.

### **Know the difference between symptoms from smoke exposure and COVID-19.**

Some symptoms, like dry cough, sore throat, and difficulty breathing can be caused by both wildfire smoke exposure and COVID-19.

Learn about symptoms of COVID-19. Symptoms like fever or chills, muscle or body aches, and diarrhea are not related to smoke exposure.

If you have any of these symptoms, the CDC COVID-19 Self-Checker can help you determine whether you need further assessment or testing for COVID-19. If you have questions after using the CDC COVID-19 Self-Checker, contact a healthcare provider.

If you have severe symptoms, like difficulty breathing or chest pain, immediately call 911 or the nearest emergency facility.

### **People with COVID-19 are at increased risk from wildfire smoke during the pandemic.**

People who currently have or who are recovering from COVID-19 may be at increased risk of health effects from exposure to wildfire smoke due to compromised heart and/or lung function related to COVID-19.

### **Know whether you are at risk from wildfire smoke during the COVID-19 pandemic.**

Some people are more at risk of harmful health effects from wildfire smoke than others.

Those most at risk include:

Children less than 18 years old

Adults aged 65 years or older

Pregnant women

People with chronic health conditions such as heart or lung disease, asthma, and diabetes

Outdoor workers People who have lower socioeconomic status, including individuals experiencing homelessness or those who have limited access to medical care

People who are immunocompromised or taking drugs that suppress the immune system

### **Know what to do if you must evacuate.**

- Pay attention to local guidance about updated plans for evacuations and shelters, including [potential shelters for your pets](#).
- Whether you decide to evacuate or are asked to evacuate by state or local authorities, [evacuate safely](#).
- When you check on neighbors and friends before evacuating, be sure to follow [social distancing](#) recommendations (staying at least 6 feet from others) and [other CDC recommendations](#) to protect yourself and others.
- If you need to go to a disaster shelter, follow CDC recommendations for staying safe and healthy in a [public disaster shelter](#) during the COVID-19 pandemic.

### **Stay informed. Know where to find information about air quality and COVID-19 in your area.**

- Use the [Air Quality Indexexternal icon](#) (AQI) to check the air quality in your area.
- Visit [airnow.govexternal icon](#) to find reliable information about wildfire smoke and air quality.

- If there is a large wildfire in your area, then there is likely an [Air Resource Advisorexternal icon](#) assigned to provide [wildfire smoke outlooksexternal icon](#).
- For further information about wildfire smoke and your health, visit, <https://www.cdc.gov/air/wildfire-smoke/default.htm>.
- Visit the [CDC COVID Data Tracker](#) for more information about COVID-19.
- Check resources from [state, local, tribal, and territorial health departments](#) for more information on COVID-19 cases and deaths in a given area.

**For more information about COVID-19, go to <https://www.cdc.gov/coronavirus/2019-ncov/index.html>**

**For more information about the health effects of wildfire smoke and reducing exposure to it:**

- [Create a Clean Room to Protect Indoor Air Quality During a Wildfireexternal icon](#)
- [DIY Box Fan Filterexternal icon](#)
- [Natural Disasters and Severe Weather: Wildfires](#)
- [Protect Yourself from Wildfire Smoke](#)
- [Wildfire Guide Factsheet: Indoor Air Filtration pdf icon\[PDF-122 KB\]external icon](#)
- [Wildfires and Indoor Air Qualityexternal icon](#)

**For more information on air quality, wildfire information, smoke forecasts, and vulnerable populations:**

- [airnow.govexternal icon](#)
- [https://airquality.weather.gov/external icon](https://airquality.weather.gov/)
- [https://inciweb.nwcg.gov/external icon](https://inciweb.nwcg.gov/)
- <https://www.cdc.gov/disasters/wildfires/links.html>

# Use of surgical face masks to reduce the incidence of the common cold among health care workers in Japan: A randomized controlled trial

[https://www.ajicjournal.org/article/S0196-6553\(08\)00909-7/fulltext](https://www.ajicjournal.org/article/S0196-6553(08)00909-7/fulltext)

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## Background

Health care workers outside surgical suites in Asia use surgical-type face masks commonly. Prevention of upper respiratory infection is one reason given, although evidence of effectiveness is lacking.

## Methods

Health care workers in a tertiary care hospital in Japan were randomized into 2 groups: 1 that wore face masks and 1 that did not. They provided information about demographics, health habits, and quality of life. Participants recorded symptoms daily for 77 consecutive days, starting in January 2008. Presence of a cold was determined based on a previously validated measure of self-reported symptoms. The number of colds between groups was compared, as were risk factors for experiencing cold symptoms.

## Results

Thirty-two health care workers completed the study, resulting in 2464 subject days. There were 2 colds during this time period, 1 in each group. Of the 8 symptoms recorded daily, subjects in the mask group were significantly more likely to experience headache during the study period ( $P < .05$ ). Subjects living with children were more likely to have high cold severity scores over the course of the study.

## Conclusion

Face mask use in health care workers has not been demonstrated to provide benefit in terms of cold symptoms or getting colds. A larger study is needed to definitively establish noninferiority of no mask use.

# Face masks to prevent transmission of influenza virus: a systematic review

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<https://www.cambridge.org/core/journals/epidemiology-and-infection/article/face-masks-to-prevent-transmission-of-influenza-virus-a-systematic-review/64D368496EBDE0AFCC6639CCC9D8BC05>

## SUMMARY

Influenza viruses circulate around the world every year. From time to time new strains emerge and cause global pandemics. Many national and international health agencies recommended the use of face masks during the 2009 influenza A (H1N1) pandemic. We reviewed the English-language literature on this subject to inform public health preparedness. There is some evidence to support the wearing of masks or respirators during illness to protect others, and public health emphasis on mask wearing during illness may help to reduce influenza virus transmission. There are fewer data to support the use of masks or respirators to prevent becoming infected. Further studies in controlled settings and studies of natural infections in healthcare and community settings are required to better define the effectiveness of face masks and respirators in preventing influenza virus transmission.

## INTRODUCTION

Pandemic influenza A (H1N1) virus emerged in Mexico in early 2009 and rapidly spread worldwide. Severity of illness now appears to be more moderate than initially feared [1, 2], although high population attack rates would be associated with significant numbers of severe infections, hospitalizations and deaths. While some governments, particularly in the developed world, have large antiviral stockpiles on hand and contracts for vaccines that are now in production, the primary interventions currently available in both developed and less-developed settings are nonpharmaceutical [3, 4]. At the population level, these can include border controls to delay cross-border transmission, and social distancing

measures such as school or workplace closures. At the individual level, interventions to reduce transmission include improved hygiene and the use of face masks, respirators, and other physical barriers [5]. We conducted a systematic review [6] to investigate the evidence supporting the effectiveness of face masks in reducing influenza virus infection under controlled and natural conditions.

## **METHODS**

### **Search strategy**

On 18 August 2009 we searched the following databases for articles published in English from January 1960 to August 2009: PubMed (1960–2009), Science Citation Index (Web of Science) (1970–2009), and the Cochrane Library (1988–2009). We searched for articles using the following search strategy: #1: ' facemask' OR ' facemasks' OR 'mask' OR 'masks' OR ' respirator' OR ' respirators' OR 'N100' OR 'N99' OR 'N95' OR 'P2' OR 'FFP2' #2: 'influenza' OR 'flu' OR ' respiratory virus' OR ' respiratory infection' OR ' respiratory tract infection' #3: #1 AND #2. The search results were surveyed for methodological articles. Review articles were excluded, but the reference lists in all retrieved review papers were searched for additional related articles. In addition, a manual search was performed with the corresponding authors' reference database.

### **Selection**

Two authors (B.J.C. and Y.Z.) independently evaluated the titles and abstracts of all studies for potential inclusion in this review. The same authors then reviewed full-length versions of selected articles to determine inclusion. When consensus was not reached, discussion and further study evaluation with other authors was used to resolve data extraction discrepancies. Articles were included in the review if they (1) described controlled volunteer studies of influenza virus filtration of face masks or respirators, (2) described observational or intervention studies of face masks or respirators to prevent influenza or influenza-like illness (ILI) in healthcare settings, (3) described observational or intervention studies of face masks or respirators to prevent influenza or ILI in community settings. Studies focused on specific non-influenza respiratory infections, such as SARS, were excluded. The initial search resulted in 279 citations. Fifty-six articles were



accepted at the abstract stage and finally 12 articles were considered relevant for inclusion in this review (Fig. 1).

## RESULTS

### Experimental volunteer studies

We identified one study that examined the efficacy of face masks in filtering influenza virus in volunteer subjects. Johnson and colleagues tested the performance of surgical and N95 masks to filter virus in nine volunteers with confirmed influenza A or B virus infection [7]. Participants coughed five times onto a Petri dish containing viral transport medium held 20 cm in front of their mouth. The experiment was repeated with subjects wearing a surgical mask, and wearing an N95 respirator. While influenza virus could be detected by RT-PCR in all nine volunteers without a mask, no influenza virus could be detected on the Petri dish specimens when participants wore either type of face mask. A limitation was that the study did not consider the role of leakage around the sides of the mask.

**Studies in healthcare settings** We identified six studies of face mask use in healthcare settings (Table 1) [8–13]. Because the study designs, participants, interventions and reported outcome measures varied markedly, we focused on describing the studies, their results, their applicability and their limitations and on qualitative synthesis rather than meta-analysis. A randomized controlled trial in Canada found no significant differences in protection against laboratory confirmed influenza infection associated with the use of surgical masks or N95 masks among nurses [absolute risk difference 0.73%, 95% confidence interval (CI) 0.8 to 7.3] with 24% of nurses in the surgical mask arm having laboratory-confirmed infection during an influenza season [8]. A randomized controlled trial in Japan allocated 32 healthcare personnel to wearing surgical face masks or not, but was underpowered to detect significant differences between arms with one observed acute respiratory illness in each arm of the study during the follow-up period [9].

A survey of 133 nurses in Hong Kong found that suboptimal adherence to wearing a face shield during high-risk procedures [adjusted odds ratio (OR) 3.56, 95% CI 1.18–10.69] was associated with higher risk of ILI, while suboptimal adherence to use of gloves and gowns were also associated with higher adjusted risk of ILI

although not statistically significant [10]. Two other cross-sectional studies found no evidence for a protective effect of face masks against infection [11, 12]. Finally, Hobday & Cason [13] speculated that natural ventilation, hand hygiene and gauze face masks were associated with fewer observed deaths in open-air hospitals in Boston during the 1918–1919 influenza A (H1N1) ‘Spanish flu’ pandemic, although there were many potential confounders. Studies in community settings We identified four randomized controlled trials that examined the effectiveness of face masks to prevent respiratory virus transmission in community settings [14–16] (Table 2). In a household-based study in Hong Kong, index cases and household members were randomized to three arms, including control, hand hygiene and hand hygiene plus surgical masks (to be worn by the index case and household members) [14]. In the primary intention-to-treat analysis there was no statistically significant difference in laboratory-confirmed influenza in household contacts across intervention groups. However when a prespecified analysis restricted attention to 154 households in which the intervention was applied within 36 hours of symptom onset in the index case, statistically significant reductions in laboratory-confirmed influenza virus infections in household contacts were observed in the face mask and hand hygiene arm (adjusted OR 0.33, 95% CI 0.13–0.87). Adherence to the face mask intervention in index cases was moderate, but poorer in household contacts. The pilot study with a similar design was underpowered to identify significant differences between study arms [15]. Another recent study randomized 145 symptomatic index cases aged 0–15 years from outpatient clinics and their household members to three arms: control, surgical masks (worn by household contacts only), or N95-type respirators (worn by household contacts only) without fit-testing [16]. There were no differences in ILI in household contacts across intervention arms. A secondary per-protocol analysis found that Table 2. adherent use of N95 or surgical masks significantly reduced the risk for ILI in household contacts (hazard ratio 0.26, 95% CI 0.09–0.77) compared to nonadherent mask use or allocation to the control arm. Aiello and colleagues described a study in which 1437 university students were randomized by dormitory to three arms: control, surgical masks alone, and surgical masks plus hand hygiene [17]. Students were followed for 6 weeks during the influenza season and assessed for clinically diagnosed or survey-reported ILI. Compared with the control group, significant reductions in ILI were observed during weeks 4–6 in the mask and hand hygiene group ranging from 35% (95% CI

9–53) to 51% (95% CI 13–73), after adjusting for vaccination and other covariates; similar reductions, although not statistically significant, were observed in the mask-only group compared to the control group. Neither mask use and hand hygiene nor mask use alone was associated with significant reduction in ILI rate cumulatively; continued subject recruitment (larger sample size) after study start, increased participation in the intervention later in the study, a late, mild influenza season, and/or interruption of the intervention for 1 week by spring break may explain this finding. The study was underpowered to determine the relative contribution of the protective effects of masks compared to hand hygiene. Finally, Lo and colleagues [18] investigated respiratory virus isolations in specimens collected primarily from in-patients and compared virus isolations in Hong Kong in 2003 with the preceding years. Declines in the number and proportions of virus isolations were attributed to population increases in hygienic measures and widespread use of face masks, as well as social distancing during the SARS epidemic. However, the study could not distinguish the relative contributions of each intervention.

## **DISCUSSION**

Our review highlights the limited evidence base supporting the efficacy or effectiveness of face masks to reduce influenza virus transmission. An important concern when determining which public health interventions could be useful in mitigating local influenza virus epidemics, and which infection control procedures are necessary to prevent nosocomial transmission, is the mode of influenza virus transmission between people and in the environment. Physical barriers would be most effective in limiting short distance transmission by direct or indirect contact and large droplet spread, while more comprehensive precautions would be required to prevent infection at longer distances via airborne spread of small (nuclei) droplet particles [19]. In healthcare settings, stringent precautions are recommended to protect against pathogens that are transmitted by the airborne route, including the use of N95-type respirators (which require fit testing), other personal protective equipment including gowns, gloves, head covers and face shields, and isolation of patients in negative pressure rooms [19]. There remains considerable controversy over the relative importance of the alternative modes of transmission for influenza virus. In a recent review, Brankston and colleagues concluded that natural influenza transmission in human beings occurs generally

over short distance rather than over long distance [20]. Based on the same evidence, Tellier had earlier concluded that aerosol transmission occurs at appreciable rates [21], and cited further evidence in an updated review [22]. Weber & Stilianakis [23] found that contact, large droplet and small droplet (aerosol) transmission are all potentially important modes of transmission for influenza virus. If airborne transmission were important, it would be less likely that surgical masks will lead to reductions in infectiousness or protection against infection, if worn by ill or uninfected people, respectively. The primary argument against airborne transmission is as much one of absence of evidence as evidence of absence. While there are documented examples of long-distance airborne transmission of other pathogens including varicella zoster virus and *Mycobacterium tuberculosis*, the literature contain few compelling examples of airborne transmission of influenza virus [20], and several reports of scenarios where airborne transmission did not occur [24–27]. Further indirect evidence such as the substantial benefit of hand hygiene to prevent influenza transmission [14] is suggestive of direct or indirect contact as one of the most important modes of transmission for influenza virus in some settings. Further observational or intervention studies conducted in different latitudes during different times of the year could help to elucidate the role of temperature and humidity in mediating modes of transmission [28]. We did not identify any experimental volunteer studies that investigated whether surgical masks or N95 respirators could protect against infection. We identified one experimental study of face mask performance which involved participants with confirmed influenza virus infection [7], and the results suggested that surgical masks may be able to reduce infectiousness. In future similar studies it would be important to consider the potential for leakage around the sides of the mask in addition to direct penetration of infectious viral particles through the mask, if the results are to have practical implications for reduction of transmission in community and other settings [29]. Further studies are needed to investigate how mask and respirator performance varies with temperature and humidity, or under working conditions when moisture in exhaled breath or sweat may build up in face masks and hinder filtration or fit [30]. Few studies have been conducted in healthcare settings, and there is limited evidence to support the effectiveness of either surgical masks or N95 respirators to protect healthcare personnel [8–13]. One recent large trial in nurses found no difference in effectiveness between surgical masks and N95 respirators, although

the confidence intervals were wide enough to include moderate effect sizes [8]. Further, larger studies are needed to confirm the noninferiority of surgical masks. Guidance provided by the World Health Organization for protection of healthcare workers against pandemic influenza A (H1N1) virus infection recommends the use of standard and droplet precautions (including surgical masks or a face shield) during most patient interactions, while N95 or equivalent respirators are recommended for aerosol-generating procedures [31]. One concern over the use of face masks or respirators in healthcare settings is the potential for negative psychosocial impacts on patients and children in particular, especially in regions outside Asia where masks are not routinely worn [32]. Long-term use of N95-type respirators is likely to lead to physical discomfort [33], and has been associated with headaches [34]. Considerable resources might be required to make available N95 respirators and other protective equipment to large numbers of healthcare personnel through the course of influenza epidemics or pandemics. Finally, there are likely to be difficulties in ensuring compliance in healthcare workers [35]. Nevertheless personal protective equipment has led to major improvements in general infection control procedures in the hospital setting [36–38] and should not be discounted due to the lack of available data examining influenza virus outcomes. Three controlled studies of face mask effectiveness in the community setting used case-ascertained designs, where ill index cases were recruited from outpatient clinics and households were followed up for 7–10 days to observe secondary transmission [14–16].

