Foundation for Health Leadership & Innovation | NC ORAL HEALTH COLLABORATIVE

Interim Mask and Face Shield Guidelines

The American Dental Association recommends providers use the highest level of PPE available in coordination with goggles or a face shield, when interacting with patients. In this guidance, the ADA outlines the different types of PPE and the associated level of protection they offer. NCOHC has also attached supporting research and evidence.

Please note: the attached documentation is only intended to serve as a reference guide and does not necessarily reflect the sole recommendation or advisement of the NC Oral Health Collaborative. It is up to the individual provider and team to determine best approaches to PPE based on most current research and guidance from agencies such as the ADA, CDC, OSHA, and OSAP.

Contents

Additional Resources

Counterfeit Respirators / Misrepresentation of NIOSH-Approval - CDC
Respiratory Protection in the Era of COVID-19

Interim Mask and Face Shield Guidelines

These recommendations align with existing CDC recommendations for patients without signs/symptoms of COVID-19.

Use the highest level of PPE available when treating patients to reduce the risk of exposure. Some risk is inherent in all scenarios. If masks with either goggles or face shields are not available, please understand there is a higher risk for infection; therefore, use your professional judgment related to treatment provided and the patient's risk factors.

Considering that patients who are asymptomatic may still be COVID-19 infectious, it should be assumed that all patients can transmit disease.

Mask Type – With Goggles or Face Shield (Understanding Mask Types)		Level of Risk*** to DHCP
	**N95**	Low
	**N95 EQUIVALENT MASK* KN/KP95, PFF2, P2, DS/DL2, KOREAN SPECIAL 1ST**	Low
	**Surgical Mask****	Moderate

**The FDA has authorized the use of masks equivalent to the N95 during the pandemic period. Manufacturers approved can be found here: https://www.fda.gov/media/136663/download*

***ASTM has established performance levels for surgical masks based on fluid resistance, bacterial filtration efficiency, particulate filtration efficiency, breathing resistance and flame spread.*

- *Level 1 masks have the least fluid resistance, bacterial filtration efficiency, particulate filtration efficiency, and breathing resistance.*
- *Level 2 masks provide a moderate barrier for fluid resistance, bacterial and particulate filtration efficiencies and breathing resistance.*
- *Level 3 masks provide the maximum level of fluid resistance recognized by ASTM and are designed for procedures with moderate or heavy amounts of blood, fluid spray or aerosol exposure.*

****ADA.org/InterimGuidanceOverview*

Professional judgment should be exercised when considering the use of gowns, foot covers and head covers.

These guidelines are intended to help dental practices lower (but not eliminate) the risk of coronavirus transmission during the current pandemic. Dental practices should not presume that following the guidelines will insulate them from liability in the case of infection. Dentists should also be aware of any relevant laws, regulations, or rules adopted in their states.

Understanding Mask Types

	 SURGICAL MASK	 N95 MASK*	 N95 EQUIVALENT MASK KN/KP95, PFF2, P2, DS/DL2, KOREAN SPECIAL 1ST*
Testing and Approval	Cleared by the U.S. Food and Drug Administration (FDA)	Evaluated, tested, and approved by NIOSH as per the requirements in 42 CFR Part 84	FDA Emergency Use Authorization (EUA)
Sizing	No	Yes. The sizing differs with each mask model. Some of the sizing options include small, small/ medium, medium, medium/large, and large.	Yes. The sizing differs with each mask model. Some of the sizing options include small, small/ medium, medium, medium/large, and large.
Intended Use and Purpose	Fluid resistant and provides the wearer protection against large droplets, splashes, or sprays of bodily or other hazardous fluids. Protects the patient from the wearer's mask emissions	Reduces wearer's exposure to particles including small particle aerosols and large droplets (only non-oil aerosols). OSHA recommends certifying the authenticity of masks to insure they provide the expected protection.	Reduces wearer's exposure to particles including small particle aerosols and large droplets (non-oil aerosols). Manufactured in compliance with standards of other countries and considered equivalent to NIOSH approved N95 masks. Authorized manufacturers are listed at: https://www.fda.gov/media/136663/download
Face Seal Fit+	Loose-fitting	Tight-fitting**	Tight-fitting**
Fit Testing+ Requirement	No	Temporary lifting of fit test enforcement requirement.	Temporary lifting of fit test enforcement requirement.
User Seal Check Requirement	No	Yes. Required each time the mask is donned (put on)	Yes. Required each time the mask is donned (put on)
Use Limitations	Disposable. Discard after each patient encounter.	Ideally should be discarded after each aerosol-generating patient encounter. It should also be discarded when it becomes damaged or deformed; no longer forms an effective seal to the face; becomes wet or visibly dirty; breathing becomes difficult; or if it becomes contaminated with blood, respiratory or nasal secretions, or other bodily fluids from patients.	Ideally should be discarded after each aerosol-generating patient encounter. It should also be discarded when it becomes damaged or deformed; no longer forms an effective seal to the face; becomes wet or visibly dirty; breathing becomes difficult; or if it becomes contaminated with blood, respiratory or nasal secretions, or other bodily fluids from patients.

**OSHA video on mask seal check: https://www.youtube.com/watch?v=pGXiUyAoEd8 .*
Facial hair may affect the fit of the mask: https://www.cdc.gov/niosh/npptl/pdfs/FacialHairWmask11282017-508.pdf

+Note: A seal test is a user test performed by the wearer every time the mask is put on to insure that the mask is properly seated to the face. If not, it needs to be adjusted. A fit test is used to determine appropriate mask size for the individual.

***A mask that does not fit does not protect you, meaning that you should not rely on it to protect you from infection.*

4/17/20

Effectiveness of N95 respirators versus surgical masks in protecting health care workers from acute respiratory infection: a systematic review and meta-analysis

Jeffrey D. Smith MSc, Colin C. MacDougall MSc, Jennie Johnstone MD PhD, Ray A. Copes MD, Brian Schwartz MD, Gary E. Garber MD

Abstract

Background: Conflicting recommendations exist related to which facial protection should be used by health care workers to prevent transmission of acute respiratory infections, including pandemic influenza. We performed a systematic review of both clinical and surrogate exposure data comparing N95 respirators and surgical masks for the prevention of transmissible acute respiratory infections.

Methods: We searched various electronic databases and the grey literature for relevant studies published from January 1990 to December 2014. Randomized controlled trials (RCTs), cohort studies and case–control studies that included data on health care workers wearing N95 respirators and surgical masks to prevent acute respiratory infections were included in the meta-analysis. Surrogate exposure studies comparing N95 respirators and surgical masks using manikins or adult volunteers under simulated conditions were summarized separately. Outcomes from clinical studies were laboratory-confirmed respiratory infection, influenza-like illness and workplace absenteeism. Outcomes from surrogate exposure studies were filter penetration, face-seal leakage and total inward leakage.

Results: We identified 6 clinical studies (3 RCTs, 1 cohort study and 2 case–control studies) and 23 surrogate exposure studies. In the meta-analysis of the clinical studies, we found no significant difference between N95 respirators and surgical masks in associated risk of (a) laboratory-confirmed respiratory infection (RCTs: odds ratio [OR] 0.89, 95% confidence interval [CI] 0.64–1.24; cohort study: OR 0.43, 95% CI 0.03–6.41; case–control studies: OR 0.91, 95% CI 0.25–3.36); (b) influenza-like illness (RCTs: OR 0.51, 95% CI 0.19–1.41); or (c) reported workplace absenteeism (RCT: OR 0.92, 95% CI 0.57–1.50). In the surrogate exposure studies, N95 respirators were associated with less filter penetration, less face-seal leakage and less total inward leakage under laboratory experimental conditions, compared with surgical masks.

Interpretation: Although N95 respirators appeared to have a protective advantage over surgical masks in laboratory settings, our meta-analysis showed that there were insufficient data to determine definitively whether N95 respirators are superior to surgical masks in protecting health care workers against transmissible acute respiratory infections in clinical settings.

Competing interests: None declared.

This article has been peer reviewed.

Accepted: Dec. 2, 2015
Online: Mar. 7, 2016

Correspondence to:
Gary Garber, gary.garber@oahpp.ca

CMAJ 2016. DOI:10.1503/cmaj.150835

Transmission of acute respiratory infections occurs primarily by contact and droplet routes, and accordingly, the use of a surgical mask, eye protection, gown and gloves should be considered appropriate personal protective equipment when providing routine care for a patient with a transmissible acute respiratory infection.[1–3] Concerns have been raised about possible acute respiratory infection spread via limited-distance airborne transmission, but this is controversial and has not been proven.[1,4–9] Also, experimental data suggest the superiority of N95 filtering facepiece respirators (N95 respirators) over surgical masks for the prevention of acute respiratory infections.[1] Randomized controlled trials (RCTs) and observational studies comparing N95 respirators and surgical masks have not shown a benefit, but they may have been underpowered.[10–17]

The lack of clarity has led to conflicting guideline recommendations regarding respiratory protective equipment for the prevention of acute respiratory infections: N95 respirators are recommended in some guidelines but not others.[18] Since the outbreak of severe acute respiratory syndrome (SARS), there has been a heightened level of controversy within Canada in determining the optimal ways to protect health care workers from respiratory pathogens. Conflicting recommendations from federal and provincial health authorities lead to confusion among heath care workers, which can result in lack of adherence to basic infection control principles and practices.

We performed a systematic review to assess and synthesize the available body of literature regarding N95 respirators versus surgical masks for the protection of health care workers against acute respiratory infections in a health care setting.

Methods

A detailed protocol developed a priori is described in Appendix 1 (available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.150835/-/DC1).

Literature search

We searched MEDLINE, Embase, the Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, Health Technology Assessment, the Collective Index of Nursing and Allied Health Literature, PsycINFO and Scopus for pertinent English-language studies published from Jan. 1, 1990, to Dec. 9, 2014. (The search strategies are available in Appendix 1, Tables S1–S9.) The search start date marks 4 years before N95 respirators became a part of standard respiratory protective equipment among health care workers in the United States.

We also conducted searches of the grey literature to obtain unpublished data. These searches were limited to the past 5 years (see Appendix 1, Table S10, for search details).

Study selection

Randomized controlled trials, prospective and retrospective cohort studies, and case–control studies were eligible for inclusion in the meta-analysis. Participants in clinical studies were health care workers in a health care setting. We defined health care worker as any worker in a health care setting who might be exposed to a patient with an acute respiratory infection. We excluded studies that solely involved protection of patients or community populations.

Surrogate exposure studies (i.e., experiments involving manikins or volunteers exposed to artificially produced aerosols) were not eligible for inclusion in the meta-analysis but were summarized to provide an overview of the laboratory-based experimental evidence for use of N95 respirators to protect against acute respiratory infections. Aerosols are defined as a suspension of very small (0.01–100 μm in diameter) particles or droplets in the air.[19] Studies with manikins or adult volunteers exposed to an aerosol simulating what might occur in a health care setting were considered.

