Health care workers have been at the forefront of the COVID-19 pandemic response and are at high risk for acquiring SARS-CoV-2 infection. Infected health care workers can transmit SARS-CoV-2 to coworkers and patients, including persons at risk for severe illness. Therefore, preventing SARS-CoV-2 infection in health care workers is essential to both maintaining an adequate health care workforce and preventing iatrogenic infections.

Along with other infection control measures in the hospital setting, personal protective equipment, including masks, is a key component of strategies to prevent SARS-CoV-2 in health care workers. However, the optimal mask type remains uncertain. N95 and equivalent respirators are designed to filter out at least 95% of airborne particles that are 0.3 microns or larger, with minimal leakage when properly fitted (1). By contrast, medical masks filter less efficiently and are loose fitting, enabling leakage, but they are more comfortable, less expensive, do not require fitting, and are more widely available. An ongoing point of contention has centered around when N95 respirators are necessary. Recommendations range from routine N95 use for procedures performed (2, 3).

Evidence on the comparative effectiveness of different mask types in health care workers has been suboptimal. Until now, the only randomized trials were from the pre-COVID-19 era and indicated similar risk for influenza-like illness with N95 respirators and medical masks (4). Observational studies found that N95 respirators were associated with decreased risk for SARS-CoV-1 infection, but the studies had methodological limitations, including potential recall bias, incomplete SARS-CoV-1 exposure measurement, and residual confounding (5). The applicability to SARS-CoV-2 of observations related to transmission of other viruses is uncertain. Subsequent observational studies in the SARS-CoV-2 era also provided insufficient evidence because of methodological limitations and inconsistent findings (6).

Two and a half years after the emergence of the COVID-19 pandemic, Loeb and colleagues (7) report the first randomized trial of N95 respirators versus medical masks in health care workers. This study was designed to determine if medical masks are noninferior to fit-tested N95 respirators for protecting health care workers during routine care of patients with known or suspected COVID-19. Overall, the trial found that the effects of medical masks versus N95 respirators on risk for SARS-CoV-2 infection confirmed by reverse transcriptase polymerase chain reaction were within the predefined noninferiority margin (hazard ratio, 1.14 [95% CI, 0.77 to 1.69]). A slightly higher proportion of participants randomly assigned to N95 respirators reported mask-related adverse events (primarily, discomfort or headaches). Strengths of the trial include the randomized design, pragmatic approach (for example, use of N95 respirators in participants randomly assigned to medical masks permitted when deemed necessary), and high mask type adherence. Despite evidence suggesting that outside exposures may be a stronger risk factor for COVID-19 than work exposures (8), a post hoc analysis found similar findings in participants with or without nonwork exposures.

The noninferiority margin used by the trial warrants closer examination. The prespecified noninferiority margin was a 5% absolute increase in COVID-19 incidence confirmed by reverse transcriptase polymerase chain reaction. This was based on preserving an estimated 50% of the observed N95 respirator benefit versus no mask from a prior retrospective study of SARS (9) and the input of health care professionals. Yet, the 5% increase represents a potential doubling of risk with medical masks—a generous noninferiority threshold which may be unacceptable to many health workers. In fact, the finding of noninferiority in this trial was consistent with up to a relative 70% increased risk.

The trial protocol also underwent several changes because of the evolution of the pandemic and availability of vaccination. These included expanded eligibility from nurses to any health care worker providing direct patient care, expansion to additional countries, permitting extended and reuse of N95 respirators, reducing follow-up from 12 to 10 weeks, expanding symptomatic criteria for COVID-19 testing, excluding previously vaccinated health care workers, continuing assessment of outcomes for 2 weeks in health care workers vaccinated during the trial, and increased sample size. These changes aimed to enhance enrollment and statistical power, maintain a pragmatic approach, and account for uptake of COVID-19 vaccinations. Although the changes do not seem to have biased findings, use of an adaptive or other flexible design could have better anticipated and addressed modifications to study methods (10).

There was substantial heterogeneity in outcomes by country. A post hoc analysis stratified by country reported hazard ratios that ranged from 0.95 in Egypt (where participants were enrolled later in the pandemic and seroprevalence was high) to 2.83 in Canada (where participants were enrolled early in the pandemic and seroprevalence was low). Among the factors that could contribute to this heterogeneity are differences in vaccine types, vaccination rates, infection control measures, local transmission dynamics, and enrollment during periods when different variants were predominantly circulating. This heterogeneity warrants caution in the interpretation of the trial findings. Nearly three quarters (74% [73 of 99]) of cases occurred in Egypt, where medical masks were within the noninferiority margin (hazard ratio, 0.95 [CI, 0.60 to 1.50]). Estimates from other countries did not meet noninferiority criteria but were based on few events (range, 5 to 11) and were very imprecise, with overlapping CIs. Therefore,
both the combined and site-specific findings are inconclusive. Yet, the stratified analysis enables one to judge that the trial findings are likely most applicable to an Omicron-predominant, high baseline COVID-19 seroprevalence setting.

The trial had other limitations. It was not designed to evaluate the effects of mask types as source control or in effectively vaccinated health care workers. The trial was unable to assess the effect of Omicron or other variants on mask effectiveness. Some subgroup analyses were post hoc, and it was not possible to determine how the findings varied according to factors affecting SARS-CoV-2 transmission, such as ventilation, use of other infection control measures, specific health care setting, or vaccination status.

Nonetheless, this trial provides the best evidence to date on comparative effectiveness of mask types in preventing SARS-CoV-2 infection in health care workers providing routine patient care. The results indicate that medical masks may be similar to N95 respirators in Omicron-era settings with high COVID-19 seroprevalence—but would not have met a more stringent noninferiority threshold (for example, 30% relative increased risk). Therefore, the results are not definitive. Decisions about mask types in health care workers should be informed by the uncertainty around the estimates and continue to account for health care worker preferences about potential tradeoffs, N95 respirator availability, and resource constraints.

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Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/Confl...m22-3219.

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