Article

Comparative effectiveness of N95, surgical or medical, and non-medical facemasks in protection against respiratory virus infection: a systematic review and network meta-analysis

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Research in context

Summary

The aim of this systematic review and network meta-analysis is to evaluate the comparative effectiveness of N95, surgical/medical, and non-medical facemasks as personal protective equipment (PPE) against respiratory virus infection.

The study incorporated 35 published and unpublished randomized controlled trials (RCTs) and observational studies investigating specific mask effectiveness against influenza virus, SARS-CoV, MERS-CoV, and SARS-CoV-2. We searched PubMed, Google Scholar, and medRxiv databases for studies published up to 5 February 2021 (PROSPERO registration: CRD42020214729). The primary outcome of interest was the rate of respiratory viral infection. The quality of evidence was estimated using the GRADE approach.

High compliance to mask-wearing conferred a significantly better protection (odds ratio [OR], 0.43; 95% confidence interval [CI], 0.23-0.82) than low compliance. N95 or equivalent masks were the most effective in providing protection against coronavirus infections (OR, 0.30; CI, 0.20–0.44) consistently across subgroup analyses of causative viruses and clinical settings. Evidence supporting the use of medical or surgical masks against influenza or coronavirus infections (SARS, MERS, and COVID-19) was weak.

Our study confirmed that the use of facemasks provides protection against respiratory viral infections in general; however, the effectiveness may vary according to the type of facemask used. Our findings encourage the use of N95 respirators or their equivalents (e.g., P2) for best personal protection in healthcare settings until more evidence on surgical and medical masks is accrued. This study highlights a substantial lack of evidence on the comparative effectiveness of mask types in community settings.

ABBREVIATIONS

AGP: aerosol generating procedure

CDC: Centers for Disease Control and Prevention

CI: confidence interval

CoV: coronavirus

GRADE: Grading of Recommendations Assessment, Development, and Evaluation

ILI: influenza-like illness

MERS: Middle East respiratory syndrome

NMA: network meta-analysis

OR: odds ratio

PICOS: population, intervention, comparator, outcomes, and setting

PPE: personal protective equipment

RCTs: randomized controlled trials

SARS: Severe acute respiratory syndrome

WHO: World Health Organization

INTRODUCTION

The coronavirus disease (COVID-19) pandemic has led to an unprecedented increase in the demand for facemasks globally. The types of facemasks currently in use include N95 respirators, surgical masks, medical masks, and non-medical masks (e.g. cloth or cotton masks)[1-4]. However, there is no established evidence or consensus on which type of facemask is superior in preventing respiratory viral infection either by the wearer or those they encounter. Different facemask guidelines recommend the use of different facemasks against COVID-19[1-4], and this is an area of concern as certain mask types may not be as capable as others in preventing respiratory viral infections. Previous systematic reviews exclusively performed pairwise comparisons of mask types[5-7], and did not evaluate the capacities of all existing mask types simultaneously, leading to the unconsolidated information on the comparative effectiveness of different facemask types.

Therefore, we conducted the first network meta-analysis (NMA) to evaluate the comparative prevention effectiveness of the most common types of facemasks (N95 respirators, surgical or medical masks, and non-medical masks) that have been used as personal protective equipment (PPE). NMA is an analytical tool that enables a single coherent ranking of multiple interventions; thus, it can provide information that helps policy makers and healthcare workers choose appropriate equipment from an array of protective equipment[8,9]. To inform optimised protective strategies for different causative viruses and clinical settings, we separately analysed comparative mask effects in various respiratory viral infections, including influenza, Middle East respiratory syndrome (MERS), severe acute respiratory syndrome (SARS), and COVID-19, in both community and healthcare settings.

METHODS

Search strategy and selection criteria

We conducted a meta-analysis following a pre-registered protocol in PROSPERO (CRD42020214729). Two researchers (MS Kim and D Seong) independently searched the PubMed, Google Scholar, and medRxiv databases from inception to 5 February 2021 using the search strategy detailed in the Supplementary Appendix (p. 2). The manual research and screening of reference lists of review articles were also conducted to include additional relevant studies that have not been retrieved through the primary search. Any conflicts were resolved by consensus, with the mediation of a third independent investigator (JI Shin).

Our research question could be summarized in PICOS (population, intervention, comparator, outcomes, and setting) as follows: people at risk of respiratory virus infection (P), adhered to facemask wearing (I), compared with either no mask-wearing or little mask-wearing (C), reduction in the risk of laboratory-confirmed viral infection (O), in health care or community settings (S). Eligible studies met the following criteria: (1) RCTs, cluster RCTs, prospective cohort studies, retrospective cohort studies, case-control studies, and cross-sectional studies; (2) studies comparing the effectiveness of N95 respirators or their equivalent (e.g., P2), surgical masks, medical masks, or non-medical (e.g., cloth or cotton) masks with each other or with not wearing masks/very low compliance to wearing masks. Studies were excluded if they did not specify the types of mask used, and did not present isolated outcomes for individual mask types. There was no limitation regarding the type of mask, compliance to wearing masks, and the fitting of the mask; however, we preferentially used results from high compliance and better mask fitting when stratified results were presented within a study. Pre-prints have been used relatively frequently in meta-analyses for the urgent topic of COVID-19[10-14] as a large amount of relevant data is still unpublished. We included pre-prints to reduce the risk of selection and publication bias and increase network density, as done elsewhere[15]. We included both RCTs and observational studies in our NMA; inclusion of real-world data from non-randomized studies has the potential to improve precision of findings from RCTs if appropriately integrated[16,17] and many previous NMAs have increased the density of network and enhanced the statistical power of findings using the approach[18-21].

Data extraction

Two investigators (D Seong and MS Kim) extracted data on the PICOS (Participants, Interventions, Comparisons, Outcomes, and Study design) for each study. Moreover, information on the following was collected: first author, publication year, study design, estimated effect sizes or number of events, population information, type of respiratory virus, details of interventions and comparisons (mask type and compliance, if applicable), and outcome of interest. The intervention group included participants wearing a specific type of mask for protection, and the control group consisted of participants not wearing a mask or those who had a very low compliance to wearing a mask. For studies involving facemask and other non-pharmaceutical interventions (i.e., hand hygiene), we extracted data from selective groups to make the facemask the only difference. The primary outcome of the current NMA was laboratory-confirmed infection of various respiratory viruses—influenza virus, SARS-CoV, MERS-CoV, and SARS-CoV-2. Disagreements were resolved by consensus, with any persistent conflict resolved by a third independent investigator (JI Shin).

Quality assessment

Two investigators (D Seong and MS Kim) evaluated the risk of bias for all included studies according to meta-analysis guidelines. The risk of bias of RCTs was assessed using the ROB2 tool[22]. The risk of bias of observational studies was assessed using the ROBINS-I tool[23]. The certainty of evidence for primary outcomes was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach specifically designed for NMA[24-27]. Using the GRADE approach, outcomes were classified as high, moderate, low, or very low certainty of evidence.

Data synthesis

This NMA assessed the effectiveness of facemasks in preventing respiratory viral infection by presenting binary outcomes as odds ratio (OR) with 95% confidence interval (CI). The frequentist framework was used to perform the NMA using STATA (Stata Corp, College Station, TX, US, version 15.0) and R software (version 3.6.0)[28]; self-programmed routines of STATA[29,30] and the 'netmeta' package in R[31] were used as described in the previous studies[15,32]. The 'netmeta' package utilises graph theoretical approach, which constructs the Moore-Penrose pseudoinverse matrix and calculates the fitted values of the network model using a weighted least squares approach[33]. Review Manager (REVMAN version 5.3; Nordic Cochrane Centre, Copenhagen, Denmark) was used for pairwise meta-analysis using inverse variance random-effects model. We applied random-effects model as we deemed that the expected heterogeneity between studies is likely to be due to real differences between studies rather than by chance.