Study designs assessed the use of National Institute for Occupational Safety and Health certified N95 respirators compared with surgical masks. Certification must have been under public health regulations (42 CFR part 84). Respirators certified under the former regulations (at 30 CFR part 11) were ineligible because they are no longer in use.[20] We also included data on European standard filtering facepiece (FFP2) respirators (standards EN149:2001 and EN149:2001+A1:2009) as data on N95 filtering facepiece respirators. We did not include data on elastomeric facepiece respirators because they are not in widespread use in health care settings. The term "surgical mask" was considered equivalent to medical masks, procedural masks, isolation masks, laser masks, fluid-resistant masks and face masks that meet bacterial and particle filtration efficiency standards required by the US Food and Drug Administration (ASTM standard F2100–11) but are not certifiable as N95 respirators. Other types of respirators and surgical masks not explicitly described here were excluded.

Data extraction and quality assessment

The primary outcome of interest from RCTs, cohort studies and case–control studies was laboratory-confirmed respiratory infection, including respiratory infections diagnosed by means of polymerase chain reaction, serology, respiratory virus culture and *Bordetella pertussis* bacterial culture. Secondary outcomes were influenza-like illness, and workplace absenteeism due to hospital-acquired respiratory infections. The outcomes extracted from surrogate exposure studies were filter penetration, face-seal leakage and total inward leakage.

Two reviewers (J.D.S. and C.C.M.) independently screened abstracts, titles and full texts as described in the selection of studies. Data extraction was conducted using an electronic spreadsheet template (completed independently by J.D.S. and C.C.M.) and compared for discrepancies. Data from surrogate exposure studies were transformed, when appropriate, from fit-factors, protection factors or filter efficiencies to penetration percentages. When necessary, one of us (J.D.S.) contacted authors for additional information (Appendix 1, Table S11).

Randomized controlled trials were explicitly assessed for bias according to the Cochrane risk-of-bias tool.[21] Cohort and case–control studies were assessed for risk of design-specific bias using the relevant Newcastle–Ottawa Scale.[22]

Outcome-specific quality of the body of evidence was assessed in duplicate by the same 2 reviewers using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework.[23,24] Disagreements were resolved through consultation with a third reviewer

(J.J.). The quality of evidence can be graded as high, moderate, low or very low.

Data synthesis

Where data could be combined for meta-analyses, these data were reported as odds ratios (ORs). We combined similar study designs only for the meta-analysis. Data were measured on dichotomous outcomes (laboratory-confirmed respiratory infection, influenza-like illness and workplace absenteeism). A random-effects analysis model and inverse variance statistical method were used for meta-analysis using Review Manager (RevMan).[25]

Cluster RCTs were adjusted for the meta-analysis with individual RCTs. We used the intraclass correlation coefficient to determine the design effect.[26] Design effect was used to determine the effective sample size.[26] When the effective sample size was not a whole number, it was rounded to the nearest whole number.

For meta-analyses involving rare events, zero cell counts were adjusted by including a correction (the reciprocal of the size of the contrasting study arm).[27]

We assessed evidence of heterogeneity using the χ^2 test and I^2 statistic; a χ^2 value less than 0.10 or an I^2 value greater than 50% indicated significant heterogeneity.[28,29] Subgroup analysis was planned if there were more than 5 pooled studies and when significant heterogeneity was present.

All statistical analyses were performed with the use of RevMan (version 5.2; The Nordic Cochrane Centre, The Cochrane Collaboration, 2012).

Results

Search results and study characteristics

We screened 8962 titles, excluded 8855 and retrieved 107 articles for full-text assessment. We selected 31 eligible articles involving 29 studies; 6 were clinical studies that we included in the meta-analysis, and 23 were surrogate exposure studies (Figure 1). No unpublished abstracts of RCTs, cohort studies or case–control studies were found.

We included 3 RCTs, 1 cohort study and 2 case–control studies in the meta-analysis.[11–17] The main characteristics of these studies are found in Table 1. All 6 studies reported laboratory-confirmed respiratory infection. Definitions of laboratory-confirmed respiratory infection differed. None of the RCTs used *B. pertussis* bacterial culture or viral culture. Neither of the RCTs by MacIntyre and colleagues[12–14] used serology. The SARS cases in the cohort study[15] and one of the case–control studies were confirmed only by serology.[16] Zhang and colleagues[17] confirmed influenza only by polymerase chain reaction. All of the RCTs reported on influenza-like illness. One RCT also reported workplace absenteeism; however, the outcome could not be confirmed to result from nosocomial respiratory infections.[11]

Effect on outcomes

No significant difference in risk of laboratory-confirmed respiratory infection was detected between health care workers using N95 respirators and those using surgical masks in the meta-analysis of the RCTs (OR 0.89, 95% confidence interval [CI] 0.64–1.24; $I^2 = 0\%$), the cohort study (OR 0.43, 95% CI 0.03–6.41) or the case–control studies (OR 0.91, 95% CI 0.25–3.36; $I^2 = 0\%$) (Figure 2). Similar results were found in 2 post-hoc meta-analyses: in one, we combined data from the 3 observational studies (OR 0.79, 95% CI 0.24–2.56; $I^2 = 0\%$); in the other, although not advised, we pooled data from all of the studies as an intellectual exercise to try to ascertain whether

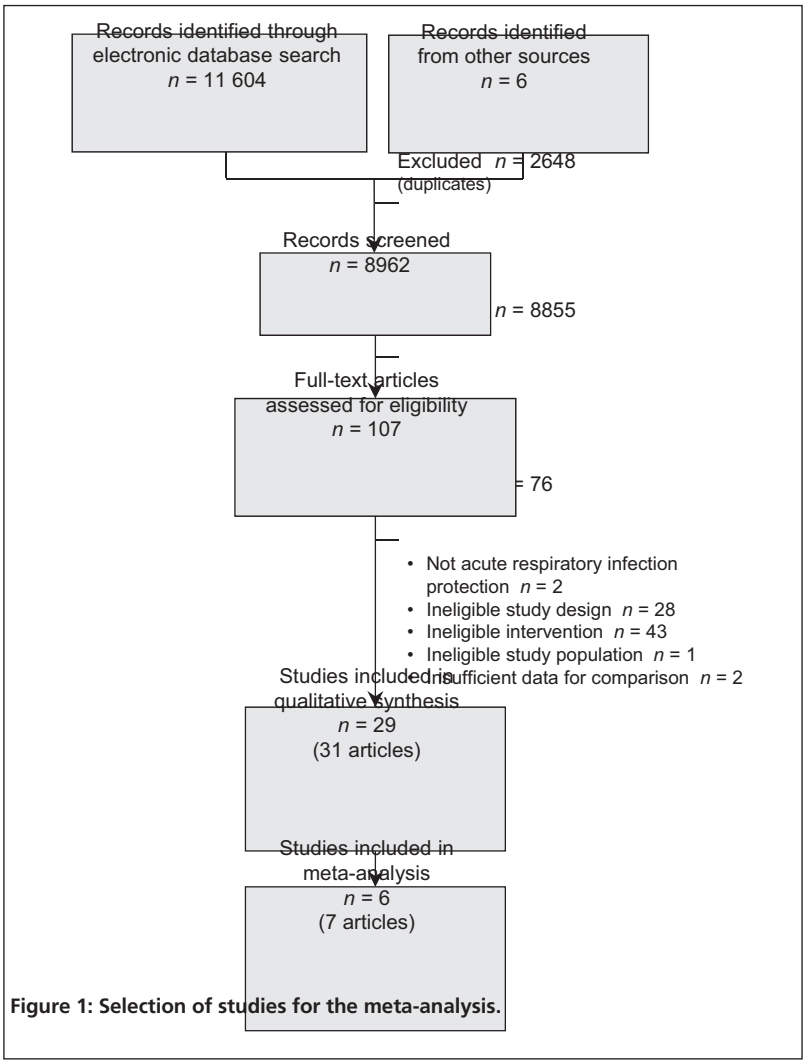


Figure 1: Selection of studies for the meta-analysis.

more precision could theoretically be obtained (OR 0.88, 95% CI 0.64–1.21; $I^2 = 0\%$).

We found no significant difference in risk of influenza-like illness between N95 respirators and surgical masks in the meta-analysis of the 3 RCTs (OR 0.51, 95% CI 0.19–1.41; $I^2 = 18\%$) (Figure 2). We also found no significant difference in risk of workplace absenteeism between N95 respirators and surgical masks in the 1 RCT that measured this outcome[11] (OR 0.92, 95% CI 0.57–1.50) (Figure 2).

Risk of bias

The risk of bias for the RCTs is summarized in Figure S1 of Appendix 1. In brief, risk-of-bias ratings were identical across each domain of the Cochrane risk-of-bias tool for all included RCTs (low risk of bias for random sequence

Table 1: Characteristics of studies included in the meta-analysis[11–17]

Study	Setting	Participants	Outcomes	Interventions	Notes
Randomized controlled trials					
Loeb et al., 2009[11]	8 hospitals in Ontario, Canada: emergency departments, acute medical units and pediatric units	446 nurses; individual-level randomization	• Laboratory-confirmed respiratory infection, influenza-like illness, workplace absenteeism • 5-wk follow-up	• Intervention: targeted use, fit-tested N95 respirator • Control: targeted use, surgical mask	• Noninferiority trial • Detection of influenza A and B, respiratory syncytial virus metapneumovirus, parainfluenza virus, rhinovirus–enterovirus, coronavirus and adenovirus
MacIntyre et al., 2011/2014[12,13]	15 hospitals in Beijing: emergency departments and respiratory wards	1441 nurses, doctors and ward clerks; cluster randomization by hospital	• Laboratory-confirmed respiratory infection, influenza-like illness • 5-wk follow-up	• Intervention 1: continual use, fit-tested N95 respirator • Intervention 2: continual use, non–fit-tested N95 respirator • Control: continual use, surgical mask	Detection of influenza A and B, respiratory syncytial virus metapneumovirus, parainfluenza virus, rhinovirus–enterovirus, coronavirus, adenovirus, *Streptococcus pneumoniae*, *Bordetella pertussis*, *Chlamydophila pneumoniae*, *Mycoplasma pneumoniae* and *Haemophilus influenzae* type B
MacIntyre et al., 2013[14]	19 hospitals in Beijing: emergency departments and respiratory wards	1669 nurses, doctors and ward clerks; cluster randomization by ward	• Laboratory-confirmed respiratory infection, influenza-like illness • 5-wk follow-up	• Intervention 1: continual use, fit-tested N95 respirator • Intervention 2: targeted use, fit-tested N95 respirator • Control: continual use, surgical mask	Detection of influenza A and B, respiratory syncytial virus metapneumovirus, parainfluenza virus, rhinovirus–enterovirus, coronavirus, adenovirus, *S. pneumoniae*, *B. pertussis*, *C. pneumoniae*, *M. pneumoniae* and *H. influenzae* type B
Cohort study					
Loeb et al., 2004[15]	2 hospitals in Ontario: coronary care units and ICUs with SARS patients	43 nurses	Laboratory-confirmed respiratory infection	• Intervention: N95 respirator • Control: surgical mask	• Retrospective • Only 20 nurses reported exposures and consistent use of facial protective equipment • Detection of SARS
Case–control studies					
Seto et al., 2003[16]	5 hospitals in Hong Kong: emergency departments and medicine units	13 infected (cases) and 241 noninfected (controls) nurses, doctors, health care assistants and domestic staff	Laboratory-confirmed respiratory infection	• N95 respirator • Surgical mask • Paper mask	• No cases in N95 respirator or surgical mask groups • 143 controls wore either surgical mask or N95 respirator • Detection of SARS
Zhang et al., 2013[17]	25 hospitals in Beijing: emergency departments, respiratory wards, ICUs, outpatient departments, technical clinic departments and management	51 infected (cases) and 204 noninfected (controls) doctors, nurses, technicians and other	Laboratory-confirmed respiratory infection	• N95 respirator • Surgical mask • Cloth mask	• Cases and controls matched 1:4 by hospital, ward, age and sex • 40 cases wore either N95 respirator or surgical mask • 159 controls wore either surgical mask or N95 respirator • Detection of pandemic H1N1 influenza virus

