N95 respirator and surgical mask effectiveness against respiratory viral illnesses in the healthcare setting: A systematic review and meta-analysis

Andrew P. Collins BS 1 | Benjamin C. Service MD 2 | Sunny Gupta MD 3 | Naser Mubarak MPH 4 | Ibrahim Mamdouh Zeini PhD, PMP, SA, CCRP 5 | Daryl C. Osbahr MD 6 | Anthony A. Romeo MD 7

1 University of Central Florida College of Medicine, Orlando, Florida, USA
2 Orlando Health Orthopedic Institute, Orlando, Florida, USA
3 Department of Orthopedics, University of Pennsylvania, Philadelphia, Pennsylvania, USA
4 University of Central Florida College of Medicine, Orlando, Florida, USA
5 AdventHealth Orthopedic Institute, Orlando, Florida, USA
6 Orthopaedic Surgery, Rothman Orthopaedic Institute Florida, Orlando, Florida, USA
7 DuPage Medical Group Musculoskeletal Institute, Chicago, Illinois, USA

Correspondence
Andrew P. Collins, University of Central Florida College of Medicine, Orlando, Florida. Email: Andrewcollins@knights.ucf.edu

Abstract

Objective: To examine the results, level of evidence, and methodologic quality of original studies regarding surgical mask effectiveness in minimizing viral respiratory illness transmission, and, in particular, the performance of the N95 respirator versus surgical mask.

Methods: Meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines with use of PubMed, MEDLINE, and the Cochrane Library databases.

Results: Eight studies (9164 participants) were included after screening 153 articles. Analyses showed statistically significant differences between N95 respirator versus surgical mask use to prevent influenza-like-illness (risk ratio [RR] = 0.81, 95% confidence interval [CI] = 0.68–0.94, P < 0.05), non-influenza respiratory viral infection (RR = 0.62, 95% CI = 0.52–0.74, P < 0.05), respiratory viral infection (RR = 0.73, 95% CI = 0.65–0.82, P < 0.05), severe acute respiratory syndrome coronavirus (SARS-CoV) 1 and 2 virus infection (RR = 0.17, 95% CI = 0.06–0.49, P < 0.05), and laboratory-confirmed respiratory viral infection (RR = 0.75, 95% CI = 0.66–0.84, P < 0.05).

Analyses did not indicate statistically significant results against laboratory-confirmed influenza (RR = 0.87, CI = 0.74–1.03, P > 0.05).

Conclusions: N95 respirator use was associated with fewer viral infectious episodes for healthcare workers compared with surgical masks. The N95 respirator was most effective in reducing the risk of a viral infection in the hospital setting from the SARS-CoV 1 and 2 viruses compared to the other viruses included in this investigation. Methodologic quality, risk of biases, and small number of original studies indicate the necessity for further research to be performed, especially in front-line healthcare delivery settings.
1 | INTRODUCTION

1.1 | Background

Following the past outbreaks of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003, Middle East respiratory syndrome coronavirus (MERS-CoV) since 2012, and the current COVID-19 pandemic, facemasks have been considered a necessity to reduce the risk of viral transmission. As with prior viral pandemics, healthcare workers are at increased risk of infection. This can reduce the numbers of available medical practitioners and resources for patient care. N95 respirators are a staple in healthcare personal protective equipment (PPE), as they reduce exposures by >95% to particulates sized 0.3 microns and must be specifically fitted to the user’s face to reduce air leakage. Unfortunately, prolonged N95 respirator use is associated with discomfort and headaches, leading to improper doffing and decreased compliance, causing increased infection rates among these non-compliant users. Surgical masks on the other hand are defined as loose-fitting devices that provide a physical barrier between the mouth and nose of the user and the immediate environment. They are designed to reduce microorganism transmission among wearers, prevent gross contamination, and fit more loosely on the user’s face.

Unlike the N95 respirator these surgical masks cannot prevent inhalation of very small airborne particles because of the lack of a filtration mechanism; however, both have shown protective effects from large droplets and sprays. Each of these mask types are essential in the healthcare setting as measures of PPE and in the community to stop the spread of viral respiratory illnesses.

1.2 | Importance

Current recommendations for airborne protection against SARS and pandemic influenza from the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) are conflicting. The May 2021 CDC guidelines recommend using respirators in low and high-risk situations, whereas the most current WHO guidelines recommend surgical masks in low-risk situations and respirators in high-risk situations. During the current COVID-19 pandemic, civilians have been purchasing N95 respirators, decreasing the supply and availability to hospitals and healthcare workers, potentially putting frontline workers at increased risk of infection. Previous studies have shown that existing clinical evidence has been inconclusive and inconsistent regarding whether N95 respirators are more effective than surgical masks for preventing viral respiratory infection among healthcare professionals. The number of randomized controlled trials (RCTs) have led to a limited amount of evidence supporting N95 respirator use versus surgical masks. Studies also did not stratify the type of surgical mask based on level of protection when comparing to N95 respirators. Ideally, clinical decision making should be founded on high levels of evidence to best protect healthcare workers from infection.

During initial presentation to first responders or in front-line settings such as the emergency department, vaccination history and immunity status are usually unknown for patients at risk for communicable illness such as COVID-19; the initial unknown state must be handled with the safety of the healthcare team in mind using PPE with the highest margin of safety. However, later in the course of care when an infectious state has been determined, directed PPE application can be used.

