Science Journal of Public Health
2022; 10(3): 142-157
http://www.sciencepublishinggroup.com/j/sjph
doi: 10.11648/j.sjph.20221003.16
ISSN: 2328-7942 (Print); ISSN: 2328-7950 (Online)

A Systematic Review and Meta-analysis of the Efficacy of Medical Masks and N95 Respirators for Protection Against Respiratory Infectious Diseases

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To cite this article:

Gaohong Wu, Qingyang Ji, Huiwen Huang, Xueping Zhu. A Systematic Review and Meta-analysis of the Efficacy of Medical Masks and N95 Respirators for Protection Against Respiratory Infectious Diseases. *Science Journal of Public Health*. Vol. 10, No. 3, 2022, pp. 142-157. doi: 10.11648/j.sjph.20221003.16

Received: May 12, 2022; **Accepted**: June 13, 2022; **Published**: June 16, 2022

Abstract: To evaluate the efficacy of N95 respirators and medical masks for protection against respiratory infectious diseases, including COVID-19. We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) and observational studies evaluating the use of N95 respirators and medical masks for protection against respiratory infectious diseases. We retrieved relevant articles published from January 1994 to January 2020 by searching the PubMed, EMBASE, Cochrane CENTRAL, and Web of Science databases. The study quality was evaluated using the Cochrane Risk of Bias tool with RevMan 5.3 software. Eleven RCTs adjusted for clustering were included in the meta-analysis. Compared with the control group, N95 respirators or medical masks conferred significant protection against respiratory infectious diseases (odds ratio (OR) = 0.20; 95% CI: 0.08–0.51). Compared to medical masks, N95 respirators conferred significant protection against respiratory infectious diseases (OR = 0.75; 95% confidence interval (CI): 0.57–0.99). Meta-analysis of 10 observational studies adjusting for clustering also suggested that N95 respirators and medical masks are effective for protection against respiratory infectious diseases (OR = 0.30; 95% CI: 0.15–0.63). Given the body of evidence through a systematic review and meta-analyses, our findings supported the use of N95 respirators or medical masks has a significantly greater protective effect against respiratory infectious diseases among medical workers compared with those who did not use these types of PPE. However, only one case report showed the effectiveness of medical masks for preventing COVID-19. Although medical masks and N95 respirators may confer significant protection against respiratory infectious diseases, there is insufficient evidence to conclude that these types of personal protective equipment offer similar protection against COVID-19. Moreover, in the absence of sufficient resources during an epidemic, medical masks and N95 respirators should be reserved for high-risk, aerosol-generating producing procedures.

Keywords: Respiratory Infectious Diseases, COVID-19, Medical Masks, N95 Respirators, Meta-analysis

1. Introduction

Respiratory infectious diseases are characterized by high infectivity and rapid epidemic contagion via multiple transmission channels that are difficult to control [1]. The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which originated in Wuhan, China, has become a major global health issue. This novel coronavirus can cause severe respiratory tract infections and lead to bronchiolitis or pneumonia, a disease designated coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO) on February 12, 2020. The high prevalence of SARS-Cov-2 infections led the WHO to declare this an international public health emergency on January 30, 2020 [2]. At present, there are no specific treatments for COVID-19, but many public health measures have been implemented to improve disease control and prevention. By contrast, face masks are quickly available and accessible at the early stage of the outbreak. Still, there is insufficient evidence to reach a consensus on the use and the types of face masks in reducing disease spread.

Medical masks and N95 respirators are a type of personal protective equipment (PPE) used by medical staff that have been shown to be highly significant for the prevention of SARS-Cov-2 [3]. During the COVID-19 pandemic, there have been reports of shortages of PPE such as N95 respirators and medical masks for medical workers [4]. There is evidence that medical masks and N95 respirators have similar protective efficacy and that N95 respirators should be reserved for aerosol-generating procedures [5]. On the other hand, if N95 respirators are more effective than medical masks for the prevention of respiratory infectious diseases, they should be prioritized for aerosol-generating procedures. In this study, we conducted a comprehensive meta-analysis of the effectiveness of N95 respirators and medical masks for protection against respiratory infectious diseases, including COVID-19, to provide scientific basis for the formulation of policies related to the use of medical masks and other PPE.

2. Methods

2.1. Systematic Review Registration

This systematic review was registered with number CRD42020179966 (https://www.crd.york.ac.uk/PROSPERO).

2.2. Search Strategy

Articles published in English from January 1994 to January 2020 which explored the relationship between wearing medical masks and protection against respiratory infectious diseases were retrieved from PubMed, EMBASE, Cochrane CENTRAL, and Web of Science databases. The following search terms were used: “Respiratory infectious diseases”, “COVID-19”, “respiratory tract infection”, “prevention”, “Medical masks” and “N95 respirators”. Logical operators (OR, NOT, AND) were used to combine keywords and subject words (Table 1).

2.3. Inclusion Criteria

Articles that met the following criteria were selected: This study design was peer-reviewed randomized controlled trials (RCTs) or observational studies (OSs); The population was medical staff; The exposure of interest was wearing medical masks or N95 respirators; The outcome of interest was the proportion of infected patients in the experimental and control groups; The settings were healthcare settings worldwide; The diagnosis of respiratory infectious diseases was required to be supported by laboratory evidence, or local clinical diagnostic criteria were applied when laboratory evidence was not be available during acute large-scale infectious diseases (Table 2) [6].

