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Review of "Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis"

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One-Minute Summary

- This paper is a systematic review and meta-analysis of observational studies on the protective effectiveness of **physical distancing**, **face masks** and **eye protection** from infection from Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) or Coronavirus Disease 2019 (COVID-19).
- 44 comparative studies (n=25,697 cases) met inclusion criteria (7 studies with 6,674 cases of COVID-19, the remainder were from SARS and MERS).
- 38 studies examined physical distancing (6 on COVID-19); a strong association was found between proximity of an exposed individual with the risk of infection (unadjusted relative risk (RR): 0.30, 95% confidence interval [CI]: 0.20-0.44; adjusted odd ratio (aOR): 0.18, 95% CI: 0.09-0.38). The absolute risk (AR) was 12.8% with shorter distance and 2.6% with further distance (risk difference (RD): -10.2%, 95% CI: -11.5 to -7.5; moderate certainty). The strength of association was larger (lower infection risk) with increasing distance (RR: 2.02 per metre, 95% CI: 1.08-3.76).
 - Tests for interaction between the different viruses, healthcare versus non-healthcare settings, and type of face mask were not statistically significant.
- 39 studies compared N95 or similar respirators use, or other surgical/cotton masks, compared to no face mask. Any mask use was associated with large reductions in infection risk (unadjusted RR: 0.34, 95% CI 0.26-0.45; aOR: 0.15, 95% CI: 0.07-0.34; AR: 3.1% with face mask versus 17.4% without; RD: -14.3%, 95% CI: -15.9 to -10.7%, low certainty)
 - The associations were significantly stronger in healthcare settings (RR: 0.30, 95% CI: 0.22-0.41) compared to non-healthcare settings (RR: 0.56, 95% CI: 0.40-0.79) (p_{interaction}=0.049).

- A subgroup analysis of protection from N95 or similar respirators compared to no mask found an aOR: 0.04, 95% CI: 0.004-0.30, and surgical or cotton masks compared to no mask with an aOR: 0.33, 95% CI: 0.17-0.61. However the difference between these two comparisons was not statistically significant (p_{interaction}=0.090). Adjusting for aerosol generating medical procedures (AGMPs) did have a statistically significant differential effect (p_{interaction}=0.048).
- In 15 studies, eye protection demonstrated significant protection (unadjusted RR: 0.34, 95% CI: 0.22-0.52; AR: 5.5% with eye protection versus 16.0% without; RD: -10.6%, 95% CI: -12.5 to -7.7; aOR: 0.22, 95% CI: 0.12-0.39, low certainty).

Additional Information

- Sensitivity analyses related to mask use that utilized a Bayesian approach incorporating data from non-coronavirus studies in preventing influenza-like illness (RR: 0.93, 95% CI: 0.83-1.05) yielded a significant association with protection from COVID-19 (aOR: 0.40, 95% [credible interval [CrI]: 0.16-0.97).
- Similarly, the authors incorporated previous meta-analysis data from randomized controlled trials (RCTs) from mostly influenza comparing N95 respirators to surgical masks (OR: 0.76, 95% CI: 0.54-1.06). This sensitivity analysis resulted in no change in the results which showed a nonstatistically significant association favouring stronger protection from N95 respirators (ratio of aOR: 0.14, 95% CI: 0.02-1.05).

PHO Reviewer's Comments

- This is a meta-analysis of the best available evidence on novel coronaviruses demonstrating that policies on physical distancing are associated with large reductions in infection, in particular that further distances are more effective, even beyond 2 metres.
- This meta-analysis supports face masks and eye protection as effective interventions to reduce the risk of COVID-19 in both healthcare, and non-healthcare, settings.
- The authors discuss a possible protective effect of N95 respirators compared to other face masks. While this result was not statistically significant the effect size was large. A major limitation of this analysis is that they combined surgical and cotton masks to compare to N95 or similar respirators. This likely biases the results toward N95 respirators. In the appendix, after removing cotton masks from the analysis, surgical masks compared to no masks found an aOR 0.20, 95%CI 0.06-0.63. In addition, when AGMPs were incorporated there was a statistically significant interaction effect suggesting there may be additional confounding in these observational studies related to N95 respirator use and AGMPs. Previous RCTs evaluating N95 respirators compared to surgical masks for influenza have not found a significant beneficial effect. This meta-analysis does not provide conclusive evidence of benefit of N95 respirators compared to surgical masks for non-AGMPs for healthcare workers caring for COVID-19 patients. However, it does provide evidence for equipoise for much needed RCTs. We are aware of one such funded trial (NCT04296643).
- At least one study (<u>Seto et al 2003</u>) was incorrectly abstracted and used in this meta-analyses that biased the results to favour N95 respirators. Further validation of the abstraction of included studies is warranted and we urge caution in interpreting these results until this validation is complete.

- Another limitation of this meta-analysis is that all included studies were observational and susceptible to varying amounts of recall, confounding, and measurement biases. Although metaanalysis of such studies can improve power to detect a significant difference, it cannot resolve the underlying biases from the original studies.
- The authors combined novel betacoronavirus data, and most of the literature was from SARS as well as MERS patients. Based on the difference in transmission dynamics of COVID-19 some of this data may not be directly applicable.

Citation

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