The Hong Kong study applied surgical face masks to index cases and their household contacts [14, 15], while the Australian study applied surgical masks or N95-type respirators to household contacts only [16]. Neither study provides conclusive evidence that face masks are effective in primary intention-to-treat analyses, although statistical power was limited. Adherence was moderate in both studies, and a per protocol analysis of the Australian study suggests that masks could be effective in reducing risk of infection [16]. In the Hong Kong study, index cases not allocated to the face mask intervention reported use of face masks, indicating some degree of contamination of the intervention, while adherence was lower in household contacts and the results may primarily support the use of masks in ill members to reduce infectiousness [14, 15]. The effectiveness of face masks is probably impacted by compliance issues in both the healthcare and

community setting [14, 15, 35]. Various studies show a lower level of compliance with face masks [14, 15] or find lower reported acceptability of face masks [39] compared to hand hygiene behaviours and other non-pharmaceutical interventions. However, these studies do not seek to explain the reduced compliance, nor do they measure levels of compliance in the midst of an outbreak of pandemic influenza. Future research endeavours should investigate the influence of cultural and socio-behavioural factors (e.g. fear, stigma, altruism) on levels of compliance during a pandemic. Use of face masks in the community was very common during the SARS epidemic in Hong Kong, but not in Singapore [40], and cultural differences could also affect compliance. Pandemic guidance provided by the World Health Organization for community settings advises that masks may be worn although effectiveness is uncertain particularly in open spaces [41]. Other health agencies, such as the US Centers for Disease Control and Prevention, are not recommending masks in the community setting, with the exception of high-risk individuals who care for the sick or spend time in large crowds in areas affected by the pandemic [42]. Wearing masks incorrectly may increase the risk of transmission [41]. Further studies of face mask use are now underway, including some with prospective designs that follow cohorts of initially uninfected people. These studies will be particularly important in addressing compliance to and effectiveness associated with sustained use of face masks beyond the acute scenarios of existing studies [14–16]. While fewer resources are required to conduct studies with outcomes based on self-reported signs and symptoms of acute respiratory infection, future studies could include acute and convalescent serology or repeated collection of clinical specimens to provide results specific to influenza virus infection. In conclusion there remains a substantial gap in the scientific literature on the effectiveness of face masks to reduce transmission of influenza virus infection. While there is some experimental evidence that masks should be able to reduce infectiousness under controlled conditions [7], there is less evidence on whether this translates to effectiveness in natural settings. There is little evidence to support the effectiveness of face masks to reduce the risk of infection. Current research has several limitations including underpowered samples, limited generalizability, narrow intervention targeting and inconsistent testing protocols, different laboratory methods, and case definitions. Further in-vivo studies of face masks in infectious individuals are warranted to determine the proportion of exhaled virus that is trapped by the

mask. More detailed volunteer challenge and volunteer transmission studies could be designed to include both infectious and susceptible participants, to evaluate the efficacy of face masks both in reducing infectiousness and reducing susceptibility. However, such studies would require substantial resources, and contrived experiments may have limited generalizability to the natural setting. Large intervention studies in healthcare and community settings are likely to provide the best evidence of the effectiveness of face masks in reducing transmission in pandemic and inter-pandemic periods and are an urgent priority to guide pandemic preparedness for second and subsequent waves of pandemic influenza A (H1N1) and future pandemics.

## **A cluster randomised trial of cloth masks compared with medical masks in healthcare workers**

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<https://bmjopen.bmj.com/content/5/4/e006577>

### Objective

The aim of this study was to compare the efficacy of cloth masks to medical masks in hospital healthcare workers (HCWs). The null hypothesis is that there is no difference between medical masks and cloth masks. Setting 14 secondary-level/tertiary-level hospitals in Hanoi, Vietnam. Participants 1607 hospital HCWs aged  $\geq 18$  years working full-time in selected high-risk wards.

### Intervention

Hospital wards were randomised to: medical masks, cloth masks or a control group (usual practice, which included mask wearing). Participants used the mask on every shift for 4 consecutive weeks. Main outcome measure Clinical respiratory illness (CRI), influenza-like illness (ILI) and laboratory-confirmed respiratory virus infection. Results The rates of all infection outcomes were highest in the cloth mask arm, with the rate of ILI statistically significantly higher in the cloth mask arm (relative risk (RR)=13.00, 95% CI 1.69 to 100.07) compared with the medical mask arm. Cloth masks also had significantly higher rates of ILI compared with the control arm. An analysis by mask use showed ILI (RR=6.64, 95% CI 1.45 to 28.65) and laboratory-confirmed virus (RR=1.72, 95% CI 1.01 to 2.94) were significantly higher in the cloth masks group compared with the medical masks group. Penetration of cloth masks by particles was almost 97% and medical masks 44%. Conclusions This study is the first RCT of cloth masks, and the results caution against the use of cloth masks. This is an important finding to inform occupational health and safety. Moisture retention, reuse of cloth masks and poor filtration may result in increased risk of infection. Further research is needed to inform the widespread use of cloth masks globally. However, as a



precautionary measure, cloth masks should not be recommended for HCWs, particularly in high-risk situations, and guidelines need to be updated.

### Strengths and limitations of this study

The use of cloth masks is widespread around the world, particularly in countries at high-risk for emerging infections, but there have been no efficacy studies to underpin their use.

This study is large, a prospective randomised clinical trial (RCT) and the first RCT ever conducted of cloth masks.

The use of cloth masks are not addressed in most guidelines for health care workers—this study provides data to update guidelines.

The control arm was ‘standard practice’, which comprised mask use in a high proportion of participants. As such (without a no-mask control), the finding of a much higher rate of infection in the cloth mask arm could be interpreted as harm caused by cloth masks, efficacy of medical masks, or most likely a combination of both.

### INTRODUCTION

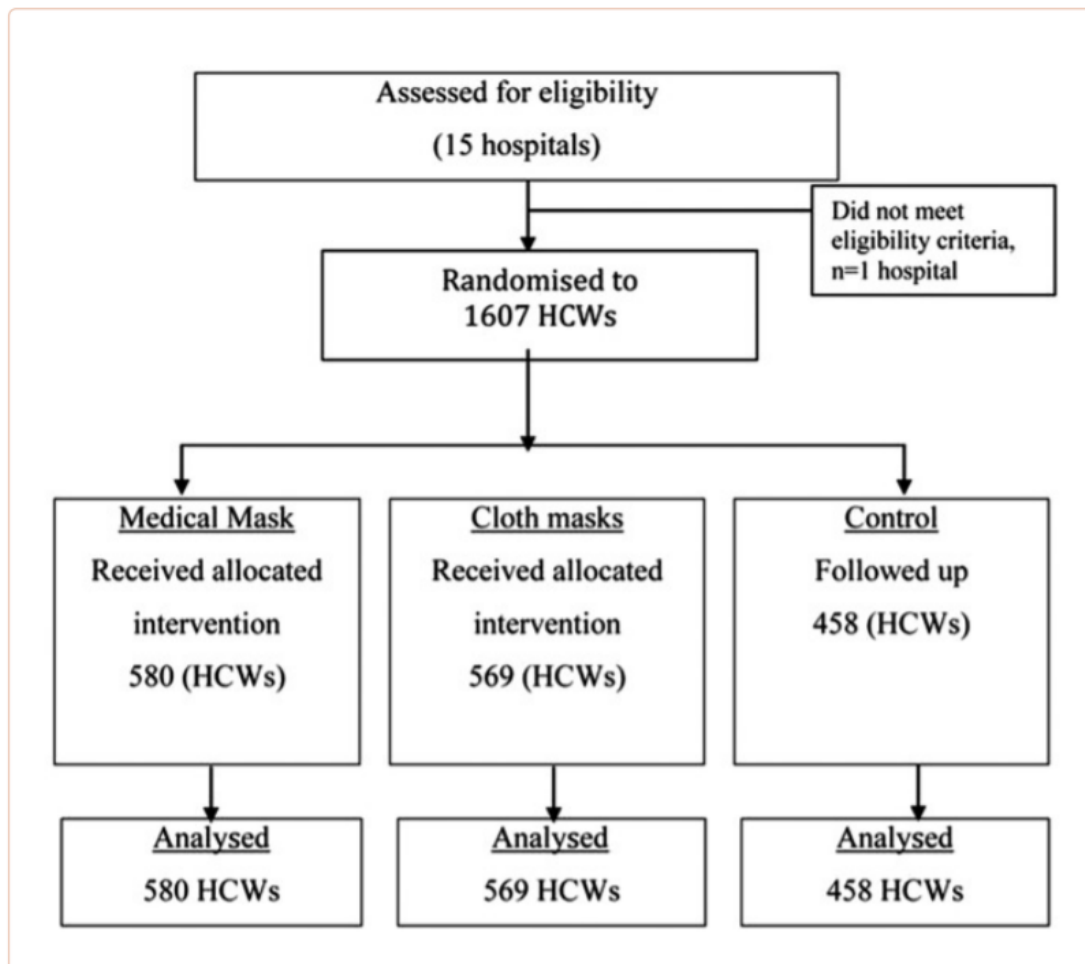
The use of facemasks and respirators for the protection of healthcare workers (HCWs) has received renewed interest following the 2009 influenza pandemic, and emerging infectious diseases such as avian influenza, Middle East respiratory syndrome coronavirus (MERS-coronavirus) and Ebola virus. Historically, various types of cloth/cotton masks (referred to here after as ‘cloth masks’) have been used to protect HCWs. Disposable medical/surgical masks (referred to here after as ‘medical masks’) were introduced into healthcare in the mid 19th century, followed later by respirators. Compared with other parts of the world, the use of face masks is more prevalent in Asian countries, such as China and Vietnam. In high resource settings, disposable medical masks and respirators have long since replaced the use of cloth masks in hospitals. Yet cloth masks remain widely used globally, including in Asian countries, which have historically been affected by emerging infectious diseases, as well as in West Africa, in the context of shortages of personal protective equipment (PPE). It has been shown that medical research

disproportionately favours diseases of wealthy countries, and there is a lack of research on the health needs of poorer countries. Further, there is a lack of high-quality studies around the use of facemasks and respirators in the healthcare setting, with only four randomised clinical trials (RCTs) to date. Despite widespread use, cloth masks are rarely mentioned in policy documents, and have never been tested for efficacy in a RCT. Very few studies have been conducted around the clinical effectiveness of cloth masks, and most available studies are observational or in vitro. Emerging infectious diseases are not constrained within geographical borders, so it is important for global disease control that use of cloth masks be underpinned by evidence. The aim of this study was to determine the efficacy of cloth masks compared with medical masks in HCWs working in high-risk hospital wards, against the prevention of respiratory infections.

## METHODS

A cluster-randomised trial of medical and cloth mask use for HCWs was conducted in 14 hospitals in Hanoi, Vietnam. The trial started on the 3 March 2011, with rolling recruitment undertaken between 3 March 2011 and 10 March 2011. Participants were followed during the same calendar time for 4 weeks of facemasks use and then one additional week for appearance of symptoms. An invitation letter was sent to 32 hospitals in Hanoi, of which 16 agreed to participate. One hospital did not meet the eligibility criteria; therefore, 74 wards in 15 hospitals were randomised. Following the randomisation process, one hospital withdrew from the study because of a nosocomial outbreak of rubella. Participants provided written informed consent prior to initiation of the trial. Randomisation Seventy-four wards (emergency, infectious/respiratory disease, intensive care and paediatrics) were selected as high-risk settings for occupational exposure to respiratory infections. Cluster randomisation was used because the outcome of interest was respiratory infectious diseases, where prevention of one infection in an individual can prevent a chain of subsequent transmission in closed settings. Epi info V.6 was used to generate a randomisation allocation and 74 wards were randomly allocated to the interventions. From the eligible wards 1868 HCWs were approached to participate. After providing informed consent, 1607 participants were randomised by ward to three arms: (1) medical masks at all times on their work shift; (2) cloth masks at all times on shift or (3) control arm (standard practice, which may 1 2 3 4 5 6 7 8–11 12 13 14 15 16 6 8 9 or may not

include mask use). Standard practice was used as control because the IRB deemed it unethical to ask participants to not wear a mask. We studied continuous mask use (defined as wearing masks all the time during a work shift, except while in the toilet or during tea or lunch breaks) because this reflects current practice in high-risk settings in Asia. The laboratory results were blinded and laboratory testing was conducted in a blinded fashion. As facemask use is a visible intervention, clinical end points could not be blinded. Figure 1 outlines the recruitment and randomisation process.



### Primary end points

There were three primary end points for this study, used in our previous mask RCTs: (1) Clinical respiratory illness (CRI), defined as two or more respiratory symptoms or one respiratory symptom and a systemic symptom; (2) influenza-like

illness (ILI), defined as fever  $\geq 38^{\circ}\text{C}$  plus one respiratory symptom and (3) laboratory-confirmed viral respiratory infection. Laboratory confirmation was by nucleic acid detection using multiplex reverse transcriptase PCR (RT-PCR) for 17 respiratory viruses: respiratory syncytial virus (RSV) A and B, human metapneumovirus (hMPV), influenza A (H3N2), (H1N1)pdm09, influenza B, parainfluenza viruses 1–4, influenza C, rhinoviruses, severe acute respiratory syndrome (SARS) associated coronavirus (SARS-CoV), coronaviruses 229E, NL63, OC43 and HKU1, adenoviruses and human bocavirus (hBoV). Additional end points included compliance with mask use, defined as using the mask during the shift for 70% or more of work shift hours. HCWs were categorised as ‘compliant’ if the average use was equal or more than 70% of the working time. HCW were categorised as ‘non-compliant’ if the average mask use was less than 70% of the working time. Eligibility Nurses or doctors aged  $\geq 18$  years working full-time were eligible. Exclusion criteria were: (1) Unable or refused to consent; (2) Beards, long moustaches or long facial hair stubble; (3) Current respiratory illness, rhinitis and/or allergy. Intervention Participants wore the mask on every shift for four consecutive weeks. Participants in the medical mask arm were supplied with two masks daily for each 8 h shift, while participants in the cloth mask arm were provided with five masks in total for the study duration, which they were asked to wash and rotate over the study period. They were asked to wash cloth masks with soap and water every day after finishing the shifts. Participants were supplied with written instructions on how to clean their cloth masks. Masks used in the study were locally manufactured medical (three layer, made of non-woven material) or cloth masks (two layer, made of cotton) commonly used in Vietnamese hospitals. The control group was asked to continue with their normal practices, which may or may not have included mask wearing. Mask wearing was measured and documented for all participants, including the control arm. Data collection and follow-up Data on sociodemographic, clinical and other potential confounding factors were collected at baseline. Participants were followed up daily for 4 weeks (active intervention period), and for an extra week of standard practice, in order to document incident infection after incubation. Participants received a thermometer (traditional glass and mercury) to measure their temperature daily and at symptom onset. Daily diary cards were provided to record number of hours worked and mask use, estimated number of patient contacts (with/without ILI) and number/type of aerosol-generating procedures

(AGPs) conducted, such as suctioning of airways, sputum induction, endotracheal intubation and bronchoscopy. Participants in the cloth mask and control group (if they used cloth masks) were also asked to document the process used to clean their mask after use. We also monitored compliance with mask use by a previously validated self-reporting mechanism. Participants were contacted daily to identify incident cases of respiratory infection. If participants were symptomatic, swabs of both tonsils and the posterior pharyngeal wall were collected on the day of reporting.

Sample collection and laboratory testing 18–23 9 8 Trained collectors used double rayon-tipped, plastic-shafted swabs to scratch tonsillar areas as well as the posterior pharyngeal wall of symptomatic participants. Testing was conducted using RT-PCR applying published methods. Viral RNA was extracted from each respiratory specimen using the Viral RNA Mini kit (Qiagen, Germany), following the manufacturer's instructions. The RNA extraction step was controlled by amplification of a RNA house-keeping gene (amplify pGEM) using real-time RT-PCR. Only extracted samples with the house keeping gene detected by real-time RT-PCR were submitted for multiplex RT-PCR for viruses. The reverse transcription and PCRs were performed in OneStep (Qiagen, Germany) to amplify viral target genes, and then in five multiplex RT-PCR: RSVA/B, influenza A/H3N2, A(H1N1) and B viruses, hMPV (reaction mix 1); parainfluenza viruses 1–4 (reaction mix 2); rhinoviruses, influenza C virus, SARS-CoV (reaction mix 3); coronaviruses OC43, 229E, NL63 and HKU1 (reaction mix 4); and adenoviruses and hBoV (reaction mix 5), using a method published by others. All samples with viruses detected by multiplex RT-PCR were confirmed by virus-specific mono nested or heminested PCR. Positive controls were prepared by in vitro transcription to control amplification efficacy and monitor for false negatives, and included in all runs (except for NL63 and HKU1). Each run always included two negatives to monitor amplification quality. Specimen processing, RNA extraction, PCR amplification and PCR product analyses were conducted in different rooms to avoid cross-contamination.

#### Filtration testing

The filtration performance of the cloth and medical masks was tested according to the respiratory standard AS/NZS1716. The equipment used was a TSI 8110

Filter tester. To test the filtration performance, the filter is challenged by a known concentration of sodium chloride particles of a specified size range and at a defined flow rate. The particle concentration is measured before and after adding the filter material and the relative filtration efficiency is calculated. We examined the performance of cloth masks compared with the performance levels—P1, P2 (=N95) and P3, as used for assessment of all particulate filters for respiratory protection. The 3M 9320 N95 and 3M Vflex 9105 N95 were used to compare against the cloth and medical masks.

### Sample size calculation

To obtain 80% power at two-sided 5% significance level for detecting a significant difference of attack rate between medical masks and cloth masks, and for a rate of infection of 13% for cloth mask wearers compared with 6% in medical mask wearers, we would need eight clusters per arm and 530 participants in each arm, and intracluster correlation coefficient (ICC) 0.027, obtained from our previous study. The design effect (deff) for this cluster randomisation trial was 1.65 ( $deff=1+(m-1)\times ICC=1+(25-1)\times 0.027=1.65$ ). As such, we aimed to recruit a sample size of 1600 participants from up to 15 hospitals.

### Analysis

Descriptive statistics were compared among intervention and control arms. Primary end points were analysed by intention to treat. We compared the event rates for the primary outcomes across study arms and calculated p values from cluster-adjusted  $\chi$  tests and ICC. We also estimated relative risk (RR) after adjusting for clustering using a log-binomial model under generalised estimating equation (GEE) framework. We checked for variables which were unequally distributed across arms, and 19–23 18 19 20 24 8 2 25 25 26 27 conducted an adjusted analysis accordingly. We fitted a multivariable log-binomial model, using GEE to account for clustering by ward, to estimate RR after adjusting for potential confounders. In the initial model, we included all the variables that had p value less than 0.25 in the univariable analysis, along with the main exposure variable (randomisation arm). A backward elimination method was used to remove the variables that did not have any confounding effect. As most participants in the control arm used a mask during the trial period, we carried out a post-hoc analysis

comparing all participants who used only a medical mask (from the control arm and the medical mask arm) with all participants who used only a cloth mask (from the control arm and the cloth arm). For this analysis, controls who used both types of mask (n=245) or used N95 respirators (n=3) or did not use any masks (n=2) were excluded. We fitted a multivariable log-binomial model, to estimate RR after adjusting for potential confounders. As we pooled data of participants from all three arms and analysed by mask type, not trial arm, we did not adjust for clustering here. All statistical analyses were conducted using STATA V.12. Owing to a very high level of mask use in the control arm, we were unable to determine whether the differences between the medical and cloth mask arms were due to a protective effect of medical masks or a detrimental effect of cloth masks. To assist in interpreting the data, we compared rates of infection in the medical mask arm with rates observed in medical mask arms from two previous RCTs, in which no efficacy of medical masks could be demonstrated when compared with control or N95 respirators, recognising that seasonal and geographic variation in virus activity affects the rates of exposure (and hence rates of infection outcomes) among HCWs. This analysis was possible because the trial designs were similar and the same outcomes were measured in all three trials. The analysis was carried out to determine if the observed results were explained by a detrimental effect of cloth masks or a protective effect of medical masks.