2.4. Exclusion Criteria

We excluded guidelines, editorials, public press articles, reviews, raw data unavailable, theoretical models and the articles published in languages other than English.

Table 1. *Search strings for the four databases.*

Database	Search string
PubMed	(masks [MeSH Terms] OR mask [Title/Abstract] OR N95 respirators [Title/Abstract] OR “medical masks” [Title/Abstract] OR “face masks” [Title/Abstract] OR “medical mask” [Title/Abstract] OR “medical masks” [Title/Abstract] OR “surgical mask” [Title/Abstract] OR “surgical masks” [Title/Abstract] OR “surgical facemask” [Title/Abstract] OR “surgical facemasks” [Title/Abstract] OR “surgical face mask” [Title/Abstract] OR “surgical face masks” [Title/Abstract] OR respiratory infectious diseases [Title/Abstract] OR COVID-19 [Title/Abstract] OR prevention [Title/Abstract] OR control [Title/Abstract] OR measure [Title/Abstract] OR evaluate [Title/Abstract] OR effect [Title/Abstract] OR Public Health [Title/Abstract] OR medical workers [Title/Abstract]
EMBASE	(“respiratory infectious diseases”: ab, ti OR “COVID-19”: ab, ti) AND (“Public Health”: ab, ti OR “medical workers”: ab, ti OR “nursing home patient”: ab, ti) AND (“prevention”: ab, ti OR “control”: ab, ti OR “measure”: ab, ti OR “evaluate”: ab, ti OR “effect”: ab, ti OR “prevent”: ab, ti OR “control”: ab, ti OR “intervention”: ab, ti OR “outcome”: ab, ti)
Web of Science	TS=(mask OR facemask OR “face mask” OR “face masks” OR “medical” OR “medical mask” OR medical “masks” OR “medical facemask” OR “medical facemasks” OR “medical face mask” OR “medical face masks” OR “N95” OR “N95 respirators” OR “surgical facemask” OR “surgical facemasks” OR “surgical face mask” OR “surgical face masks” OR Infectious Diseases OR Respiratory infectious diseases OR “COVID-19” OR “prevention” OR “control” OR “prevention and control” OR PPE OR “measur” OR “evaluat” OR “effect” OR “Public Health” OR “medical workers”) AND TS=(“healthcare worker” OR “healthcare workers” OR “health care worker” OR “health care workers” OR “health-care worker” OR “health-care workers” OR “healthcare professional” OR “healthcare professionals” OR “health care professional” OR “health care professionals” OR “health-care professional” OR “health-care professionals” OR staff OR “healthcare personnel” OR “health care personnel” OR “health-care personnel”)
Cochrane CENTRAL	Respiratory infectious diseases OR COVID-19 in Title, Abstract, Keywords, AND “medical masks” OR “N95 respirators” OR “mask” in Title, Abstract, Keywords, AND practice OR control OR measur OR evaluat OR effect OR prevent OR prevention and control OR intervention OR outcome in Title, Abstract, Keywords, Publication Year from 1994 to 2020 in Trials

Table 2. *The diagnosis of respiratory infectious diseases.*

Type	Diagnostic criteria
Clinical diagnosis	One of the following two conditions is met: 1 Cough, expectoration, lung moist rales, and one of the following conditions: (1) Fever; (2) The total number of leukocytes and/or the proportion of neutrophils increased; (3) X-ray showed inflammatory infiltration in the lung. 2 Chronic respiratory disease secondary acute infection, and etiological changes or X-ray chest film showing obvious changes.
Etiological diagnosis	The clinical diagnosis can be made if one of the following six conditions is met: 1 The same pathogen was isolated from sputum on two consecutive occasions. 2 The number of pathogenic bacteria isolated by quantitative culture of sputum bacteria was $\geq 10^6$ cfu/ml. 3 Pathogens were isolated from blood culture or pleural fluid. 4 The number of pathogens in the lower respiratory tract secretion was $\geq 10^5$ cfu/ml. The number of pathogens in BALF $\geq 10^4$ cfu/ml; The number of pathogens in patients with chronic obstructive pulmonary disease was $\geq 10^3$ cfu/ml. 5 Non-respiratory bacteria were isolated from sputum or lower respiratory tract samples. 6 Evidence of etiological diagnosis by immunoserology and histopathology.

2.5. Data Extraction

Data extraction was conducted in two stages: first, the literature was screened by two researchers according to inclusion criteria. The screened literature was then searched and evaluated by two other researchers according to the inclusion criteria and exclusion criteria. To avoid errors, a pre-designed form was used to select the study characteristics, baseline patient characteristics, outcomes and definitions included in the literature, and any inconsistencies in recommendations were resolved through consultation. The main data extracted were as follows: the number of medical staff who insisted on wearing masks and those who did not insist on wearing masks.