In this NMA, the rank hierarchy for each mask type was investigated using the surface under the cumulative rank curve (SUCRA) of the P rank score of R[34]. We assessed the consistency of evidence between direct and indirect comparisons where $p < 0.05$ under the design-by-treatment interaction random-effects model or inconsistency factors with 95% credible intervals containing 0 was deemed a lack of consistency[35]. As consistency could be considered as statistical measure of transitivity[36], transitivity assumption was estimated along with consistency test. The net heat plot was constructed to visualise the inconsistency matrix[35]. Heterogeneity was measured using the I^2 value, with $I^2 > 50\%$ indicating moderate-to-high heterogeneity. Publication bias was assessed using comparison-adjusted funnel plots and Egger's test[29]. A two-sided P-value of <0.05 was considered statistically significant.

Subgroup analysis

Subgroup analyses were performed for virus types (influenza virus, SARS-CoV, MERS-CoV, and SARS-CoV-2), clinical settings (health care setting and community setting), and study design (RCT and observational study) as planned in priori. Post hoc subgroup analysis for usual healthcare setting (patient contact) versus aerosol-generating procedure (AGP) was further conducted given that increasing evidence has supported the difference in the risk of infection in those settings[37,38].

RESULTS

Study characteristics

A total of 5,892 articles were identified through an initial search, and an additional 54 articles were identified from other sources after reviewing references (Figure 1). Duplicates and irrelevant studies were excluded; hence, a total of 185 articles were selected. After screening the full text of the articles to identify studies meeting the prespecified inclusion and exclusion criteria, 35 articles were included in the final meta-analysis. Among them, 8 studies were conducted in non-healthcare settings, and 27 studies investigated mask effectiveness in healthcare settings. Twelve studies were randomized or cluster-randomized controlled trials and 23 studies were observational studies. The PICOS data of individual studies and reference list of included studies are described in Supplementary Tables 1 and 2 (pp 4-14). The risk of bias in the included studies was generally low to moderate (Supplementary Appendix pp. 46–80).

In pairwise meta-analysis and NMA, heterogeneity (I^2) ranged from 0% to 53.7% (Supplementary Appendix pp. 15–45). Inconsistencies in NMA outcomes were evaluated to identify disagreement between direct and indirect assessments; global inconsistency was found in results of coronavirus (overall), coronavirus (healthcare setting), and COVID-19. Networks of eligible comparisons are shown in Figure 2. The certainty of evidence (GRADE) for the primary outcomes is depicted in Table 1.

Overall effect of wearing masks against respiratory viral infections

Wearing masks, regardless of the type, was associated with a reduced risk of infection from all respiratory viruses (OR, 0.50; 95% CI, 0.37–0.68; GRADE, low), SARS-CoV/MERS-CoV (OR, 0.30; 95% CI, 0.14–0.63; GRADE, low), and SARS-CoV-2 (OR, 0.49; 95% CI, 0.31–0.78; GRADE, low), but not with the risk of infection from influenza virus (OR, 0.71; 95% CI, 0.42–1.21; GRADE, moderate) (Figure 3). High adherence to wearing masks was associated with a lower risk of respiratory viral infection relative to low adherence (Figure 3).

Comparative effectiveness of facemasks against influenza

The use of facemask, including medical/surgical masks (OR, 0.75; 95% CI, 0.51–1.09; GRADE, moderate), N95 or equivalent masks (OR, 0.84; 95% CI, 0.56–1.28; GRADE, moderate), and non-medical masks (OR, 1.29; 95% CI, 0.24–6.94; GRADE, very low), was not associated with reduced infection from influenza virus, similar to the non-use of facemasks or a very low compliance to wearing masks in all studies (Figure 4A). The results were consistent in subgroup analyses of RCTs (Figure 4B) and observational studies (Figure 4C).

Comparative effectiveness of facemasks against coronaviruses

Only wearing N95 or equivalent masks (OR, 0.30; 95% CI, 0.20–0.44; GRADE, low) was associated with a decreased risk infection from all coronaviruses (SARS-CoV, MERS-

CoV, and SARS-CoV-2). The results were similar for assessment of the comparative effectiveness of masks against SARS and MERS (Figure 5B) and COVID-19 (Figure 5C).

Comparative effectiveness of facemasks in healthcare and community settings

No facemask type, was associated with a reduced influenza infection rate in healthcare settings (Figure 6A) and community settings (Figure 6B). For all coronavirus infections, including SARS, MERS, and COVID-19, in healthcare settings, the use of N95 or equivalent mask was associated with a lower infection rate (OR, 0.29; 95% CI, 0.19–0.44; GRADE, low), but not the use of medical/surgical masks (Figure 6C); the results were consistent in subgroup analysis particularly limited to mask effectiveness during AGP (Supplementary Figure 1). Insufficient data were collected on the effectiveness of N95 or equivalent masks against coronavirus infection in community settings (Figure 6D).

DISCUSSION

We conducted the first NMA to evaluate the comparative effectiveness of facemasks against various respiratory viral infections (influenza, MERS, SARS, and COVID-19) in both community and healthcare settings. This NMA mainly focused on using facemask as PPE (i.e., to protect the uninfected wearer) rather than as source control or transmission prevention, and as such, the interpretation of the results was confined to this regard. Our study revealed that the use of facemasks provides protection against respiratory viral infections in general, but the effectiveness may vary according to the type of facemask used. The N95 respirator or its equivalent was the most effective mask type, while evidence supporting the use of medical or surgical masks against influenza or coronavirus infections (SARS, MERS, and COVID-19) was weak.

The current facemask guidelines for COVID-19 vary from one organisation to another[6]. The World Health Organization (WHO) recommends non-medical masks for the general population; medical/surgical masks for individuals aged >60 years, those with underlying medical conditions, the frail, and/or those attending the ill; and respirator masks including N95 masks for healthcare workers in settings where procedures that may aerosolize the virus are performed[1]. While our findings agree with the use of N95 or equivalent in the healthcare setting for both usual patient contact and AGP, this study highlights insufficient evidence on the effectiveness of medical or surgical masks in community settings. The Centers for Disease Control and Prevention (CDC) advises the use of non-medical masks with multiple layers for community dwellers and advocates the reservation of medical/surgical masks or N95 respirators for healthcare workers[2]. Although we acknowledge that identifying the optimal mask distribution strategy based on mask effectiveness and supply is complicated, our finding raises the concern that non-medical masks may not provide sufficient protection against respiratory viral infections as our results show very large CIs and even an increased OR toward infection in community settings (Figure 6D), which leads to the belief that non-medical masks are less likely to be shown to be effective even after accumulation of more evidence. The findings of this study support that N95 or equivalent (e.g. P2) masks should be the primary choice, and further investigations on N95 or equivalent masks, including effects of reusing N95 masks or extending their use period[39-41], would be useful in mitigating the demand and supply imbalance and protecting the globe against current and future respiratory infection pandemics.