## RESULTS

A total of 1607 HCWs were recruited into the study. The participation rate was 86% (1607/1868). The average number of participants per ward was 23 and the mean age was 36 years. On average, HCWs were in contact with 36 patients per day during the trial period (range 0–661 patients per day, median 20 patients per day). The distribution of demographic variables was generally similar between arms ( table 1). Figure 2 shows the primary outcomes for each of the trial arms. The rates of CRI, ILI and laboratory-confirmed virus infections were lowest in the medical mask arm, followed by the control arm, and highest in the cloth mask arm.

Table 1

Demographic and other characteristics by arm of randomisation

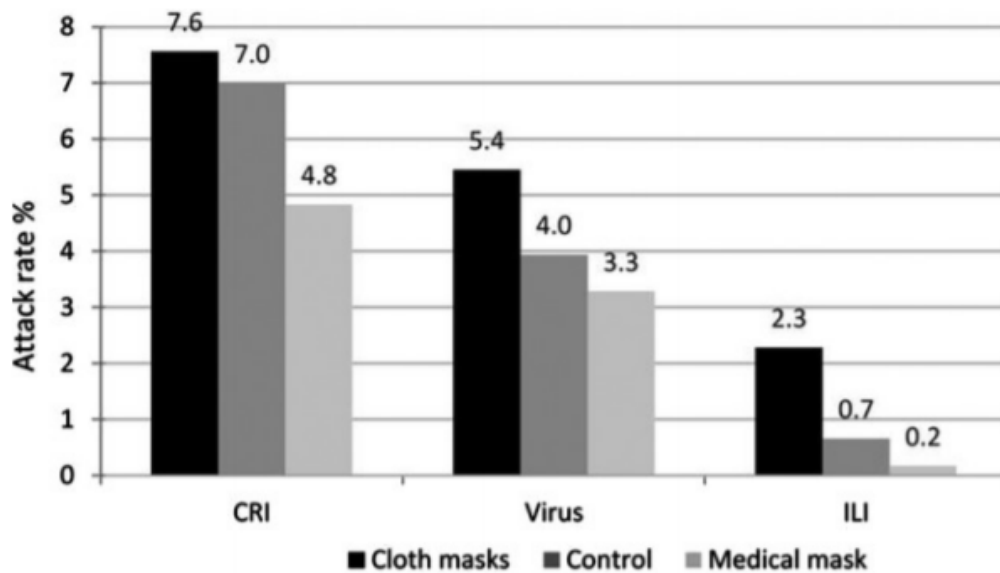
<b>Variable</b>	<b>Medical mask (% and 95% CI) (n=580)</b>	<b>Cloth mask (% and 95% CI) (n=569)</b>	<b>Control (% and 95% CI) (n=458)</b>
Gender (male)	112/580 19.3 (16.2 to 22.8)	133/569 23.4 (20.0 to 27.1)	112/458 24.5 (20.6 to 28.7)
Age (mean)	36 (35.6 to 37.3)	35 (34.6 to 36.3)	36 (35.1 to 37.0)
Education (postgraduate)	114/580 19.7 (16.5 to 23.1)	99/569 17.4 (14.3 to 20.8)	78/458 17.0 (13.7 to 20.8)
Smoker (current/ex)	78/580 13.4 (10.8 to 16.5)	79/569 13.9 (11.1 to 17.0)	66/458 14.4 (11.3 to 18.0)
Pre-existing illness*	66/580 11.4 (9.0 to 14.2)	70/569 12.3 (9.8 to 15.3)	47/458 10.3 (7.8 to 13.4)
Influenza vaccination (yes)	21/580 3.6 (2.4 to 5.4)	21/569 3.7 (2.4 to 5.6)	15/458 3.3 (2.0 to 5.3)
Staff (doctors)	176/580 30.3 (26.6 to 34.3)	165/569 29.0 (25.3 to 32.9)	134/458 29.3 (25.1 to 33.7)
Number of hand washings per day (geometric mean)†	14 (13.8 to 15.4)	11 (10.9 to 11.9)	12 (11.5 to 12.7)

\*Includes asthma, immunocompromised and others.

†'Hand wash' variable was created by taking average of the number of hand washes performed by a healthcare worker (HCW) over the trial period. The variable was log transformed for the multivariate analysis.

‡'Number of patients had contact with' variable was created by taking average of the number of patients in contact with a HCW over the trial period. Median and range is presented in the table.





[Open in a separate window](#)

Figure 2

Outcomes in trial arms (CRI, clinical respiratory illness; ILI, influenza-like illness; Virus, laboratory-confirmed viruses).

Table 2 shows the intention-to-treat analysis. The rate of CRI was highest in the cloth mask arm, followed by the control arm, and lowest in the medical mask arm. The same trend was seen for ILI and laboratory tests confirmed viral infections. In intention-to-treat analysis, ILI was significantly higher among HCWs in the cloth masks group (RR=13.25 and 95% CI 1.74 to 100.97), compared with the medical masks group. The rate of ILI was also significantly higher in the cloth masks arm (RR=3.49 and 95% CI 1.00 to 12.17), compared with the control arm. Other outcomes were not statistically significant between the three arms.

Table 2

Intention-to-treat analysis

	<b>CRI</b> <b>N (%)</b>	<b>RR</b> <b>(95% CI)</b>	<b>ILI</b> <b>N (%)</b>	<b>RR</b> <b>(95% CI)</b>	<b>Laboratory- confirmed</b> <b>viruses N (%)</b>	<b>RR</b> <b>(95% CI)</b>
Medical mask*	28/580 (4.83)	Ref	1/580 (0.17)	Ref	19/580 (3.28)	Ref
Cloth masks†	43/569 (7.56)	1.57 (0.99 to 2.48)	13/569 (2.28)	<b>13.25 (1.74 to 100.97)</b>	31/569 (5.45)	1.66 (0.95 to 2.91)
Control‡	32/458 (6.99)	1.45 (0.88 to 2.37)	3/458 (0.66)	3.80 (0.40 to 36.40)	18/458 (3.94)	1.20 (0.64 to 2.26)

Bold typeface indicates statistically significant. \*p Value from cluster adjusted  $\chi^2$  tests is 0.510 and intracluster correlation coefficients is 0.065.

†p Value from cluster adjusted  $\chi^2$  tests is 0.028 and intracluster correlation coefficients is 0.029.

‡p Value from cluster adjusted  $\chi^2$  tests is 0.561 and intracluster correlation coefficients is 0.068.

CRI, clinical respiratory illness; ILI, influenza-like illness; RR, relative risk.

Among the 68 laboratory-confirmed cases, 58 (85%) were due to rhinoviruses. Other viruses detected were hMPV (7 cases), influenza B (1 case), hMPV/rhinovirus co-infection (1 case) and influenza B/rhinovirus co-infection (1 case) ([table 3](#)). No influenza A or RSV infections were detected.

Table 3

Type of virus isolated

Study arm	hMPV	Rhino	Influenza B virus	hMPV & rhino	Influenza B virus & rhino	Total
Medical masks arm	1	16	1	1	0	19
Cloth mask arm	4	26	0	0	1	31
Control arm	2	16	0	0	0	18
Total	7	58	1	1	1	68

hMPV, human metapneumovirus; Rhino, rhinoviruses.

Compliance was significantly higher in the cloth mask arm (RR=2.41, 95% CI 2.01 to 2.88) and medical masks arm (RR=2.40, 95% CI 2.00 to 2.87), compared with the control arm. [Figure 3](#) shows the percentage of participants who were compliant in the three arms. A post-hoc analysis adjusted for compliance and other potential confounders showed that the rate of ILI was significantly higher in the cloth mask arm (RR=13.00, 95% CI 1.69 to 100.07), compared with the medical masks arm ([table 4](#)). There was no significant difference between the medical mask and control arms. Hand washing was significantly protective against laboratory-confirmed viral infection (RR=0.66, 95% CI 0.44 to 0.97).

Table 4

Multivariable cluster-adjusted log-binomial model to calculate RR for study outcomes

	<b>CRI RR (95% CI)</b>	<b>ILI RR (95% CI)</b>	<b>Laboratory-confirmed viruses RR (95% CI)</b>
Medical masks arm	Ref	Ref	Ref
Cloth mask arm	1.56 (0.97 to 2.48)	<b>13.00 (1.69 to 100.07)</b>	1.54 (0.88 to 2.70)
Control arm	1.51 (0.90 to 2.52)	4.64 (0.47 to 45.97)	1.09 (0.57 to 2.09)
Male	0.67 (0.41 to 1.12)	1.03 (0.34 to 3.13)	0.65 (0.34 to 1.22)
Vaccination	0.83 (0.27 to 2.52)	1.74 (0.24 to 12.56)	1.27 (0.41 to 3.92)
Hand washing	0.91 (0.66 to 1.26)	0.94 (0.40 to 2.20)	<b>0.66 (0.44 to 0.97)</b>
Compliance	1.14 (0.77 to 1.69)	1.86 (0.67 to 5.21)	0.86 (0.53 to 1.40)

Bold typeface indicates statistically significant. CRI, clinical respiratory illness; ILI, influenza-like illness; RR, relative risk.

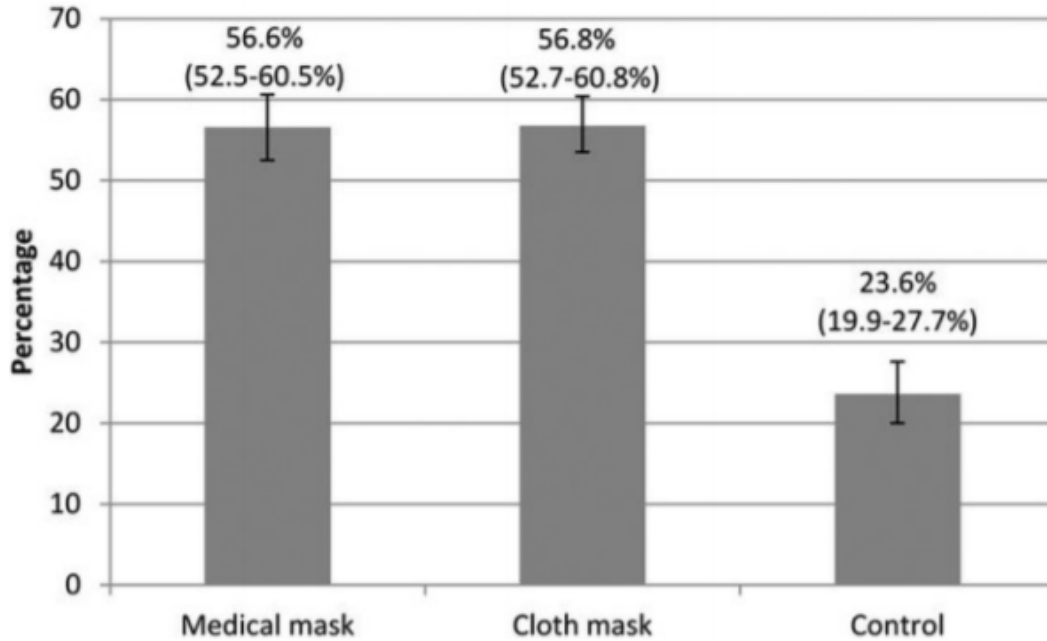


Figure 3

Compliance with the mask wearing—mask wearing more than 70% of working hours.

In the control arm, 170/458 (37%) used medical masks, 38/458 (8%) used cloth masks, and 245/458 (53%) used a combination of both medical and cloth masks during the study period. The remaining 1% either reported using a N95 respirator (n=3) or did not use any masks (n=2).

Table 5 shows an additional analysis comparing all participants who used only a medical mask (from the control arm and the medical mask arm) with all participants who used only a cloth mask (from the control arm and the cloth arm). In the univariate analysis, all outcomes were significantly higher in the cloth mask group, compared with the medical masks group. After adjusting for other factors, ILI (RR=6.64, 95% CI 1.45 to 28.65) and laboratory-confirmed virus (RR=1.72, 95% CI 1.01 to 2.94) remained significantly higher in the cloth masks group compared with the medical masks group.

Table 5

Univariate and adjusted analysis comparing participants who used medical masks and cloth masks\*

	Univariate RR (95% CI)	Adjusted RR (95% CI)
<b>CRI</b>		
Medical mask (35/750, 4.67%)	Ref	Ref
Cloth mask (46/607, 7.58%)	<b>1.62 (1.06 to 2.49)</b>	1.51 (0.97 to 2.32)
Male	0.60 (0.32 to 1.12)	0.58 (0.31 to 1.08)
Vaccination	0.66 (0.17 to 2.62)	0.68 (0.17 to 2.67)
Hand washing	0.81 (0.58 to 1.15)	0.84 (0.59 to 1.20)
Compliance	1.01 (1.00 to 1.03)	1.01 (1.00 to 1.02)
<b>ILI</b>		
Medical mask (2/750, 0.27%)	Ref	Ref
Cloth mask (13/607, 2.14%)	<b>8.03 (1.82 to 35.45)</b>	<b>6.64 (1.45 to 28.65)</b>
Male	0.95 (0.27 to 3.35)	0.92 (0.26 to 3.22)
Vaccination	1.87 (0.25 to 13.92)	1.97 (0.27 to 14.45)
Hand washing	0.56 (0.24 to 1.27)	0.61 (0.23 to 1.57)
Compliance	1.04 (1.01 to 1.08)	1.04 (1.00 to 1.08)
<b>Laboratory-confirmed viruses</b>		
Medical mask (22/750, 2.93%)	Ref	Ref
Cloth mask (34/607, 5.60%)	<b>1.91 (1.13 to 3.23)</b>	<b>1.72 (1.01 to 2.94)</b>
Male	0.64 (0.30 to 1.33)	0.61 (0.29 to 1.27)
Vaccination	0.97 (0.24 to 3.86)	1.03 (0.26 to 4.08)

Bold typeface indicates statistically significant. \*The majority (456/458) of HCWs in the control arm used a mask. Controls who exclusively used a medical mask were categorised and analysed with the medical mask arm participants; and controls who exclusively wore a cloth mask were categorised and analysed with the cloth mask arm.

CRI, clinical respiratory illness; HCWs, healthcare workers; ILI, influenza-like illness; RR, relative risk.

[Table 6](#) compares the outcomes in the medical mask arm with two previously published trials.<sup>8,9</sup> This shows that while the rates of CRI were significantly higher in one of the previously published trials, the rates of laboratory-confirmed viruses were not significantly different between the three trials for medical mask use.

Table 6

A comparison of outcome data for the medical mask arm with medical mask outcomes in previously published RCTs

	CRI N (%)	RR (95% CI)	ILI N (%)	RR (95% CI)	Laboratory- confirmed viruses N (%)	RR (95% CI)
Vietnam trial	28/580 (4.83)	Ref	1/580 (0.17)	Ref	19/580 (3.28)	Ref
Published RCT China 1 <sup>8</sup>	33/492 (6.70)	1.40 (0.85 to 2.26)	3/492 (0.61)	3.53 (0.37 to 33.89)	13/492 (2.64)	0.80 (0.40 to 1.62)
Published RCT China 2 <sup>9</sup>	98/572 (17.13)	<b>3.54 (2.37 to 5.31)</b>	4/572 (0.70)	4.06 (0.45 to 36.18)	19/572 (3.32)	1.01 (0.54 to 1.89)

Bold typeface indicates statistically significant. CRI, Clinical respiratory illness; ILI, influenza-like illness; RCT, randomised clinical trial; RR, relative risk.

On average, HCWs worked for 25 days during the trial period and washed their cloth masks for 23/25 (92%) days. The most common approach to washing cloth masks was self-washing (456/569, 80%), followed by combined self-washing and hospital laundry (91/569, 16%), and only hospital laundry (22/569, 4%). Adverse events associated with facemask use were reported in 40.4% (227/562) of HCWs in the medical mask arm and 42.6% (242/568) in the cloth mask arm (p value 0.450). General discomfort (35.1%, 397/1130) and breathing problems (18.3%, 207/1130) were the most frequently reported adverse events. Laboratory tests showed the penetration of particles through the cloth masks to be very high (97%) compared with medical masks (44%) (used in trial) and 3M 9320 N95 (<0.01%), 3M Vflex 9105 N95 (0.1%).