2.6. Literature Quality Assessment

The quality of the methodology in the included studies was evaluated by using Cochrane Risk of Bias tool [7]. The quality of RCTs was evaluated using RevMan 5.3 software. The risk of bias was evaluated from six perspectives: choice bias, performance bias, measurement bias, attrition bias, reporting bias and other biases (Table 3). According to the criteria for low, unclear and high risk, the quality of the methodology of the included studies was divided into three levels as follows: Mild bias: four or more of the above six items are low risk; moderate bias: two or three of the above six items are low risk; severe bias: none or only one of the above six items is low risk.

Table 3. *Cochrane risk of bias assessment form.*

Evaluation items	Evaluation content	
Choice bias	Random sequence generation	The method of generating random assignment sequence is described in detail, which is convenient for evaluation of the comparability between groups.
	Assignment hidden	The method of hiding random distribution sequence is described in detail, which is convenient for judging whether the distribution of intervention measures can be predicted.
Performance bias	Blind method for researchers and subjects	The method of blinding used to prevent researchers and subjects from knowing the intervention measures is described in detail. This provides information that can be used to judge whether the blinding method is effective.
Measurement bias	Blind evaluation of research results	The method of blinding used to prevent the evaluators of the research results from knowing the intervention measures is described in detail. This provides information that can be used to judge whether the blinding method is effective.
Attrition bias	Integrity of result data	The data for each major outcome indicator, including those of subjects who were lost or withdrew from the study, are reported completely. Including subjects who were lost or withdrew, the total number of people in each group (compared with the total number of randomly enrolled people), and the reasons for the loss of interview/withdrawal are clearly reported, so as to facilitate assessment of the relevant treatment by the system evaluator.
Reporting bias	Selective reporting of research results	The information described can be used by system evaluators to judge the possibility of selective reporting of research results and relevant information.
Other biases	Other sources of bias	In addition to the above biases, the information provided can be used to assess the existence of other bias factors. If a question or factor is mentioned in the plan, corresponding answers are required.

2.7. Statistical Methods

RevMan 5.3 software provided by the Cochrane Collaboration was used to conduct this meta-analysis of the proportions of medical mask use between the experimental and control groups. Q and I^2 tests were used to evaluate the heterogeneity of the included studies (Q tests is the traditional method in the heterogeneity test of meta-analysis; I^2 tests can measure the degree of difference among multiple research effects, and can describe the percentage of variation caused by inter research in the total variation). When $I^2 \leq 50\%$ and $P > 0.1$, a fixed effect model was used to merge the data; when $I^2 > 50\%$ or $P < 0.1$, a random effect model was used to merge the data. The odds ratio (OR) and 95% confidence interval (CI) were used to express the enumeration data. $P < 0.05$ was considered to indicate statistical significance.

Document retrieval flow chart (Figure 1).

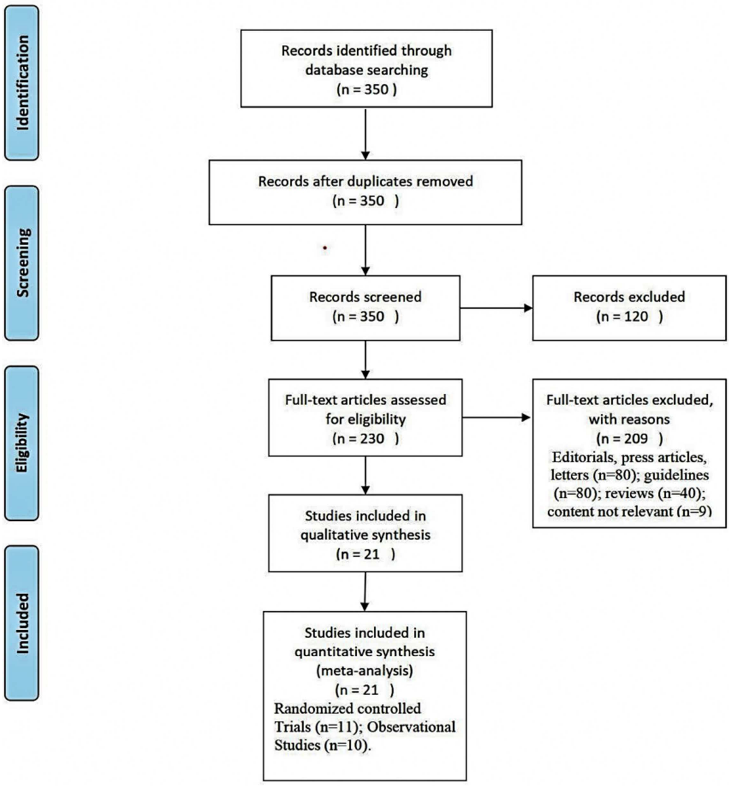


Figure 1. *Summary of the literature search and inclusion process.*

3. Results

3.1. Literature Search Results

After searching 350 papers from four databases, 21 articles were included in the final screening (Figure 1). We searched the full text of 230 articles and excluded 209 that did not meet our inclusion criteria. Finally, we selected 11 RCTs (Table 4, Table 5) and 10 OSs (Table 6). Five of the RCTs analyzed the effectiveness of N95 respirators versus medical masks for protection against respiratory infectious diseases. There was no real evidence to suggest publication bias (Figure 2).