Although N95 or equivalent masks were effective against coronavirus infections (e.g. SARS, MERS, and COVID-19), they did not show effectiveness in preventing influenza virus infections (Figure 4). Four potential explanations are provided for this discrepancy. First, we investigated laboratory-confirmed influenza infection, rather than clinically diagnosed influenza (i.e., standard CDC classification of fever ≥37.8 °C plus cough or sore throat) or influenza-like illness (ILI); this is because the clinical diagnosis cannot guarantee if the person was indeed infected by influenza virus given the numerous respiratory viruses (i.e., respiratory syncytial virus, adenovirus, and rhinovirus) can induce similar symptoms. This different focus of outcome may in part explain our counterintuitive results on mask effectiveness against influenza infection, considering previous studies have made conclusions for mask effectiveness in light of ILI[42,43]. Second, there was a consistent trend towards reduced influenza infection with facemasks (Figure 3 and 4); given the imprecision of the effect estimates for wearing masks against influenza according to GRADE (Table 1), we cannot yet discount facemasks' effectiveness in prevention of influenza infection. Third, the poor effectiveness of masks against influenza may be attributable to the higher aerosol transmission potency of influenza virus compared to that of coronaviruses[44,45]. The higher aerosol potency of influenza virus may allow more particles to be penetrated through unfitted masks. Lastly, the difference in the findings can be possibly explained by a higher adherence to wearing masks in pandemic settings than during the seasonal spread of influenza[6]. The global effect of SARS, MERS, and COVID-19 led to unprecedentedly high standards, regulations, and education regarding facemask usage, and this may have contributed to a significant reduction in the numbers of coronavirus infections. This is also supported by our result that higher compliance to masks significantly reduced respiratory viral infection (Figure 3).

This study does not claim the ineffectiveness of surgical or medical masks nor does it oppose their use. Their effect directions were consistently toward lower risk for infection but with substantial imprecision according to GRADE, which may reflect a lack of statistical power rather than absence of actual effectiveness. Moreover, facemasks can be used to block the spread of droplets by an infected person (source control), as well as PPE[46,47]. Since the present study mainly focused on the protection of uninfected wearer but not the source control or transmission, the interpretation of the results on surgical and medical masks should be limited to protection. Wearing medical or surgical masks can still be meaningful in preventing transmissions of influenza virus and coronavirus as they can serve as shields to prevent the spreading of droplets carrying the infectious viruses from infected persons[48-50]. Laboratory findings insisted that wearing of surgical masks or KN95 respirators reduced the number of particles emitted from breath and coughing[51], even without proper fit testing[52].

This study has several limitations. First, in contrast to the wealth of RCTs investigating mask potencies for preventing influenza virus infection, there is one RCT investigating mask effectiveness against COVID-19. Thus, analysis of mask usage against coronaviruses was performed primarily based on observational studies, which may be prone to reporting, selection, and confounding biases. To account for such biases, we evaluated the certainty of evidence using the GRADE framework[24] and downgraded the evidence level for limited study design and any detection of bias. Second, individual studies were heterogeneous in terms of causative viruses, settings, protocols for wearing facemasks, and participants' compliance. We conducted various subgroup analyses to address these issues and reached relatively low heterogeneity, ranged from I^2 0% to 53.7%, compared to previous meta-analysis investigating facemask effectiveness (I^2 ranging from 48% to 87%)[5]. Lastly, it is observed in the GRADE framework that certainty of evidence for medical or surgical masks are generally lower than that for N95 or equivalent (Table 1). This may support the necessity for reappraisal of surgical/medical masks after more studies are published. Although the certainty of evidence is yet suboptimal, this study presents the highest level of evidence to date.

Coronaviruses are a serious public health threat, as demonstrated during the previous SARS and MERS epidemics and the current COVID-19 pandemic. Our study demonstrated that the use of facemasks provides protection against respiratory viral infections in general. Among various types of facemasks, it is likely safer to use N95 or equivalent in healthcare settings as PPE for the moment until more evidence on other types of masks are realized.

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Author Contribution Statement

MS Kim, D Seong, and JI Shin contributed to the study concept and design. MS Kim and D Seong identified and acquired relevant trials and extracted data. MS Kim and D Seong drafted the protocol for this study. MS Kim analyzed the data. MS Kim, Han Li, and JH Kim wrote the first draft of the manuscript. MS Kim finalized the manuscript. SK Chung, Y Park, and M Lee contributed to evaluating the Risk of Biases. SW Lee, DK Yon, KH Lee, M Solmi, E Dragioti, A Koyanagi, L Jacob, A Kronbichler, K Tizaoui, S Cargnin, S Terrazzino, SH Hong, RA Ghayda, J Radua, H Oh, S Lee, K Kostev, S Ogino, I-M Lee, E Giovannucci, Y Barnett, L Butler, D McDermott, P-C Ilie, and JI Shin contributed to the interpretation of data and critical revision of the manuscript. JI Shin, E Dragioti, Ai Koyanagi, A Kronbichler, S Ogino, and I-M Lee provided statistical advice or supervised the statistical interpretations. All authors saw and approved the final submitted version.

Conflict of interest disclosure

No conflict of interest declared

Data Availability Statement

The data that supports the findings of this study are available in the supplementary material of this article

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Table 1. Certainty of evidence evaluated with Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework for primary outcomes

Comparisons **(vs. Control)**	Comparison No.	OR (95% CI), p-value	Study design†	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	GRADE
Overall mask effect									
Preventive effect of wearing mask (any type) on respiratory viral infection									
Overall respiratory viral infection	22	0.50 (0.37, 0.68), **p<0.001**	Observational study	Not serious	Not serious	Not serious	Not serious	Not serious	Low
Influenza	8	0.71 (0.42, 1.21), p=0.208	RCT	Not serious	Not serious	Not serious	Serious	Not serious	Moderate
SARS/MERS	6	0.30 (0.14, 0.63), **p=0.001**	Observational study	Serious	Not serious	Not serious	Not serious	Not serious	Low‡
COVID-19	8	0.49 (0.31, 0.78), **p=0.003**	Observational study	Not serious	Not serious	Not serious	Not serious	Not serious	Low
Compliance (vs. low compliance)									
High adherence to mask behavior	6	0.43 (0.23, 0.82), **p=0.010**	Observational study	Not serious	Serious	Not serious	Not serious	Not serious	Very Low
Per specific mask type									
Influenza virus infection									
Medical and surgical mask	17	0.75 (0.51, 1.09), p=0.132	RCT	Not serious	Not serious	Not serious	Serious	Not serious	Moderate
N95 or equivalent	11	0.84 (0.56, 1.28), p=0.417	RCT	Not serious	Not serious	Not serious	Serious	Not serious	Moderate
Non-medical mask	1	1.29 (0.24, 6.94), p=0.767	Observational study	Not serious	Not serious	Not serious	Very serious	Not serious	Very Low
Coronavirus infection, overall (SARS, MERS, and COVID-19)									
N95 or equivalent	14	0.30 (0.20, 0.44), **p<0.001**	Observational study	Not serious	Not serious	Not serious	Not serious	Serious	Low‡
Medical or surgical mask	14	0.72 (0.51, 1.01), p=0.057	Observational study	Not serious	Not serious	Not serious	Serious	Serious	Very Low
Non-medical mask	2	0.77 (0.29, 2.07), p=0.605	Observational study	Not serious	Not serious	Not serious	Serious	Serious	Very Low
SARS/MERS infection									
N95 or equivalent	8	0.24 (0.13, 0.46), **p<0.001**	Observational study	Not serious	Not serious	Not serious	Not serious	Serious	Low‡
Medical and surgical mask	7	0.70 (0.38, 1.30), p=0.259	Observational study	Not serious	Not serious	Not serious	Serious	Serious	Very Low
COVID-19 infection									
N95 or equivalent	6	0.30 (0.17, 0.55), **p<0.001**	Observational study	Not serious	Not serious	Not serious	Not serious	Serious	Low‡
Medical or surgical mask	7	0.71 (0.44, 1.14), p=0.156	Observational study	Serious	Not serious	Not serious	Serious	Serious	Very Low
Non-medical mask	2	0.73 (0.25, 2.14), p=0.566	Observational study	Not serious	Not serious	Not serious	Serious	Serious	Very Low
Health care settings									
Influenza virus infection									
Medical or surgical mask	10	0.65 (0.28, 1.49), p=0.309	RCT	Not serious	Not serious	Not serious	Serious	Not serious	Moderate
N95 or equivalent	9	0.72 (0.31, 1.69), p=0.451	RCT	Not serious	Not serious	Not serious	Serious	Not serious	Moderate