1.3 | Goals of this investigation

Recent increases in the number of RCTs of N95 respirator and surgical mask use for protection against viral respiratory illnesses have increased the pool of data. A systematic review and meta-analysis from 2020 studied the effectiveness of N95 respirators versus surgical masks against influenza, including related RCTs. This current study of existing literature is aimed to assess the level of evidence provided in these studies and analyze the data assessing N95 respirator use versus surgical mask use for the prevention not only of influenza but also other viral respiratory illness from all original research studies.

2 | METHODS

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The primary focus was on the association of N95 respirator and surgical mask effectiveness in reducing viral respiratory disease infection and the level of evidence supporting these data.

2.1 | Data sources and search

We searched the MEDLINE, PubMed, and Cochrane Library databases through May 14, 2021, to analyze published original research and systematic reviews evaluating the use and effectiveness of N95 respirators and surgical masks to prevent respiratory viral illness transmission without a specified time frame. The search strategy used for the PubMed database is seen in Table 1; these search terms were adjusted for use in the MEDLINE and Cochrane Library databases. In addition to the initial search, systematic reviews were identified and used to locate other RCTs, case-control studies, and cohort studies that did not appear in our original search, with no specified time frame.
TABLE 1  Search terminology used in the PubMed database

| Column 1 | Column 2 | Column 3 | Column 4 |
|----------|----------|----------|----------|
| “Viral respiratory infection” | “Personal protective equipment” | “Transmission” | “Healthcare worker” |
| Coronavirus | PPE | Spread | Physician |
| COVID-19 | N95 | Aerosol | “Healthcare Staff” |
| SARS-CoV-2 | N99 | Infect* | Doctor |
| Airborne viral infection | N100 | Mortality | Nurse |
| MERS-CoV | R95 | “Respiratory Droplets” | Surgeon |
| SARS-CoV-1 | P95 | “Contaminated Surfaces” | “Healthcare Worker” |
| H1N1 | P99 | Fomite | Operating room |
| HAdV-7 | P100 | Carrier | |
| HAdV | PAPR | |
| H5N1 | FFR | |

Abbreviations: FFR, filtering facepiece respirator; HAdV, human adenovirus; HAdV-7, human adenovirus serotype 7; MERS-CoV, Middle East respiratory syndrome coronavirus; PAPR, powered air purifying respirator; PPE, personal protective equipment; SARS-CoV, severe acute respiratory syndrome coronavirus.

FIGURE 1  Literature search and article screening process. Abbreviation: PPE, personal protective equipment

2.2  Study selection and data extraction

Two reviewers independently screened articles based on title and abstract, then full text (Figure 1). Reviewers extracted data from the included studies and disagreements were resolved by discussion to come to a consensus. All studies that met the inclusion criteria were used and sensitivity analyses were run for each result group to minimize study selection bias.
Level of evidence was determined for each study according to the Oxford Centre for Evidence-Based Medicine.\textsuperscript{19,20} Outcomes of research classified as level I or II evidence are generally considered as high-level evidence, and studies at level III, IV, and V are considered low-level evidence. All disagreements were resolved by discussion between reviewers.

Inclusion criteria for this study were based on (1) participant type: humans with influenza, influenza-like illness, or other respiratory viral infections; (2) study type: randomized controlled trial, non-randomized controlled study, case-control study, and cohort study; (3) intervention: N95 respirator and surgical mask; (4) outcome: laboratory-confirmed viral infection, laboratory-confirmed influenza-like infection, laboratory-confirmed respiratory infection, positive clinical diagnosis of respiratory viral illness; and (5) study setting in hospitals. Selection of multiple study types were chosen to display the potentially widespread level of evidence in data.

Exclusion criteria were (1) non-human experimental laboratory studies, (2) non-healthcare setting, (3) studies without mention of specific PPE type effectiveness, (4) cloth or other non-medical grade mask use, (5) theoretical models, (6) conference presentations, (7) self-reported illness as outcome measure, (8) studies assessing only bacterial colonization or infection, and (9) studies assessing viral infection only in bacterial coinfection.

### 2.3 Risk of bias assessment

Reviewers assessed the risk of bias of the RCTs included in this review, following the Cochrane Risk of Bias tool.\textsuperscript{21} This assessment included identification of several types of biases that could affect the quality of the RCT, including but not limited to selection bias, performance bias, detection bias, attrition bias, reporting bias, and an overall consolidation and classification of these biases among 3 levels (high, some, and low risk). Studies with negative methodology regarding these previously mentioned types of biases were determined to be at high risk of overall bias. Studies that did not specifically report these methods were labeled some risk of bias. Those that used strict methodology to account for such biases were noted as low risk of bias. Disagreements among bias classification were resolved by discussion.

### 2.4 Data synthesis and statistical analysis

All data analyses were performed using the program R version 3.4.3. Studies that presented comparable data with similar interventions and outcome results were pooled together for joint analysis of the larger sample size. The effect of these studies was conducted using risk ratios (RR) with 95% confidence intervals (CIs) for the dichotomous data. One-factor-at-a-time sensitivity analyses revealed that results were unchanged when excluding individual studies from each pooled analysis. Results were pooled by grouped infection type; influenza: influenza A and influenza B; non-influenza: adenovirus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, and rhinovirus-enterovirus; all respiratory viral infection: influenza and non-influenza viruses; and SARS-CoV-1 and SARS-CoV-2 viral infection.