Note: ICU = intensive care unit, SARS = severe acute respiratory syndrome.

generation, incomplete outcome data, selective reporting and "other" bias; unclear risk of bias for allocation concealment; and high risk of bias for blinding of participants) except for blinding of outcome assessment, which was rated as unclear risk of bias for the RCT by

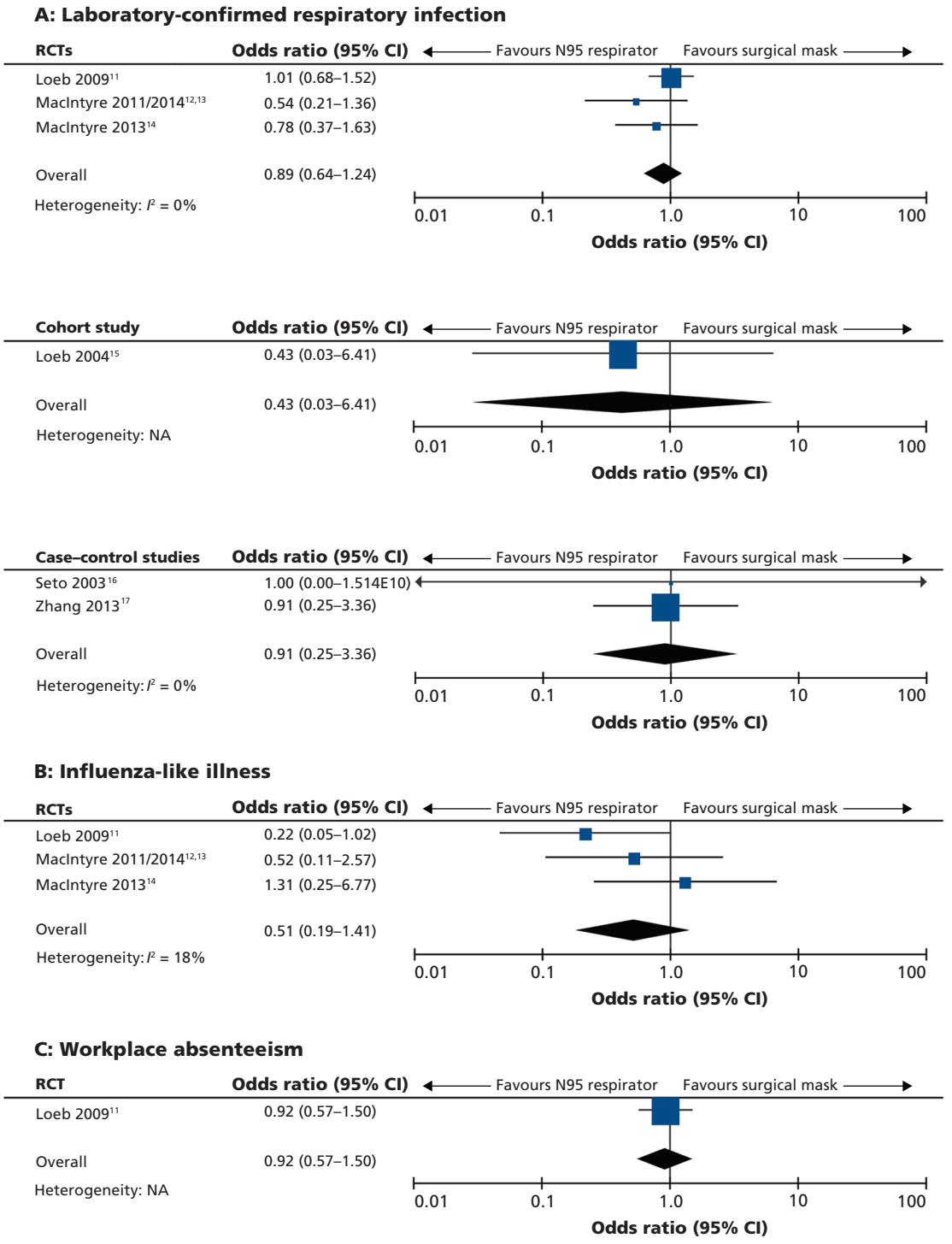


Figure 2: Results of meta-analysis to determine effectiveness of N95 respirators versus surgical masks in protecting health care workers against acute respiratory infection. Outcomes were (A) laboratory-confirmed respiratory infection, (B) influenza-like illness and (C) workplace absenteeism. Values less than 1.0 favour N95 respirator. CI = confidence interval, NA = not applicable, RCT = randomized controlled trial.

Loeb and colleagues[11] but as high risk of bias for the other 2 RCTs.[12–14]

Risk of bias for the cohort and case–control studies is summarized in Table S12 of Appendix 1. In brief, the cohort study[15] received a rating of 6 stars, one of the case–control studies received 3 stars,[16] and the other case–control study received 6 stars.[17]

Outcome-specific quality of evidence

The ratings of importance and outcome-specific quality of evidence that we assessed using the GRADE approach are summarized in Table S13 of Appendix 1. In brief, laboratory-confirmed respiratory infection was deemed a critically important outcome for decision-making with low-quality evidence from RCTs, and an important outcome for decision-making with very-low-quality evidence from observational studies. Influenza-like illness was rated as an important outcome for decision-making with very-low-quality evidence from RCTs. Work-related absenteeism was considered not an important outcome for decision-making with very-low-quality evidence from 1 RCT.

We did not conduct subgroup analyses because no significant heterogeneity was detected. No meaningful sensitivity analyses could be performed because too few studies were included.

Summary of surrogate exposure studies

Twenty-three surrogate exposure studies were included.[30–53] Their outcomes and general methods (e.g., participants, particles used for exposure, number and type of respirator or surgical mask used, flow rates and breathing rates of manikins, size of challenge particles and range of particle size measured) are summarized in Appendix 2 (available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.150835/-/DC1). In general, compared with surgical masks, N95 respirators showed less filter penetration, less face-seal leakage and less total inward leakage under the laboratory experimental conditions described.

Interpretation

Results of our systematic review and meta-analysis show that there was no significant difference between N95 respirators and surgical masks when used by health care workers to prevent transmission of acute respiratory infections from patients. However, wide 95% CIs from our meta-analysis must be interpreted as insufficient evidence to determine whether there is a clinically significant difference. Findings from the surrogate exposure studies suggest that N95 respirators are superior to surgical masks for filter penetration, face-seal leakage and total inward leakage under laboratory conditions.

It was not surprising to find that N95 respirators were generally more efficient filters with better face-seal characteristics than surgical masks when tested in the laboratory. However, transmission of acute respiratory infections is a complex process that may not be appropriately replicated by surrogate exposure studies. Because the face seal is important for the efficiency of the N95 respirator, fit-testing is recommended for health care workers.[2] N95 respirators are often considered uncomfortable for regular use, and improper wearing or adjustment of the respirator because of discomfort could lead to inadvertent face contamination, thus negating the potential protective benefit.[54,55] Furthermore, we do not have an adequate understanding of the number, size and dispersion of the droplets that contain live, infectious particles produced by infected patients.[56] A laboratory-based study reported data that humans infected with influenza rarely produce aerosols that contain infectious viral particles.[57] In 2 other laboratory studies, participants infected with influenza produced droplets containing viral RNA, but viral RNA could not be detected on manikin headforms or on filters of breathing manikins at distances as close as 0.1 m following participants breathing, counting, coughing or laughing.[7]

Limitations

Despite our study's many strengths, including a comprehensive search strategy for published data and grey literature, and a thorough review and assessment for risk of bias and quality of evidence using validated tools, limitations of this review should be acknowledged.

None of the studies included in the meta-analysis, except the RCT by Loeb and colleagues,[11] independently audited compliance with the intervention. Potential confounding due to concurrent interventions (e.g., gloves, gowns and hand hygiene practices) as part of routine and additional precautions for droplet transmission were not accounted for by our meta-analysis.

We did not assess the impact of harms associated with mask and respirator use that could negatively affect the efficacy of the assigned intervention because it was out of the scope of our review.[55]

Acute respiratory infections may have been acquired during the study from community exposures rather than nosocomial exposure. In one of the RCTs,[12,13] transmission may have occurred via contamination of provided respiratory protective equipment during storage and reuse of masks and respirators throughout the workday.

Only 2 respiratory virus seasons were assessed by the 3 RCTs; in one trial,[14] the peak period of one of these influenza seasons was missed, and in another trial,[11] the H1N1 outbreak in 2009 halted the study during the other respiratory season. Year-to-year strain variation of influenza necessitates additional data from other seasons during peak periods.

The weighting of the meta-analysis was influenced by the laboratory-confirmed respiratory infection outcome of serology used in one of the RCTs.[11] However, health care workers who received influenza vaccination were appropriately excluded from analysis based only on serology.

Bias due to lack of blinding in all studies was a key factor in the relatively low GRADE quality assessment, and it is impossible to overcome because the health care workers would know which mask they were wearing.

Finally, these results are not generalizable to infections transmitted primarily through airborne routes (i.e., tuberculosis, measles and varicella) or to protection from acute respiratory infections during aerosol-generating medical procedures.[3]

Conclusion

Although N95 respirators appeared to have a protective advantage over surgical masks in laboratory settings, our meta-analysis showed that there were insufficient data to determine definitively whether N95 respirators are superior to surgical masks in protecting health care workers against transmissible acute respiratory infections in clinical settings. Additional, large RCTs are needed to detect a potentially clinically important difference owing to small event rates. Initial guidelines on preventing acute respiratory infection relied on surrogate exposure data and data extrapolated from the protection of health care workers against tuberculosis because clinical evidence did not exist at that time.[58,59] Randomized controlled trials conducted in clinical settings represent the most valid information to evaluate the effectiveness of N95 respirators. They are more relevant to real clinical situations and report actual outcomes in health care workers, and therefore they are the best evidence on effectiveness to inform policy-making.