Non-medical mask	1	1.29 (0.24, 6.94), p=0.767	Observational study	Not serious	Not serious	Not serious	Very serious	Not serious	Very Low
Coronavirus infection, overall (SARS, MERS, and COVID-19)									
N95 or equivalent	14	0.29 (0.19, 0.44), **p<0.001**	Observational study	Not serious	Not serious	Not serious	Not serious	Serious	Low‡
Medical or surgical mask	12	0.69 (0.44, 1.07), p=0.097	Observational study	Serious	Not serious	Not serious	Serious	Serious	Very Low
Community settings									
Influenza virus infection									
Medical or surgical mask	7	0.76 (0.47, 1.20), p=0.239	RCT	Serious	Not serious	Not serious	Serious	Not serious	Low
N95 or equivalent	2	3.50 (0.44, 27.97), p=0.237	RCT	Not serious	Not serious	Not serious	Very serious	Not serious	Low
Coronavirus infection, overall (SARS, MERS, and COVID-19)									
Medical or surgical mask	2	0.78 (0.53, 1.12), p=0.150	Observational study	Serious	Not serious	Not serious	Serious	Not serious	Very Low
Non-medical mask	1	1.29 (0.48, 3.45), p=0.612	Observational study	Not serious	Not serious	Not serious	Serious	Not serious	Very Low

†: dominant study design. ‡upgraded by one for a large magnitude of effect. RCT = randomized controlled trial.

Rationale:
Study design: If randomized trials form the majority of evidence base, the quality rating starts at “high”. If observational studies form the majority of evidence, base the quality rating starts at “low”.
Risk of bias: Downgraded for failure to conceal random allocation or blind participants in randomized controlled trials or failure to adequately control for confounding in observational studies.
Inconsistency: Downgraded if direct and indirect evidence are not coherence as demonstrated by the difference in point estimates and the lack of overlap in the 95% confidential intervals (CIs) between direct and indirect evidence (Global incoherence tests such as Q statistic to assess consistency under the assumption of a full design-by-treatment interaction random effects model were used as supplementary information for judgement).
Indirectness. Downgraded if there present substantial differences in study characteristics (PICO) that may modify treatment effect in the direct comparisons (such as A v C and B v C) that form the basis for the indirect estimate of effect of the comparison of interest (A v B), or the result is solely derived from indirect comparisons.
Imprecision: Downgraded when cases are small; or 95% CIs are wide and include or are close to null effect.
Publication bias: Downgraded when substantial asymmetry is observed in funnel plot or p<0.10 in egger’s test.

GRADE Definition (suggested by Puhan et al. in “A GRADE Working Group approach for rating the quality of treatment effect estimates from network meta-analysis”):
High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: We are moderately confident in the effect estimate i.e. the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality: Our confidence in the effect estimate is limited i.e. the true effect may be substantially different from the estimate of the effect.
Very low quality: We have very little confidence in the effect estimate i.e. the true effect is likely to be substantially different from the estimate of effect.

Figure legend

Fig. 1 PRISMA diagram showing selection of articles for pairwise and network meta-analysis

Fig. 2 Network of eligible comparisons for respiratory viruses
(A) Influenza virus. (B) Coronavirus (including SARS, MERS, and COVID-19). (C) SARS (SARS-CoV) and MERS (MERS-CoV). (D) COVID-19 (SARS-CoV-2). Control includes no mask wearing, or mask wearing at very low frequencies. Non-medical masks include cloths or cotton masks. Lines indicate direct comparisons of agents, and the thickness of line corresponds to the number of trials in the comparison. The size of node corresponds to the number of studies that involve the intervention. SARS = Severe Acute Respiratory Syndrome. MERS = Middle East Respiratory Syndrome. COVID-19 = Coronavirus Disease-19.

Fig. 3 Pairwise meta-analysis for the impact of wearing masks and adhering to mask behavior on the risk of infection to respiratory viral diseases
Control includes no mask wearing, or mask wearing at very low frequencies. SARS = Severe Acute Respiratory Syndrome. MERS = Middle East Respiratory Syndrome. COVID-19 = Coronavirus Disease-19.

Fig. 4 Network meta-analysis of different types of facemask compared with control (no mask or very low frequencies) for influenza virus infections
Risk of laboratory-confirmed infection by influenza virus in (A) overall, (B) RCTs, and (C) observational studies. Effect estimates are presented in odds ratios (ORs) with 95% CI. Facemasks are ranked by surface under the cumulative ranking curve (SUCRA) value. RCT = randomized controlled trial.

Fig. 5 Network meta-analysis of different types of facemask compared with control (no mask or very low frequencies) for coronavirus infections
Rate of diagnosed with coronavirus infection. (A) Risk of overall coronavirus infection (SARS, MERS, and COVID-19), (B) SARS (SARS-CoV) and MERS(MERS-CoV), and (C) COVID-19 (SARS-CoV-2). Effect estimates are presented in odds ratios (ORs) with 95% CI. Facemasks are ranked by surface under the cumulative ranking curve (SUCRA) value. SARS = Severe Acute Respiratory Syndrome. MERS = Middle East Respiratory Syndrome. COVID-19 = Coronavirus Disease-19.

Fig. 6 Network meta-analysis of different types of facemask compared with control (no mask or very low frequencies) for respiratory viral infections in health care and non-health care settings
(A) Risk of influenza virus infection in health care setting, (B) risk of influenza virus infection in community setting, (C) risk of coronavirus infection (SARS, MERS, and COVID-19) in health care setting, and (D) risk of coronavirus infection (SARS, MERS, and COVID-19) in community setting. For studies that investigated mask effectiveness separately for usual care and aerosol-generating procedure (AGP) within the health care setting, results from usual care were preferentially used for the analysis. Effect estimates are presented in odds ratios (ORs) with 95% CI. Facemasks are ranked by surface under the cumulative ranking curve (SUCRA) value.