### 3 RESULTS

#### 3.1 Search results and study characteristics

The details of our literature search and screening process of articles are found in Figure 1. In total, we included 4 RCTs,\textsuperscript{22-15} 3 case control studies,\textsuperscript{25-27} and 1 retrospective cohort study.\textsuperscript{28} The characteristics of these studies are found in Table 2. The included studies were published between 2003 and 2020 and involved a total of 9164 participants located in Canada, China, and the United States. The number of participants included in the RCTs ranged from 422 to 5180, and the number of those in the other studies ranged from 38 to 199. All included studies took place in a hospital setting and examined an adult study population of healthcare workers to assess mask type PPE effectiveness against respiratory viral disease infection. Each of the included studies met all inclusion criteria and did not fail the exclusion criteria.

#### 3.2 Level of evidence

Of the RCTs, all were level I evidence, whereas the case-control studies and retrospective cohort study were level III evidence. Of these included studies, 50% presented level I evidence, and 50% presented level III evidence. However, of the 4 included RCTs, only 1 presented statistically significant results measuring our primary outcomes, and none of the individual case-control or retrospective cohort studies had statistically significant findings regarding mask type effectiveness differences. The non-RCTs did present statistically significant findings regarding the general protective effect of N95 respirators and surgical masking practices versus infection rates.

#### 3.3 Risk of bias

The summary of results of the Cochrane Risk of Bias tool can be seen in Table 3. None of the studies reported an assessment of compliance with the protocol regarding surgical mask or respirator use. Blinding of participants and personnel (performance bias) was taken as the main factor for deciding the overall risk of bias of a study. Overall, 1 of the included RCTs was deemed high risk of bias, 1 had some risk, and 2 had low risk.

The Loeb et al. study\textsuperscript{22} was found to have unknown random sequence generation and allocation concealment, increasing the possibility of selection bias. However, it was classified as low risk as there was no performance bias. The MacIntyre 2013 study\textsuperscript{24} had unknown allocation concealment, blinding of participants and personnel, and blinding of outcome assessment. These findings placed the study into
| Level of evidence | Author and year  | Study type | Setting | Participants | Interventions | Outcomes | Laboratory detection |
|-------------------|------------------|------------|---------|--------------|---------------|----------|----------------------|
| I                 | Loeb 2009        | RCT        | Hospital: Ontario, Canada; 8 hospitals included; emergency departments, pediatric units, and acute medical units | 446 nurses; individual-level randomization | Non-inferiority trial; Intervention: targeted use of fit-tested N95 respirator; Control: targeted use of surgical mask | Laboratory-confirmed respiratory infection, influenza-like illness, workplace absenteeism; with 5-week follow-up | Influenza A and B, RSV, metapneumovirus, parainfluenza virus, rhinovirus-enterovirus, coronavirus, and adenovirus |
| I                 | MacIntyre 2011   | RCT        | Hospital: Beijing, China; 15 hospitals; respiratory units and emergency departments | 1441 ward clerks, nurses, and doctors; clusters randomized by ward | Intervention 1: continual use of fit-tested N95 respirator; Intervention 2: continual use of non-fit-tested N95 respirator; Control: continual use of surgical mask | Laboratory-confirmed respiratory infection and influenza-like illness; with 5-week follow-up | Influenza A and B, RSV, metapneumovirus, parainfluenza virus, rhinovirus-enterovirus, coronavirus, and adenovirus |
| I                 | MacIntyre 2013   | RCT        | Hospital: Beijing, China; 19 hospitals; Respiratory wards and emergency departments | 1669 ward clerks, nurses, and doctors; clusters randomized by ward | Intervention (1): continual use of fit-tested N95 respirator; Intervention (2): targeted use of fit-tested N95 respirator; Control: continual use of surgical mask | Laboratory-confirmed respiratory infection and influenza-like illness; with 5-week follow-up | Influenza A and B, RSV, metapneumovirus, parainfluenza virus, rhinovirus-enterovirus, coronavirus, and adenovirus |
| I                 | Radonovich 2019  | RCT        | Hospital: United States; 7 hospitals; primary care settings, dental clinics, pediatric and adult clinics, dialysis clinics, EDs, urgent care clinics, emergency transport services | 5180 nurses/trainees, clinical support staff, clerical staff, physicians, social workers, housekeepers; cluster randomized by outpatient clinic/setting | Effectiveness study; Intervention: targeted use of fit-tested N95 respirator; Control: targeted use of medical mask | Laboratory-confirmed respiratory infection, influenza, respiratory illness, influenza-like illness, acute respiratory illness; with 12-week follow-up | Influenza A and B, RSV, metapneumovirus, parainfluenza virus, rhinovirus-enterovirus, coronavirus, coxsackie/echovirus |
### TABLE 2 (Continued)

| Level of evidence | Author and year | Study type | Setting | Participants | Interventions | Outcomes | Laboratory detection |
|-------------------|-----------------|------------|---------|--------------|--------------|----------|----------------------|
| III               | Seto 2003       | Case-control | Hospital: Hong Kong, China; 5 hospitals; ED and medicine units | 13 infected staff; 241 non-infected staff; includes nurses, doctors, healthcare assistants, and domestic staff | Protective measure usage; including masks (paper, surgical, and N95 respirator), gloves, gowns, and hand-washing | Clinical diagnosis of severe acute respiratory syndrome (SARS) | Clinical diagnosis |
| III               | Zhang 2012      | Case-control | Hospital: Beijing, China; 25 hospitals, emergency departments, respiratory wards, intensive care units, outpatient departments | 51 infected staff; 204 non-infected staff; includes doctors, nurses, technicians | Intervention (1): Usage of N95 respirator; Intervention (2): usage of surgical mask; Intervention (3): usage of cloth mask; Control: non-infected participants | Laboratory diagnosis of H1N1 respiratory infection | Detection of H1N1 using RT-PCR |
| III               | Guo 2020        | Case-control | Hospital: Wuhan, China; 8 hospitals; Orthopedic surgeons | 24 infected orthopedic surgeons, 48 control group uninfected | Intervention (1): Usage of N95 Respirator; Intervention (2): Wearing respirators or masks continually; Control: Uninfected orthopedic surgeons at the same hospitals as the infected | Laboratory and clinical diagnosis of COVID-19 | Detection of COVID-19 by pathogen test and hematologic examination; Clinical diagnosis in some participants |
| III               | Loeb 2004       | Retrospective cohort study | Hospital: Toronto, Canada; 2 hospitals, critical care units | 43 nurses total; 8 of 32 who entered a SARS patient’s room were infected | Intervention (1): consistent mask usage; Intervention (2): continual N95 respirator usage; Control: inconsistent mask usage | Clinical diagnosis of SARS | Clinical diagnosis |