References

1. Siegel JD, Rhinehart E, Jackson M, et al. 2007 guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *Am J Infect Control* 2007;35:S65-164.
2. *Routine practices and additional precautions: in all health care settings, 3rd ed*. In: Ontario Agency for Health Protection and Promotion, Provincial Infectious Diseases Advisory Committee. Toronto: Queen's Printer for Ontario; 2012. Available: www.publichealthontario.ca/en/eRepository/RPAP_All_HealthCare_Settings_Eng2012.pdf (accessed 2014 Dec. 12).
3. Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care. Geneva: World Health Organization; 2014. Available: www.who.int/csr/bioriskreduction/infection_control/publication/en/ (accessed 2014 Dec. 9).
4. Chung SJ, Ling ML, Seto WH, et al. Debate on MERS-CoV respiratory precautions: Surgical mask or N95 respirators? *Singapore Med J* 2014;55:294-7.
5. Brankston G, Gitterman L, Hirji Z, et al. Transmission of influenza A in human beings. *Lancet Infect Dis* 2007;7:257-65.
6. Hall CB. The spread of influenza and other respiratory viruses: complexities and conjectures. *Clin Infect Dis* 2007;45:353-9.
7. Tang JW, Gao CX, Cowling BJ, et al. Absence of detectable influenza RNA transmitted via aerosol during various human respiratory activities — experiments from Singapore and Hong Kong. *PLoS One* 2014;9:e107338.
8. Tellier R. Review of aerosol transmission of influenza A virus. *Emerg Infect Dis* 2006;12:1657-62.
9. Roy CJ, Milton DK. Airborne transmission of communicable infection — the elusive pathway. *N Engl J Med* 2004;350:1710-2.
10. Clynes N. Surgical masks vs N95 respirators for preventing influenza. *JAMA* 2010;303:937-8, author reply 938-9.
11. Loeb M, Dafoe N, Mahony J, et al. Surgical mask vs N95 respirator for preventing influenza among health care workers: a randomized trial. *JAMA* 2009;302:1865-71.
12. MacIntyre CR, Wang Q, Cauchemez S, et al. A cluster randomized clinical trial comparing fit-tested and non-fit-tested N95 respirators to medical masks to prevent respiratory virus infection in health care workers. *Influenza Other Respir Viruses* 2011;5:170-9.
13. MacIntyre CR, Wang Q, Rahman B, et al. Efficacy of face masks and respirators in preventing upper respiratory tract bacterial colonization and co-infection in hospital healthcare workers. *Prev Med* 2014;62:1-7.
14. MacIntyre CR, Wang Q, Seale H, et al. A randomized clinical trial of three options for N95 respirators and medical masks in health workers. *Am J Respir Crit Care Med* 2013;187:960-6.
15. Loeb M, McGeer A, Henry B, et al. SARS among critical care nurses, Toronto. *Emerg Infect Dis* 2004;10:251-5.
16. Seto WH, Tsang D, Yung RW, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* 2003;361:1519-20.
17. Zhang Y, Seale H, Yang P, et al. Factors associated with the transmission of pandemic (H1N1) 2009 among hospital healthcare workers in Beijing, China. *Influenza Other Respir Viruses* 2013;7:466-71.
18. Chughtai AA, Seale H, MacIntyre CR. Availability, consistency and evidence-base of policies and guidelines on the use of mask and respirator to protect hospital health care workers: a global analysis. *BMC Res Notes* 2013;6:216.
19. National Institute for Occupational Safety and Health (NIOSH). *Workplace safety and health topics: aerosols*. Atlanta: US Centers for Disease Control and Prevention; 2010. Available: www.cdc.gov/niosh/topics/aerosols/ (accessed 2014 Dec. 10).
20. National Institute for Occupational Safety and Health (NIOSH). *NIOSH guide to the selection and use of particulate respirators*. Atlanta: US Centers for Disease Control and Prevention; 1996. Available: www.cdc.gov/niosh/docs/96-101/ (accessed 2015 Oct. 20).
21. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
22. Wells GA, Shea B, O'Connell D, et al. *The Newcastle–Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses*. Ottawa: The Ottawa Hospital; 2011. Available: www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed 2014 Oct. 22).
23. GRADEpro [computer program]. Hamilton (ON): McMaster University; 2014. Available: www.guidelinedevelopment.org (accessed 2014 Nov. 20).
24. GRADE Working Group. Grading the quality of evidence and the strength of recommendations. Available: www.gradeworkinggroup.org/intro.htm (accessed 2014 Apr. 30).
25. Higgins JPT, Green S, editors. *Cochrane handbook for systematic reviews of interventions, version 5.1.0*. Oxford (UK): Cochrane Collaboration; 2011. Available: handbook.cochrane.org/ (accessed 2014 Jan. 26).
26. Killip S, Mahfoud Z, Pearce K. What is an intracluster correlation coefficient? Crucial concepts for primary care researchers. *Ann Fam Med* 2004;2:204-8.
27. Sweeting MJ, Sutton AJ, Lambert PC. What to add to nothing? Use and avoidance of continuity corrections in meta-analysis of sparse data. *Stat Med* 2004;23:1351-75.
28. Higgins JP, Thomphson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;21:1539-58.
29. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557-60.
30. Bałazy A, Toivola M, Adhikari A, et al. Do N95 respirators provide 95% protection level against airborne viruses, and how adequate are surgical masks? *Am J Infect Control* 2006;34:51-7.

31. Bischoff WE, Reid T, Russell GB, et al. Transocular entry of seasonal influenza-attenuated virus aerosols and the efficacy of N95 respirators, surgical masks, and eye protection in humans. *J Infect Dis* 2011;204:193-9.
32. Checchi L, Montevecchi M, Moreschi A, et al. Efficacy of three face masks in preventing inhalation of airborne contaminants in dental practice. *J Am Dent Assoc* 2005;136:877-82.
33. Davidson CS, Green CF, Gibbs SG, et al. Performance evaluation of selected N95 respirators and surgical masks when challenged with aerosolized endospores and inert particles. *J Occup Environ Hyg* 2013;10:461-7.
34. Davidson C, Green CF, Panlilio AL, et al. Method for evaluating the relative efficiency of selected N95 respirators and surgical masks to prevent the inhalation of airborne vegetative cells by healthcare personnel. *Indoor Built Environ* 2011;20:265-77.
35. Derrick JL, Li PT, Tang SP, et al. Protecting staff against airborne viral particles: in vivo efficiency of laser masks. *J Hosp Infect* 2006;64:278-81.
36. Diaz KT, Smaldone GC. Quantifying exposure risk: surgical masks and respirators. *Am J Infect Control* 2010;38:501-8.
37. Duling MG, Lawrence RB, Slaven JE, et al. Simulated workplace protection factors for half-facepiece respiratory protective devices. *J Occup Environ Hyg* 2007;4:420-31.
38. Gawn J, Clayton M, Makison C, et al. *Evaluating the protection afforded by surgical masks against influenza bioaerosols: gross protection of surgical masks compared to filtering facepiece respirators*. Norwich (UK): Health and Safety Executive; 2008. Available: www.hse.gov.uk/research/rrpdf/rr619.pdf (accessed 2014 June 3).
39. Grinshpun SA, Haruta H, Eninger RM, et al. Performance of an N95 filtering facepiece particulate respirator and a surgical mask during human breathing: two pathways for particle penetration. *J Occup Environ Hyg* 2009;6:593-603.
40. He X, Reponen T, McKay RT, et al. Effect of particle size on the performance of an N95 filtering facepiece respirator and a surgical mask at various breathing conditions. *Aerosol Sci Technol* 2013;47:1180-7.
41. He X, Reponen T, McKay R, et al. How does breathing frequency affect the performance of an N95 filtering facepiece respirator and a surgical mask against surrogates of viral particles? *J Occup Environ Hyg* 2014;11:178-85.
42. Lawrence RB, Duling MG, Calvert CA, et al. Comparison of performance of three different types of respiratory protection devices. *J Occup Environ Hyg* 2006;3:465-74.
43. Lee SA, Grinshpun SA, Reponen T. Respiratory performance offered by N95 respirators and surgical masks: human subject evaluation with NaCl aerosol representing bacterial and viral particle size range. *Ann Occup Hyg* 2008;52:177-85.
44. Li Y, Wong T, Chung J, et al. In vivo protective performance of N95 respirator and surgical facemask. *Am J Ind Med* 2006;49: 1056-65.
45. Lindsley WG, King WP, Thewlis RE, et al. Dispersion and exposure to a cough-generated aerosol in a simulated medical examination room. *J Occup Environ Hyg* 2012;9:681-90.
46. Mansour MM, Smaldone GC. Respiratory source control versus receiver protection: impact of facemask fit. *J Aerosol Med Pulm Drug Deliv* 2013;26:131-7.
47. 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;32:1166-9.
48. Noti JD, Lindsley WG, Blachere FM, et al. Detection of infectious influenza virus in cough aerosols generated in a simulated patient examination room. *Clin Infect Dis* 2012;54:1569-77.
49. Qian Y, Willeke K, Grinshpun SA, et al. Performance of N95 respirators: filtration efficiency for airborne microbial and inert particles. *Am Ind Hyg Assoc J* 1998;59:128-32.
50. Rengasamy S, Eimer BC. N95-companion measurement of C_{out}/C_{in} ratios for two N95 filtering facepiece respirators and one surgical mask. *J Occup Environ Hyg* 2013;10:527-32.
51. Rengasamy S, Eimer BC, Szalajda J. A quantitative assessment of the total inward leakage of NaCl aerosol representing submicron size bioaerosol through N95 filtering facepiece respirators and surgical masks. *J Occup Environ Hyg* 2014;11:388-96.
52. Wen Z, Yu L, Yang W, et al. Assessment the protection performance of different level personal respiratory protection masks against viral aerosol. *Aerobiologia* 2013;29:365-72.
53. Zou Z, Yao M. Airflow resistance and bio-filtering performance of carbon nanotube filters and current facepiece respirators. *J Aerosol Sci* 2015;79:61-71.
54. Rebmann T, Carrico R, Wang J. Physiologic and other effects and compliance with long-term respirator use among medical intensive care unit nurses. *Am J Infect Control* 2013;41:1218-23.
55. Jefferson T, Del Mar CB, Dooley L, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. *Cochrane Database Syst Rev* 2011;(7):CD006207.
56. Morawska L. Droplet fate in indoor environments, or can we prevent the spread of infection? *Indoor Air* 2006;16:335-47.
57. Milton DK, Fabian MP, Cowling BJ, et al. Influenza virus aerosols in human exhaled breath: particle size, culturability, and effect of surgical masks. *PLoS Pathog* 2013;9:e1003205.
58. Bozzi CJ, Burwen DR, Dooley SW, et al. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care facilities, 1994. *MMWR Recomm Rep* 1994;43(RR-13):1-132.
59. Gammaitoni L, Nucci MC. Using a mathematical model to evaluate the efficacy of TB control measures. *Emerg Infect Dis* 1997;3:335-42.

