

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

A Randomized Trial

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INFLUENZA CAUSES ANNUAL EPIDEMICS of respiratory illness worldwide and is the most important cause of medically attended acute respiratory illness.^{1,2} Moreover, there is increasing concern about the recently declared influenza pandemic due to 2009 influenza A(H1N1) in humans.³⁻⁵

Transmission of influenza can occur by coughing or sneezing where infectious particles of variable size, ranging from approximately 0.1 to 100 μm , may be inhaled.⁶ 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 μm) can occur,⁷⁻¹¹ the exact nature of transmission of influenza that occurs

For editorial comment see p 1903.

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.

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in nonexperimental settings is not well understood.¹² 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,¹³⁻¹⁵ 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.¹⁶ 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 accept-

able 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.¹⁷ Nurses had a qualitative fit testing using the saccharin or Bitrex protocol.¹⁷

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 $\geq 38^{\circ}\text{C}$), 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 flocculated 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).¹⁸ 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 $\geq 38^{\circ}\text{C}$).¹⁹ 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.²⁰ For the primary analysis, the dif-

ference 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.²¹

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.²²

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% drop-out 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 sur-

gical 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 ≥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

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

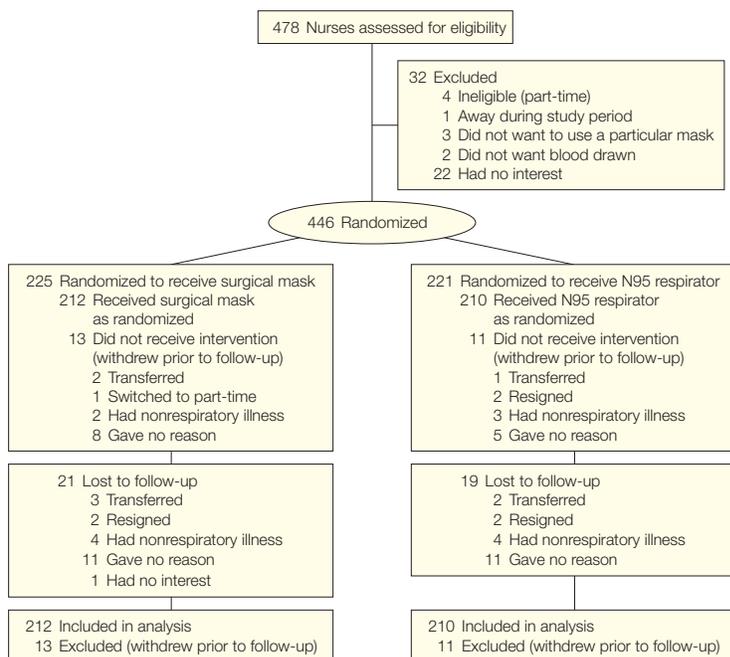


Table 1. Characteristics of 446 Nurse Participants in the Surgical Mask and N95 Respirator Groups

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 ^a	3 (1.3)	3 (1.3)
Pregnancy	5 (2.2)	2 (0.9)
Other ^b	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)

^aImmunosuppressive medications for transplantation (n=1), rheumatoid arthritis (n=3), uveitis (n=1), and Crohn disease (n=1).
^bIncludes 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).

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 RT-PCR or ≥ 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 respirator 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 infec-

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 ^a	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) ^b	25 (11.8)	21 (10)	-1.79 (-7.73 to 4.15)	.55
≥ 4 -Fold rise in serum titers A/Brisbane/10/2007 (H3N2) ^b	42 (19.8)	49 (23.3)	3.52 (-4.32 to 11.36)	.38
≥ 4 -Fold rise in serum titers B/Florida/4/2006 ^b	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) ^b	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.

^aInfluenza 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.

^bIncludes 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 ^a	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 ^b	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 ^c	9 (4.3)	12 (5.7)	1.47 (-2.68 to 5.62)	.49
Total ^d	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.

^aRefers to respiratory syncytial virus type B only because no type A was detected.

^bRefers to parainfluenza 3 only because no parainfluenza 1, 2, or 4 was detected.

^cRefers to coronaviruses OC43, 229E, NL63, and HKU1.

^dTotals 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 ^a	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.

^aInfluenza-like illness was defined as the presence of both cough and temperature 38°C or greater.

tion 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 influenza-like 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.

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.²³⁻²⁸ 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.²⁹ 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, age-specific 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.²¹ It is for this reason that the number of participants with influenza-like illness, defined by fever and cough alone,¹⁹ 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.