Table 4. *Summary of RCTs assessing the effectiveness of masks for protection against respiratory infectious diseases (n = 7).*

Author	Journal	Year of publication	Study design	virus types	Mask type	Experimental group (n)		Control group (n)		OR	95%CI
						Infected	Non-infected	Infected	Non-infected		
Steo [8]. Asia	*Lancet*	2003	RCTs	coronaviruses	N95	0	10	92	28	0.01	0.00–0.26
Al-Asmary [9]. Asia	*Int J Infect Dis*	2007	RCTs	coronaviruses	N95	10	110	4	16	0.36	0.10–1.30
Ng [10]. Asia	*Infect Control Hosp Epidemiol*	2008	RCTs	coronaviruses	Medical	10	100	20	20	0.10	0.04–0.25
Yang [11]. Asia	*Braz J Infect Dis*	2010	RCTs	coronaviruses	Medical	73	140	44	76	0.90	0.56–1.44
MacIntyre [12]. Oceania	*INFLUENZA OTHER RESP*	2011	RCTs	respiratory syncytial viruses	N95	5	995	100	400	0.02	0.01–0.05
MacIntyre [12]. Oceania	*INFLUENZA OTHER RESP*	2011	RCTs	respiratory syncytial viruses	Medical	13	500	15	466	0.81	0.38–1.72
MacIntyre [13]. Oceania	*Prev Med*	2014	RCTs	respiratory syncytial viruses	N95	3	946	40	410	0.03	0.01–0.11
MacIntyre [13]. Oceania	*Prev Med*	2014	RCTs	respiratory syncytial viruses	Medical	32	510	39	442	0.71	0.44–1.15
MacIntyre [14]. Oceania	*BMJ Open*	2015	RCTs	respiratory syncytial viruses	Medical	15	600	25	440	0.44	0.23–0.84

Table 5. *Summary of RCTs assessing the effectiveness of medical masks versus N95 respirators for protection against respiratory infectious diseases (n = 6).*

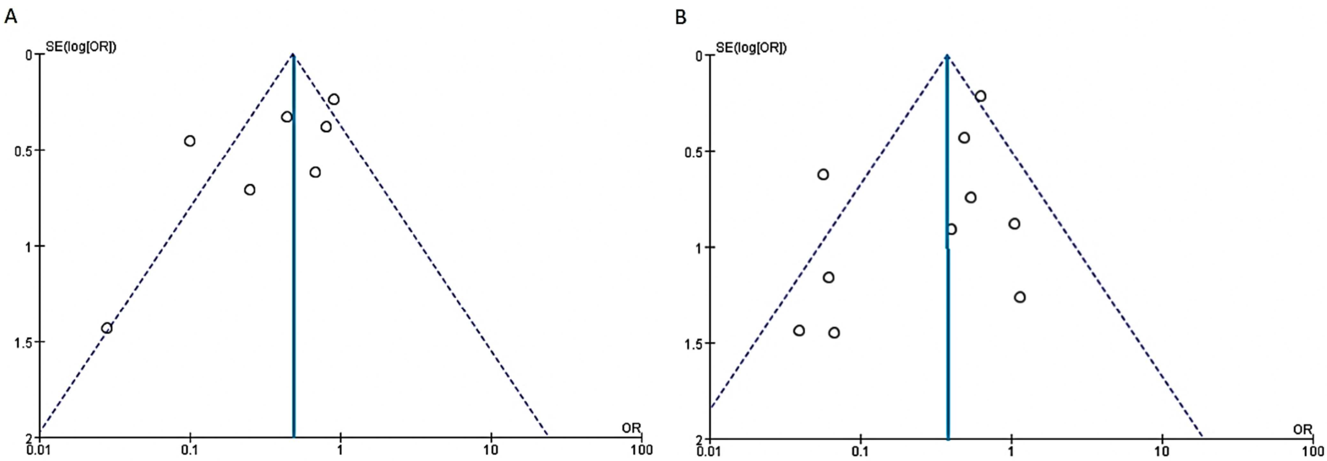
Author	Journal	Year of publication	Study design	N95 group (n)		Medical group (n)		OR	95%CI
				Infected	Non-infected	Infected	Non-infected		
Loeb [15]. North America	*JAMA*	2009	RCTs	126	663	113	675	1.14	0.86–1.50
MachIntyre [16]. Oceania	*Int J Infect Dis*	2009	RCTs	25	533	34	248	0.34	0.20–0.59
MachIntyre [12]. Oceania	*Influenza and Other Respiratory Viruses*	2011	RCTs	19	2828	21	1455	0.47	0.25–0.87
MachIntyre [17]. Oceania	*Am J Respir Crit Care Med*	2013	RCTs	58	2266	73	1991	0.70	0.49–0.99
MacIntyre [13]. Oceania	*Prev Med*	2014	RCTs	43	906	41	901	1.04	0.67–1.62
Radonovich [18]. North America	JAMA	2019	RCTs	650	6886	776	7228	0.88	0.79–0.98

Table 6. *Summary of OSs assessing the effectiveness of masks for protection against respiratory infectious diseases (n = 10).*