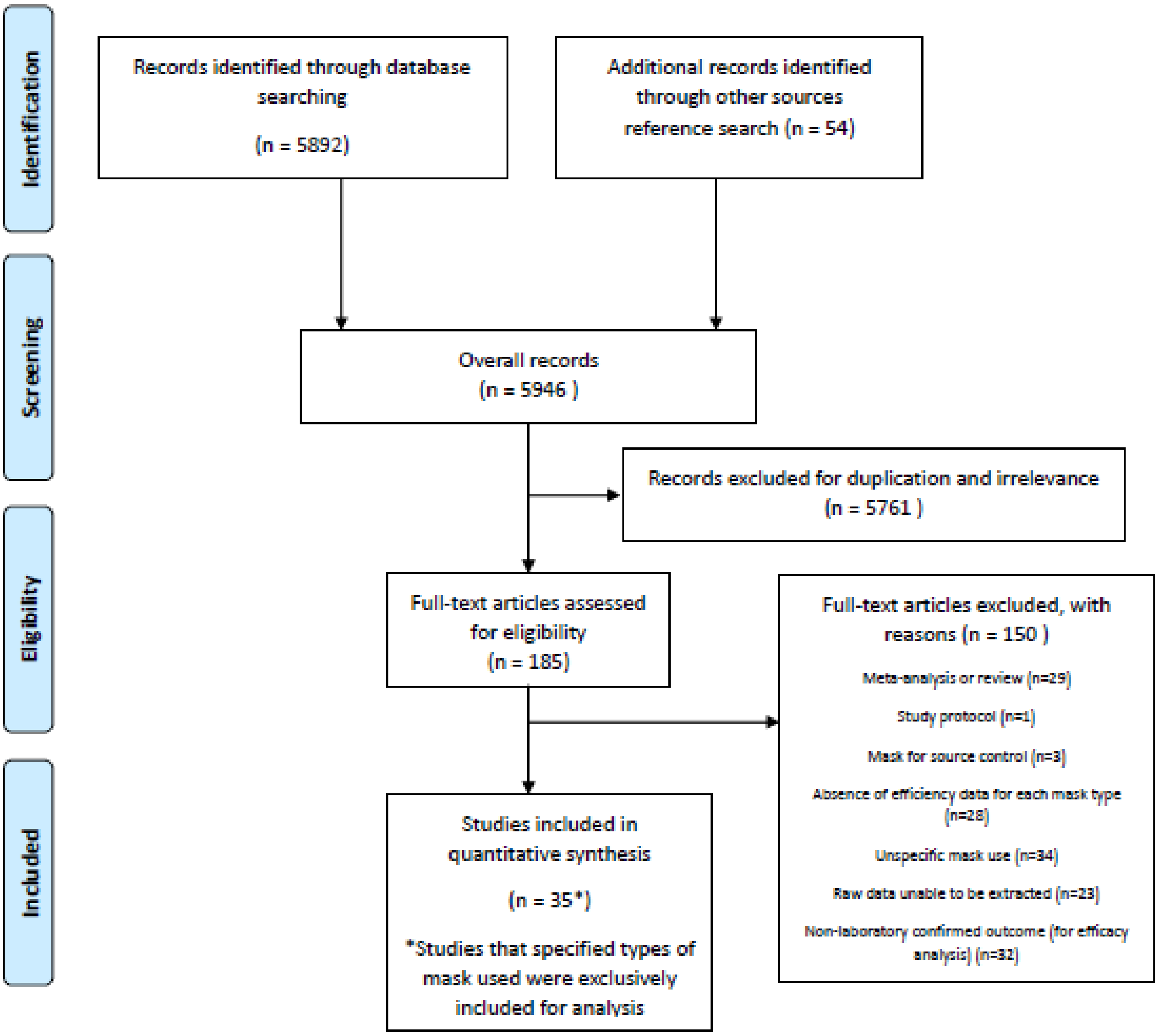
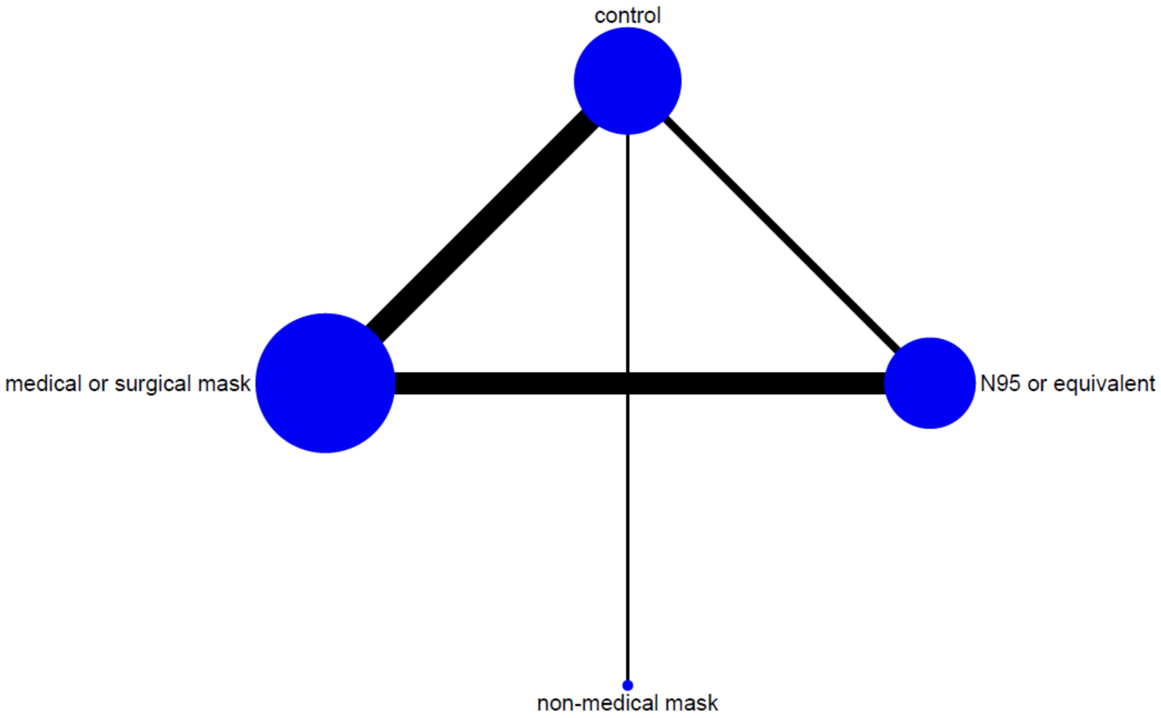
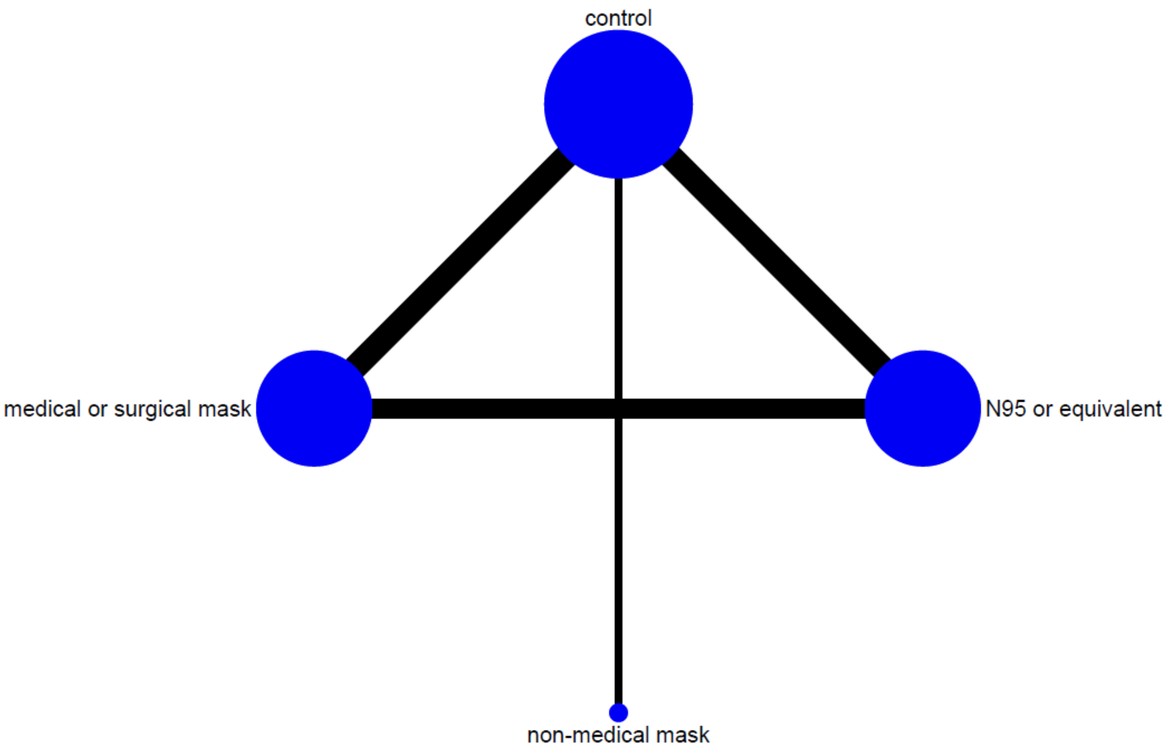