Abbreviations: RCT, randomized controlled trial; RSV, respiratory syncytial virus; RT-PCR, reverse transcription polymerase chain reaction
### TABLE 3 Risk of bias in RCTs

| Author and year       | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Overall risk-of-bias judgment |
|-----------------------|---------------------------------------------|----------------------------------------|-------------------------------------------------------------|------------------------------------------------|----------------------------------------|---------------------------------|-------------------------------|
| Loeb 2009             | ?                                           | ?                                     | +                                                            | +                                              | +                                      | +                              | Low                           |
| MacIntyre 2011        | +                                           | ?                                     | -                                                            | ?                                              | +                                      | +                              | High                          |
| MacIntyre 2013        | +                                           | ?                                     | ?                                                            | ?                                              | +                                      | +                              | Some                          |
| Radonovich 2019       | +                                           | ?                                     | +                                                            | +                                              | +                                      | +                              | Low                           |

Abbreviation: RCT, randomized controlled trial.

**FIGURE 2** Results of N95 respirator effectiveness versus surgical masks against influenza-like illness. Abbreviations: LCL, lower confidence limit; POP, population; RR, risk ratio; UCL, upper confidence limit; WGT, weight.

"some bias" classification owing to the increased likelihood of performance and detection biases.

### 3.4 Effectiveness of masking practices

Results of N95 respirator use versus surgical masks against influenza-like illness (laboratory confirmed and clinical diagnoses of influenza) were addressed in 4 RCTs and 1 case-control study, involving 8911 participants (Figure 2). The pooled analysis demonstrated a statistically significant result with an RR with 95% CI of 0.81 (0.68–0.94, \( P < 0.05 \)). A sensitivity analysis excluding each trial individually showed no change in pooled result significance when analyzed.

Results of N95 respirator use versus surgical masks against non-influenza respiratory viral infections (adenovirus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, and rhinovirus-enterovirus) were addressed by RCTs, 2 case-control studies, and 1 retrospective cohort study, involving 8543 participants (Figure 3). Only 1 of the studies presented statistically significant results (RR = 0.78, 95% CI = 0.64–0.94, \( P < 0.05 \)). A sensitivity analysis excluding each trial individually showed no change in pooled result significance when analyzed.

Results of N95 respirator use versus surgical masks against SARS and COVID-19 (SARS-CoV 1 and 2 viruses) were measured by 2 case-control studies, involving 215 participants (Figure 5). Overall, the pooled analysis from the studies was statistically significant (RR = 0.17, 95% CI = 0.06–0.49, \( P < 0.05 \)). The relative risk of 0.17 suggests that wearing an N95 respirator reduces the risk of a SARS-CoV 1 and 2 viral infection to 17% of this population wearing the surgical mask.

The results of N95 respirator use versus surgical masks against laboratory-confirmed respiratory infection were assessed by 4 RCTs and 1 case-control study, involving 8911 participants (Figure 6). The pooled result was statistically significant, reporting a decreased risk among N95 respirator use versus surgical masks against laboratory-confirmed respiratory infection (RR = 0.75, 95% CI = 0.66–0.84, \( P < 0.05 \)).
FIGURE 3  Results of N95 respirator effectiveness versus surgical masks against non-influenza respiratory viral infection. Abbreviations: LCL, lower confidence limit; POP, population; RR, risk ratio; UCL, upper confidence limit; WGT, weight.

FIGURE 4  Results of N95 respirator effectiveness versus surgical masks against respiratory viral infection. Abbreviations: LCL, lower confidence limit; POP, population; RR, risk ratio; UCL, upper confidence limit; WGT, weight.

FIGURE 5  Results of N95 respirator effectiveness versus surgical masks against SARS and COVID-19 (SARS-CoV-1 and SARS-CoV-2). Abbreviations: LCL, lower confidence limit; POP, population; RR, risk ratio; SARS, severe acute respiratory syndrome; UCL, upper confidence limit; WGT, weight.

FIGURE 6  Results of N95 respirator effectiveness versus surgical masks against laboratory-confirmed respiratory viral infection. Abbreviations: LCL, lower confidence limit; POP, population; RR, risk ratio; UCL, upper confidence limit; WGT, weight.
The results of N95 respirator use versus surgical masks against laboratory-confirmed influenza were assessed by 4 RCTs, involving 8712 participants (Figure 7). Overall, the pooled result was not statistically significant, reporting no significant difference in the risk of laboratory-confirmed influenza with N95 respirator use versus surgical masks (RR = 0.87, 95% CI = 0.74–1.03, P > 0.05).