Author	Journal	Year of publication	Study design	virus types	Mask type	Experimental group (n)		Control group (n)		OR	95%CI
						Infected	Non-infected	Infected	Non-infected		
Seto [8]. Asia	*Lancet*	2003	OSs	coronaviruses	N95	0	11	100	156	0.07	0.00–1.16
Seto [8]. Asia	*Lancet*	2003	OSs	coronaviruses	Medical	0	30	51	123	0.04	0.66
Scales [19]. North America	*EMERG INFECT DIS*	2003	OSs	coronaviruses	Medical	3	20	3	18	1.06	0.02–0.19
Scales [19]. North America	*EMERG INFECT DIS*	2003	OSs	coronaviruses	N95	1	5	3	18	1.13	0.10–13.44
Teleman [20]. Asia	*Epidemiol Infect*	2004	OSs	coronaviruses	N95	3	177	23	77	0.06	0.02–0.19
Yin [21]. Asia	*Zhonghua Liu Xing Bing Xue Za Zhi*	2004	OSs	coronaviruses	Medical	46	74	156	158	0.63	0.41–0.97
Loeb [15]. North America	JAMA	2004	OSs	influenza virus	N95	2	16	5	16	0.40	0.07–2.37
Loeb [15]. North America	*JAMA*	2004	OSs	influenza virus	Medical	1	29	5	9	0.06	0.01–0.61
Nishiura [22]. Asia	*Jpn J Infect Dis*	2005	OSs	coronaviruses	Medical	8	42	35	90	0.49	0.21–1.15
Wilder-Smith [23]. Asia	*Emerg Infect Dis*	2005	OSs	coronaviruses	N95	3	6	34	37	0.54	0.13–2.35

3.2. Randomized Controlled Trials

Assessment of the risk bias of 11 RCTs [8-18] using RevMan 5.3 software showed moderate overall bias (Figure 3).



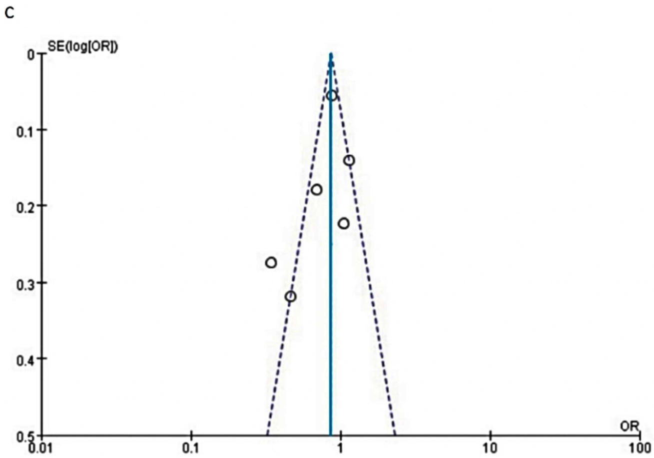


Figure 2. *Analysis of publication bias of RCTs and OSs.*

(A) RCTs effect of mask compared to no mask.
Funnel plot and egger's test assessing publication bias in RCTs investigating the effectiveness of medical masks for protection against respiratory infectious diseases; Harbord's estimated bias coefficient: -0.58; $P = 0.599$.
(B) OSs effect of mask compared to no mask.
Funnel plot and egger's test assessing publication bias in OSs comparing the effectiveness of masks for protection against respiratory infectious diseases; Harbord's estimated bias coefficient: 0.40; P = 0.635.
(C) RCTs effect of N95 respirators compared to medical masks.
Funnel plot and egger's test assessing publication bias in RCTs investigating the effectiveness of medical masks and N95 respirators for protection against respiratory infectious diseases; Harbord's estimated bias coefficient: -0.44; $P = 0.491$.
Funnel plots were generated to evaluate publication bias in RCT and OSs. The unadjusted effect estimates in some studies correspond to their standard errors. The real line and dotted line represent the aggregate effect estimates of different standard errors and their 95% CI, respectively. To determine publication bias, the Harbord test of small-study effects was used to assess funnel plot asymmetry.