Fig. 1 PRISMA diagram showing selection of articles for pairwise and network meta-analysis

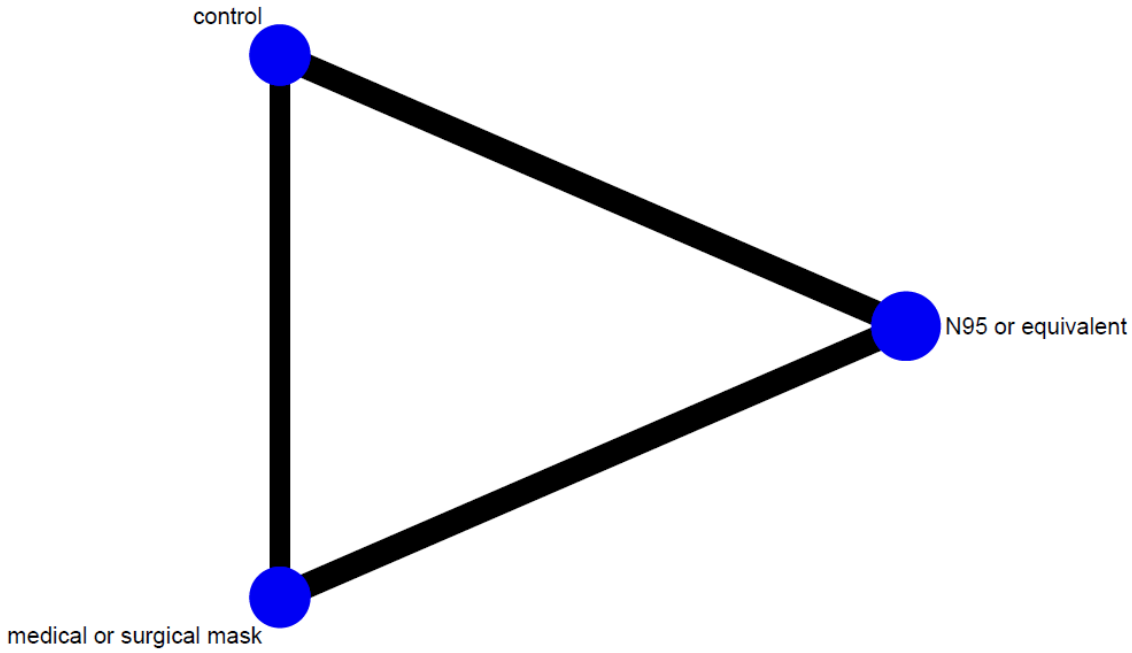
A Influenza virus



B Coronavirus (SARS, MERS, and COVID-19)



C SARS (SARS-CoV) and MERS(MERS-CoV)



D COVID-19 (SARS-CoV-2)

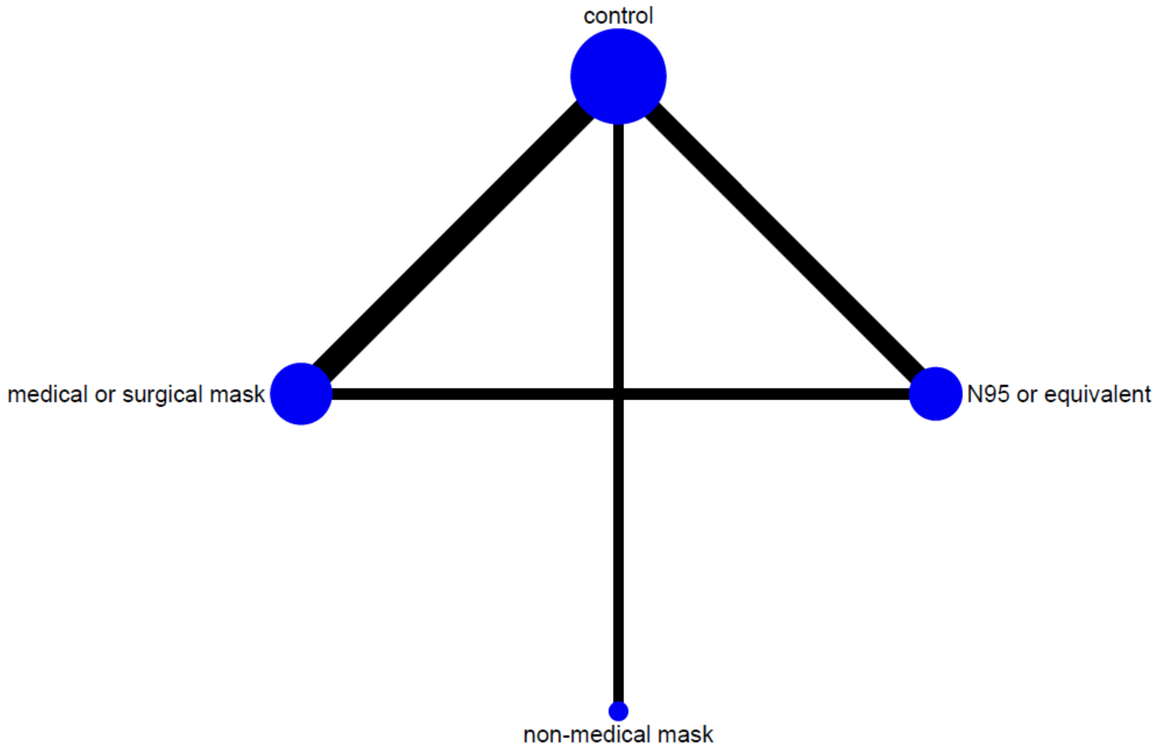


Fig. 2 Network of eligible comparisons for respiratory viruses
(A) Influenza virus. (B) Coronavirus (including SARS, MERS, and COVID-19). (C) SARS (SARS-CoV) and MERS (MERS-CoV). (D) COVID-19 (SARS-CoV-2). Control includes no mask wearing, or mask wearing at very low frequencies. Non-medical masks include cloths or cotton masks. Lines indicate direct comparisons of agents, and the thickness of line corresponds to the number of trials in the comparison. The size of node corresponds to the number of studies that involve the intervention. SARS = Severe Acute Respiratory

Syndrome. MERS = Middle East Respiratory Syndrome. COVID-19 = Coronavirus Disease-19.