4 LIMITATIONS

This study is not without limitations. The overall study risk of biases poses a limitation to the quality of evidence included in this meta-analysis. Additionally, all the included trials were potentially heterogeneous in their surgical masking type, as they did not disclose the manufacturers. Although mostly consistent, the viruses assessed by each of the trials was not uniform; these viruses may transmit, reproduce, and mutate uniquely. Likely the largest limitation of each of the included studies was the lack of masking compliance assessment. Despite these limitations, an examination of the included articles showed that they each described very similar overall techniques when comparing masking effectiveness in the hospital setting.

5 DISCUSSION

This meta-analysis has shown that much of the research studying N95 respirator and surgical mask effectiveness to reduce viral respiratory disease transmission in the hospital setting is of high-level evidence but is limited in the number of studies available. However, of these 4 RCTs that presented high-level evidence, 1 was at high risk of biased judgment, 1 had some risk, and only 2 had low risk, as determined by the Cochrane Risk of Bias tool. These studies were considered at risk of bias owing to the lack of blinding of participants and personnel. However, it is practically difficult to blind participants who must know what type of mask they are wearing. Other risks of bias not addressed by the Centre for Evidence-Based Medicine criteria include risk of type II error owing to relatively small sample sizes and no measure of PPE compliance in the studies. The latter could pose a strong limitation to the N95 respirator functionality and is a known factor in reducing protective effectiveness of the PPE. The lack of uniform prestudy and poststudy antibody and polymerase chain reaction (PCR) testing could also lead to a selection bias in these studies. Participants in the studies may have been infected and asymptomatic or previously infected with no presence of current antigen for PCR analysis.

This meta-analysis of the included RCTs displayed no statistically significant differences in N95 respirator versus surgical mask effectiveness in reducing laboratory-confirmed influenza. However, pooled results were statistically significant for decreased risk of influenza-like-illness, non-influenza respiratory viral infection, respiratory viral infection, SARS-CoV 1 and 2 viruses, and laboratory-confirmed respiratory viral infections. Of these significant results, only 1 was a laboratory-confirmed method, whereas the others relied (at least partially) on clinical diagnoses, placing the included studies at risk for reporting bias and misdiagnosis. The laboratory-confirmed methods were not uniform among the studies, as they tested for various different respiratory viral infections.

Healthcare professionals have stated discomfort, most often headaches, associated with N95 respirator use. Because healthcare professionals are often required to wear these respirators for prolonged periods to protect against infection, side effects of use may become a deterrent to compliance. A 2017 study showed an inverse relationship between level of compliance of wearing N95 respirators and risk of clinical respiratory infection. In all studies comparing the effects of N95 respirators, it is difficult to ensure participant compliance throughout the study, because of the discomfort associated with wearing the masks. This decreased compliance associated with N95 respirator use may lead to respirator manipulation and adjustment, as well as frequent removal and reapplication, affecting the study outcomes comparing the respirators versus surgical masks. Although the aerosol particle filtration ability of the N95 respirator is a distinguishing feature between it and the surgical mask in a laboratory setting with ideal compliance, the discomfort associated with wearing these masks in a work environment may inhibit healthcare workers from closely following respirator use protocols.

In vitro studies have shown that surgical mask particulate filtration efficiency for 0.1 micron aerosol particles and bacterial filtration efficiency of 3.0 micron *Staphylococcus aureus* aerosol particles are consistently >96%, implying the surgical mask’s high performance to reduce infection transmission. These laboratory studies have also indicated increased filter performance and simulated-workplace protection factors with fit-tested N95 respirators than surgical masks. High rates of influenza virus recovery from contaminated surgical masks and N95 respirators has also been reported, whereas improper doffing of PPE such as N95 respirators, face shields, and surgical masks have been
shown to cause self-contamination with viral respiratory illnesses. These findings highlight the need for understanding the interpretation of data of the included studies for this meta-analysis and detail the possibility of confounding variables, such as non-compliance from strict N95 respirator use protocol.

Although much of the discussion in the literature regards the comparison of surgical masks to N95 masks or other respirators, their intended functions are quite different. The N95 and powered air purifying respirators (PAPR) are designed to protect the wearer from the environment by reducing particle inhalation, but surgical masks are designed to reduce spread of infection from the wearer and prevent gross contamination during surgery. Their functions are inherently separate, but their application in the healthcare setting has significant overlap when treating patients during a viral disease outbreak or pandemic. Among PAPRs and N95 respirators to reduce viral respiratory infection, neither has demonstrated clinical effectiveness over the other in decreasing infection during aerosol generating procedures. Additionally, there is limited evidence that in the healthcare setting, N95 respirators provide enhanced protection over aerosol viral transmission compared to surgical masks. Like the PAPR recommendations, these are precautionary principles rather than evidence-based protocols. Although we demonstrated that N95 respirators are recommended in healthcare workers for SARS-CoV viruses, CDC guidelines released in April 2021 for public mask use states to avoid use of masks that are prioritized for healthcare workers, such as N95 respirators.