Affiliations: Public Health Ontario (Smith, MacDougall, Johnstone, Copes, Schwartz, Garber); Department of Medicine (Johnstone), University of Toronto; Dalla Lana School of Public Health (Copes, Schwartz), University of Toronto, Toronto, Ont.; Department of Medicine (Garber), University of Ottawa, Ottawa, Ont.

Contributors: Jeffrey Smith drafted the protocol and data extraction template, and performed the literature screening, data extraction and analysis. Colin MacDougall provided input for all stages of the project, and performed screening and data extraction. Jennie Johnstone provided input and made revisions on the protocol, data extraction template and analyses. Ray Copes, Brian Schwartz and Gary Garber were involved in the study conception. Gary Garber oversaw the project. Jeffrey Smith drafted the manuscript, and Colin MacDougall, Jennie Johnstone, Ray Copes, Brian Schwartz and Gary Garber provided critical feedback on the manuscript. All of the authors approved the final version to be published and agreed to act as guarantors of the work.

Acknowledgement: The authors are grateful for the contributions of the Library Services team at Public Health Ontario in the development, refinement and execution of the search strategy for this review.

THE JOURNAL OF PROFESSIONAL EXCELLENCE
Dimensions OF DENTAL HYGIENE

Ask The Expert

What Level of Mask Should Dental Hygienists Use?

What level of mask should dental hygienists use when completing typical activities, such as X-rays and patient care? I use level 3, but would level 2 would be sufficient?

By Kandis V. Garland, RDH, MS **On** **Jun 5, 2018** 0

QUESTION: What level of mask should dental hygienists use when completing typical activities, such as X-rays and patient care? I use level 3, but would level 2 would be sufficient?

ANSWER: The Occupational Safety and Health Administration (OSHA) mandates the use of personal protective equipment (PPE) to protect oral health professionals from disease transmission, specifically from bloodborne pathogens such as hepatitis B and human immunodeficiency virus.[1] The United States Centers for Disease Control and Prevention's (CDC) *Guidelines for Infection Control in Dental Health-Care Settings—2003* discuss the use of PPE to prevent splash and spatter to the skin and mucous membranes (eyes, nose, and mouth).[2] Splash, spatter, and aerosols that are potentially infectious from blood, saliva, and microorganisms are generated by handpieces, powered instrumentation, and rinsing. PPE includes surgical face masks, eyewear, gloves, and protective clothing such as lab coats.

The US Food and Drug Administration (FDA) considers surgical face masks one-time-use disposable medical devices.[3] There are many types of masks available, ranging from minimum performance to m

potential for splash/spatter require masks with higher levels of filtration. Whereas, tasks without splash/spatter/aerosol potential, such as for brief examinations or when exposing radiographs, can be performed with masks that have little or no filtration.[4,5]

With more than 12,000 standards, the American Society for Testing and Materials Standards (ASTM) is a global organization that develops voluntary guidance for a variety of industries and products to aid in quality control, product safety, and recommended usage and application.[6] ASTM standard F2100-11 provides specifications for surgical face masks that includes bacterial filtration efficiency (BFE), sub-micron particulate filtration (PFE), delta P differential pressure, fluid resistance, and flammability.[6] Molinari and Nelson state: "95% of dental aerosols are 5.0 microns or less in diameter and cannot be seen."[5] So masks with at least 95% BFE and PFE are preferable in the dental setting during procedures that generate aerosols, such as powered scaling and handpiece use. ASTM levels are classified into three levels of protection (low, moderate, high) to help clinicians decide which mask is appropriate for the task at hand.

Level 1 masks (low protection at $\geq$ 95% BFE and PFE) are suitable for brief examinations, exposing radiographs, and cleaning tasks. Level 2 masks (moderate protection at $\geq$ 98% BFE and PFE) are preferable for procedures that involve a moderate level of aerosols such as hand instrumentation and sealants. Level 3 masks have a high level of protection (at $\geq$ 98% BFE and PFE) and are used for procedures involving high levels of aerosols such as ultrasonic scaling, surgical procedures, and crown preparation.

A level 2 mask would be sufficient for exposing radiographs and routine dental hygiene procedures such as hand scaling; however, a level 3 mask would be preferred if performing tasks such as ultrasonic instrumentation. Depending on the frequency of powered instrumentation use, it might be wise to continue to use level 3 masks.

The 2003 CDC guidelines recommend masks be changed between patients, when they become wet from breath or splash, and during patient care with highly aerosolized procedures (every 20 minutes).[2] Wet masks can lead to microbial penetration, making the mask ineffective.[2] Masks should create a seal covering the nose and mouth[2] and be comfortable without any gaps, which may allow microorganisms to penetrate. Compliance with masks depends on comfort, temperature, and breathability. Delta P differential penetration represents the air flow measured in mmH20/cm[2] so a mask with a higher delta P differential provides better filtration but less breathability.[6]

Masks are a required part of routine safe patient care and the selection depends on several factors including ASTM level for type of procedure being performed, comfort, and cost.

REFERENCES

1. Occupational Safety and Health Administration. Bloodborne Pathogens Standard Regulations (Standard 29 CFR. 1910.1030). Available at: osha.gov/pls/oshaweb/owadisp.show_document?

2. Kohn WG, Collins AS, Cleveland JL, et al. Guidelines for infection control in dental health-care settings —2003. *MMWR Recomm Rep*. 2003;52(RR-17):1–61.
3. Food and Drug Administration (FDA). Guidance for Industry and FDA Staff: Surgical Masks. Available at: fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm072549.htm. Accessed May 8, 2018.
4. Molinari J, Nelson P. Face masks what to wear and when. *The Dental Advisor.* October 18, 2014.
5. Molinari J, Nelson P. Face mask performance: Are you protected? Available at: medicom.com/uploads/files/Medicom%20Face%20Mask%20Performance
6. %20Article_v3(1).pdf. Accessed May 8, 2018.
7. American Society for Testing and Materials Standards (ASTM). ASTM F2100–11. Standard Specification for Performance of Materials Used in Medical Face Masks. Available at: astm.org/Standards/F2100.htm. Accessed May 8, 2018.

The Ask the Expert column features answers to your most pressing clinical questions provided by *Dimensions of Dental Hygiene's* online panel of key opinion leaders, including: Jacqueline J. Freudenthal, RDH, MHE, on anesthesia; Nancy K. Mann, RDH, MSEd, on cultural competency; Claudia Turcotte, CDA, RDH, MSDH, MSOSH, on ergonomics; Van B. Haywood, DMD, and Erin S. Boyleston, RDH, MS, on esthetic dentistry; Michele Carr, RDH, MA, and Rachel Kearney, RDH, MS, on ethics and risk management; Durinda Mattana, RDH, MS, on fluoride use; Kandis V. Garland, RDH, MS, on infection control; Mary Kaye Scaramucci, RDH, MS, on instrument sharpening; Stacy A. Matsuda, RDH, BS, MS, on instrumentation; Karen Davis, RDH, BSDH, on insurance coding; Cynthia Stegeman, EdD, RDH, RD, LD, CDE, on nutrition; Olga A.C. Ibsen, RDH, MS, on oral pathology; Jessica Y. Lee, DDS, MPH, PhD, on pediatric dentistry; Bryan J. Frantz, DMD, MS, and Timothy J. Hempton, DDS, on periodontal therapy; Ann Eshenaur Spolarich, RDH, PhD, on pharmacology; and Caren M. Barnes, RDH, MS, on polishing. Log on to dimensionsofdentalhygiene.com/asktheexpert to submit your question.

From *Dimensions of Dental Hygiene*. June 2018;16(6):46.

Kandis V. Garland, RDH, MS

Kandis V. Garland, RDH, MS, is an associate professor in the Department of Dental Hygiene at Idaho State University in Pocatello, as well as health and safety coordinator and clinic director. Her research, which she presents nationally, focuses on infection control. Garland is a member of the Organization for Safety, Asepsis and Prevention and *Dimensions of Dental Hygiene's* Peer Review Panel.

Appendix A: Authorized Respirators
Updated: May 7, 2020

The Authorized Respirators

Authorized respirators should be used in accordance with CDC's recommendations. For the most current CDC recommendations on optimizing respirator use, please visit CDC's webpage: Strategies for Optimizing the Supply of N95 Respirators.

Authorized Imported, Non-NIOSH Approved Respirators Manufactured in China

Manufacturer	Respirator Model(s)	Country of Manufacture
3M	9001, 9002, 9501, 9501+, 9501V+, 9502, 9502+, 9502V+, 9505+, 9541, 9541V, 9542, 9542V, 9552, 9552V	China
AOK Tooling Ltd. (aka Shenzhonghai Medical)	20130040, 20130045A, 20180021, 20130038, 20190019	China
Bei Bei Safety Co Ltd.	B702, B702V, B704, B704V	China
BYD Precision Manufacture Co. Ltd.	BYD KN95 Particulate Respirator (Model Number: DG3101)	China
Fujian Kang Chen Daily Necessities Co, Ltd.	K0450, 57793	China
Guangzhou Harley Commodity Company Limited	L-103V KN95	China
Guangzhou Powecom Labor Insurance Supplies Co., LTD	KN95	China

HeiQ Materials AG	HVB-FFP2-01	China
Hangzhou San Qiang Safety Protection Products Co., Ltd.	9420 (FFP2), 9420V (FFP2), 9480 (FFP2), 9480V (FFP2), 9980V (FFP3), 9920V (FFP3)	China
Rizhao Sanqi Medical & Health Articles Co., Ltd	RIZ100CVb, 3Q KN95, 3Q FFP2 NR, RIZQ100Sb, 3Q KN95 9505	China
Shanghai Dasheng Health Products Manufacture Company, Ltd.	DTC3X-1, DTC3X-2, DTC3X-3, DTC3B-1	China
Suzhou Bolisi Medical Technology Co., Ltd	BS-9501L, BS-9501FL, BS-9502C, BS-9502FC	China
Suzhou Sanical Protective Product Manufacturing Co., Ltd	Model 8015, Model 9015	China
Weini Technology Development Co., Ltd	FFP2 NR E-300, FFP2 NR E-680, FFP2 NR 952, FFP2 NR F-820	China

JAMA | Original Investigation

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

Lewis J. Radonovich Jr, MD; Michael S. Simberkoff, MD; Mary T. Bessesen, MD; Alexandria C. Brown, PhD; Derek A. T. Cummings, PhD; Charlotte A. Gaydos, MD; Jenna G. Los, MLA; Amanda E. Krosche, BS; Cynthia L. Gibert, MD; Geoffrey J. Gorse, MD; Ann-Christine Nyquist, MD; Nicholas G. Reich, PhD; Maria C. Rodriguez-Barradas, MD; Connie Savor Price, MD; Trish M. Perl, MD; for the ResPECT investigators

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 influenzalike 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.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT01249625

JAMA. 2019;322(9):824-833. doi:10.1001/jama.2019.11645

Visual Abstract

Editorial page 817

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The ResPECT investigators appear at the end of the article.

