CJEM Journal Club

Surgical mask versus N95 respirator for preventing influenza among health care workers: a randomized trial

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Clinical question
Are surgical masks inferior to N95 respirators in reducing influenza infection in health care workers?
Article chosen
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.
Objective
To evaluate the effectiveness of N95 respirators compared to standard surgical masks in reducing influenza infection in health care workers.

BACKGROUND

N95 respirators are costly and require specialized training prior to use. The assumption is that N95 respirators provide greater protection against influenza virus exposure. However, there is uncertainty about optimal personal respiratory devices in the prevention of influenza as N95 respirators have not been directly compared to standard surgical masks or even to the absence of protection. The study aimed to determine whether surgical masks were as effective as the N95 respirators.

POPULATION STUDIED

Four hundred forty-six nurses in emergency departments, medical units, and pediatric units in eight tertiary care hospitals.

STUDY DESIGN

This study was a noninferiority, multicentre, randomized trial. Randomization was conducted centrally in permuted blocks of four with investigators and laboratory personnel blinded to the randomization process and allocation.

OUTCOMES

The primary outcome was laboratory-confirmed influenza diagnosed either by polymerase chain reaction (PCR) or a fourfold rise in hemagglutinin titres. The a priori noninferiority criterion was satisfied if the lower limit of the 95% CI for the reduction in the incidence of influenza (N95 respirator group minus surgical mask group) was greater than −9%. Secondary outcomes were detection of several noninfluenza viruses by PCR, influenza-like illness, work-related absenteeism, and physician visits for respiratory illness.

RESULTS

Of 478 nurses assessed for study inclusion, 446 were randomly assigned to either the N95 group (n = 221) or the surgical mask group (n = 225). There were no significant differences in baseline characteristics between the two groups. Forty patients were lost to follow-up (n = 21 in the surgical mask group, n = 19

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in the N95 group). Intention-to-treat (ITT) analysis was conducted on 422 subjects. No significant difference was found in the two groups in terms of influenza infection (23.6% surgical masks v. 22.9% N95 respirators, absolute risk increase [ARI] −0.7%, $p = 0.86$), thus meeting the authors' predefined criteria for noninferiority. Given that ITT analyses in noninferiority trials may increase the chance of finding no difference, the authors also conducted a per protocol analysis (only patients with complete follow-up) of the primary outcome. Influenza infection rates from the per protocol analysis once again indicated noninferiority (33.9% surgical masks v. 37.7% N95 respirators, ARI 3.85%, $p = 0.43$). No significant difference was observed in the secondary outcomes between the two groups.

STUDY CONCLUSIONS

The authors concluded that the protection provided by an N95 respirator is not superior to that provided by a standard surgical mask.

COMMENTARY

This study compared influenza outcome rates diagnosed using multiple methods in a real-world situation.[1] Although N95 respirators are not routinely recommended for seasonal influenza, they may have a role in personal protection against novel strains of influenza with pandemic potential such as H1N1. This article demonstrated that health care workers in various hospital settings are no more likely to experience influenza when they wear surgical masks than if they wear an N95 respirator while caring for patients with influenza.

When we think of randomized controlled trials comparing two or more interventions, we typically think of an outcome that demonstrates whether an intervention is superior to the control or comparator by some prespecified amount. However, there are situations in which one might wish to determine if an intervention is as good as or not worse than the control, again according to some prespecified amount. The reason for conducting such a trial is that the intervention has another advantage, such as being safer or less expensive, and might therefore prove to be a suitable replacement. In this particular study, the authors sought to determine if surgical masks were noninferior to the more expensive N95 respirators in preventing influenza among health care workers.

There are four requirements for reporting a noninferiority trial:

1. The noninferiority margin is defined.
2. The sample size calculation is based on the noninferiority margin.
3. The data are analyzed by both ITT and per protocol.
4. The confidence interval for the result is provided.[2,3]

In this article, the authors calculated the sample size based on a noninferiority margin defined as follows: "the lower limit of the 95% confidence interval (CI) for the reduction in incidence (N95 respirator minus surgical group) was greater than −9%." In other words, the incidence (reported as a percentage) of influenza cases in the N95 group subtracted by the incidence of influenza cases in the surgical mask group is greater than −9%. They first report this using ITT analysis, in which the outcomes are analyzed according to the group to which the subjects were randomized: 22.9% (N95 influenza incidence) − 23.6% (surgical mask influenza incidence) = −0.7% (95% CI −8.8% to 7.3%). The lower limit of the 95% CI, −8.8%, is greater than the prespecified −9% for noninferiority. However, ITT analysis is a conservative measure of treatment effect. Therefore, in noninferiority trials, ITT may be biased toward finding no difference.[4] For that reason, the authors also analyzed the data per protocol: 37.7% (N95 influenza incidence) − 33.9% (surgical mask influenza incidence) = 3.8% (95% CI −5.7% to 13.4%). In this case, the lower limit of the 95% CI, −5.7%, is also greater than the prespecified −9% for noninferiority. Hence, surgical masks are not inferior to N95 masks in preventing influenza in health care workers. What remains to be studied is how these masks compare to no mask at all or to comprehensive vaccination in protecting health care workers against influenza.

Several study limitations have been alleged in letters to the editor. These are mostly based on the lack of measurements performed during the study period and might be considered important study limitations in an efficacy trial. For example, that authors did not collect data regarding the frequency of device changing.[5] According to the study protocol, the subjects were mandated to use masks or respirators only once per patient encounter.[6] Although high levels of compliance were observed for a limited number of audits, exact

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compliance with mask use cannot be ascertained. However, if less compliance with the N95 occurred, thereby favouring the inferiority hypothesis, it is likely due to a characteristic of the respirator rather than collective premeditated noncompliance by participants in the N95 group. This also suggests that recommending that health care workers wear the N95 respirator without enforcing rigid compliance will not lower infection rates as intended.

Another concern has been raised about the difference in filtering capabilities among surgical masks.[7] Although this was not taken into account—again a reflection of real-world circumstances in which health care workers will use whichever mask is available—there is a lack of evidence showing a difference between various surgical masks. A clinical trial to examine this difference would need to ensure 100% compliance and would have to preclude health care workers from nonclinical sources of influenza exposure. The similarity in event rates between the groups also suggests no significant difference.[6] Daily (nonclinical) exposures to influenza were not measured even though they likely played a large role in influenza transmission, meaning that all cases of influenza transmission cannot be attributed to barrier failure.[8] This is important and once again demonstrates that this is an effectiveness trial and not an efficacy trial because there is no reason to believe that in the multiple patient care areas of the multiple hospitals in which the study was conducted, nonclinical exposures were collectively greater in the N95 group. This favours the inferiority hypothesis despite the similar prognostic factors of the two groups.

CONCLUSIONS

Standard surgical masks are no worse than N95 respirators in reducing health care worker infection with influenza and can be used safely in the emergency department for patients suspected of having influenza.

Competing interests: None declared.

Keywords: critical appraisal, H1N1, infectious disease, personal protective equipment (PPE)

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