The recent study by Fischer et al. established varying relative droplet count during speech using different mask types in a reproducible optic measurement. Their findings demonstrated that fitted N95 respirators and surgical masks both have a similar effectiveness in reducing droplet expulsion. In contrast, the popular mask types among the public, such as bandanas and neck gaiters, showed no statistically significant reduction in droplet count when compared to an unmasked speaker. A similar study examining a Schlieren optical technique to visualize droplets tested fitted N95 respirators and surgical masks during coughing. The findings showed that the tighter fitting N95 had low velocity turbulent air mass expulsion through the mask itself. In comparison, surgical masks had less direct expulsion of air through the mask and more escaping through the top, bottom, and sides of the mask, which was expected because of the mask’s looser fit. The results from these trials displayed that both surgical masks and N95 respirators are effective at reducing droplet expulsion during speech and turbulent air during coughing into the surrounding space, and surgical masks have a greater likelihood of particulate leak through the loose perimeter of the mask. The results from Fischer et al., when paired with the results from this current analysis, demonstrate the importance of the N95 in the clinical setting when there is a risk of aerosolization and when caring for patients at risk for infection with airborne spread. These risks do not apply to the general public, especially when social distancing policies and appropriate quarantine measures are implemented for infected and high-risk individuals (eg., known exposure to test-positive person).

The included studies did not specify the type of surgical mask used and whether the mask type was consistent throughout the trial, posing a limitation of our current analysis. Laboratory trials have shown that medical masks and face masks have variable protective effects to those around the user by filtering expelled droplets during speech. With various manufacturers supplying surgical masks of multiple types, the variation in their design may affect data collected in these studies. Another limitation is healthcare worker compliance with mask use and N95 use in these healthcare settings had not been tracked in the included studies and is likely not uniform. The potential variation in compliance may skew the results found in the studies that are participating in particularly high-risk aerosolization environments to favor N95 respirators.

The nature of this meta-analysis is limited by the size and nature of the included studies. Many of the studies analyzed a heterogeneous group of viral illnesses that spread, reproduce, and potentially mutate in vastly different ways. This limits the specificity of their results when attempting to compare the results to a pandemic such as with COVID-19. However, many RNA respiratory viral pathogens included in our analyses have similarities to the SARS-CoV-2 virus, including RNA positive sense viruses (rhinovirus-enterovirus) and RNA negative sense viruses (influenza, RSV, and parainfluenza). These viruses each interact with host cell proteins in the upper respiratory tract similarly to the SARS-CoV-2 viral spike protein interaction with host angiotensin-converting enzyme 2. These viral infections are most often spread via droplets generated by coughing, sneezing, or talking but may also spread by airborne transmission, especially in indoors environments. Of note, both the SARS-CoV-2 and influenza virus have been speculated to possess airborne transmission ability. The respiratory droplet size of both influenza and other mixed viruses, including coronaviruses, is similar, and <4.7 microns. Because of the similarities of the particle size, infection location, and cellular entry, it is feasible to assume some overlap between the results of other respiratory viral infections and the SARS-CoV-2 virus.

There is a risk of type II error in this small group of included RCTs because of the limited size of the populations being studied. There is also a risk of publication bias that we cannot determine owing to the limited number of related RCTs. Additionally; the number of RCTs and other studies that fulfilled the inclusion criteria for the analysis was small. Finally, these studies were performed before vaccine development for COVID-19, but with other vaccines available (eg., influenza). Vaccine administration for a given virus does not guarantee immunity and viral mutation can also limit vaccine effectiveness, which necessitates the ongoing use of optimal PPE especially for front-line physicians and healthcare team. The effect of vaccines on PPE effectiveness warrants further investigation and is beyond the scope of this analysis.

The authors recommend that further RCTs that compare surgical masks to N95 respirators (1) assess compliance with surgical mask and respirator use; (2) analyze viral illness in each group with PCR and antibody-based assays before, during, and after the study period for all participating healthcare workers; (3) study a single viral pathogen; (4) focus the study location on a single treatment setting (eg, emergency
Results comparing N95 respirators and surgical masks for influenza-like-illness (including clinical diagnoses) (Figure 2) and laboratory-confirmed influenza infection (Figure 7) showed statistically significant and insignificant results, respectively. This dichotomy highlights the importance of study design in these trials, as the clinical influenza diagnoses may have included other viral or bacterial pathogens presenting as influenza. This demonstrates that the influenza-like illness and influenza infection outcomes are different in nature and should not be grouped for analysis. These results suggest that N95 respirators are not beneficial over surgical masks against influenza but have a protective effect for preventing non-influenza respiratory viral illness. However, data analyzed regarding laboratory-confirmed influenza are at risk for type II error and compliance failure; these limitations suggest that further research is needed with regard to the potential safety benefits of N95 use when treating patients with laboratory-confirmed influenza.

Although many viral illnesses have shown to follow similar transmission patterns, others exhibit unique behaviors, as witnessed during the COVID-19 pandemic. Results show a statistically significant decrease in SARS and COVID-19 illness with N95 respirator use, compared to surgical masks. The RR associated with N95 respirator use compared to surgical masks for these viruses was 0.17, indicating a number needed to treat of just 1.2 to prevent additional infection in the healthcare team. The SARS-CoV-2 virus has shown to exhibit transmission from clinically asymptomatic patients who are unknowingly shedding the virus and exposing other inpatients, outpatients, and healthcare professionals to the risk of contracting COVID-19.38,46,47 In settings with high institutional and regional COVID-19 infection rates, N95 respirator use may help prevent transmission not only from patients but also from other members of the medical team. Hospitals and healthcare systems are a common environment of COVID-19 transmission, causing healthcare workers to be increasingly affected by the pandemic.48 Because of the virus’ reproduction, transmissibility, and high R0 value (basic reproduction number),49 the meta-analysis pooled results in this review might not have universal generalizability. Owing to variations in regional prevalence and other institutional policies, these data demonstrate that N95 respirators are a necessary resource to protect front-line physicians and all healthcare workers in the emergency setting because of high-risk procedures such as intubation that may lead to aerosolization of viral particles. The results of this investigation support the stringent use of N95 respirators by the emergency medicine team and also in the hospital setting when there is likelihood of exposure to COVID-19 and other respiratory viral illnesses either from patient care or other healthcare workers. As the data regarding the efficacy of N95 respirators have shown the superiority to prevent respiratory viral infection compared to surgical masks, the authors advise against the use of surgical masks for prevention of viral transmission, especially in high-risk settings such as the initial ED evaluation and during further hospital-based care of patients with laboratory test-positive infection. The authors also recommend that first responders use N95 respirators to enhance their protection when caring for patients who are at risk for viral disease such as COVID-19.