## DISCUSSION

We have provided the first clinical efficacy data of cloth masks, which suggest HCWs should not use cloth masks as protection against respiratory infection. Cloth masks resulted in significantly higher rates of infection than medical masks,

and also performed worse than the control arm. The controls were HCWs who observed standard practice, which involved mask use in the majority, albeit with lower compliance than in the intervention arms. The control HCWs also used medical masks more often than cloth masks. When we analysed all mask-wearers including controls, the higher risk of cloth masks was seen for laboratory-confirmed respiratory viral infection. 8 9 The trend for all outcomes showed the lowest rates of infection in the medical mask group and the highest rates in the cloth mask arm. The study design does not allow us to determine whether medical masks had efficacy or whether cloth masks were detrimental to HCWs by causing an increase in infection risk. Either possibility, or a combination of both effects, could explain our results. It is also unknown whether the rates of infection observed in the cloth mask arm are the same or higher than in HCWs who do not wear a mask, as almost all participants in the control arm used a mask. The physical properties of a cloth mask, reuse, the frequency and effectiveness of cleaning, and increased moisture retention, may potentially increase the infection risk for HCWs. The virus may survive on the surface of the facemasks, and modelling studies have quantified the contamination levels of masks. Self contamination through repeated use and improper doffing is possible. For example, a contaminated cloth mask may transfer pathogen from the mask to the bare hands of the wearer. We also showed that filtration was extremely poor (almost 0%) for the cloth masks. Observations during SARS suggested double-masking and other practices increased the risk of infection because of moisture, liquid diffusion and pathogen retention. These effects may be associated with cloth masks. We have previously shown that N95 respirators provide superior efficacy to medical masks, but need to be worn continuously in high-risk settings to protect HCWs. Although efficacy for medical masks was not shown, efficacy of a magnitude that was too small to be detected is possible. The magnitude of difference between cloth masks and medical masks in the current study, if explained by efficacy of medical masks alone, translates to an efficacy of 92% against ILI, which is possible, but not consistent with the lack of efficacy in the two previous RCTs. Further, we found no significant difference in rates of virus isolation in medical mask users between the three trials, suggesting that the results of this study could be interpreted as partly being explained by a detrimental effect of cloth masks. This is further supported by the fact that the rate of virus isolation in the no-mask control group in the first Chinese RCT was



3.1%, which was not significantly different to the rates of virus isolation in the medical mask arms in any of the three trials including this one. Unlike the previous RCTs, circulating influenza and RSV were almost completely absent during this study, with rhinoviruses comprising 85% of isolated pathogens, which means the measured efficacy is against a different range of circulating respiratory pathogens. Influenza and RSV predominantly transmit through droplet and contact routes, while Rhinovirus transmits through multiple routes, including airborne and droplet routes. The data also show that the clinical case definition of ILI is non-specific, and captures a range of pathogens other than influenza. The study suggests medical masks may be protective, but the magnitude of difference raises the possibility that cloth masks cause an increase in infection risk in HCWs. Further, the filtration of the medical mask used in this trial was poor, making extremely high efficacy of medical masks unlikely, particularly given the predominant pathogen was rhinovirus, which spreads by the airborne route. Given the obligations to HCW occupational health and safety, it is important to consider the potential risk of using cloth masks. In many parts of the world, cloth masks and medical masks may be the only options available for HCWs. Cloth masks have been used in West Africa during the Ebola outbreak in 2014, due to shortages of PPE, (personal communication, M Jalloh). The use of cloth masks is recommended by some health organisations, with caveats. In light of our study, and the obligation to ensure occupational health and safety of HCWs, cloth masks should not be recommended for HCWs, particularly during AGPs and in high-risk settings such as emergency, infectious/respiratory disease and intensive care wards. Infection control guidelines need to acknowledge the widespread real-world practice of cloth masks and should comprehensively address their use. In addition, other important 29 30 31 8 9 9 8 9 8 9 32 33 34–36 infection control measure such as hand hygiene should not be compromised. We confirmed the protective effects of hand hygiene against laboratory-confirmed viral infection in this study, but mask type was an independent predictor of clinical illness, even adjusted for hand hygiene. A limitation of this study is that we did not measure compliance with hand hygiene, and the results reflect self-reported compliance, which may be subject to recall or other types of bias. Another limitation of this study is the lack of a no-mask control group and the high use of masks in the controls, which makes interpretation of the results more difficult. In addition, the quality of paper and cloth masks varies widely around the world, so the results

may not be generalisable to all settings. The lack of influenza and RSV (or asymptomatic infections) during the study is also a limitation, although the predominance of rhinovirus is informative about pathogens transmitted by the droplet and airborne routes in this setting. As in previous studies, exposure to infection outside the workplace could not be estimated, but we would assume it to be equally distributed between trial arms. The major strength of the randomised trial study design is in ensuring equal distribution of confounders and effect modifiers (such as exposure outside the workplace) between trial arms. Cloth masks are used in resource-poor settings because of the reduced cost of a reusable option. Various types of cloth masks (made of cotton, gauze and other fibres) have been tested in vitro in the past and show lower filtration capacity compared with disposable masks. The protection afforded by gauze masks increases with the fineness of the cloth and the number of layers, indicating potential to develop a more effective cloth mask, for example, with finer weave, more layers and a better fit. Cloth masks are generally retained long term and reused multiple times, with a variety of cleaning methods and widely different intervals of cleaning. Further studies are required to determine if variations in frequency and type of cleaning affect the efficacy of cloth masks. Pandemics and emerging infections are more likely to arise in low-income or middle-income settings than in wealthy countries. In the interests of global public health, adequate attention should be paid to cloth mask use in such settings. The data from this study provide some reassurance about medical masks, and are the first data to show potential clinical efficacy of medical masks. Medical masks are used to provide protection against droplet spread, splash and spray of blood and body fluids. Medical masks or respirators are recommended by different organisations to prevent transmission of Ebola virus, yet shortages of PPE may result in HCWs being forced to use cloth masks. In the interest of providing safe, low-cost options in low income countries, there is scope for research into more effectively designed cloth masks, but until such research is carried out, cloth masks should not be recommended. We also recommend that infection control guidelines be updated about cloth mask use to protect the occupational health and safety of HCWs.

## N95 Respirators vs Medical Masks for Preventing Influenza Among Health Care Personnel A Randomized Clinical Trial

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<https://jamanetwork.com/journals/jama/fullarticle/2749214>

**IMPORTANCE** Clinical studies have been inconclusive about the effectiveness of N95 respirators and medical masks in preventing health care personnel (HCP) from acquiring workplace viral respiratory infections. **OBJECTIVE** To compare the effect of N95 respirators vs medical masks for prevention of influenza and other viral respiratory infections among HCP.

**DESIGN, SETTING, AND PARTICIPANTS** A cluster randomized pragmatic effectiveness study conducted at 137 outpatient study sites at 7 US medical centers between September 2011 and May 2015, with final follow-up in June 2016. Each year for 4 years, during the 12-week period of peak viral respiratory illness, pairs of outpatient sites (clusters) within each center were matched and randomly assigned to the N95 respirator or medical mask groups.

**INTERVENTIONS** Overall, 1993 participants in 189 clusters were randomly assigned to wear N95 respirators (2512 HCP-seasons of observation) and 2058 in 191 clusters were randomly assigned to wear medical masks (2668 HCP-seasons) when near patients with respiratory illness.

**MAIN OUTCOMES AND MEASURES** The primary outcome was the incidence of laboratory-confirmed influenza. Secondary outcomes included incidence of acute respiratory illness, laboratory-detected respiratory infections, laboratory-confirmed respiratory illness, and influenzalike illness. Adherence to interventions was assessed. **RESULTS** Among 2862 randomized participants (mean [SD] age, 43 [11.5] years; 2369 [82.8%] women), 2371 completed the study and accounted for 5180 HCP-seasons. There were 207 laboratory-confirmed influenza infection events (8.2% of HCP-seasons) in the N95 respirator group and 193 (7.2% of HCP-seasons) in the medical mask group (difference, 1.0%, [95% CI, -0.5% to 2.5%];  $P = .18$ ) (adjusted odds ratio [OR], 1.18 [95% CI, 0.95-1.45]). There were 1556 acute respiratory illness events in the respirator group vs 1711 in the mask group (difference, -21.9 per 1000 HCP-seasons [95% CI, -48.2 to 4.4];  $P = .10$ ); 679 laboratory-detected respiratory infections in the respirator group vs 745 in the mask group (difference, -8.9 per 1000 HCP-seasons, [95% CI, -33.3 to 15.4];  $P = .47$ ); 371 laboratory-confirmed respiratory illness events in the respirator group vs 417 in the mask group (difference, -8.6 per 1000 HCP-seasons [95% CI, -28.2 to 10.9];  $P = .39$ ); and 128 influenza like illness events in the respirator group vs 166 in the mask group (difference, -11.3 per 1000 HCP-seasons [95% CI, -23.8 to 1.3];  $P = .08$ ). In the respirator group,

89.4% of participants reported “always” or “sometimes” wearing their assigned devices vs 90.2% in the mask group.

**CONCLUSIONS AND RELEVANCE** Among outpatient health care personnel, N95 respirators vs medical masks as worn by participants in this trial resulted in no significant difference in the incidence of laboratory-confirmed influenza.

Health care personnel (HCP) who are routinely exposed to viral respiratory infections in the workplace<sup>1</sup> may transmit infection to others. It is widely recognized that HCP, as a group, incompletely adhere to infection prevention recommendations and practice standards. Inpatient respiratory protection studies suggest adherence rates vary from 10% to 84%.<sup>2-4</sup> While laboratory studies designed to achieve 100% intervention adherence have shown that N95 filtering facepiece respirators are more efficacious than medical masks at reducing exposure to aerosols,<sup>5</sup> comparative clinical effectiveness studies have been inconclusive.<sup>3,4,6</sup> Some experts argue that N95 respirators and medical masks are equivalent in clinical settings.<sup>2,7</sup> Pragmatic effectiveness trials are increasingly recognized as an essential component of medical evidence, in part because efficacy studies may overestimate effectiveness and true adherence.<sup>8</sup> Disposable N95 respirators and medical masks are both worn by HCP for self-protection; however, these masks have different intended uses. N95 respirators are designed to prevent the wearer from inhaling small airborne particles,<sup>9</sup> must meet filtration requirements,<sup>10</sup> and fit tightly to the wearer’s face, limiting facial seal leakage. Medical masks, frequently called surgical masks, are intended to prevent microorganism transmission from the wearer to the patient. Medical masks fit the face loosely and do not reliably prevent inhalation of small airborne particles. However, medical masks prevent hand-to-face contact and facial contact with large droplets and sprays.<sup>11</sup> Clinical evidence is inconclusive regarding whether N95 respirators are more effective than medical masks for preventing viral respiratory infection among HCP, including influenza,<sup>3,4,6,12</sup> accounting for differing practices<sup>2</sup> and positions held by clinical,<sup>7</sup> public health,<sup>13,14</sup> and regulatory organizations.<sup>15</sup> The objective of this study was to compare<sup>13</sup> the effectiveness of N95 respirators vs medical masks worn by HCP in clinical practice for prevention of workplace-acquired influenza and other viral respiratory infections in geographically diverse, high-exposure, outpatient settings.

## METHODS

**Study Sites and Institutional Review Boards** The Respiratory Protection Effectiveness Clinical Trial (ResPECT) was approved by the human subjects research board at the National Institute for Occupational Safety and Health (protocol #10-NPPTL-O5XP) and the institutional review boards (IRBs) at the 7 participating health systems, as previously described,<sup>16</sup> and approved or exempted by IRBs at the analysis and sample storage sites. All participants were permitted to participate for 1 or more years and gave written consent for each year of participation. Study intervention sites included outpatient settings at the Children’s Hospital Colorado (Aurora),

Denver Health Medical Center (Denver, Colorado), Johns Hopkins Health System (Baltimore, Maryland), Michael E. DeBakey Veterans Affairs (VA) Medical Center (Houston, Texas), VA Eastern Colorado Healthcare System (Denver), Washington DC VA Medical Center, and VA New York Harbor Healthcare System (New York). Sample storage and data analysis sites were the VA St Louis Healthcare System and St Louis University (St Louis, Missouri), University of Florida (Gainesville), University of Massachusetts (Amherst), and University of Texas Southwestern Medical Center (Dallas).

### Design and Oversight

This cluster randomized, multicenter, pragmatic effectiveness trial<sup>16</sup> conducted between September 2011 and May 2015, with final follow-up on June 28, 2016, compared the effect of N95 respirators, used as recommended during the 2009 H1N1 pandemic,<sup>13</sup> and medical masks, used as recommended to prevent seasonal influenza<sup>17,18</sup> and other viral respiratory infections and illnesses, among HCP.<sup>17</sup> The investigators were blinded to the randomization until completion of the study and analysis. An independent data and safety monitoring board assessed the data. Additional details are included in Supplement 1, including the statistical analysis plan and the full protocol that was previously published in an abridged format.<sup>16</sup>

### Participants and Setting

This trial was conducted in diverse outpatient settings serving adult and pediatric patients with a high prevalence of acute respiratory illness, including primary care facilities, dental clinics, adult and pediatric clinics, dialysis units, urgent care facilities and emergency departments, and emergency transport services. All participants in a cluster worked in the same outpatient clinic or outpatient setting. A cluster randomized design was used to improve adherence and increase indirect effects associated with participants in a cluster using the same intervention. Participants were aged at least 18 years, employed at one of the 7 participating health systems, and self-identified as routinely positioned within 6 feet (1.83 m) of patients. Participants were full-time employees (defined as direct patient care for approximately  $\geq 24$  hours weekly) and worked primarily at the study site (defined as  $\geq 75\%$  of working hours). Exclusion criteria were medical conditions precluding safe participation or anatomic features that could interfere with respirator fit, such as facial hair or third-trimester pregnancy. Participants self-identified race and sex using fixed categories; these variables were collected because facial anthropometrics related to race and sex may influence N95 respirator fit. Participants kept diaries that included signs and symptoms of respiratory illness, annual influenza vaccination status, and exposure to household and community members with respiratory illness. Participants also recorded their participation in aerosol-generating procedures and exposure to patients, coworkers, or both with respiratory illness daily. Participants were categorized for exposure risk by occupational roles.

## Procedures, Interventions, and Group Allocation

Each year, participating sites were cluster randomized to have participants wear N95 respirators<sup>13</sup> or medical masks,<sup>17,18</sup> as previously described.<sup>16</sup> N95 respirator models studied were the 3M Corporation 1860, 1860S, and 1870 (St Paul, Minnesota) and the Kimberly Clark Technol Fluidshield PFR95-270, PFR95-274 (Dallas, Texas); medical mask models were the Precept 15320 (Arden, North Carolina) and Kimberly Clark Technol Fluidshield 47107 (Dallas, Texas). Within each medical center, for each study year, pairs of clusters (clinics and other settings) were matched by the number of participants, health services delivered, patient population served, and additional personal protective equipment. One cluster was randomly assigned to the medical mask group and one to the N95 respirator group. Random allocation of clusters required using constrained randomization, a process that maintains random assignment and balance between groups.<sup>19</sup> Computer-generated random sequences of group assignments were generated by an individual not involved in the study implementation and data analyses. Random sequences of assignment assured that every participant in each season had an equal probability of being assigned to the N95 respirator and medical mask groups and allowed participants to switch groups between seasons. Occupational Safety and Health Administration– accepted fit testing<sup>15</sup> of N95 respirators was conducted annually for all study participants. Participants were instructed to wear their assigned protective devices (ie, N95 respirators or medical masks) during the 12-week period (the intervention period) during which the incidence of viral respiratory illness and infections was expected to be highest that year, as predicted by the ALERT algorithm<sup>20</sup> developed for this trial. Participants were instructed to put on a new device whenever they were positioned within 6 feet (1.83 m) of patients with suspected or confirmed respiratory illness. Hand hygiene was recommended to all participants in accordance with Centers for Disease Control and Prevention guidelines.<sup>13,17,18</sup> Infection prevention policies were followed at each study site. Participants volunteered to participate for up to 12 weeks each intervention period, for a total of 48 weeks of intervention spanning 4 consecutive viral respiratory seasons.

## Surveillance, Outcomes, and Measures of Effectiveness

Study personnel obtained swabs of the anterior nares and oropharynx<sup>21</sup> (FLOQSwabs UTM, Diagnostic Hybrids) from participants who self-reported symptoms of respiratory illness (Box 1). Symptomatic swabs were collected within 24 hours of self-report, and again if signs or symptoms persisted beyond 7 days. If symptomatic participants were not at work, samples were self-obtained using a structured process and shipped to the study laboratory. During each 12-week intervention period, 2 random swabs were obtained from all participants, typically while asymptomatic. Additionally, each year, paired serum samples obtained from all participants were assayed for influenza hemagglutinin levels before and after peak viral respiratory season. The prespecified primary outcome was the incidence of laboratory-confirmed influenza, defined as detection of influenza A or B virus by reverse-transcription polymerase chain reaction<sup>22</sup> in an upper respiratory specimen collected within 7 days of

symptom onset; detection of influenza from a randomly obtained swab from an asymptomatic participant; or influenza seroconversion (symptomatic or asymptomatic), defined as at least a 4-fold rise in hemagglutination inhibition antibody titers to influenza A or B virus between pre-season and post-season serological samples deemed not attributable to vaccination. Individuals experiencing seroconversion were not required to have a detected symptomatic illness to meet the defined outcome. Influenza reagents used in the hemagglutination inhibition antibody assays were obtained from the International Reagent Resource Program, established by the Centers for Disease Control and Prevention.

Secondary outcome measures were the incidence of 4 measures of viral respiratory illness and infection: (1) acute respiratory illness (Box 1) with or without laboratory confirmation; (2) laboratory-detected respiratory infection, defined as detection of a respiratory pathogen by polymerase chain reaction or serological evidence of infection with a respiratory pathogen during the study surveillance period(s), which was added to the protocol prior to data analysis; (3) laboratory confirmed respiratory illness, identified as previously described,<sup>23</sup> defined as self-reported acute respiratory illness plus the presence of at least 1 polymerase chain reaction– confirmed viral pathogen (Box 2) in a specimen collected from the upper respiratory tract within 7 days of the reported symptoms and/or at least a 4-fold rise from pre-intervention to post-intervention serum antibody titers to influenza A or B virus; and (4) influenza-like illness, defined as temperature of at least 100°F (37.8°C) plus cough and/or a sore throat, with or without laboratory confirmation.

#### Adherence to Group Assignment and Infection Prevention and Control Practices

Participants were reminded to adhere to protective device and hand hygiene instructions by signage posted at study sites, email, and by study personnel in person. Adherence to assigned devices were reported daily by participants as “always,” “sometimes,” “never,” or “did not recall.” In addition, study personnel observed participants’ device-wearing behaviors as they entered and exited patient care rooms by conducting unannounced, inconspicuous visits to randomly selected study sites throughout the intervention period. However, to preserve patient confidentiality, monitors were not permitted to enter patient care rooms.