Corresponding Author: Lewis J. Radonovich Jr, MD, National Personal Protective Technology Laboratory, Centers for Disease Control and Prevention, 626 Cochrans Mill Rd, B141, R108, Pittsburgh, PA 15236 (mto5@cdc.gov).

Health care personnel (HCP) who are routinely exposed to viral respiratory infections in the workplace[1] 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%.[2-4] 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,[5] comparative clinical effectiveness studies have been inconclusive.[3,4,6] Some experts argue that N95 respirators and medical masks are equivalent in clinical settings.[2,7] Pragmatic effectiveness trials are increasingly recognized as an essential component of medical evidence, in part because efficacy studies may overestimate effectiveness and true adherence.[8]

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,[9] must meet filtration requirements,[10] 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.[11]

Clinical evidence is inconclusive regarding whether N95 respirators are more effective than medical masks for preventing viral respiratory infection among HCP, including influenza,[3,4,6,12] accounting for differing practices[2] and positions held by clinical,[7] public health,[13,14] and regulatory organizations.[15] The objective of this study was to compare[13] 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.

Key Points

Question Is the use of N95 respirators or medical masks more effective in preventing influenza infection among outpatient health care personnel in close contact with patients with suspected respiratory illness?

Findings In this pragmatic, cluster randomized clinical trial involving 2862 health care personnel, there was no significant difference in the incidence of laboratory-confirmed influenza among health care personnel with the use of N95 respirators (8.2%) vs medical masks (7.2%).

Meaning As worn by health care personnel in this trial, use of N95 respirators, compared with medical masks, in the outpatient setting resulted in no significant difference in the rates of laboratory-confirmed influenza.

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-05XP) and the institutional review boards (IRBs) at the 7 participating health systems, as previously described,[16] 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[16] 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,[13] and medical masks, used as recommended to prevent seasonal influenza[17,18] and other viral respiratory infections and illnesses, among HCP.[17] 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.[16]

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 ≥24 hours weekly) and worked primarily at the study site (defined as ≥75% of working hours). Exclusion criteria were medical conditions precluding safe participation or anatomic features that

Box 1. Criteria for Acute Respiratory Illness[a]

Signs
Coryza
Fever (temperature >37.8 °C)
Lymphadenopathy
Tachypnea (respiratory rate >25/min)

Symptoms
Arthralgias/myalgias/body aches
Chills
Cough
Diarrhea
Dyspnea
Fatigue
Headache
Malaise
Other gastrointestinal systems
Sore throat
Sputum production
Sweats
Vomiting/nausea

[a] An acute respiratory illness was defined as the presence of at least 1 sign or 2 symptoms listed, representing a change from baseline.

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[13] or medical masks,[17,18] as previously described.[16] 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.[19] 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[15] 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[20] 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.[13,17,18] 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[21] (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[22] 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 preseason and postseason 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,[23] 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 preintervention to postintervention serum antibody titers to influenza A or B virus; and (4) influenzalike illness, defined as temperature of at least 100°F (37.8°C) plus cough and/or a sore throat, with or without laboratory confirmation.

Box 2. Respiratory Pathogens Assayed by Polymerase Chain Reaction

- Adenoviruses
- Coxsackie/echoviruses
- Coronavirus HKU1
- Coronavirus NL63
- Coronavirus OC43
- Coronavirus 229E
- Human metapneumovirus
- Human rhinovirus
- Influenza A
- Influenza B
- Parainfluenza virus type 1
- Parainfluenza virus type 2
- Parainfluenza virus type 3
- Parainfluenza virus type 4a
- Parainfluenza virus type 4b
- Respiratory syncytial virus type A
- Respiratory syncytial virus type B

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

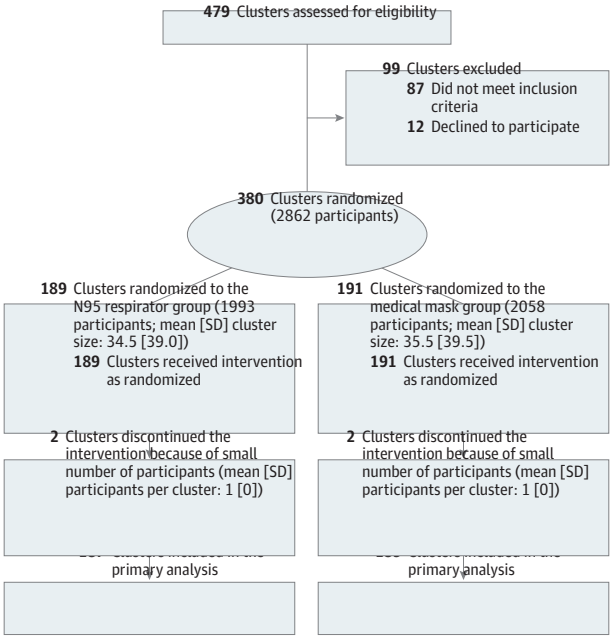
Although we identified no standard definition of a "clinically significant difference," this study[16] was designed to detect a 25% relative reduction in the incidence of laboratory-confirmed influenza or respiratory illness, based on expert opinion, rather than an absolute reduction, which has been described in a previous study.[6] 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 χ^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.[23] 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 χ^2 tests. Mean workplace and household rates of exposure to respiratory illness were compared using mixed-effects logistic regression. For

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



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).

Results

Participants

The study sites were randomized to provide 380 cluster-seasons 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)

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)[a]	No. (%) Medical Mask (n = 2668 HCP-Seasons)[a]
Age, mean (SD), y	43 (11.5)	43 (11.6)
Sex		
Men	378 (15.0)	420 (15.7)
Women	2134 (85.0)	2248 (84.3)
Ethnicity		
Hispanic or Latino	397 (15.8)	427 (16)
Race	(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)
Occupation		
Nurse/nursing trainee	1049 (41.8)	1085 (40.7)
Clinical care support staff[b]	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)
Occupational risk[c]		
High	1492 (59.4)	1594 (59.7)
Medium	295 (11.7)	318 (11.9)
Low	724 (28.8)	755 (28.3)
Patient population		
Adult	1409 (56.1)	1486 (55.7)
Pediatric	573 (22.8)	557 (20.9)
Adult and pediatric	530 (21.1)	625 (23.4)
Clinic type		
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)
Site		
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)
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	(n = 2444)	(n = 2598)
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.

[a] Unless otherwise specified.

[b] Staff who have direct patient contact, such as clinical medical assistants and clinical technicians.

[c] 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.

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 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
Influenza (primary outcome)										
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
All events[a]										
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
Secondary Outcomes										
Acute respiratory illness	235	234	354	446	398	519	569	512	1556	1711
Laboratory-detected respiratory infection[b]	47	71	165	201	217	260	250	213	679	745
Laboratory-confirmed respiratory illness[b]	26	31	91	116	111	150	143	120	371	417
Influenzalike illness	13	10	30	45	22	50	63	61	128	166

[a] 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.

[b] 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.

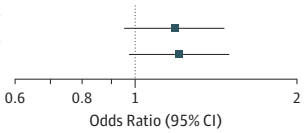
Respiratory viruses are primarily transmitted by large droplets. Because a fraction of respiratory viruses may be transmitted by aerosol, N95 respirators have been presumed to provide better protection than medical masks against viral respiratory infections in health care settings.[2] However, definitive evidence of greater clinical effectiveness of N95 respirators is lacking. A well-designed trial[6] 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[3,4] (and a pooled analysis[12]) concluded that N95 respirators may be more effective than medical masks; however, these studies were limited by uncertain clinical significance of end points.[24] 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.[2,7,13,18,24,25]

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

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

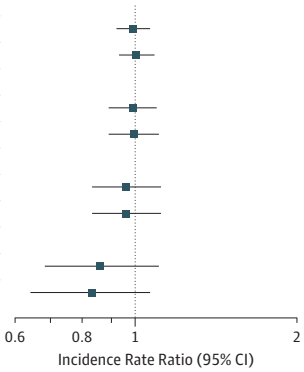
A Primary outcome

	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)
Influenzalike 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.

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[3,4,6,12,26-28] 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.[2,7,14,17,29] 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.[30] Third, despite being intentionally conducted as a pragmatic effectiveness trial,[8] 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.

ARTICLE INFORMATION

Accepted for Publication: July 25, 2019.

Author Affiliations: National Personal Protective Technology Laboratory, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Pittsburgh, Pennsylvania (Radonovich); Veterans Affairs New York Harbor Healthcare System, New York (Simberkoff); New York University School of Medicine, New York (Simberkoff); Veterans Affairs Eastern Colorado Healthcare System, Denver (Bessesen); University of Colorado School of Medicine, Aurora (Bessesen, Nyquist, Price); University of Massachusetts, Amherst (Brown, Reich); University of Florida, Gainesville (Cummings); Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland (Cummings, Perl); Johns Hopkins School of Medicine, Baltimore, Maryland (Gaydos, Los, Krosche); Weill Cornell Medicine, New York, New York (Krosche); Veterans Affairs Medical Center, Washington, DC (Gibert); George Washington University School of Medical and Health Sciences, Washington, DC (Gibert); Veterans Affairs St Louis Healthcare System, St Louis, Missouri (Gorse); St Louis University School of Medicine, St Louis, Missouri (Gorse); Children's Hospital Colorado, Aurora (Nyquist); Michael E. DeBakey Veterans Affairs Medical Center, Houston, Texas (Rodriguez-Barradas); Baylor College of Medicine, Houston, Texas (Rodriguez-Barradas); Denver Health Medical Center, Denver, Colorado (Price); University of Texas Southwestern Medical Center, Dallas (Perl).

Author Contributions: Drs Perl and Radonovich had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Radonovich, Simberkoff, Cummings, Gaydos, Gorse, Reich, Perl.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Radonovich, Simberkoff, Cummings, Gaydos, Nyquist, Reich, Perl.
Critical revision of the manuscript for important intellectual content: Radonovich, Bessesen, Brown, Cummings, Gaydos, Los, Krosche, Gibert, Gorse, Nyquist, Reich, Rodriguez-Barradas, Price, Perl.
Statistical analysis: Brown, Cummings, Reich.
Obtained funding: Cummings, Perl.
Administrative, technical, or material support: Radonovich, Simberkoff, Bessesen, Cummings, Gaydos, Los, Krosche, Gorse, Nyquist, Rodriguez-Barradas, Price, Perl.
Supervision: Radonovich, Simberkoff, Cummings, Los, Nyquist, Reich, Price, Perl.
Other - execution of study design; data management and monitoring: Los.
Other - Site principal investigator for conduct of study and also contributed ongoing input on conduct and analysis of study: Gibert.
Other - laboratory testing support: Gaydos.
Other - recruiting patients: Price.