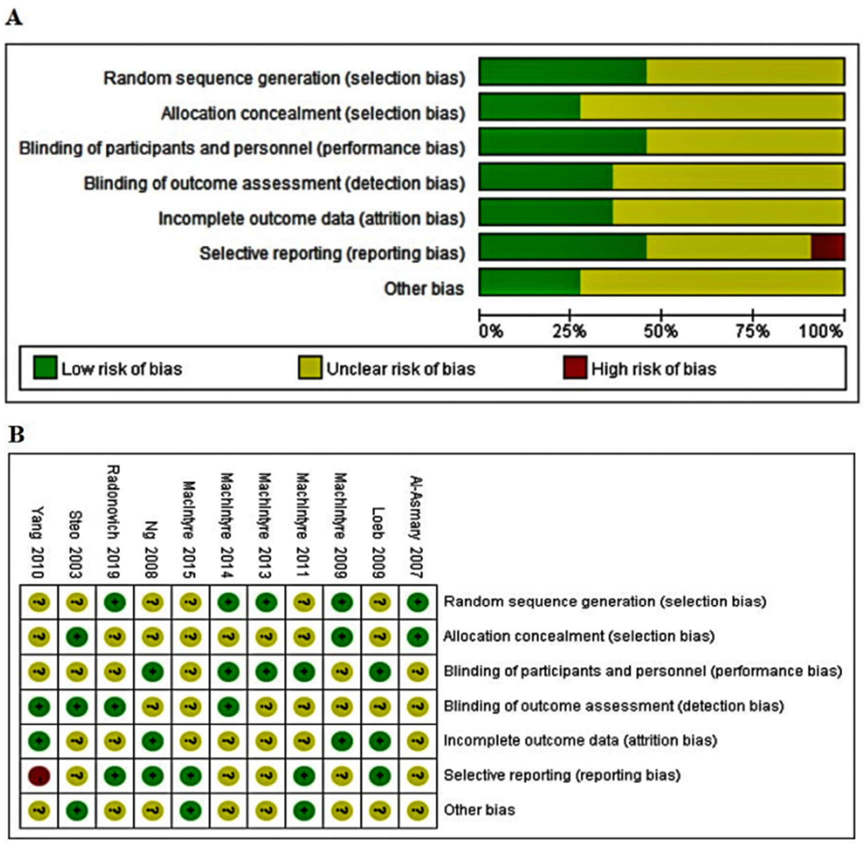
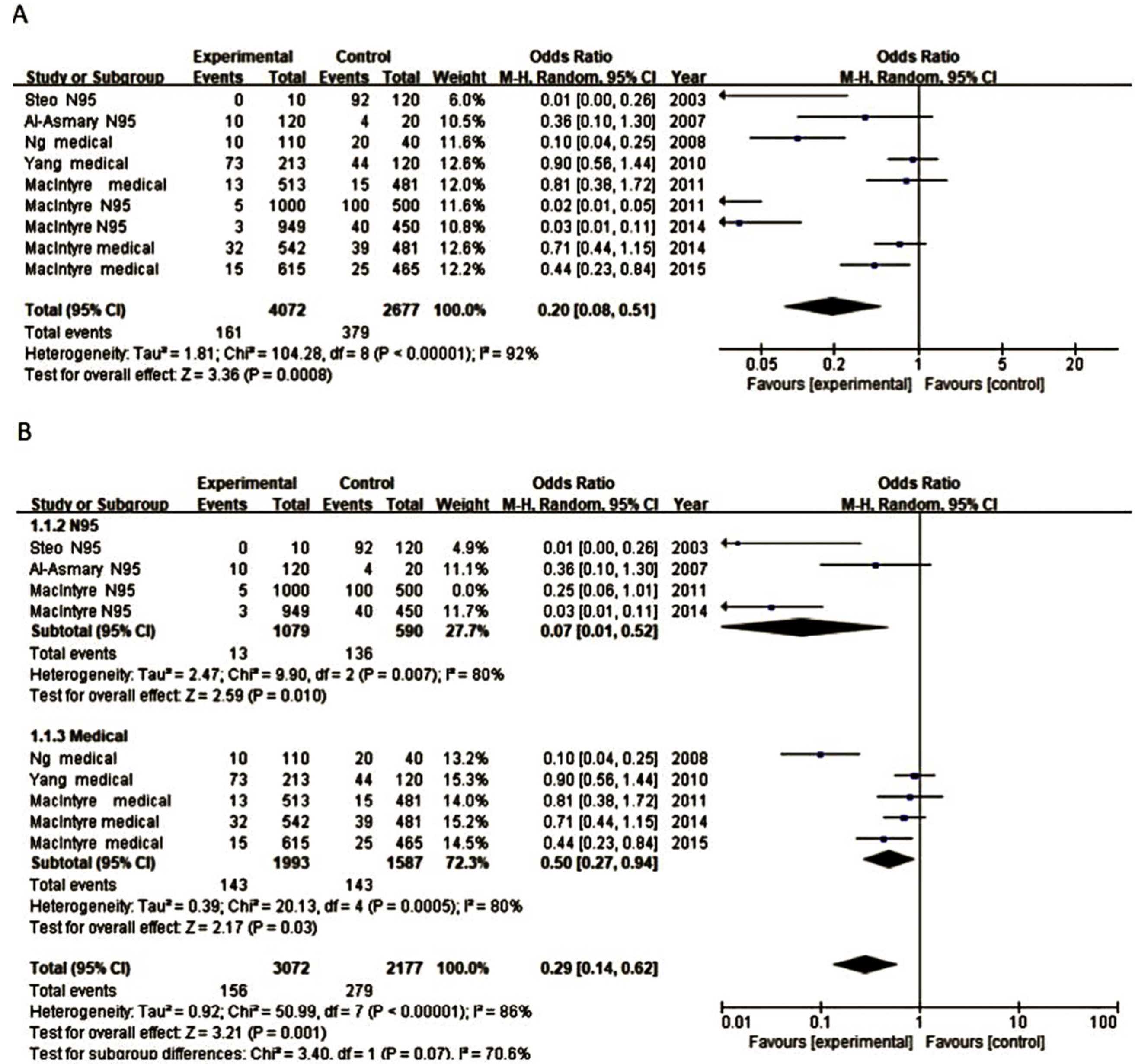


Figure 3. *Assessment of the risk bias of 11 RCTs.*

(A) Percentage of RCTs with high, low or uncertain risk of bias in each domain.
(B) RCTs received a high (red), low (green) or uncertain (yellow) risk of bias score for each of the domains.