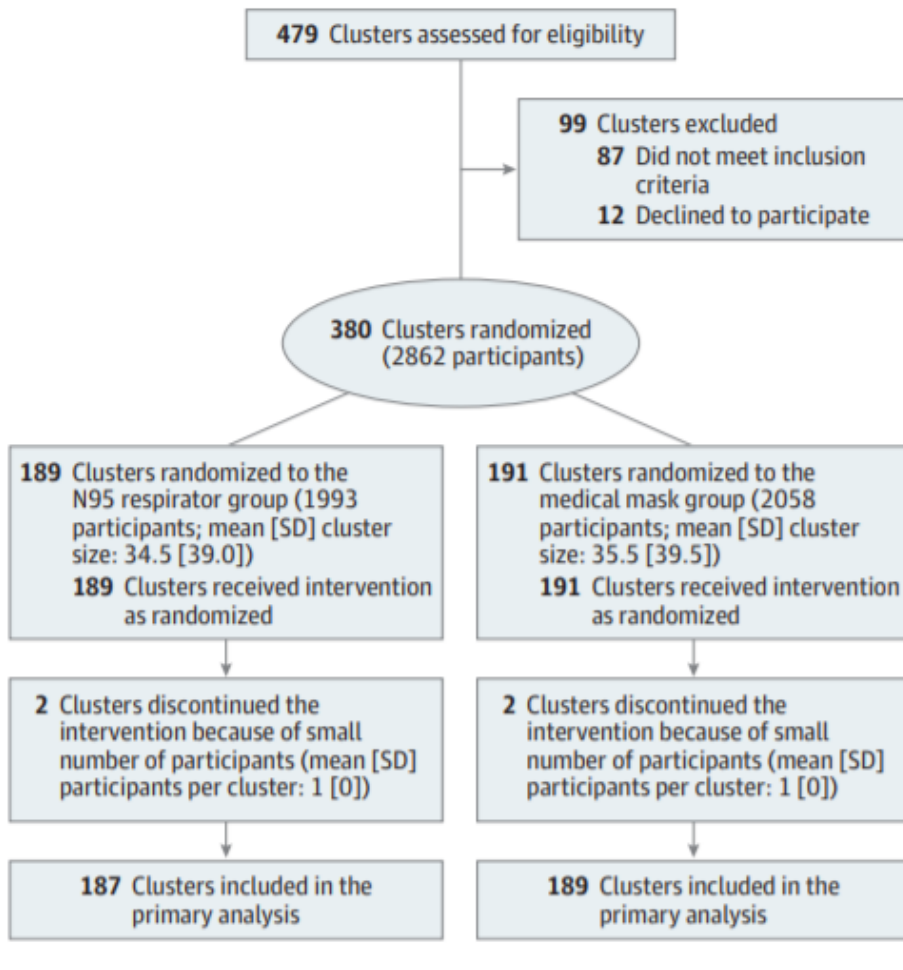
#### Statistical Analyses

Although we identified no standard definition of a “clinically significant difference,” this study<sup>16</sup> was designed to detect a 25% relative reduction in the incidence of laboratory-confirmed influenza or respiratory illness, based on expert opinion, rather than an absolute reduction, which has been described in a previous study.<sup>6</sup> The total sample size required to provide 80% power to show a 25% reduction in the incidence of laboratory-confirmed influenza in the N95 respirator group compared with the medical mask group, with a type I error rate of .05, was 10 024 participant-sessions, and the sample size needed to provide 80% power to show a 25% reduction in the incidence of laboratory-confirmed respiratory illness was 5104 participant-seasons. Comparative effects of the interventions were estimated for the

primary and secondary outcomes by calculating odds ratios (ORs; for binary outcomes) and incidence rate ratios (IRRs; for count outcomes) between participant clusters randomly assigned to wear N95 respirators or medical masks. Laboratory-confirmed influenza was modeled using logistic regression and viral respiratory infection and illness outcomes were modeled using Poisson regression. Unadjusted and adjusted analyses (both prespecified) were conducted according to the statistical analysis plan (Supplement 2). The primary outcome was an adjusted analysis, as specified in the statistical analysis plan. Prespecified covariates used in adjusted analyses included age, sex, race, number of household members younger than 5 years, occupation risk level (defined as low, medium, or high), binary season-specific influenza vaccination status, the proportion of daily exposures to others with respiratory illness, categorical self-reported adherence to hand hygiene, and intervention group assignment. Prespecified adherence rates were calculated as the proportion of reports of adherence in each group reporting “always,” “sometimes,” “never,” or “did not recall.” Comparison of proportions between groups were done using  $\chi^2$  statistics and comparisons of binomial proportions. Analyses included random effects to account for correlation of outcomes at site-level and individual-level random effects to account for correlation of outcomes at the individual level for participants who participated for multiple seasons. The primary analysis used available data on all randomized participants for the primary comparison of the intervention. A per-protocol analysis, conducted at the same time as the primary analysis, included only individuals who completed at least 8 weeks of study participation. A sensitivity analysis was conducted using imputation to assign outcomes to participants who did not complete the study. Missing outcomes were imputed using standard multiple imputation techniques, creating multiple imputed data sets with no missing values for each analysis.<sup>23</sup> Details of this analysis are described in Supplement 2. Intervention group withdrawal rates and time to withdrawal were compared to assess for potential bias. In an additional sensitivity analysis, observed and self-reported exposures and adherence were compared using Pearson  $\chi^2$  tests. Mean workplace and household rates of exposure to respiratory illness were compared using mixed-effects logistic regression. For all calculations, a 2-sided type I error probability of .05 was used. Because of the potential for type I error due to multiple comparisons, findings for analyses of secondary end points should be interpreted as exploratory. All statistical analyses were performed in R version 3.3.3 (R Foundation).



**Figure 1. Study Site Enrollment, Randomization, Follow-up, and Analysis in a Study of the Effect of N95 Respirators vs Medical Masks for Preventing Laboratory-Confirmed Influenza Among Health Care Personnel**



## Results

### Participants

The study sites were randomized to provide 380 clusterseasons of observation over 4 consecutive intervention periods. Of the 2862 participants, 1416 participated for more than 1 year or intervention period. Among 2862 unique randomized participants (mean [SD] age, 43 [11.5] years; 2369 [82.8%] women), 2371 completed the ResPECT protocol over the course of 48 weeks of intervention spanning 4 years. Among these individuals, 1446 participated in one 12-week intervention period, 723 participated in two 12-week intervention periods, and 693 participated in 3 or more 12-week intervention periods, accounting for 5180 HCP-seasons enrolled and randomized from 137 medical centers. Following randomization, 491 participants

withdrew or were excluded because the cluster size was below a preestablished threshold of 2. Overall, 4689 HCP-seasons were included in the per-protocol analysis (2243 in the N95 respirator group and 2446 in the medical mask group; Figure 1). Some members of the primary analytic cohort did not complete all weeks of the study and were missing serological outcomes. Data were missing because of early withdrawal in 189 of 2512 participants (7.5%) in the N95 respirator group and 145 of 2668 (5.4%) in the medical mask group. In the per-protocol analysis, data were missing from 16 of 2243 participants (0.7%) in the N95 respirator group and 28 of 2446 (1.1%) in the medical mask group. Baseline characteristics of the participants in the N95 respirator and medical mask groups were similar (Table 1). Daily workplace exposure to respiratory illness was reported 22.5% of the time in the N95 group and 21.6% of the time in the medical mask group, while weekly household exposure to respiratory illness was reported 3.6% of the time in the N95 respirator group and 3.4% of the time in the medical mask group (Table 1).

### Illness Surveillance and Effectiveness

In the primary analysis, the incidence of laboratory-confirmed influenza infection events occurred in 207 of 2512 HCP-seasons (8.2%) in the N95 respirator group and 193 of 2668 HCP-seasons (7.2%) in the medical mask group, (difference, 1.0% [95% CI, -0.5% to 2.5%];  $P = .18$ ) (adjusted OR, 1.18 [95% CI, 0.95-1.45]). Regarding secondary outcomes, there were 1556 acute respiratory illness events in the N95 respirator group (incidence rate [IR], 619.4 per 1000 HCP-seasons) vs 1711 in the medical mask group (IR, 641.3 per 1000 HCP-seasons) (difference, -21.9 per 1000 HCP-seasons [95% CI, -48.2 to 4.4];  $P = .10$ ; adjusted IRR, 0.99 [95% CI, 0.92-1.06]). There were 679 laboratory-detected respiratory infection events in the N95 respirator group (IR, 270.3 per 1000 HCP-seasons) vs 745 in the medical mask group (IR, 279.2 per 1000 HCP-seasons) (difference, -8.9 per 1000 HCP-seasons [95% CI, -33.3 to 15.4];  $P = .47$ ; adjusted IRR, 0.99 [95% CI, 0.89- 1.09]) (Table 2 and Figure 2). Overall, 371 laboratory-confirmed respiratory illness events occurred in the N95 respirator group (IR, 147.7 per 1000 HCP-seasons) vs 417 in the medical mask group (IR, 156.3 per 1000 HCP-seasons) (difference, -8.6 per 1000 HCP-seasons [95% CI, -28.2 to 10.9];  $P = .39$ ; adjusted IRR, 0.96 [95% CI, 0.83-1.11]). There were 128 influenzalike illness events in the N95 respirator group (IR, 51.0 per 1000 HCP-seasons) vs 166 in the medical mask group (IR, 62.2 per 1000 HCP-seasons) (difference, -11.3 per 1000 HCP-seasons [95% CI, -23.8 to 1.3];  $P = .08$ ; adjusted IRR, 0.86 [95% CI, 0.68-1.10]). Results were similar in the adjusted primary analysis and per-protocol analyses (Figure 2).

### Intervention, Adherence, and Adverse Events

Adherence was reported on daily surveys 22 330 times in the N95 respirator group and 23 315 times in the medical mask group. "Always" was reported 14 566 (65.2%) times in the N95 respirator group and 15 186 (65.1%) times in the medical mask group; "sometimes," 5407 (24.2%) times in the N95 respirator group and 5853 (25.1%) times in the medical mask group; "never," 2272 (10.2%) times in the N95 respirator group and 2207 (9.5%) times in the medical mask group; and "did not recall," 85 (0.4%) times in the N95 respirator group and 69 (0.3%)

times in the medical mask group. Participant-reported adherence could not be assessed in 784 participants (31.2%) in the N95 respirator group and 822 (30.8%) in the medical mask group (P = .84)

because of lack of response to surveys or lack of adherence opportunities (ie, participants did not encounter an individual with respiratory signs or symptoms). Analyzed post hoc, participant adherence was reported as always or sometimes 89.4% of the time in the N95 respirator group and 90.2% of the time in the medical mask group. Additional details about adherence are included in Supplement 1. No serious study-related adverse events were reported. Nineteen participants reported skin irritation or worsening acne during years 3 and 4 at one study site in the N95 respirator group.

#### Per-Protocol Analysis and Sensitivity Analysis

Results of the per-protocol analysis can be seen in Figure 2. A sensitivity analysis assessed whether there was evidence for bias in self-reported outcomes based on group assignment. In a prespecified multiple-imputation analysis, the rates of laboratory-confirmed influenza infection events were 204 of 2243 HCP seasons (9.1%) in the N95 respirator group and 190 of 2446 HCP-seasons (7.8%) in the medical mask group. Quantitative data are available in Supplement 3.

**Table 1. Health Care Personnel (HCP) Demographic Characteristics, Risk Factors, and Site Enrollment in a Study of the Effect of N95 Respirators vs Medical Masks for Preventing Laboratory-Confirmed Influenza**

Characteristic	No. (%)	
	N95 Respirator (n = 2512 HCP-Seasons) <sup>a</sup>	Medical Mask (n = 2668 HCP-Seasons) <sup>a</sup>
Age, mean (SD), y	43 (11.5)	43 (11.6)
<b>Sex</b>		
Men	378 (15.0)	420 (15.7)
Women	2134 (85.0)	2248 (84.3)
<b>Ethnicity</b>		
Hispanic or Latino	397 (15.8)	427 (16)
<b>Race</b>		
	(n = 2447)	(n = 2600)
White	1282 (52.4)	1334 (51.3)
Black	720 (29.4)	782 (30.1)
Other	232 (9.5)	252 (9.7)
Asian	195 (8.0)	210 (8.1)
American Indian or Alaska Native	14 (0.6)	13 (0.5)
Native Hawaiian or other Pacific Islander	4 (0.2)	9 (0.3)
<b>Occupation</b>		
Nurse/nursing trainee	1049 (41.8)	1085 (40.7)
Clinical care support staff <sup>b</sup>	574 (22.9)	627 (23.5)
Administrative/clerical	332 (13.2)	337 (12.6)
Other occupation	213 (8.5)	224 (8.4)
Physician/advanced practitioner/physician trainee	207 (8.2)	240 (9.0)
Registration/clerical reception	94 (3.7)	106 (4.0)
Social worker/pastoral care	35 (1.4)	29 (1.1)
Environmental services/housekeeping	8 (0.3)	19 (0.7)
<b>Occupational risk<sup>c</sup></b>		
High	1492 (59.4)	1594 (59.7)
Medium	295 (11.7)	318 (11.9)
Low	724 (28.8)	755 (28.3)
<b>Patient population</b>		
Adult	1409 (56.1)	1486 (55.7)
Pediatric	573 (22.8)	557 (20.9)
Adult and pediatric	530 (21.1)	625 (23.4)
<b>Clinic type</b>		
Primary care	1734 (69.0)	1881 (70.5)
Emergent/urgent care	665 (26.5)	700 (26.2)
Emergency transport	42 (1.7)	33 (1.2)
Specialty care	40 (1.6)	29 (1.1)
Dental/dialysis	31 (1.2)	25 (0.9)
<b>Site</b>		
Johns Hopkins Health System	882 (35.1)	859 (32.2)
Denver Health	534 (21.3)	521 (19.5)
VA New York Harbor Healthcare System	375 (14.9)	433 (16.2)
The Michael E. DeBakey VA Medical Center	233 (9.3)	287 (10.8)
Washington DC VA Medical Center	183 (7.3)	204 (7.6)
VA Eastern Colorado Healthcare System	177 (7.0)	211 (7.9)
Children's Hospital Colorado	128 (5.1)	153 (5.7)

(continued)

**Table 1. Health Care Personnel (HCP) Demographic Characteristics, Risk Factors, and Site Enrollment in a Study of the Effect of N95 Respirators vs Medical Masks for Preventing Laboratory-Confirmed Influenza (continued)**

Characteristic	No. (%)	
	N95 Respirator (n = 2512 HCP-Seasons) <sup>a</sup>	Medical Mask (n = 2668 HCP-Seasons) <sup>a</sup>
Comorbid conditions		
Asthma	255 (10.2)	284 (10.6)
Other systemic disease	104 (4.1)	118 (4.4)
Other respiratory disease	49 (2.0)	37 (1.4)
Cardiac disease	41 (1.6)	34 (1.3)
Chronic obstructive pulmonary disease	6 (0.2)	6 (0.2)
Influenza vaccination status		
Vaccinated	1993 (79.3)	2048 (76.8)
Not vaccinated	451 (18.0)	550 (20.6)
Other risk factors		
Eyeglasses wearer	960 (38.2)	999 (37.4)
Household members aged <5 y	606 (24.1)	630 (23.6)
Contact lens wearer	371 (14.8)	349 (13.1)
Tobacco smoker	210 (8.4)	234 (8.8)
Exposure to respiratory illness, %		
Daily workplace	22.5	21.6
Weekly household	3.6	3.4

Abbreviation: VA, veterans affairs.

<sup>a</sup> Unless otherwise specified.

<sup>b</sup> Staff who have direct patient contact, such as clinical medical assistants and clinical technicians.

<sup>c</sup> Occupational risk based on direct patient contact, such as physical examination and/or performance of high-risk procedures (intubation, airway suctioning, nebulizer treatments, nasopharyngeal aspiration) for high risk, direct patient contact for medium risk, and no or minimal direct patient contact for low risk.

Table 2. Primary and Secondary Outcomes in a Study of the Effect of N95 Respirators vs Medical Masks for Preventing Laboratory-Confirmed Influenza Among Health Care Personnel

Primary and Secondary Outcome Events	No.									
	2011-2012		2012-2013		2013-2014		2014-2015		Totals	
	N95 Respirator	Medical Mask	N95 Respirator	Medical Mask	N95 Respirator	Medical Mask	N95 Respirator	Medical Mask	N95 Respirator	Medical Mask
<b>Influenza (primary outcome)</b>										
Polymerase chain reaction-detected										
Influenza A	2	3	19	19	8	12	37	28	66	62
Influenza B	0	3	8	11	2	1	1	4	11	19
Hemagglutination inhibition assay-detected										
Influenza A	5	9	30	23	38	38	55	47	128	117
Influenza B	0	2	10	11	12	13	14	10	36	36
<b>All events<sup>a</sup></b>										
Influenza A	6	10	43	37	46	42	85	65	180	154
Influenza B	0	5	15	18	12	14	15	13	42	50
All influenza	6	15	58	55	58	56	100	78	222	204
Laboratory-confirmed influenza	6	13	52	52	55	51	94	77	207	193
<b>Secondary Outcomes</b>										
Acute respiratory illness	235	234	354	446	398	519	569	512	1556	1711
Laboratory-detected respiratory infection <sup>b</sup>	47	71	165	201	217	260	250	213	679	745
Laboratory-confirmed respiratory illness <sup>b</sup>	26	31	91	116	111	150	143	120	371	417
Influenzalike illness	13	10	30	45	22	50	63	61	128	166

<sup>a</sup> Influenza events were defined as the number of influenza infections attributed to the combination of polymerase chain reaction detection and hemagglutination

inhibition assay serologies. Instances in which polymerase chain reaction and hemagglutination inhibition assay were both positive counted as 1 event.

<sup>b</sup> All respiratory viruses assayed, including influenza.