In conclusion, this meta-analysis demonstrated a protective effect with use of N95 respirators compared to surgical masks when assessing influenza, non-influenza respiratory viral infection, respiratory viral infection, SARS-CoV viruses, and laboratory-confirmed respiratory viral infection. No significant increased protective effect was identified for laboratory-confirmed influenza. This suggests that N95 respirator use is protective for medical professionals and all healthcare workers who encounter viral respiratory diseases.

Pooled analysis of recent evidence published during the COVID-19 pandemic showed a statistically significant protective effect of N95 respirators for the SARS-CoV-2 virus. The data support use of N95 respirators for all healthcare workers when evaluating potentially infected patients in the ED and also when treating COVID-19 positive patients with known active disease.

Level of evidence analysis of N95 respirator and surgical mask effectiveness in a healthcare setting consists of many high-level evidence RCTs and some low-level evidence case-control and retrospective cohort studies. Significant heterogeneity exists with regard to assessment of viral transmission and the types of viral illnesses studied. This meta-analysis highlights the necessity for more robust research to help guide institutional and national policies regarding PPE use during the COVID-19 pandemic and with other viral disease outbreaks in the future.

ACKNOWLEDGMENTS
The authors received no source of external funding for this review.

CONFLICTS OF INTEREST
The authors report no conflicts of interest pertaining to this work. For full listing of conflicts of interest, please see American Academy of Orthopaedic Surgeons Conflicts of Interest disclosures.

AUTHOR CONTRIBUTIONS
All authors contributed to data analysis, drafting or revision of the article, gave final approval of the final version to be published, and agreed to be accountable for all aspects of the work. APC: Manuscript preparation. BCS: Manuscript editing. SG: Manuscript editing. NM: Data analysis and figure assembly. IMZ: Coordination of research. DCO: Manuscript editing. AAR: Manuscript editing

ORCID
Andrew P. Collins BS https://orcid.org/0000-0001-7159-1782

REFERENCES
1. Therapeutic Options for COVID-19 Patients. Centers for Disease Control and Prevention. www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html. Accessed May 1, 2021.
2. Jefferson T, Del Mar CB, Dooley L, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database Syst Rev. 2020;11:CD006207.
3. Interim guidance for managing healthcare personnel with SARS-CoV-2 infection or exposure to SARS-CoV-2. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assessment-hcp.html. Accessed May 1, 2021.

4. Qian Y, Wilke K, Grinshpun SA, Donnelly J, Coffey CC. Performance of N95 respirators: filtration efficiency for airborne microbial and inert particles. Am Ind Hyg Assoc J. 1998;59(2):128-132.

5. Lim EC, Seet RC, Lee KH, Wilder-Smith EP, Chuah BY, Ong BK. Headaches and the N95 face-mask amongst healthcare providers. Acta Neurol Scand. 2006;113(3):199-202.

6. Chen X, Chughtai AA, MacIntyre CR. Herd protection effect of N95 respirators in healthcare workers. J Int Med Res. 2017;45(6):1760-1767.

7. Lawrence RB, Duling MG, Calvert CA, Coffey CC. Comparison of performance of three different types of respiratory protection devices. J Occup Environ Hyg. 2006;3(9):465-474.

8. Derrick JL, Gomersall CD. Protecting healthcare staff from severe acute respiratory syndrome: filtration capacity of multiple surgical masks. J Hosp Infect. 2005;59(4):365-368.

9. 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.

10. Eikenberry SE, Mancuso M, Iboi E, et al. To mask or not to mask: modeling the potential for face mask use by the general public to curtail the COVID-19 pandemic. Infect Dis Model. 2020;5:293-308.

11. Prevention strategies for seasonal influenza in healthcare settings. Centers for Disease Control and Prevention. http://www.cdc.gov/flu/professionals/infectioncontrol/healthcaresettings.htm. Accessed June 6, 2021.

12. Prevention, Identification and Management of Health Worker in the Context of COVID-19. World Health Organization. https://www.who.int/publications/i/item/10665-336265 Published October 30, 2020. Accessed June 6, 2021.

13. Yeung W, Ng K, Fong JMN, Sng J, Tai BC, Chia SE. Assessment of proficiency of N95 mask donning among the general public in Singapore. JAMA Netw Open. 2020;3(5):e209670.

14. 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.

15. Radonovich LJ, Simberkoff MS, Bessesen MT, et al. N95 respirators vs medical masks for preventing influenza among health care personnel: a randomized clinical trial. JAMA. 2019;322(9):824-833.

16. Long Y, Hu T, Liu L, et al. Effectiveness of N95 respirators versus surgical masks against influenza: a systematic review and meta-analysis. J Evid Based Med. 2020;13(2):93-101.

17. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med. 2009;6(7):e1000100.