3.2.1. Mask Use Versus No Mask Use for Protection Against Respiratory Infectious Diseases

Nine RCTs compared respiratory infectious diseases risk in medical staff wearing masks to that of convenience-selected controls wearing no masks. Wearing N95 respirators or medical masks conferred significantly greater protection against respiratory infectious diseases (OR = 0.20; 95% CI: 0.08–0.51; $P < 0.05$) (Figure 4A). Because of heterogeneity, the data were divided for subgroup analysis according to the following: medical masks and N95 respirators; virus types; geographic locations. Subgroup analysis showed that heterogeneity of the data for medical mask use was $I^2 = 80\%$ ($P = 0.005$) and the heterogeneity for N95 respirator use was $I^2 = 80\%$ ($P = 0.0007$), the heterogeneity of the data for coronaviruses was $I^2 = 92\%$ ($P < 0.00001$) and the heterogeneity for respiratory syncytial virus was $I^2 = 93\%$ ($P < 0.00001$), the heterogeneity of the data for Asia was $I^2 = 88\%$ ($P < 0.0001$) and the heterogeneity for Oceania was $I^2 = 95\%$ ($P < 0.00001$). These results showed that the heterogeneity of the data for medical mask and N95 respirator use, coronaviruses and influenza virus, Asia and Oceania was very large. Therefore, the heterogeneity of the data in the included studies has little relationship with the differences in effects associated with the use of medical masks vs. N95 respirators and coronaviruses vs. influenza virus or the geographic location in Asia vs. Oceania, and may be caused by other factors (Figure 4B, 4C and 4D).



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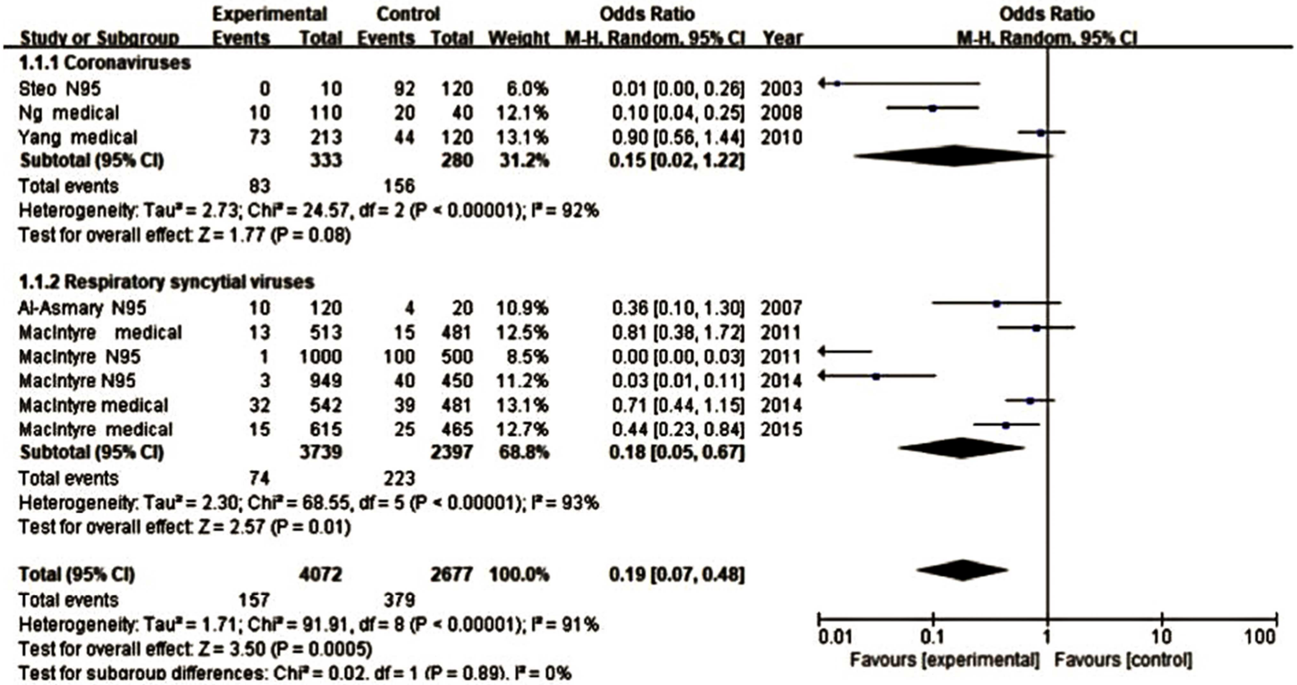