## DISCUSSION

In this pragmatic, cluster randomized trial that involved multiple outpatient sites at 7 health care delivery systems across a wide geographic area over 4 seasons of peak viral respiratory illness, there was no significant difference between the effectiveness of N95 respirators and medical masks in preventing laboratory-confirmed influenza among participants routinely exposed to respiratory illnesses in the workplace. In addition, there were no significant differences between N95 respirators and medical masks in the rates of acute respiratory illness, laboratory-detected respiratory infections, laboratory-confirmed respiratory illness, and influenzalike illness among participants. A sensitivity analysis suggested that the primary analysis reported was fairly robust to the missing outcome data with quantitative outcomes varying by less than 5%. This supports the finding that neither N95 respirators nor medical masks were more effective in preventing laboratory confirmed influenza or other viral

respiratory infection or illness among participants when worn in a fashion consistent with current US clinical practice. Respiratory viruses are primarily transmitted by large droplets. Because a fraction of respiratory viruses may be transmitted by aerosol, N95 respirators have been presumed to provide better protection than medical masks against viral respiratory infections in health care settings.<sup>2</sup> However, definitive evidence of greater clinical effectiveness of N95 respirators is lacking. A well-designed trial<sup>6</sup> found the effectiveness of medical masks to be noninferior to N95 respirators, but the trial was stopped prematurely and was limited by small sample size. Two additional studies<sup>3,4</sup> (and a pooled analysis<sup>12</sup>) concluded that N95 respirators may be more effective than medical masks; however, these studies were limited by uncertain clinical significance of end points.<sup>24</sup> The current study was undertaken because of remaining uncertainty based on previous studies, which made it challenging for infection control clinicians to effectively implement respiratory protection programs in health care settings.<sup>2,7,13,18,24,25</sup> This trial was designed to assess clinical effectiveness, taking into account many challenges of working in outpatient health care settings. This study had several strengths, including the pragmatic design; wide US geographic and climatic distribution; varied adult and pediatric outpatient settings, including emergency departments; and enrollment spanning 4 seasons of peak viral respiratory illness. Respiratory samples were obtained from symptomatic and asymptomatic participants to determine the incidence of viral respiratory infection, including individuals that were subclinical but still potentially transmissible. Influenza vaccination status information was collected. This trial was cluster randomized to avoid mixing of interventions in each clinic and clinical setting and to minimize cross-contamination from different HCP behaviors, conducted at 7 medical centers among frontline HCP in varied clinical settings with high exposure risk, and sufficiently powered to detect the predefined difference in laboratory-confirmed respiratory illness. Previous effectiveness studies<sup>3,4,6,12,26-28</sup> have met some, but not all, of these characteristics and have been inconclusive, contributing to the uncertainty and controversy among experts determining public health guidance, regulatory requirements, and health care delivery practices.<sup>2,7,14,17,29</sup> In the current study, findings were consistent across all laboratory-based outcomes and clinical syndromes. Results for the primary and secondary outcomes were in opposite directions (ie, one IRR was associated with increased risk and the other with decreased risk), although the differences were nonsignificant, further supporting a finding of no significant difference in the effectiveness of N95 respirators vs medical masks for prevention of influenza or other respiratory illness.

### Limitations

This study has several limitations. First, the criteria for viral polymerase chain reaction testing may have missed participants who were infected but asymptomatic. Unrecognized infections may have increased the probability of finding no difference between interventions, even if a difference existed. Second, self-reporting of symptoms in daily diaries likely underestimated illness among HCP who often work while ill.<sup>30</sup> Third, despite being intentionally conducted as a pragmatic effectiveness trial,<sup>8</sup> incomplete participant adherence to assigned protective devices could have contributed to more unprotected exposures, increasing the probability of finding no

difference between interventions even if a difference existed. However, participant-reported data indicates this did not differ by study group. Fourth, participants were not instructed to wear protective devices outside the workplace, which may have biased the results toward finding no difference between groups, although the rates of adherence did not differ by study group and household exposure was reported as much lower than workplace exposure. Fifth, only 2 N95 respirator and medical mask models were studied, limiting the ability to generalize about the protectiveness of other models. Sixth, the sample size required to definitively determine whether N95 respirators or medical masks are more effective for protection from laboratory-confirmed influenza in the health care setting required approximately 10 000 participant seasons, which was not feasible with the available funding or resources. However, the morbidity and mortality associated with a wide range of viral respiratory infections, including novel and emerging pathogens, renders a secondary outcome in this study, laboratory-confirmed respiratory illness, important.

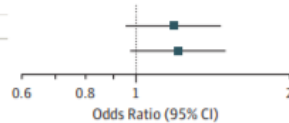
## CONCLUSIONS

Among outpatient HCP, N95 respirators vs medical masks as worn by participants in this trial resulted in no significant difference in the incidence of laboratory-confirmed influenza.

**Figure 2. Primary and Secondary Outcomes of Influenza and Respiratory Illnesses and Adjusted Risk Estimates Among Health Care Personnel in the N95 Respirator Group vs the Medical Mask Group**

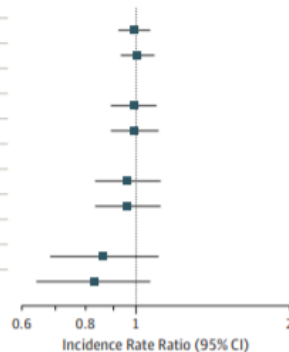
### A Primary outcome

	N95 Respirator Events/Seasons	Medical Mask Events/Seasons	Incidence Rate Ratio (95% CI)
Laboratory-confirmed influenza			
ITT cohort	207/2512	193/2668	1.18 (0.95-1.45)
PP cohort	204/2243	190/2446	1.20 (0.97-1.48)



### B All secondary outcomes

	N95 Respirator Events/Seasons	Medical Mask Events/Seasons	Incidence Rate Ratio (95% CI)
Acute respiratory illness			
ITT cohort	1556/2512	1711/2668	0.99 (0.92-1.06)
PP cohort	1512/2243	1656/2446	1.00 (0.93-1.08)
Laboratory-detected respiratory infection			
ITT cohort	679/2512	745/2668	0.99 (0.89-1.09)
PP cohort	664/2243	733/2446	0.99 (0.89-1.10)
Laboratory-confirmed respiratory illness			
ITT cohort	371/2512	417/2668	0.96 (0.83-1.11)
PP cohort	361/2243	406/2446	0.96 (0.83-1.11)
Influenza-like illness			
ITT cohort	128/2512	166/2668	0.86 (0.68-1.10)
PP cohort	121/2243	161/2446	0.83 (0.64-1.06)



The adjusted relative risks for the N95 respirator and medical mask groups for both the intention-to-treat (ITT) and per-protocol (PP) groups for the primary outcome and the other predetermined secondary outcomes. Values above 1 indicate higher relative odds or risk in the N95 respirator group compared with the medical mask group.



## **Surgical Mask vs N95 Respirator for Preventing Influenza Among Health Care Workers**

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Context Data about the effectiveness of the surgical mask compared with the N95 respirator for protecting health care workers against influenza are sparse. Given the likelihood that N95 respirators will be in short supply during a pandemic and not available in many countries, knowing the effectiveness of the surgical mask is of public health importance.

Objective To compare the surgical mask with the N95 respirator in protecting health care workers against influenza.

Design, Setting, and Participants Noninferiority randomized controlled trial of 446 nurses in emergency departments, medical units, and pediatric units in 8 tertiary care Ontario hospitals.

Intervention Assignment to either a fit-tested N95 respirator or a surgical mask when providing care to patients with febrile respiratory illness during the 2008-2009 influenza season.

Main Outcome Measures The primary outcome was laboratory-confirmed influenza measured by polymerase chain reaction or a 4-fold rise in hemagglutinin titers. Effectiveness of the surgical mask was assessed as noninferiority of the surgical mask compared with the N95 respirator. The criterion for noninferiority was met if the lower limit of the 95% confidence interval (CI) for the reduction in incidence (N95 respirator minus surgical group) was greater than -9%.

Results Between September 23, 2008, and December 8, 2008, 478 nurses were assessed for eligibility and 446 nurses were enrolled and randomly assigned the intervention; 225 were allocated to receive surgical masks and 221 to N95 respirators. Influenza infection occurred in 50 nurses (23.6%) in the surgical mask group and in 48 (22.9%) in the N95 respirator group (absolute risk difference,

-0.73%; 95% CI, -8.8% to 7.3%; P=.86), the lower confidence limit being inside the noninferiority limit of -9%.

**Conclusion** Among nurses in Ontario tertiary care hospitals, use of a surgical mask compared with an N95 respirator resulted in noninferior rates of laboratory confirmed influenza.

**INFLUENZA CAUSES ANNUAL EPIDEMICS** of respiratory illness worldwide and is the most important cause of medically attended acute respiratory illness.<sup>1,2</sup> Moreover, there is increasing concern about the recently declared influenza pandemic due to 2009 influenza A(H1N1) in humans.<sup>3-5</sup> Transmission of influenza can occur by coughing or sneezing where infectious particles of variable size, ranging from approximately 0.1 to 100  $\mu\text{m}$ , may be inhaled.<sup>6</sup> This range of particles has a yet undefined but possibly important role in transmission. Although data from animal models and human experimental studies suggest that short-range inhalational transmission with small droplet nuclei (10  $\mu\text{m}$ ) can occur,<sup>7-11</sup> the exact nature of transmission of influenza that occurs in nonexperimental settings is not well understood.<sup>12</sup> As a consequence, considerable uncertainty exists about the effectiveness of personal respiratory devices against influenza for health care workers. During a pandemic, reducing transmission of influenza to health care workers may not only help support the health care workforce, but may also prevent influenza transmission to patients. Other personal protective strategies, such as effective vaccines or antiviral drugs, may be limited in availability. Given the likelihood that N95 respirators will be in short supply during a pandemic and unavailable in many countries, understanding the relative effectiveness of personal respiratory protective equipment is important. There are few comparative studies of respiratory protective devices,<sup>13-15</sup> and data comparing the surgical mask with the N95 respirator among health care workers are sparse. We conducted a randomized trial to compare the surgical mask with the N95 respirator in health care workers. We hypothesized that the surgical mask, which is less expensive and more widely available than the N95 respirator, offers similar protection to the N95 respirator among health care workers at highest risk for exposure to influenza.

**METHODS** **Participants** We enrolled nurses who worked in emergency departments, medical units, and pediatric units in 8 Ontario tertiary care

hospitals, of which 6 were within the greater Toronto area. Six of the 8 hospitals were university affiliated teaching hospitals (range of bed size, 310-400) and 2 were community hospitals (bed sizes, 256 and 400). Participants were enrolled from a total of 22 units, which included 9 acute medical units, 7 emergency departments, and 6 pediatric units. There were an average of 34 beds (range, 14-60 beds) on the medical units and an average of 27 beds (range, 19-38) on the pediatric units. Nurses expected to work full-time (defined as 37 hours per week) on study units during the 2008-2009 influenza season were eligible. Nurses had to provide current fit-test certification. Nurses who could not pass a fit test were excluded from the study. The research protocol was approved by the McMaster University research ethics review board. All participants gave written informed consent. Interventions Randomization was performed centrally by an independent clinical trials coordinating group such that investigators were blind to the randomization procedure and group assignment and was stratified by center in permuted blocks of 4 participants. It was not possible to conceal the identity of the N95 respirator or the surgical mask since manipulating these devices would interfere with their function. Laboratory personnel conducting hemagglutinin inhibition assays, polymerase chain reaction (PCR), and viral culture for influenza were blinded to allocation. Nurses allocated to the surgical mask group were required to wear the brand of surgical mask already in use at their hospital. Following the severe acute respiratory syndrome (SARS) outbreak in Ontario, use of such a surgical mask was required by the Ministry of Health and Long-Term Care when providing care to or when within 1 m of a patient with febrile respiratory illness, defined as symptoms of a body temperature 38°C or greater and new or worsening cough or shortness of breath.<sup>16</sup> Nurses were instructed in proper placement of the surgical mask according to the manufacturer's recommendations. Since fit testing is mandatory for nurses in Ontario, the majority of nurses in the study had been fit tested prior to enrollment; additional fit testing was conducted for nurses who had not been fit tested in 2008. Using a standard protocol, a technician showed the participant how to position the respirator and fasten the strap and determine whether it provided an acceptable fit. The nurse was asked to wear the most comfortable mask for at least 5 minutes to assess fit. Adequacy of the respiratory fit was assessed using standard criteria, including chin placement, adequate strap tension, appropriate respirator size, fit across nose bridge, tendency of respirator

to slip, and position of mask on face and cheeks. The nurse then conducted a user seal check.<sup>17</sup> Nurses had a qualitative fit testing using the saccharin or Bitrex protocol.<sup>17</sup> Nurses were asked to begin using the surgical mask or N95 respirator when caring for patients with febrile respiratory illness at the beginning of the influenza season, which was defined as 2 or more consecutive isolations of influenza per week in each study region. Nurses wore gloves and gowns when entering the room of a patient with febrile respiratory illness, which was routine practice. For aerosol-generating procedures (such as intubation or bronchoscopy), as long as tuberculosis was not suspected, nurses continued to use the respiratory device they were assigned to. We had planned to stop the study at the end of influenza season. However, because of the 2009 influenza A(H1N1) pandemic, the study was stopped on April 23, 2009, when the Ontario Ministry of Health and Long-Term Care recommended N95 respirators for all health care workers taking care of patients with febrile respiratory illness. Follow-up All participants were assessed for signs and symptoms of influenza twice weekly using Web-based questionnaires. Response to the questionnaire was monitored centrally and participants who failed to provide a response were contacted and asked to complete the questionnaire. If a new symptom was reported, the study nurse was notified and a flocked nasal specimen (Copan Italia, Brescia, Italy) was obtained by the participants. They were trained to insert the swab into the left or right nostril and rotate the swab at least 3 times and to conduct self-swabbing if any of 1 of the following symptoms or signs were present: fever (temperature

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38°C), cough, nasal congestion, sore throat, headache, sinus problems, muscle aches, fatigue, earache, ear infection, or chills. We also provided participants with tympanic thermometers. To assess household exposures between study groups, we asked participants whether household members (spouses, roommates, or children) had experienced influenza-like illness over the study period. Outcomes The primary outcome of this study was laboratory-confirmed influenza. This was defined by either the detection of viral RNA using reverse-transcriptase (RT) PCR from nasopharyngeal and flocked nasal specimens or at least a 4-fold rise in serum antibodies to circulating influenza strain antigens. All nasopharyngeal or nasal specimens were tested for influenza and other respiratory viruses with the xTAG Respiratory Virus Panel test (Luminex Molecular Diagnostics, Toronto, Ontario, Canada).<sup>18</sup> This multiplex PCR assay detects influenza A virus subtypes

H1 (seasonal), H3, and H5 as well as the majority of other viruses that cause respiratory illness in humans. Blood specimens for serology were obtained prior to enrollment and at the end of the follow-up period. Serological infection was defined by detection of 4-fold or greater increase in influenza-specific hemagglutinin inhibition assay titer between baseline and convalescent serum samples using guinea pig erythrocytes and the antigens circulating A/Brisbane/59/2007(H1N1)- like virus; A/Brisbane/10/2007(H3N2)- like virus; B/Florida/4/2006-like virus; and A/TN/1560/09(H1N1), the circulating pandemic influenza virus. For A/Brisbane/59/2007(H1N1)-like virus, A/Brisbane/10/2007(H3N2)- like virus, and B/Florida/4/2006-like virus, we restricted serological criteria of infection to nurses who did not receive the trivalent 2008-2009 influenza vaccine to reduce misclassification due to vaccine response. Secondary outcomes included detection of the following noninfluenza viruses by PCR: parainfluenza virus types 1, 2, 3, and 4; respiratory syncytial virus types A and B; adenovirus; metapneumovirus; rhinovirus-enterovirus; and coronaviruses OC43, 229E, SARS, NL63, and HKU1. Influenza-like illness was defined as the presence of cough and fever (temperature

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38°C).<sup>19</sup> Work-related absenteeism and physician visits for respiratory illness were also assessed. Audits To assess compliance of participants with the assigned mask or N95 respirator, we conducted audits during what we anticipated was peak influenza period, from March 11 to April 3, 2009. Medical and pediatric hospital study units at all centers with nurses participating in the study were contacted by telephone daily by a research assistant to assess whether there were patients admitted to the unit in droplet precautions for influenza or febrile respiratory illness. If there were such cases and if the primary nurse for the patient was enrolled in our study, a trained auditor was sent to the unit to observe for compliance. The auditor was instructed to stand a short distance from the patient isolation room to remain inconspicuous but within distance to accurately record the audit. Auditors were asked to remain on the unit until they recorded the type of protective equipment worn by the participant prior to the participant entering the isolation room. To maintain patient confidentiality and to remain anonymous to the study participant, no audits were conducted within the patient's room. Once an audit was conducted, the session was completed. Audits were conducted both on weekdays and on weekends during day and evening

shifts. Assessment of hand hygiene was not conducted. Statistical Analysis The effectiveness of the surgical mask was assessed through a noninferiority analysis relative to the N95 respirator.<sup>20</sup> For the primary analysis, the difference in the incidence of laboratory confirmed influenza between the N95 respirator group and surgical mask group was estimated and the corresponding 2-sided 95% confidence interval (CI) was calculated. We used the Fisher exact test to assess statistical significance in contingency tables having expected cell frequencies less than 5. Noninferiority to the N95 respirator was achieved if the lower limit of the 95% CI for the reduction in incidence (N95 respirator minus surgical group) was greater than the prespecified noninferiority limit of -9%. Assuming an event rate of 20% in controls, this limit was selected on a clinical basis considering that laboratory confirmed influenza would include asymptomatic cases in addition to symptomatic cases of influenza. Infection detected by serology can account for up to 75% of cases of laboratory confirmed influenza where febrile illness is not present.<sup>21</sup> Since we did not anticipate severe outcomes (eg, mortality) in the study sample, we used a similar approach for influenza-like illness, work-related absenteeism, and physician visits for respiratory illness. All participants who had follow-up data collected (ie, had not withdrawn prior to any follow-up after they had been randomized) were included in the analysis. Since intention to-treat analyses in noninferiority trials may be biased toward finding no difference, we also conducted an analysis of our primary outcome using only data from participants with complete follow-up.<sup>22</sup> To avoid lack of independence associated with counting multiple outcomes, each specific outcome in a participant was only counted once. With a power of 90% and a 2-sided type-I error rate of 5%, the required sample would be 191 participants in each group for a noninferiority test assuming an absolute risk reduction of 12% in the N95 respirator group compared with the surgical mask. If the absolute reduction was assumed to be 10%, a statistical power of 80% would be maintained. The absolute risk reductions selected were based on consensus by clinician investigators. Assuming a 10% dropout rate, we estimated that a total of 420 participants would be needed. SAS version 9.1.3 (SAS Institute, Cary, North Carolina) was used to conduct the analyses. RESULTS Between September 23, 2008, and December 8, 2008, 478 nurses were assessed for eligibility and 446 participants from 8 centers in Ontario were enrolled. They were then randomly assigned the intervention, 225 to the surgical mask and 221 to the N95 respirator (FIGURE). The mean age of

participants was 36.2 years, 94% of them were female, and study groups were well balanced in terms of demographics (TABLE 1). Vaccination status was similar: 68 participants (30.2%) in the surgical mask group and 62 (28.1%) in the N95 respirator group had received 2008-2009 trivalent inactivated influenza vaccine. Follow-up began January 12, 2009, and ended April 23, 2009. Mean (SD) duration of follow-up was similar between groups: 97.9 (16.1) days in the surgical group and 97.2 (18.0) days in the N95 respirator group. There were 24 participants who withdrew from the study with no follow-up—13 in the surgical mask group and 11 in the N95 respirator group—because of resignation or transfer (n=5), working part-time (n=1), no response (n=13), or illness (n=5) (Figure). None of the health care workers withdrew because of respiratory illness. Of the resulting 422 (all of whom were in the analysis), follow-up was complete in 386 (91.4%), and 403 (95.5%) had acute and convalescent sera collected. There were 223 nasal specimens obtained (115 in the surgical mask group and 108 in the N95 respirator group). Laboratory-confirmed influenza (by RT-PCR or