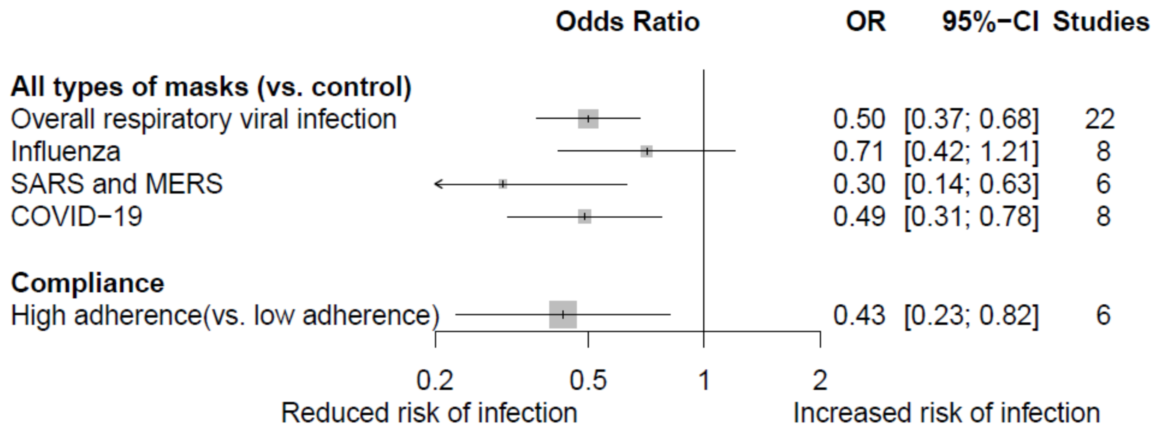
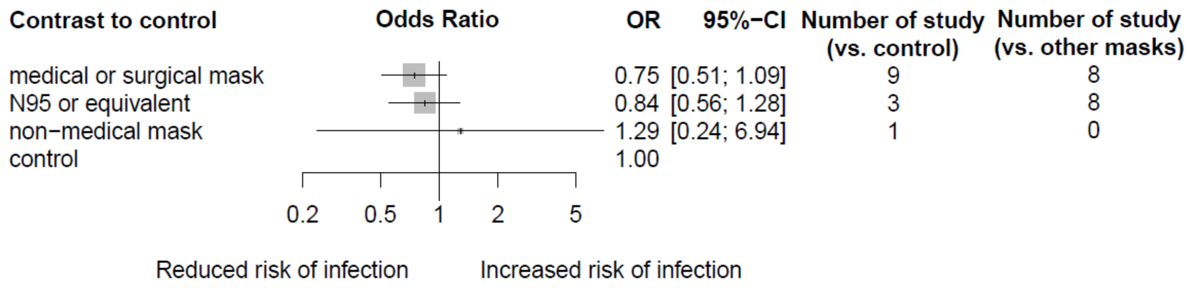


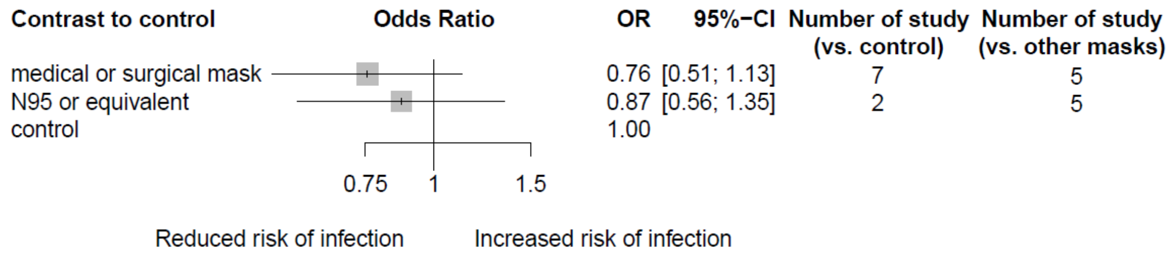
Fig. 3 Pairwise meta-analysis for the impact of wearing masks and adhering to mask behavior on the risk of infection to respiratory viral diseases

Control includes no mask wearing, or mask wearing at very low frequencies. SARS = Severe Acute Respiratory Syndrome. MERS = Middle East Respiratory Syndrome. COVID-19 = Coronavirus Disease-19.

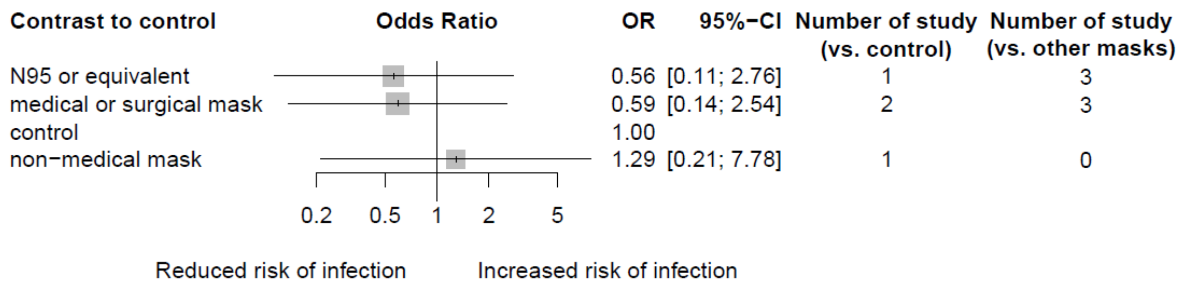
A Influenza (overall)



B Influenza (RCTs)



C Influenza (observational studies)