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REFERENCES

- Langley JM, Faughnan ME. Prevention of influenza in the general population. *CMAJ*. 2004;171(10):1213-1222.
- Thompson WW, Shay DK, Weintraub E, et al. Influenza-associated hospitalizations in the United States. *JAMA*. 2004;292(11):1333-1340.
- Dawood FS, Jain S, Finelli L, et al; Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. *N Engl J Med*. 2009;360(25):2605-2615.
- Cohen J, Enserink M. Swine flu: after delays, WHO agrees: the 2009 pandemic has begun. *Science*. 2009;324(5934):1496-1497.
- Neumann G, Noda T, Kawaoka Y. Emergence and pandemic potential of swine-origin H1N1 influenza virus. *Nature*. 2009;459(7249):931-939.
- Nicas M, Nazaroff WW, Hubbard A. Toward understanding the risk of secondary airborne infection: emission of respirable pathogens. *J Occup Environ Hyg*. 2005;2(3):143-154.
- Snyder MH, Stephenson EH, Young H, et al. Infectivity and antigenicity of live avian-human influenza A reassortment virus: comparison of intranasal and aerosol routes in squirrel monkeys. *J Infect Dis*. 1986;154(4):709-711.
- Loosli CG, Lemon HM, Robertson OH, Appel E. Experimental airborne influenza infection: I, influence of humidity on survival of virus in air. *Proc Soc Exp Biol Med*. 1943;53:205-206.
- Alford RH, Kasel JA, Gerone PJ, Knight V. Human influenza resulting from aerosol inhalation. *Proc Soc Exp Biol Med*. 1966;122(3):800-804.
- Munster VJ, de Wit E, van den Brand JM, et al. Pathogenesis and transmission of swine-origin 2009 A(H1N1) influenza virus in ferrets. *Science*. 2009;325(5939):481-483.
- Maines TR, Jayaraman A, Belser JA, et al. Transmission and pathogenesis of swine-origin 2009 A(H1N1) influenza viruses in ferrets and mice. *Science*. 2009;325(5939):484-487.
- Brankston G, Gitterman L, Hirji Z, Lemieux C, Gardam M. Transmission of influenza A in human beings. *Lancet Infect Dis*. 2007;7(4):257-265.
- Agah R, Cherry JD, Garakian AJ, Chapin M. Respiratory syncytial virus (RSV) infection rate in personnel caring for children with RSV infections: routine isolation procedure vs routine procedure supplemented by use of masks and goggles. *Am J Dis Child*. 1987;141(6):695-697.
- MacIntyre CR, Cauchemez S, Dwyer DE, et al. Face mask use and control of respiratory virus transmission in households. *Emerg Infect Dis*. 2009;15(2):233-241.
- Cowling BJ, Chan KH, Fang VJ, et al. Face-masks and hand hygiene to prevent influenza transmission in households: a randomized trial [published online August 3, 2009]. *Ann Intern Med*. <http://www.annals.org/cgi/content/full/0000605-200910060-00142v1#FN>.
- Preventing respiratory illnesses: protecting patient and staff: infection control and surveillance standards for febrile respiratory illness (FRI) in non-outbreak conditions in acute care hospitals [September 2005]. Ministry of Health and Long-Term Care, Public Health Division, Provincial Infectious Diseases Advisory Committee. http://www.health.gov.on.ca/english/providers/program/infectious/diseases/best_prac/bp_fri_080406.pdf. Accessed September 11, 2009.
- OSHA Technical Manual: section XIII: chapter 2: respiratory protection. US Department of Labor. http://www.osha.gov/dts/osta/otm/otm_viii/otm_viii_2.html. Accessed September 21, 2009.
- Mahony J, Chong S, Merante F, et al. Development of a respiratory virus panel test for detection of twenty human respiratory viruses by use of multiplex PCR and a fluid microbead-based assay. *J Clin Microbiol*. 2007;45(9):2965-2970.
- Call SA, Vollenweider MA, Hornung CA, Simel DL, McKinney WP. Does this patient have influenza? *JAMA*. 2005;293(8):987-997.
- Piaggio G, Elbourne DR, Altman DG, Pocock SJ, Evans SJ; CONSORT Group. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT statement. *JAMA*. 2006;295(10):1152-1160.
- Monto AS, Koopman JS, Longini IM Jr. Tecumseh study of illness: XIII, influenza, infection, and disease, 1976-1981. *Am J Epidemiol*. 1985;121(6):811-822.
- Gotzsche PC. Lessons from and cautions about noninferiority and equivalence randomized trials. *JAMA*. 2006;295(10):1172-1174.
- Brosseau LM, McCullough NV, Vesley D, Vincent JH. Mycobacterial aerosol collection efficiency of respirator and surgical mask filters under varying conditions of flow and humidity. *Appl Occup Environ Hyg*. 1997;12(6):435-445.
- Cooper DW, Hinds WC, Price JM, Weker R, Yee HS. Common materials for emergency respiratory protection: leakage tests with a manikin. *Am Ind Hyg Assoc J*. 1983;44(10):720-726.
- McCullough NV, Brosseau LM, Vesley D. Collection of three bacterial aerosols by respirator and surgical mask filters under varying conditions of flow and relative humidity. *Ann Occup Hyg*. 1997;41(6):677-690.
- Mitakakis TZ, Tovey ER, Yates DH, et al. Particulate masks and non-powdered gloves reduce latex allergen inhaled by healthcare workers. *Clin Exp Allergy*. 2002;32(8):1166-1169.
- Tuomi T. Face seal leakage of half masks and surgical masks. *Am Ind Hyg Assoc J*. 1985;46(6):308-312.
- Willeke K, Qian YG, Donnelly J, Grinshpun S, Ulevic V. Penetration of airborne microorganisms through a surgical mask and a dust/mist respirator. *Am Ind Hyg Assoc J*. 1996;57(4):348-355.
- Influenza transmission and the role of personal protective respiratory equipment: an assessment of the evidence. Expert Panel on Influenza and Personal Protective Respiratory Equipment, Council of Canadian Academies. [http://www.scienceadvice.ca/documents/\(2007-12-19\)_Influenza_PPPE_Final_Report.pdf](http://www.scienceadvice.ca/documents/(2007-12-19)_Influenza_PPPE_Final_Report.pdf). Accessed September 11, 2009.