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4-fold rise in serum titers) occurred in 50 nurses (23.6%) in the surgical mask group and in 48 (22.9%) in the N95 respirator group (absolute risk difference, -0.73%; 95% CI, -8.8% to 7.3%; P=.86), indicating noninferiority of the surgical mask (TABLE 2). The diagnosis of influenza was made by RT-PCR in 6 nurses (2.8%) in the surgical mask group (5 influenza A and 1 influenza B) and 4 (1.8%) in the N95 respirator group (1 influenza A and 3 influenza B) (absolute risk difference, -0.93%; 95% CI, -3.82% to 1.97%; P=.75). Four of the influenza A cases detected by PCR were H1 (all in the surgical mask group). The serology results are summarized in Table 2. Notably, 8.0% in the surgical mask group and 11.9% in the N95 respirator group had a 4-fold or greater rise in serum titers to A/TN/1560/09(H1N1), the circulating pandemic swine influenza strain. Noninferiority was demonstrated between the surgical mask group and the N95 respirator group for 2009 influenza A(H1N1) (absolute risk difference, 3.89%; 95% CI, -1.82% to 9.59%; P=.18). When the analysis was conducted using only the data from participants with complete follow-up visits, laboratory-confirmed influenza (by RTPCR or

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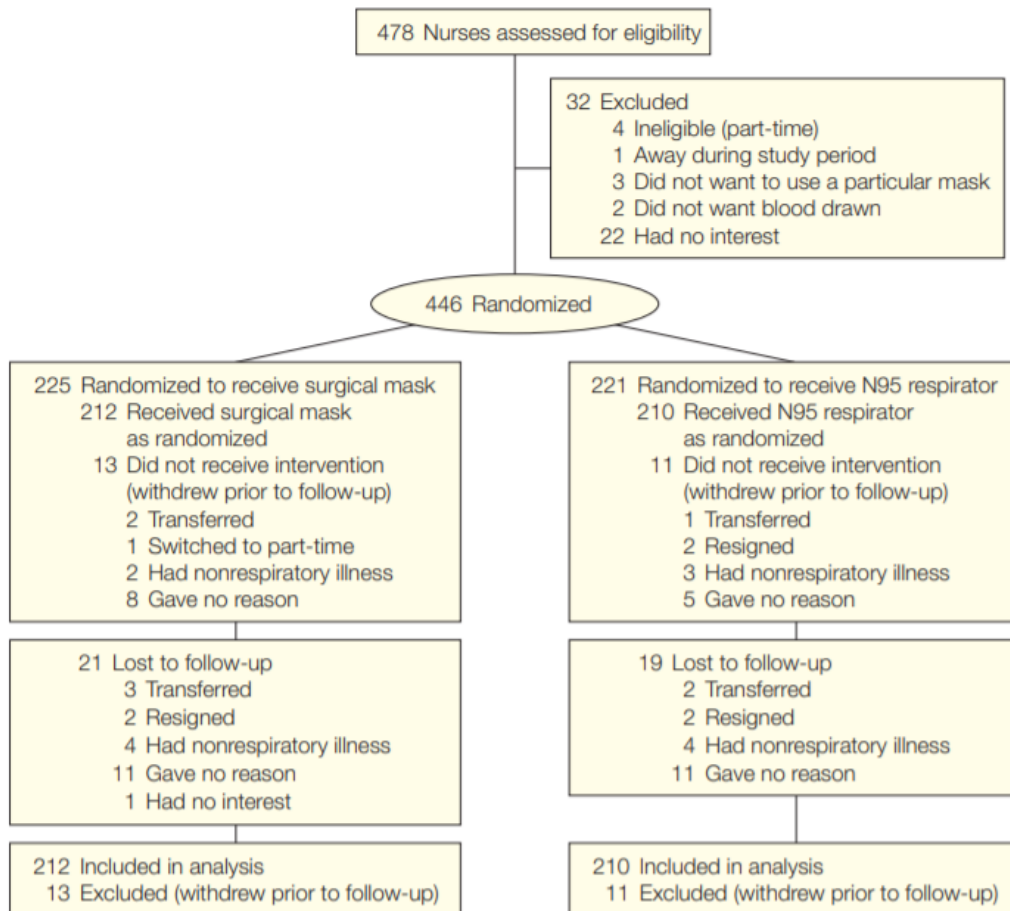
4-fold rise in serum titers) occurred in 66 nurses (33.9%) in the surgical mask group and in 72 (37.7%) in the N95 respirator group (absolute risk difference,

3.85%; 95% CI, -5.71% to 13.41%; P=.43), indicating noninferiority. No adenoviruses; no respiratory syncytial virus type A; and no parainfluenza 1, 2, and 4 viruses were detected by PCR. There were no significant differences between the surgical mask and N95 respirator groups in respiratory syncytial virus type B, metapneumovirus, parainfluenza 3, rhinovirus/enterovirus, or coronaviruses. The lower CIs for the differences were greater than -9%, meeting our criteria for noninferiority (TABLE 3). All 52 (100%) of those having infection with a respiratory virus other than influenza had 1 or more symptoms, but they did not meet the influenza-like illness definition. Nine nurses (4.2%) in the surgical mask group and 2 nurses (1.0%) in the N95 respirator group met our criteria for influenza-like illness (absolute risk difference, -3.29%; 95% CI, -6.31% to 0.28%; P=.06) (TABLE 4). All 11 had laboratory-confirmed influenza. A significantly greater number of nurses in the surgical mask group (12, or 5.66%) reported fever compared with the N95 respirator group (2, or 0.9%; P=.007). There was no significant difference in nurses who reported cough, nasal congestion, headache, sore throat, myalgia, fatigue, earache, or ear infection. Of the 44 nurses in each group who had influenza diagnosed by serology, 29 (65.9%) in the surgical mask group and 31 (70.5%) in the N95 respirator group had no symptoms. There were 13 physician visits (6.1%) for respiratory illness among those in the surgical mask group compared with 13 (6.2%) in the N95 respirator group (absolute risk difference, -0.06%; 95% CI, -4.53% to 4.65%; P=.98). Forty-two participants (19.8%) in the surgical mask group reported an episode of work-related absenteeism compared with 39 (18.6%) in the N95 respiratory group (absolute risk difference, -1.24%; 95% CI, -8.75% to 6.27%; P=.75) (Table 4). There were no episodes of lower respiratory tract infection among participants. There were no adverse events reported by participants. Fifty-five participants (25.9%) in the surgical mask group vs 47 (22.4%) in the N95 respirator group reported a spouse or roommate with influenzalike illness (P=.39). Forty-eight participants (22.6%) in the surgical mask group vs 43 (20.5%) in the N95 respirator group reported a child with influenza-like illness (P=.59). Over the 2-week audit period, there were 18 episodes of patients admitted to units in droplet precautions for influenza or febrile respiratory illness where the nurse providing care for the patient had been enrolled in our study. The results of the audit demonstrated that all 11 participants (100%) allocated to surgical masks and 6 of 7 participants (85.7%)



allocated to N95 respirators were wearing the device to which they had been assigned.

**Figure.** Flow Diagram for Trial of Surgical Mask vs N95 Respirator



**Table 1.** Characteristics of 446 Nurse Participants in the Surgical Mask and N95 Respirator Groups

Characteristic	No. (%)	
	Surgical Mask (n = 225)	N95 Respirator (n = 221)
Age, mean (SD) [range], y	36.5 (10.6) [21-62]	35.8 (10.6) [21-60]
Female sex	212 (94.2)	208 (94.1)
Vaccinated against influenza	68 (30.2)	62 (28.1)
≥1 Coexisting conditions	22 (9.8)	26 (11.8)
Asthma	10 (4.4)	12 (5.4)
Diabetes	3 (1.3)	6 (2.7)
Metabolic	2 (1.0)	4 (1.8)
Immunocompromised <sup>a</sup>	3 (1.3)	3 (1.3)
Pregnancy	5 (2.2)	2 (0.9)
Other <sup>b</sup>	6 (2.7)	3 (1.3)
Distribution by hospital unit		
Medical	55 (24.4)	52 (23.5)
Pediatric	58 (26.2)	62 (28.1)
Emergency	112 (49.8)	107 (48.4)

<sup>a</sup>Immunosuppressive medications for transplantation (n = 1), rheumatoid arthritis (n=3), uveitis (n=1), and Crohn disease (n=1).

<sup>b</sup>Includes chronic renal failure (n = 1), coronary artery disease (n = 1), liver disease (n=2), seizures/brain disorder (n=2), and connective tissue disease (n=4).

**Table 2.** Comparison of Laboratory-Confirmed Influenza Between the Surgical Mask and N95 Respirator Groups

	No. (%)		Absolute Risk Difference, % (95% CI)	P Value
	Surgical Mask (n = 212)	N95 Respirator (n = 210)		
Laboratory-confirmed influenza <sup>a</sup>	50 (23.6)	48 (22.9)	-0.73 (-8.8 to 7.3)	.86
RT-PCR influenza A	5 (2.4)	1 (0.5)	-1.88 (-4.13 to 0.36)	.22
RT-PCR influenza B	1 (0.5)	3 (1.4)	0.96 (-0.89 to 2.81)	.37
≥4-Fold rise in serum titers A/Brisbane/59/2007 (H1N1) <sup>b</sup>	25 (11.8)	21 (10)	-1.79 (-7.73 to 4.15)	.55
≥4-Fold rise in serum titers A/Brisbane/10/2007 (H3N2) <sup>b</sup>	42 (19.8)	49 (23.3)	3.52 (-4.32 to 11.36)	.38
≥4-Fold rise in serum titers B/Florida/4/2006 <sup>b</sup>	15 (7.1)	19 (9.0)	2.0 (-3.0 to 7.17)	.46
≥4-Fold rise in serum titers A/TN/1560/09 (H1N1) <sup>b</sup>	17 (8.0)	25 (11.9)	3.89 (-1.82 to 9.59)	.18

Abbreviations: CI, confidence interval; RT-PCR, reverse-transcriptase polymerase chain reaction.

<sup>a</sup>Influenza detected by 1 or more of the following: RT-PCR A, RT-PCR B, and ≥4-fold rise in serum titers to A/Brisbane/59/2007(H1N1), A/Brisbane/10/2007(H3N2), and B/Florida/4/2006. Serology includes only nonvaccinated nurses.

<sup>b</sup>Includes both vaccinated and nonvaccinated nurses. Two hundred ninety-four nurses were not vaccinated (147 in each group).

**Table 3.** Comparison of RT-PCR Results for Other Respiratory Viruses Between the Surgical Mask and N95 Respirator Groups

	No. (%)		Absolute Risk Difference, % (95% CI)	P Value
	Surgical Mask (n = 212)	N95 Respirator (n = 210)		
Respiratory syncytial virus <sup>a</sup>	2 (0.9)	1 (0.5)	-0.47 (-2.07 to 1.13)	>.99
Metapneumovirus	4 (1.9)	3 (1.4)	-0.46 (-1.98 to 2.89)	>.99
Parainfluenza virus <sup>b</sup>	1 (0.5)	2 (1.0)	0.48 (-1.12 to 2.09)	.62
Rhinovirus-enterovirus	8 (3.8)	10 (4.8)	0.99 (-2.87 to 4.85)	.62
Coronavirus <sup>c</sup>	9 (4.3)	12 (5.7)	1.47 (-2.68 to 5.62)	.49
Total <sup>d</sup>	20 (9.4)	22 (10.5)	1.04 (-4.67 to 6.76)	.72

Abbreviations: CI, confidence interval; RT-PCR, reverse-transcriptase polymerase chain reaction.

<sup>a</sup>Refers to respiratory syncytial virus type B only because no type A was detected.

<sup>b</sup>Refers to parainfluenza 3 only because no parainfluenza 1, 2, or 4 was detected.

<sup>c</sup>Refers to coronaviruses OC43, 229E, NL63, and HKU1.

<sup>d</sup>Totals are less than sums because more than 1 virus was detected in some participants.

**Table 4.** Clinical Outcomes Between the Surgical Mask and N95 Respirator Groups

	No. (%)		Absolute Risk Difference, % (95% CI)	P Value
	Surgical Mask (n = 212)	N95 Respirator (n = 210)		
Physician visits for respiratory illness	13 (6.1)	13 (6.2)	-0.06 (-4.53 to 4.65)	.98
Influenza-like illness <sup>a</sup>	9 (4.2)	2 (1.0)	-3.29 (-6.31 to 0.28)	.06
Work-related absenteeism	42 (19.8)	39 (18.6)	-1.24 (-8.75 to 6.27)	.75

Abbreviation: CI, confidence interval.

<sup>a</sup>Influenza-like illness was defined as the presence of both cough and temperature 38°C or greater.

## COMMENT

Our data show that the incidence of laboratory-confirmed influenza was similar in nurses wearing the surgical mask and those wearing the N95 respirator. Surgical masks had an estimated efficacy within 1% of N95 respirators. Based on the prespecified definition, the lower CI for the difference in effectiveness of the surgical mask and N95 mask was within -9% and the statistical criterion of noninferiority was met. That is, surgical masks appeared to be no worse, within a prespecified margin, than N95 respirators in preventing influenza. Transmission by small droplet spread would be compatible with greater protection with the

N95 mask compared with the surgical mask where efficiency estimates range from 2% to 92% for particles smaller than 20 µm in diameter.<sup>23-28</sup> The fact that attack rates were similar may suggest that small aerosols did not dominate transmission. One frequently cited concern about the surgical mask is its inability to obtain an appropriate seal compared with the N95 respirator.<sup>29</sup> Based on the results of this trial, this concern does not seem to be associated with an increased rate of infection of influenza or other respiratory viruses. Influenza attack rates among health care workers in non-outbreak settings are sparse. Our data provide estimates of an attack rate (23%) in a largely unvaccinated cohort of nurses followed closely during a period of relatively mild influenza-like illness and into the beginning of what is now considered a pandemic period. Given that serology captures exposure over the entire season and that nurses have repeated exposures, this rate of infection was not unexpected. Our serological data in unvaccinated nurses were 20% for H3N2, 10% for H1N1, and 8% for influenza B. In a community-based study, agespecific rates of infection for those aged 30 to 39 years by serology was 16% for H3N2, approximately 5% for H1N1, and 5% for influenza B.<sup>21</sup> It is for this reason that the number of participants with influenza-like illness, defined by fever and cough alone,<sup>19</sup> were relatively few compared with the number with laboratory-confirmed influenza. Given that there was no difference in laboratory-confirmed influenza between study groups, the higher proportion of nurses in the surgical mask group with influenza-like illness, although not statistically significant, was unexpected. The results of seroconversion to 2009 influenza A(H1N1) (10%) was unexpected given that the convalescent specimens were obtained from April 23 to May 15, 2009. This attack rate may suggest that 2009 influenza A(H1N1) was circulating in Ontario before April 2009. An alternative explanation for this high rate of seroconversion may be cross-reaction due to exposure to seasonal H1N1. Strengths of this study include individual-level randomization, comprehensive laboratory-confirmed outcome assessment with PCR and serological evaluation, follow-up over an entire influenza season, and excellent participant follow-up. There are a number of limitations of this study. Compliance with the intervention could not be assessed for all participants. Only 1 room entry was recorded per observation and the auditor did not enter the isolation room to assess whether the participant removed the respirator protection. Audits were only conducted on medical and pediatric units, not in the emergency department. Had there been poor

compliance with the N95 respirator, this could have biased the study toward noninferiority. However, the results from our audited sample suggest excellent adherence. This is in keeping with the fact that all hospitals in the study were in Ontario, which was affected by the SARS outbreak and where use of personal protective equipment is mandated and audited by the Ontario Ministry of Labour. We acknowledge that our protocol did not account for the effect of indirect contact because hand hygiene and use of gloves and gowns were not monitored. An imbalance in hand hygiene between study groups, with worse adherence in the N95 group, would have biased the study toward noninferiority. However, individual-level randomization and stratified randomization within hospitals would help balance any differences in adherence to hand hygiene between study groups. Because the use of gloves and gowns when entering the room of a patient with febrile respiratory illness was standard practice in our study hospitals, variability of use would likely have been minimal. It is also impossible to determine whether participants acquired influenza due to hospital or community exposure. However, our data on household exposure suggest that such exposures were balanced between intervention groups. We acknowledge that not surveying participants' coworkers about influenza-like illness was a limitation. Since we did not collect information on droplet isolation precautions, a greater exposure of N95 respirator nurses vs surgical mask nurses to patients on droplet precautions would have biased the study toward noninferiority. However, the fact that the nurses were well balanced on each ward and in the number of specimens obtained on each unit would minimize the chance of such differential exposure having occurred. The major implication of this study is that protection with a surgical mask against influenza appears to be similar to the N95 respirator, meeting criteria for noninferiority. Our findings apply to routine care in the health care setting. They should not be generalized to settings where there is a high risk for aerosolization, such as intubation or bronchoscopy, where use of an N95 respirator would be prudent. In routine health care settings, particularly where the availability of N95 respirators is limited, surgical masks appear to be noninferior to N95 respirators for protecting health care workers against influenza.