Conflict of Interest Disclosures: Dr Bessesen reported receiving grants from the Department of Veterans Affairs during the conduct of the study. Dr Brown reported receiving grants from the US Department of Veterans Affairs during the conduct of the study. Dr Cummings reported receiving grants from the Centers for Disease Control and Prevention, the National Institutes of Health, and MedImmune outside the submitted work and the Biomedical Advanced Research and Development Authority during the conduct of the study. Ms Los reported receiving grants from Centers for Disease Control and Prevention, the Veterans Health Administration, and the Biodefense Advanced Research and Development Agency during the conduct of the study. Dr Gibert reported receiving financial support for the conduct of the study, including research personnel, from the Veterans Health Administration during the conduct of the study. Dr Gorse reported receiving grants from the US Department of Veterans Affairs during the conduct of the study. Dr Nyquist reported receiving grants from the Centers for Disease Control and Prevention/Division of Healthcare Quality Promotion, the National Institute for Occupational Safety and Health, and the Veterans Health Administration during the conduct of the study; personal fees and nonfinancial support from Sequirus outside the submitted work; and serving on a policy making committee regarding infectious disease for the American Academy of Pediatrics Committee on Infectious Diseases. Dr Reich reported receiving grants from Veterans Health Administration during the conduct of the study. Dr Rodriguez-Barradas reported receiving grants from Veterans Affairs Central Office during the conduct of the study. Dr Perl reported receiving grants from the Centers for Disease Control and Prevention and Biomedical Advanced Research and Development Authority during the conduct of the study and grants from Medimmune outside the submitted work. No other disclosures were reported.

Funding/Support: This trial was funded by the US Centers for Disease Control and Prevention, Veterans Health Administration, and the Biodefense Advanced Research and Development Agency.

Role of the Funder/Sponsor: The sponsors were not involved in data collection, analysis, or interpretation; writing of the manuscript; or the decision to submit the manuscript. The sponsors reviewed and made technical comments about the study protocol prior to enrollment and the final manuscript prior to submission for publication.

Group Information: For the ResPECT Team (Contributors): The Johns Hopkins University and Health System (Baltimore, MD): Trish M. Perl, MD, MSc; Justin Getka, BA; Tina Hoang, MS; Rose Kajih, PharmD; Amanda Krosche, BS; Meghan Kubala, MS, MD: Jenna Los, MLA; Liandra Presser, MD; Kathleen Pulice, MS; Margaret Spach, DDS. VA New York Harbor Healthcare System (New York, NY): Michael S. Simberkoff, MD; Cynthia Akagbosu, BA, MA; Madeline Dansky, BA; Benedict J. Frederick, BA; Marilyn Last, RN; Scott Laverie, RN; Courtney Pike, BA; Shefali Rikhi, BS; Nicole Spector, RN; Christine A. Reel-Brander, RN. Denver Health & Hospital Authority (Denver, CO): Connie Price, MD; Katie Gorman, BS; Amy Irwin, DNP, RN; Sean O'Malley; Kevin Silva, BS. UT Southwestern Medical Center (Dallas, TX) Trish M. Perl, MD, MSc; Deepa Raj, MPH; VA Eastern Colorado Healthcare System (Aurora, CO): Mary Bessesen, MD; Jill C. Adams BSN, BA; Shannon Kingery, BS; Stefanie Tuder, BS; Erron Fritchman-Palmer, MPH. Children's Hospital Colorado (Denver, CO): Ann-Christine Nyquist, MD, MSPH; Megan Gorski, BA. VA Washington DC Medical Center (Washington, DC): Cynthia Gibert, MD, MSc; Laura Chopko, BA; Kathy Haines, MSW, MPH; Caitlin Langhorne, MPH; Dana Silver, BA; Courtney Southard, MPH. VA Michael C. DeBakey Medical Center (Houston, TX): Maria C. Rodriguez-Barradas MD; Barbara Kertz, MS; Mahwish Mushtaq, MD, MPH; Blanca Vargas, MD. Centers for Disease Control and Prevention, National Institute for Occupational Safety & Health (Pittsburgh, PA): Edward Fisher, MS; Ronald Shaffer, PhD; Lewis J. Radonovich, MD. Veteran's Health Administration Office of Public Health (Gainesville, FL): Aaron Eagan, MPH, RN; Lewis J. Radonovich, MD. HandyMetrics Corporation (Toronto, Ontario, Canada): Melanie Lipka, BS; Michael Tsang, PhD. Laboratory Core at Johns Hopkins University (Baltimore, MD): Charlotte Gaydos, DrPH, Jeffrey Holden, MA; Alexandra Valsamakis, MD, PhD. Laboratory Core at VA St Louis Healthcare System and St Louis University School of Medicine (St Louis, MO): Geoffrey J. Gorse, MD; Michelle Mitchell, BS; Gira B. Patel, MS; Yinyi Yu, BS. REDCap Core at Johns Hopkins University (Baltimore, MD): Andre Hackman, BA, Michael Sherman, BS. Statistical and Epidemiologic Core (University of Florida, Gainesville): Brooke A. Borgert MS., Derek A.T. Cummings, PhD, MPH, MSc.; Susan Rattigan (University of Massachusetts, Amherst): Alexandria C. Brown, PhD; Nicholas G. Reich, PhD (Johns Hopkins University, Baltimore, MD); Justin Lessler, PhD, MHS, MS.

Disclaimer: The findings and conclusions in this article are the authors' own and do not necessarily represent the views of the National Institute for Occupational Safety and Health, the Centers for Disease Control and Prevention, the Department of Veterans Affairs, or other affiliates. Mention of product names does not imply endorsement. All information and materials in this article are original.

Data Sharing Statement: See Supplement 4.

Additional Contributions: We thank the members of the data and safety monitoring board, Daniel Morgan, MD (University of Maryland, Baltimore), Elizabeth Colantuoni, PhD (Johns Hopkins Bloomberg School of Public Health, Baltimore), and Tia Powell, MD (Albert Einstein College of Medicine, Bronx). We also thank David Weissman, MD (National Institute for Occupational Safety and Health) and Michael Hodgson, MD (Occupational Safety and Health Administration). None of our consults were financially compensated for their expertise, support, and guidance throughout the study. We are immensely grateful to the study personnel and coordinators, the supporting clinical staff, and, most importantly, the participants.

REFERENCES

1. Goins WP, Talbot HK, Talbot TR. Health care-acquired viral respiratory diseases. *Infect Dis Clin North Am*. 2011;25(1):227-244. doi:10.1016/j.idc.2010.11.010

2. Institute of Medicine. *Preparing for an Influenza Pandemic: Personal Protective Equipment for Healthcare Workers*. Washington, DC: National Academies Press; 2008.

3. MacIntyre CR, Wang Q, Cauchemez S, et al. A cluster randomized clinical trial comparing fit-tested and non-fit-tested N95 respirators to medical masks to prevent respiratory virus infection in health care workers. *Influenza Other*

Respir Viruses. 2011;5(3):170-179. doi:10.1111/j.1750-2659.2011.00198.x

4. MacIntyre CR, Wang Q, Seale H, et al. A randomized clinical trial of three options for N95 respirators and medical masks in health workers. *Am J Respir Crit Care Med*. 2013;187(9):960-966. doi:10.1164/rccm.201207-1164OC

5. Noti JD, Lindsley WG, Blachere FM, et al. Detection of infectious influenza virus in cough aerosols generated in a simulated patient examination room. *Clin Infect Dis*. 2012;54(11):1569-1577. doi:10.1093/cid/cis237

6. Loeb M, Dafoe N, Mahony J, et al. Surgical mask vs N95 respirator for preventing influenza among health care workers: a randomized trial. *JAMA*. 2009;302(17):1865-1871. doi:10.1001/jama.2009.1466

7. Rupp ME, Whitley R, Nutty C. *Letter on Federal PPE Guidance*. Washington, DC: Infectious Diseases Society of America/Society for Healthcare Epidemiology of America/Association of Professionals in Infection Control and Epidemiology. https://www.idsociety.org/globalassets/idsa/policy--advocacy/current_topics_and_issues/infection-prevention--control/comments/1100509-shea-idsa-apic-letter-re-ppe-guidance.pdf. Published November 5, 2009. Accessed March 28, 2019.

8. Ford I, Norrie J. Pragmatic trials. *N Engl J Med*. 2016;375(5):454-463. doi:10.1056/NEJMra1510059

9. Janssen L, Ettinger H, Graham S, Shaffer R, Zhuang Z. The use of respirators to reduce inhalation of airborne biological agents. *J Occup Environ Hyg*. 2013;10(8):D97-D103. doi:10.1080/15459624.2013.799964

10. Determination of particulate filter efficiency level of N95 series filters against solid particulates for non-powered, air-purifying respirators standard testing procedure. Pittsburgh, PA: National Institute for Occupational Safety and Health; 2016.https://www.cdc.gov/niosh/npptl/stps/pdfs/TEB-APR-STP-0059-508.pdf.

11. Lipp A, Edwards P. Disposable surgical face masks for preventing surgical wound infection in clean surgery. The Cochrane Library website. http://www.cochranelibrary.com/. Published April 26, 2016. Accessed March 28, 2019.

12. MacIntyre CR, Chughtai AA, Rahman B, et al. The efficacy of medical masks and respirators against respiratory infection in healthcare workers. *Influenza Other Respir Viruses*. 2017;11(6):511-517. doi:10.1111/irv.12474

13. Interim recommendations for facemask and respirator use to reduce 2009 influenza A (H1N1) virus transmission. Centers for Disease Control and Prevention website. https://www.cdc.gov/h1n1flu/masks.htm. Published September 24, 2009. Accessed December 6, 2016.

14. Infection control webinar. World Health Organization website. http://www.who.int/gpsc/5may/news/webinars/infection_control_webinar_20100413.ppt. Published April 10, 2010. Accessed March 28, 2019.

15. US Department of Labor. 1910.134 -Respiratory protection standard. Washington, DC: Occupational Safety and Health Administration. https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=12716. Accessed March 28, 2019.

16. Radonovich LJ Jr, Bessesen MT, Cummings DA, et al. The respiratory protection effectiveness clinical trial (ResPECT): a cluster-randomized comparison of respirator and medical mask effectiveness against respiratory infections in healthcare personnel. *BMC Infect Dis*. 2016;16:243. doi:10.1186/s12879-016-1494-2

17. Siegel JD, Rhinehart E, Jackson M, Chiarello L; Health Care Infection Control Practices Advisory Committee. 2007 Guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *Am J Infect Control*. 2007;35(10)(suppl 2):S65-S164. doi:10.1016/j.ajic.2007.10.007

18. Centers for Disease Control and Prevention. Updated guidance: prevention strategies for seasonal influenza in healthcare setting. Government Publishing Office website. https://www.gpo.gov/fdsys/pkg/FR-2010-06-22/html/2010-15015.htm. Published June 22, 2010. Accessed March 28, 2019.