18. Moher D, Liberati A, Tetzlaff J, Altman DG, Group PRISMA. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097.

19. Oxford Centre for Evidence-based medicine: Levels of Evidence (March 2009). Centre for Evidence-Based Medicine (CEBM), University of Oxford. https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-basedmedicine-levels-of-evidence-march-2009. Accessed April 15, 2021.

20. JBJS, Inc. Journals Level of Evidence. JBJS. Inc. Journals level of evidence: JBJS. https://journals.lww.com/jbjsjournal/pages/journals-level-of-evidence.aspx. Accessed October 22, 2021.

21. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions Version 6.2. Cochrane Databases, www.training.cochrane.org/handbook. Published February 2021. Accessed March 13, 2021.

22. 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.

23. Maclntyre 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.

24. Maclntyre 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.

25. 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(9368):1519-1520.

26. Guo X, Wang J, Hu D, et al. Survey of COVID-19 disease among orthopaedic surgeons in Wuhan, People’s Republic of China. J Bone Joint Surg Am. 2020;102(10):847-854.

27. 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(3):466-471.

28. Loeb M, McGeer A, Henry B, et al. SARS among critical care nurses, Toronto. Emerg Infect Dis. 2004;10(2):251-255.

29. Bowling BJ, Zhou Y, Ip DK, Leung GM, Aiello AE. Face masks to prevent transmission of influenza virus: a systematic review. Epidemiol Infect. 2010;138(4):449-456.

30. Oberg T, Brousseau LM. Surgical mask filter and fit performance. Am J Infect Control. 2008;36(4):276-282.

31. Blachere FM, Lindsley WG, McMillen CM, et al. Assessment of influenza virus exposure and recovery from contaminated surgical masks and N95 respirators. J Virol Methods. 2018;260:98-106.

32. Suen LKP, Guo YP, Tong DWK, et al. Self-contamination during doffing of personal protective equipment by healthcare workers to prevent Ebola transmission. Antimicrob Resist Infect Control. 2018;7:157.

33. Balazy A, Toiviola M, Adhkari A, Sivasubramani SK, Reponen T, Grinshpun SA. Do N95 respirators provide 95% protection level against airborne viruses, and how adequate are surgical masks?. Am J Infect Control. 2006;34(2):51-57.

34. Licina A, Silvers A, Stuart RL. Use of powered air-purifying respirator (PAPR) by healthcare workers for preventing highly infectious viral diseases-a narrative review and critical appraisal of evidence. Am J Infect Control. 2021;49(4):492-499.

35. Graiton J, McLawes ML. Protecting healthcare workers from pandemic influenza: n95 or surgical masks?. Crit Care Med. 2010;38(2):657-667.

36. Your guide to masks. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/about-face-coverings.html. Accessed May 14, 2021.

37. Fischer EP, Fischer MC, Grass D, Henrion I, Warren WS, Westman azyl A, Toivola M, Adhikari A, Sivasubramani SK, Reponen T, Grinshpun SA. Do N95 respirators provide 95% protection level against airborne microbial and inert particles. Sci Adv. 2020;6(36):eabd3083.

38. Tang JW, Liebner TJ, Craven BA, Settles GS. A schlieren optical study of the human cough with and without wearing masks for aerosol infection control. J R Soc Interface. 2009;6(1):5727-5736.

39. Li R, Pei S, Chen B, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2). Science. 2020;368(6490):489-493.

40. Ceccharelli M, Berretta M, Venanzi Rullo E, Nunnari G, Cacopardo B. Differences and similarities between Severe Acute Respiratory Syndrome (SARS)-CoronaVirus (CoV) and SARS-CoV-2. Would a
rose by another name smell as sweet?. Eur Rev Med Pharmacol Sci. 2020;24(5):2781-2783.

42. Tellier R. Review of aerosol transmission of influenza A virus. Emerg Infect Dis. 2006;12(11):1657-1662.

43. Noorimotlagh Z, Jaafarzadeh N, Martinez SS, Mirzaee SA. A systematic review of possible airborne transmission of the COVID-19 virus (SARS-CoV-2) in the indoor air environment. Environ Res. 2021;193:110612.

44. Fennelly KP. Particle sizes of infectious aerosols: implications for infection control. Lancet Respir Med. 2020;8(9):914-924.

45. Amanat F, Krammer F. SARS-CoV-2 vaccines: status report. Immunity. 2020;52(4):583-589.

46. Li C, Ji F, Wang L, et al. Asymptomatic and human-to-human transmission of SARS-CoV-2 in a 2-Family Cluster, Xuzhou, China. Emerg Infect Dis. 2020;26(7):1626-1628.

47. Kimball A, Hatfield KM, Arons M, et al. Public health—Seattle & King County; CDC COVID-19 investigation team. asymptomatic and presymptomatic SARS-CoV-2 infections in residents of a long-term care skilled nursing facility, King County, Washington, March 2020. MMWR Morb Mortal Wkly Rep. 2020;69(13):377-381.

48. Interim guidance for managing healthcare personnel with SARS-CoV-2 infection or exposure to SARS-CoV-2. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html. Accessed October 22, 2021.

49. D’Arienzo M, Coniglio A. Assessment of the SARS-CoV-2 basic reproduction number, R0, based on the early phase of COVID-19 outbreak in Italy. Biosaf Health. 2020;2(2):57-59.

How to cite this article: Collins AP, Service BC, Gupta S, et al. N95 respirator and surgical mask effectiveness against respiratory viral illnesses in the healthcare setting: A systematic review and meta-analysis. JACEP Open. 2021;2:e12582. https://doi.org/10.1002/emp2.12582