## Universal Masking in Hospitals in the Covid-19 Era

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As the SARS-CoV-2 pandemic continues to explode, hospital systems are scrambling to intensify their measures for protecting patients and health care workers from the virus. An increasing number of frontline providers are wondering whether this effort should include universal use of masks by all health care workers. Universal masking is already standard practice in Hong Kong, Singapore, and other parts of Asia and has recently been adopted by a handful of U.S. hospitals. We know that wearing a mask outside health care facilities offers little, if any, protection from infection. Public health authorities define a significant exposure to Covid-19 as face-to-face contact within 6 feet with a patient with symptomatic Covid-19 that is sustained for at least a few minutes (and some say more than 10 minutes or even 30 minutes). The chance of catching Covid-19 from a passing interaction in a public space is therefore minimal. In many cases, the desire for widespread masking is a reflexive reaction to anxiety over the pandemic. The calculus may be different, however, in health care settings. First and foremost, a mask is a core component of the personal protective equipment (PPE) clinicians need when caring for symptomatic patients with respiratory viral infections, in conjunction with gown, gloves, and eye protection. Masking in this context is already part of routine operations for most hospitals. What is less clear is whether a mask offers any further protection in health care settings in which the wearer has no direct interactions with symptomatic patients. There are two scenarios in which there may be possible benefits. The first is during the care of a patient with unrecognized Covid-19. A mask alone in this setting will reduce risk only slightly, however, since it does not provide protection from droplets that may enter the eyes or from fomites on the patient or in the environment that providers may pick up on their hands and carry to their mucous membranes (particularly given the concern that mask wearers may have an increased tendency to touch their faces). More compelling is the

possibility that wearing a mask may reduce the likelihood of transmission from asymptomatic and minimally symptomatic health care workers with Covid-19 to other providers and patients. This concern increases as Covid-19 becomes more widespread in the community. We face a constant risk that a health care worker with early infection may bring the virus into our facilities and transmit it to others. Transmission from people with asymptomatic infection has been well documented, although it is unclear to what extent such transmission contributes to the overall spread of infection.<sup>1-3</sup> More insidious may be the health care worker who comes to work with mild and ambiguous symptoms, such as fatigue or muscle aches, or a scratchy throat and mild nasal congestion, that they attribute to working long hours or stress or seasonal allergies, rather than recognizing that they may have early or mild Covid-19. In our hospitals, we have already seen a number of instances in which staff members either came to work well but developed symptoms of Covid-19 partway through their shifts or worked with mild and ambiguous symptoms that were subsequently diagnosed as Covid-19. These cases have led to large numbers of our patients and staff members being exposed to the virus and a handful of potentially linked infections in health care workers. Masking all providers might limit transmission from these sources by stopping asymptomatic and minimally symptomatic health care workers from spreading virus-laden oral and nasal droplets. What is clear, however, is that universal masking alone is not a panacea. A mask will not protect providers caring for a patient with active Covid-19 if it's not accompanied by meticulous hand hygiene, eye protection, gloves, and a gown. A mask alone will not prevent health care workers with early Covid-19 from contaminating their hands and spreading the virus to patients and colleagues. Focusing on universal masking alone may, paradoxically, lead to more transmission of Covid-19 if it diverts attention from implementing more fundamental infection control measures. Such measures include vigorous screening of all patients coming to a facility for symptoms of Covid-19 and immediately getting them masked and into a room; early implementation of contact and droplet precautions, including eye protection, for all symptomatic patients and erring on the side of caution when in doubt; rescreening all admitted patients daily for signs and symptoms of Covid-19 in case an infection was incubating on admission or they were exposed to the virus in the hospital; having a low threshold for testing patients with even mild symptoms potentially attributable to a viral respiratory infection (this includes patients with



pneumonia, given that a third or more of pneumonias are caused by viruses rather than bacteria); requiring employees to attest that they have no symptoms before starting work each day; being attentive to physical distancing between staff members in all settings (including potentially neglected settings such as elevators, hospital shuttle buses, clinical rounds, and work rooms); restricting and screening visitors; and increasing the frequency and reliability of hand hygiene. The extent of marginal benefit of universal masking over and above these foundational measures is debatable. It depends on the prevalence of health care workers with asymptomatic and minimally symptomatic infections as well as the relative contribution of this population to the spread of infection. It is informative, in this regard, that the prevalence of Covid-19 among asymptomatic evacuees from Wuhan during the height of the epidemic there was only 1 to 3%.<sup>4,5</sup> Modelers assessing the spread of infection in Wuhan have noted the importance of undiagnosed infections in fueling the spread of Covid-19 while also acknowledging that the transmission risk from this population is likely to be lower than the risk of spread from symptomatic patients.<sup>3</sup> And then the potential benefits of universal masking need to be balanced against the future risk of running out of masks and thereby exposing clinicians to the much greater risk of caring for symptomatic patients without a mask. Providing each health care worker with one mask per day for extended use, however, may paradoxically improve inventory control by reducing one-time uses and facilitating centralized workflows for allocating masks without risk assessments at the individual-employee level. There may be additional benefits to broad masking policies that extend beyond their technical contribution to reducing pathogen transmission. Masks are visible reminders of an otherwise invisible yet widely prevalent pathogen and may remind people of the importance of social distancing and other infection-control measures. It is also clear that masks serve symbolic roles. Masks are not only tools, they are also talismans that may help increase health care workers' perceived sense of safety, well-being, and trust in their hospitals. Although such reactions may not be strictly logical, we are all subject to fear and anxiety, especially during times of crisis. One might argue that fear and anxiety are better countered with data and education than with a marginally beneficial mask, particularly in light of the worldwide mask shortage, but it is difficult to get clinicians to hear this message in the heat of the current crisis. Expanded masking protocols' greatest contribution may be to reduce the transmission of anxiety,

over and above whatever role they may play in reducing transmission of Covid-19. The potential value of universal masking in giving health care workers the confidence to absorb and implement the more foundational infection-prevention practices described above may be its greatest contribution.

# Effectiveness of N95 respirators versus surgical masks against influenza: A systematic review and meta-analysis

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## Abstract

### Objective

Previous meta-analyses concluded that there was insufficient evidence to determine the effect of N95 respirators. We aimed to assess the effectiveness of N95 respirators versus surgical masks for prevention of influenza by collecting randomized controlled trials (RCTs).

### Methods

We searched PubMed, EMBASE and The Cochrane Library from the inception to January 27, 2020 to identify relevant systematic reviews. The RCTs included in systematic reviews were identified. Then we searched the latest published RCTs from the above three databases and searched ClinicalTrials.gov for unpublished RCTs. Two reviewers independently extracted the data and assessed risk of bias. Meta-analyses were conducted to calculate pooled estimates by using RevMan 5.3 software.

### Results

A total of six RCTs involving 9 171 participants were included. There were no statistically significant differences in preventing laboratory-confirmed influenza (RR = 1.09, 95% CI 0.92-1.28,  $P > .05$ ), laboratory-confirmed respiratory viral infections (RR = 0.89, 95% CI 0.70-1.11), laboratory-confirmed respiratory infection (RR = 0.74, 95% CI 0.42-1.29) and influenzalike illness (RR = 0.61, 95% CI 0.33-1.14) using N95 respirators and surgical masks. Meta-analysis indicated a protective effect of N95 respirators against laboratory-confirmed bacterial colonization (RR = 0.58, 95% CI 0.43-0.78).

## Conclusion

The use of N95 respirators compared with surgical masks is not associated with a lower risk of laboratory-confirmed influenza. It suggests that N95 respirators should not be recommended for general public and nonhigh-risk medical staff those are not in close contact with influenza patients or suspected patients.

## 1 INTRODUCTION

Severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) have mortality rates about 10% and 37%, respectively.<sup>1</sup> Since the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), facemasks have been considered to be vitally important to reduce the risk of infection because vaccination or specific anti-infective treatments are unavailable.<sup>2, 3</sup> N95 respirators are used to prevent users from inhaling small airborne particles and must fit tightly to the user's face. Surgical masks are designed to protect wearers from microorganism transmission and fit loosely to the user's face.<sup>5,6</sup> Although surgical masks cannot prevent inhalation of small airborne particles, both of them can protect users from large droplets and sprays.<sup>7, 8</sup>

There are conflicting recommendations for severe acute respiratory syndrome (SARS) and pandemic influenza: the World Health Organization (WHO) recommends using masks in low-risk situations and respirators in high-risk situations, but the Centers for Disease Control and Prevention (CDC) recommends using respirators in both low and high-risk situations.<sup>9</sup> However, N95 respirators may play a limited role in low-resource settings, where there are a finite number of N95 respirators, or it may be unaffordable.<sup>9</sup> Also, previous meta-analyses concluded there was insufficient evidence to determine the effect of N95 respirators due to a small number of studies that is prone to lack of statistical power.<sup>10, 11</sup> Additionally, these meta-analyses were limited by the small number of included randomized control trials (RCTs). More rigorous RCTs of comparing N95 respirators with surgical masks against influenza published in recent years were not included in previous meta-analyses.<sup>12-14</sup>

In light of the growing number of RCTs of masks use for protecting against influenza, this systematic review and meta-analysis aimed to assess the effectiveness of N95 respirators versus surgical masks for prevention of influenza.

## 2 METHODS

This meta-analysis was conducted based on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.<sup>15</sup>

### 2.1 Inclusion and exclusion criteria

Inclusion criteria were (1) study type: RCT (including cluster-randomized trial) and nonrandomized controlled study; (2) participants: humans with influenza (including pandemic strains, seasonal influenza A or B viruses and zoonotic viruses such as swine or avian influenza), and other respiratory viral infections (as a proxy for influenza); (3) intervention and comparator: N95 respirators versus surgical masks; (4) primary outcome: laboratory-confirmed influenza; (5) secondary outcomes: laboratory-confirmed respiratory viral infections, laboratory-confirmed bacterial colonization, laboratory-confirmed respiratory infection, and influenzalike illness; and (6) settings: hospital or community. RCTs were selected due to the potential possibility of high evidence level. Exclusion criteria were (1) theoretical models; (2) human/nonhuman experimental laboratory studies; and (3) conference abstract.

### 2.2 Search strategy

We searched PubMed, EMBASE, and The Cochrane Library databases from inception to January 27, 2020, to identify published systematic reviews on evaluating the use of masks for preventing influenza. Search strategy in PubMed could be found in Table 1, and the strategy was adequately adjusted to use in other databases. Then, primary RCTs included in the systematic reviews were identified. Additionally, we conducted an additional search to identify RCTs published in the past five years from January 27, 2015, to January 27, 2020, using the databases and search strategies described above. We also searched for ClinicalTrials.gov to obtain unpublished data. There were no publication status and language restrictions on selecting the studies.

### 2.3 Study selection and data extraction

Two reviewers independently screened the articles based on the titles, abstracts and full texts. Then, two reviewers independently extracted the following data from included studies: first author, publication year, country, disease, details of study

population and intervention, study design, sample size, settings, and results. All disagreements were resolved by discussion.

#### 2.4 Risk of bias assessment

Two reviewers independently assessed the risk of bias of the selected RCTs using the Cochrane Risk of Bias tool,<sup>16</sup> which includes domains on random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, and selective reporting. For each RCT, every domain was judged among 3 levels: high risk, unclear risk, and low risk. Disagreements were resolved by discussion.

#### 2.5 Data analysis

All statistical analyses were performed using Review Manager (RevMan) version 5.3. Comparable data from studies with similar interventions and outcomes were pooled using forest plots. Relative risk (RR) with 95% confidence intervals (CIs) for dichotomous data was used as the effect measure. Between-study heterogeneity was assessed using the  $I^2$  for each pooled estimate.<sup>17</sup> We adopted a random-effects model for heterogeneity  $P < .10$ . We performed a subgroup analysis based on the settings (hospital, community) due to the possibility of clinical heterogeneity. A sensitivity analysis was conducted to evaluate the robustness of the results by excluding individual studies for each forest plot. Funnel plots were planned to assess publication bias. Because of the small number of studies available for each pooled estimate, we failed to assess publication bias.

### 3 RESULTS

#### 3.1 Search results and study characteristics

The details on the literature search and screening process can be found in Figure 1. Excluded studies and reasons for exclusion were shown in Table 2. In total, we included six RCTs<sup>12, 18-22</sup> and found no unpublished data of RCTs from ClinicalTrials.gov. The characteristics of these RCTs were presented in Table 3. The included studies published between 2009 and 2019. A total of 9171 participants in Canada, Australia, China, or America were included, and the number of participants in each RCT ranged from 435 to 5180 patients. The follow-up duration varied from 2 to 15 weeks. Five studies included participants in hospitals,<sup>12, 18, 20-22</sup> and one in households.<sup>19</sup> Because of different definitions

of outcome in included studies, we redefined the laboratory-confirmed respiratory infection as respiratory influenza, other viruses or bacteria infection.

### 3.2 Risk of bias

The results of the risk of bias assessment can be found in Figure 2. Five studies reported the computer-generated random sequences, while only one mentioned randomization. All studies did not mention allocation concealment. Participants and trial staff were not blinded in two studies, and the other two studies failed to mention the blinding of participants and personnel. Four studies did not report whether the outcome assessors were blinded. All studies had complete outcome data or described comparable numbers and reasons for withdrawal across groups and prespecified outcomes.

### 3.3 Effectiveness

Five RCTs involving 8444 participants reported laboratory-confirmed influenza.[12](#), [18-21](#) Meta-analysis with fixed-effects model revealed that there was no statistically significant differences in preventing influenza using N95 respirators and surgical masks (RR = 1.09, 95% CI 0.92-1.28,  $P > .05$ ) (Figure 3). The results of subgroup analyses were consistent with this regardless of the hospital or the community. The results of the sensitivity analysis were not altered after excluding each trial.

Four RCTs[18-21](#) involving 3264 participants reported laboratory-confirmed respiratory viral infections. Meta-analysis with fixed-effects model revealed that there were no statistically significant differences in preventing respiratory viral infections using N95 respirators and surgical masks (RR = 0.89, 95% CI 0.70-1.11,  $P > .05$ ) (Figure 4). The results of subgroup analyses were consistent regardless of the hospital or the community. However, the sensitivity analysis after excluding the trial by Loeb et al[18](#) showed a significant effect of N95 respirators on preventing respiratory viral infections (RR = 0.61, 95% CI 0.39-0.98,  $P < .05$ ).

Two RCTs[21](#), [22](#) involving 2538 participants reported laboratory-confirmed bacterial colonization. Meta-analysis with fixed-effects model revealed that compared with surgical masks, N95 respirators significantly reduced bacterial colonization in hospitals (RR = 0.58, 95% CI 0.43-0.78,  $P < .05$ ) (Figure 5). The

sensitivity analysis showed that the results did not change after excluding each trial.

Two RCTs<sup>12, 22</sup> involving 6621 participants reported laboratory-confirmed respiratory infection. Meta-analysis with random-effects model revealed that there were no statistically significant differences in preventing respiratory infection using N95 respirators and surgical masks in hospitals (RR = 0.74, 95% CI 0.42-1.29,  $P > .05$ ) (Figure 6). However, the sensitivity analysis after excluding the trial by Radonovich et al<sup>12</sup> showed a significant effect of N95 respirators on preventing respiratory infection (RR = 0.53, 95% CI 0.35-0.82,  $P < .05$ ).

Five RCTs involving 8444 participants reported influenza like illness.<sup>12, 18-21</sup> Meta-analysis with random-effects model revealed that there were no statistically significant differences in preventing influenza like illness using N95 respirators and surgical masks (RR = 0.61, 95% CI 0.33-1.14,  $P > .05$ ) (Figure 7). The results of subgroup analyses indicated that statistically significant superiority of N95 respirators over surgical masks against influenza like illness (RR = 0.37, 95% CI 0.20-0.71,  $P < .05$ ) in the community (only one RCT). The sensitivity analysis showed results remained unchanged after excluding each trial.

#### 4 DISCUSSION

This meta-analysis showed that there were no statistically significant differences in preventing laboratory-confirmed influenza, laboratory-confirmed respiratory viral infections, laboratory-confirmed respiratory infection and influenza-like illness using N95 respirators and surgical masks. N95 respirators provided a protective effect against laboratory-confirmed bacterial colonization. In subgroup analysis, similar results could be found in the hospital and community for laboratory-confirmed influenza and laboratory-confirmed respiratory viral infections. However, sensitivity analysis showed unstable results for the prevention of laboratory-confirmed respiratory viral infections and laboratory-confirmed respiratory infection.

Through the course of influenza pandemics, large numbers of facemasks may be required to use in long periods to protect people from infections.<sup>23</sup> Using N95 respirators is likely to result in discomfort, for example, headaches.<sup>23</sup> A previous study<sup>3</sup> reported that there was an inverse relationship between the level of compliance with wearing an N95 respirator and the risk of clinical respiratory



illness. It is difficult to ensure high compliance due to this discomfort of N95 respirators in all studies.

The reason for the similar effects on preventing influenza for the use of N95 respirators *versus* surgical masks may be related to low compliance to N95 respirators wear,<sup>23</sup> which may lead to more frequent doffing compared with surgical masks.<sup>13</sup> Although N95 respirators may confer superior protection in laboratory studies designing to achieve 100% intervention adherence,<sup>24</sup> the routine use of N95 respirators seems to be less acceptable due to more significant discomfort in real-world practice.<sup>11</sup> Therefore, the benefit of N95 respirators of fitting tightly to faces is offset or subjugated.<sup>13</sup> However, it should be noted that the surgical masks are primarily designed to protect the environment from the wearer, whereas the respirators are supposed to protect the wearer from the environment.<sup>25</sup>

There are several limitations to this study. First, some RCTs had a high risk of bias due to lack of allocation concealment and blinding; although it is impractical to blind participants who would know the type of masks they are wearing. Second, the number of included studies focusing on the community was small. Consequently, the results of the subgroup analysis might be unreliable. Third, we identified RCTs from published systematic reviews, which may result in the omission of relative RCTs. Finally, there might be publication bias, and we cannot assess it due to an insufficient number of included RCTs.

In conclusion, the current meta-analysis shows the use of N95 respirators compared with surgical masks is not associated with a lower risk of laboratory-confirmed influenza. It suggests that N95 respirators should not be recommended for the general public and nonhigh risk medical staffs those are not in close contact with influenza patients or suspected patients.