19. Moulton LH. Covariate-based constrained randomization of group-randomized trials. *Clin Trials*. 2004;1(3):297-305. doi:10.1191/1740774504cn024oa

20. Reich NG, Cummings DA, Lauer SA, et al. Triggering interventions for influenza: the ALERT algorithm. *Clin Infect Dis*. 2015;60(4):499-504. doi:10.1093/cid/ciu749

21. de la Tabla VO, Masiá M, Antequera P, et al. Comparison of combined nose-throat swabs with nasopharyngeal aspirates for detection of pandemic influenza A/H1N1 2009 virus by real-time reverse transcriptase PCR. *J Clin Microbiol*. 2010;48(10):3492-3495. doi:10.1128/JCM.01105-10

22. Tang YW, Lowery KS, Valsamakis A, et al. Clinical accuracy of a PLEX-ID flu device for simultaneous detection and identification of influenza viruses A and B. *J Clin Microbiol*. 2013;51(1):40-45. doi:10.1128/JCM.01978-12

23. Azur MJ, Stuart EA, Frangakis C, Leaf PJ. Multiple imputation by chained equations: what is it and how does it work? *Int J Methods Psychiatr Res*. 2011;20(1):40-49. doi:10.1002/mpr.329

24. Bessesen MT, Savor-Price C, Simberkoff M, Reich NG, Pavia AT, Radonovich LJ. N95 respirators or surgical masks to protect healthcare workers against respiratory infections: are we there yet? *Am J Respir Crit Care Med*. 2013;187(9):904-905. doi:10.1164/rccm.201303-0581ED

25. Sartor C, Zandotti C, Romain F, et al. Disruption of services in an internal medicine unit due to a nosocomial influenza outbreak. *Infect Control Hosp Epidemiol*. 2002;23(10):615-619. doi:10.1086/501981

26. Jacobs JL, Ohde S, Takahashi O, Tokuda Y, Omata F, Fukui T. Use of surgical face masks to reduce the incidence of the common cold among health care workers in Japan: a randomized controlled trial. *Am J Infect Control*. 2009;37(5):417-419. doi:10.1016/j.ajic.2008.11.002

27. Offeddu V, Yung CF, Low MSF, Tam CC. Effectiveness of masks and respirators against respiratory infections in healthcare workers: a systematic review and meta-analysis. *Clin Infect Dis*. 2017;65(11):1934-1942. doi:10.1093/cid/cix681

28. Smith JD, MacDougall CC, Johnstone J, Copes RA, Schwartz B, Garber GE. Effectiveness of N95 respirators versus surgical masks in protecting health care workers from acute respiratory infection: a systematic review and meta-analysis. *CMAJ*. 2016;188(8):567-574. doi:10.1503/cmaj.150835

29. Peterson K, Novak D, Stradtman L, Wilson D, Couzens L. Hospital respiratory protection practices in 6 U.S. states: a public health evaluation study. *Am J Infect Control*. 2015;43(1):63-71. doi:10.1016/j.ajic.2014.10.008

30. Chiu S, Black CL, Yue X, et al. Working with influenza-like illness: presenteeism among US health care personnel during the 2014-2015 influenza season. *Am J Infect Control*. 2017;45(11):1254-1258. doi:10.1016/j.ajic.2017.04.008

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

A Randomized Trial

Mark Loeb, MD, MSc
Nancy Dafoe, RN
James Mahony, PhD
Michael John, MD
Alicia Sarabia, MD
Verne Glavin, MD
Richard Webby, PhD
Marek Smieja, MD
David J. D. Earn, PhD
Sylvia Chong, BSc
Ashley Webb, BS
Stephen D. Walter, PhD

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.

Trial Registration clinicaltrials.gov Identifier: NCT00756574

JAMA. 2009;302(17):1865-1871 www.jama.com

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.

Author Affiliations: Departments of Pathology and Molecular Medicine (Drs Loeb, Mahony, and Smieja and Ms Dafoe), Medicine (Dr Loeb), Clinical Epidemiology and Biostatistics (Drs Loeb, Smieja, Earn, and Walter), and Mathematics and Statistics (Dr Earn), Michael G. DeGroote Institute for Infectious Disease Research (Drs Loeb, Mahony, Smieja, and Earn), McMaster University, Hamilton, Ontario, Canada; St Joseph's Hospital Regional Virology Laboratory, Hamilton (Dr Mahony and Ms Chong); Departments of Pathology and Microbiology and Immunology, University of Western Ontario, London (Dr John); Department of Microbiology, Credit Valley Hospital, Mississauga, Ontario (Dr Sarabia); Joseph Brant Memorial Hospital, Burlington, Ontario (Dr Glavin); and World Health Organization Collaborating Center for Studies on the Ecology of Influenza in Animals and Birds, St Judes Children's Hospital, Memphis, Tennessee (Dr Webby and Ms Webb).
Corresponding Author: Mark Loeb, MD, MSc, McMaster University, 1200 Main St W, Hamilton, ON L8N 3Z5, Canada (loebm@mcmaster.ca).

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 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.[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 ≥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).[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 ≥38°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 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.[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% 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.

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

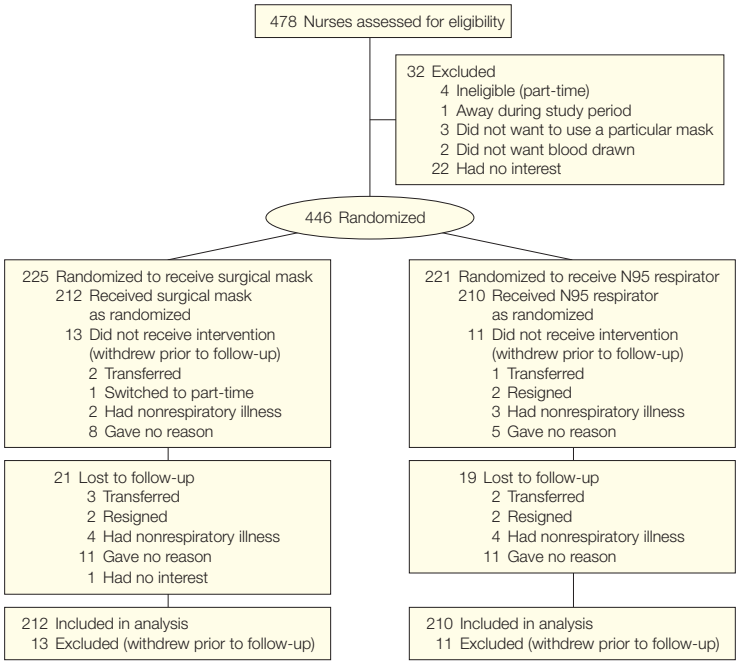


Table 1. Characteristics of 446 Nurse Participants in the Surgical Mask and N95 Respirator Groups

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)

[a] Immunosuppressive medications for transplantation (n=1), rheumatoid arthritis (n=3), uveitis (n=1), and Crohn disease (n=1).
[b] 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).

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

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 coronoviruses. 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 infec-

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

	No. (%)			
	Surgical Mask (n = 212)	N95 Respirator (n = 210)	Absolute Risk Difference, % (95% CI)	*P* Value
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.
[a]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.
[b]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. (%)			
	Surgical Mask (n = 212)	N95 Respirator (n = 210)	Absolute Risk Difference, % (95% CI)	*P* Value
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.
[a]Refers to respiratory syncytial virus type B only because no type A was detected.
[b]Refers to parainfluenza 3 only because no parainfluenza 1, 2, or 4 was detected.
[c]Refers to coronaviruses OC43, 229E, NL63, and HKU1.
[d]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. (%)			
	Surgical Mask (n = 212)	N95 Respirator (n = 210)	Absolute Risk Difference, % (95% CI)	*P* Value
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.
[a]Influenza-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.

Published Online: October 1, 2009 (doi:10.1001/jama.2009.1466).
Author Contributions: Dr Loeb had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Loeb, Webby, Smieja, Earn, Walter.
Acquisition of data: Loeb, Dafoe, Mahony, John, Sarabia, Glavin, Chong, Webb.
Analysis and interpretation of data: Loeb, Smieja, Chong, Walter.
Drafting of the manuscript: Loeb, Dafoe.
Critical revision of the manuscript for important intellectual content: Loeb, Mahony, John, Sarabia, Glavin, Webby, Smieja, Earn, Chong, Webb, Walter.
Statistical analysis: Loeb, Walter.
Obtained funding: Loeb, Walter.
Administrative, technical, or material support: Dafoe, John, Sarabia, Smieja, Earn, Chong, Webb.
Study supervision: Loeb, Mahony, Webby.
Financial Disclosures: None reported.
Funding/Support: This study was supported by the Public Health Agency of Canada.
Role of the Sponsor: The funding organization had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

REFERENCES

1. Langley JM, Faughnan ME. Prevention of influenza in the general population. *CMAJ*. 2004;171(10):1213-1222.
2. Thompson WW, Shay DK, Weintraub E, et al. Influenza-associated hospitalizations in the United States. *JAMA*. 2004;292(11):1333-1340.
3. 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.
4. Cohen J, Enserink M. Swine flu: after delays, WHO agrees: the 2009 pandemic has begun. *Science*. 2009;324(5934):1496-1497.
5. Neumann G, Noda T, Kawaoka Y. Emergence and pandemic potential of swine-origin H1N1 influenza virus. *Nature*. 2009;459(7249):931-939.
6. 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.
7. 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.
8. 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.
9. Alford RH, Kasel JA, Gerone PJ, Knight V. Human influenza resulting from aerosol inhalation. *Proc Soc Exp Biol Med*. 1966;122(3):800-804.
10. 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.
11. 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.
12. 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.
13. 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.
14. 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.
15. Cowling BJ, Chan KH, Fang VJ, et al. Facemasks 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.
16. 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.
17. 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.
18. 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.
19. Call SA, Vollenweider MA, Hornung CA, Simel DL, McKinney WP. Does this patient have influenza? *JAMA*. 2005;293(8):987-997.
20. 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.
21. 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.
22. Gotzsche PC. Lessons from and cautions about noninferiority and equivalence randomized trials. *JAMA*. 2006;295(10):1172-1174.
23. 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.
24. 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.
25. 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.
26. 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.
27. Tuomi T. Face seal leakage of half masks and surgical masks. *Am Ind Hyg Assoc J*. 1985;46(6):308-312.
28. Willeke K, Qian YG, Donnelly J, Grinshpun S, Ulevicius V. Penetration of airborne microorganisms through a surgical mask and a dust/mist respirator. *Am Ind Hyg Assoc J*. 1996;57(4):348-355.
29. 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_PPRE_Final_Report.pdf. Accessed September 11, 2009.