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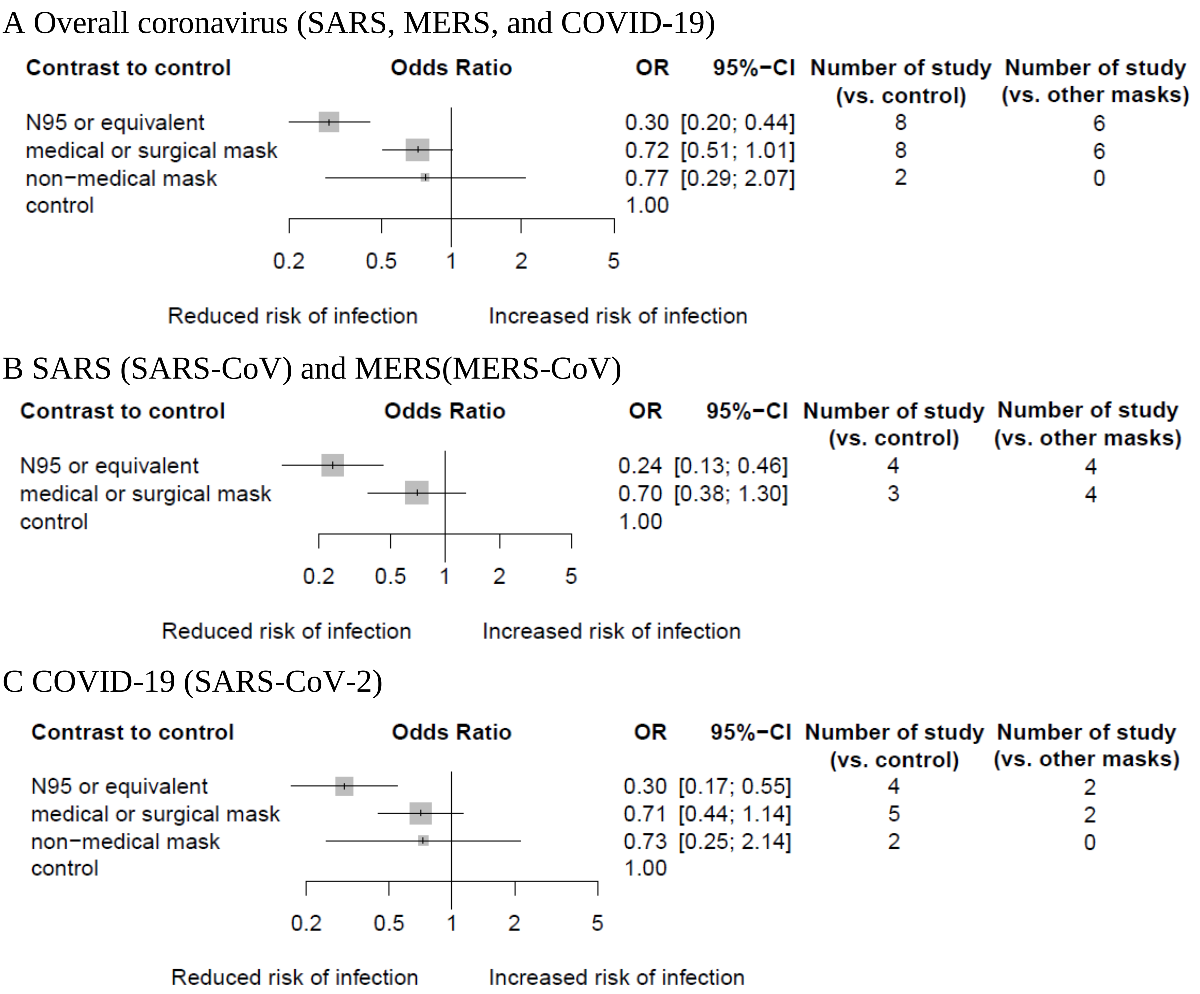

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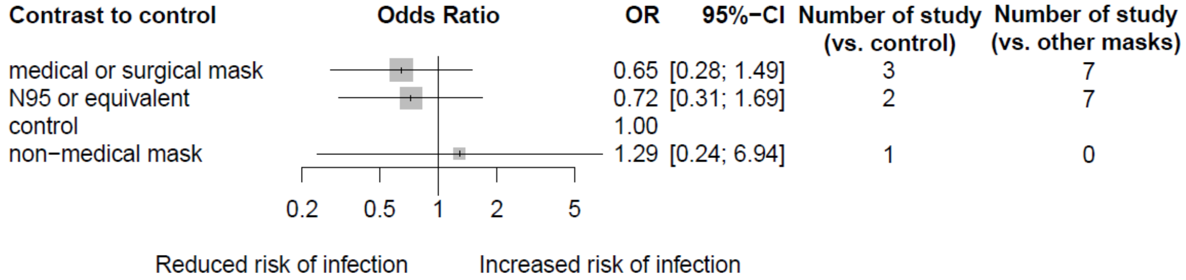
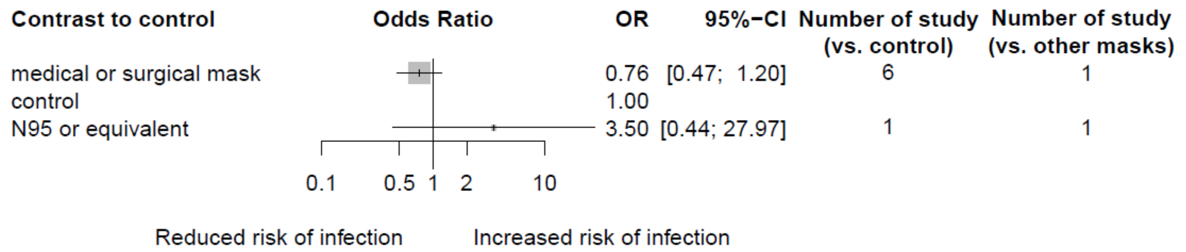
Rate of diagnosed with coronavirus infection. (A) Risk of overall coronavirus infection (SARS, MERS, and COVID-19), (B) SARS (SARS-CoV) and MERS(MERS-CoV), and (C) COVID-19 (SARS-CoV-2). Effect estimates are presented in odds ratios (ORs) with 95% CI. Facemasks are ranked by surface under the cumulative ranking curve (SUCRA) value. SARS = Severe Acute Respiratory Syndrome. MERS = Middle East Respiratory Syndrome. COVID-19 = Coronavirus Disease-19.

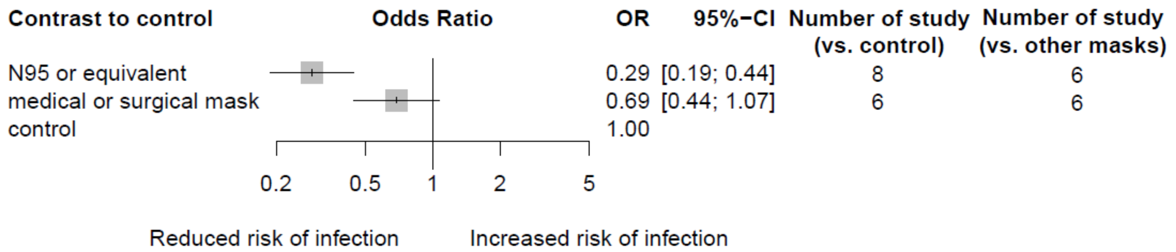
A Influenza virus infection in health care setting



B Influenza virus infection in community setting



C Coronavirus infection (SARS, MERS, and COVID-19) in health care setting



D Coronavirus infection (SARS, MERS, and COVID-19) in community setting

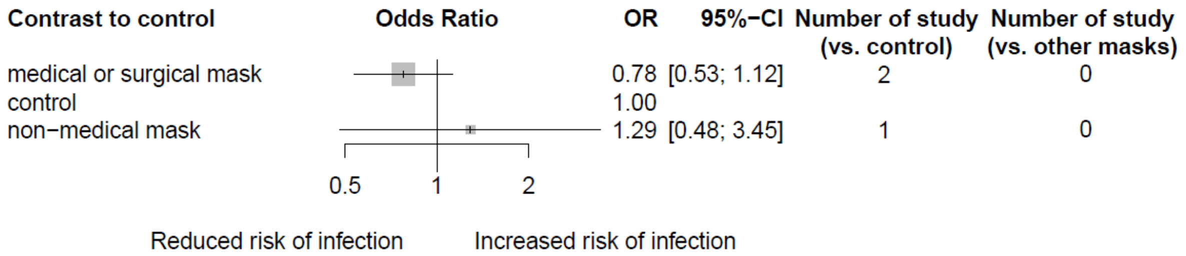


Fig. 6 Network meta-analysis of different types of facemask compared with control (no mask or very low frequencies) for respiratory viral infections in health care and non-health care settings

(A) Risk of influenza virus infection in health care setting, (B) risk of influenza virus infection in community setting, (C) risk of coronavirus infection (SARS, MERS, and COVID-19) in health care setting, and (D) risk of coronavirus infection (SARS, MERS, and COVID-19) in community setting. For studies that investigated mask effectiveness separately for usual care and aerosol-generating procedure (AGP) within the health care setting, results from usual care were preferentially used for the analysis. Effect estimates are presented in odds ratios (ORs) with 95% CI. Facemasks are ranked by surface under the cumulative ranking curve (SUCRA) value.