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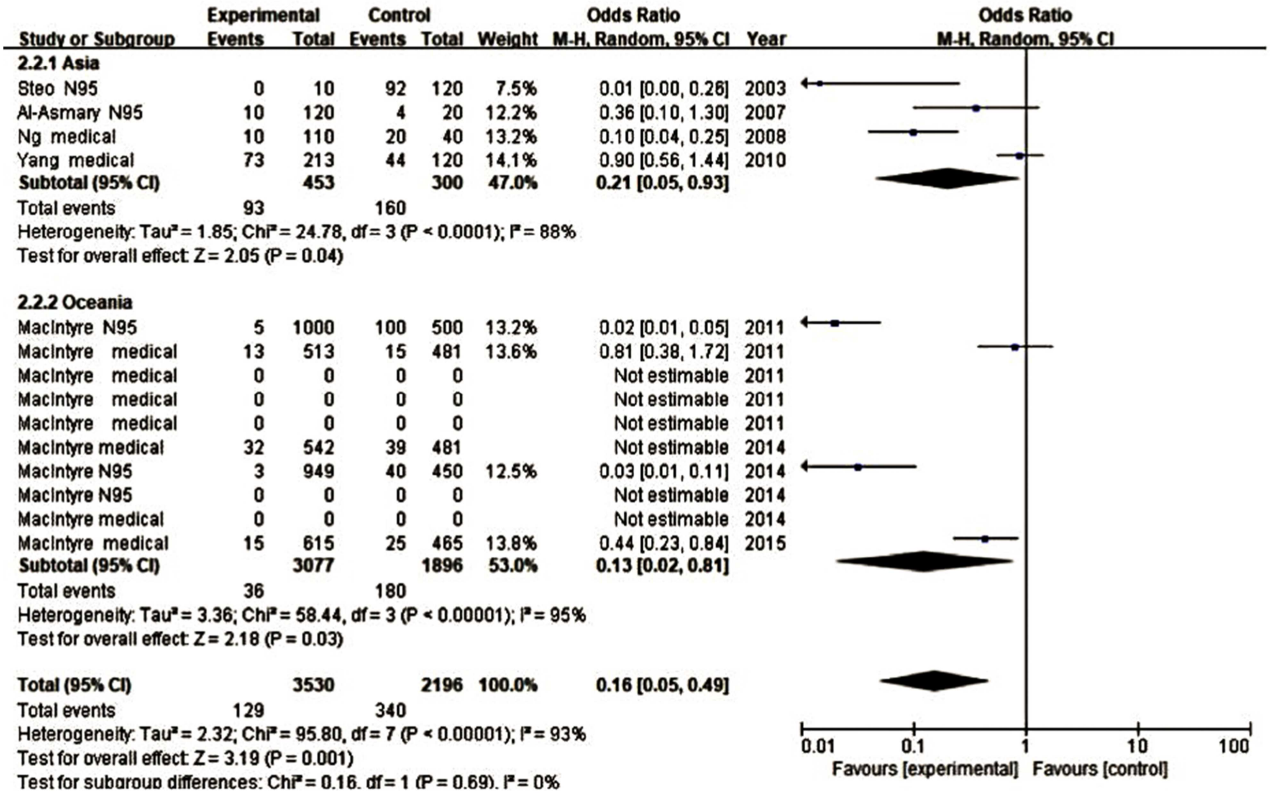


Figure 4. *Meta-analysis of RCTs assessing the protective effects of N95 respirators and medical masks against respiratory infectious diseases.*

(A) Meta-analysis of the effect of wearing N95 respirators and medical masks for protection against respiratory infectious diseases.
(B) Subgroup analysis of the effect of wearing N95 respirators and medical masks for protection against respiratory infectious diseases.
(C) Subgroup analysis of the effect of wearing masks for protection against different types of viruses.
(D) Subgroup analysis of the effect of wearing N95 respirators and medical masks for protection against respiratory infectious diseases in different geographic locations.

3.2.2. Medical Mask Use Versus N95 Respirator Use for Protection Against Respiratory Infectious Diseases

Six RCTs compared the use of medical masks and N95 respirators for protection against respiratory infectious diseases [12, 13, 15-18]. Compared with medical masks, N95 respirators were significantly more effective in protecting against respiratory infectious diseases (OR = 0.75; 95% CI: 0.57–0.99; $P < 0.05$) (Figure 5).

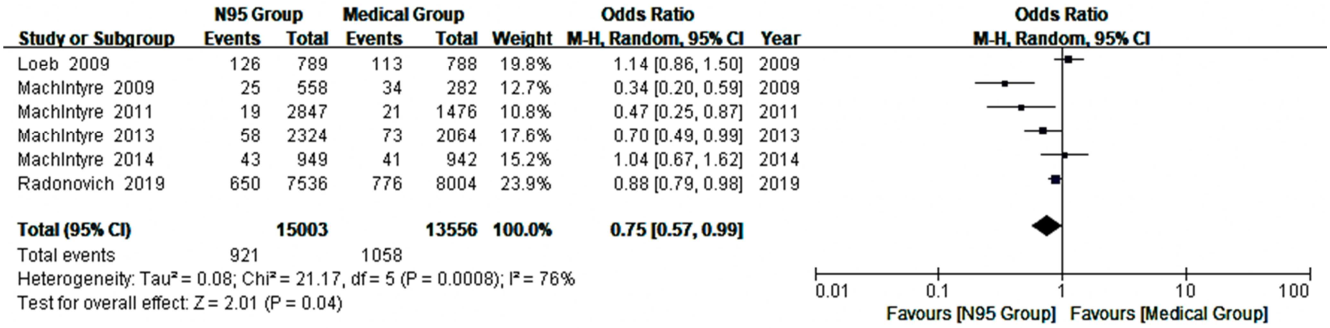


Figure 5. *Meta-analysis of RCTs comparing the protective effects of medical masks and N95 respirators against respiratory infectious diseases.*

3.3. Observational Studies

Assessment of the risk bias of nine OSs [17-23] using RevMan 5.3 software showed moderate overall bias (Figure 6).

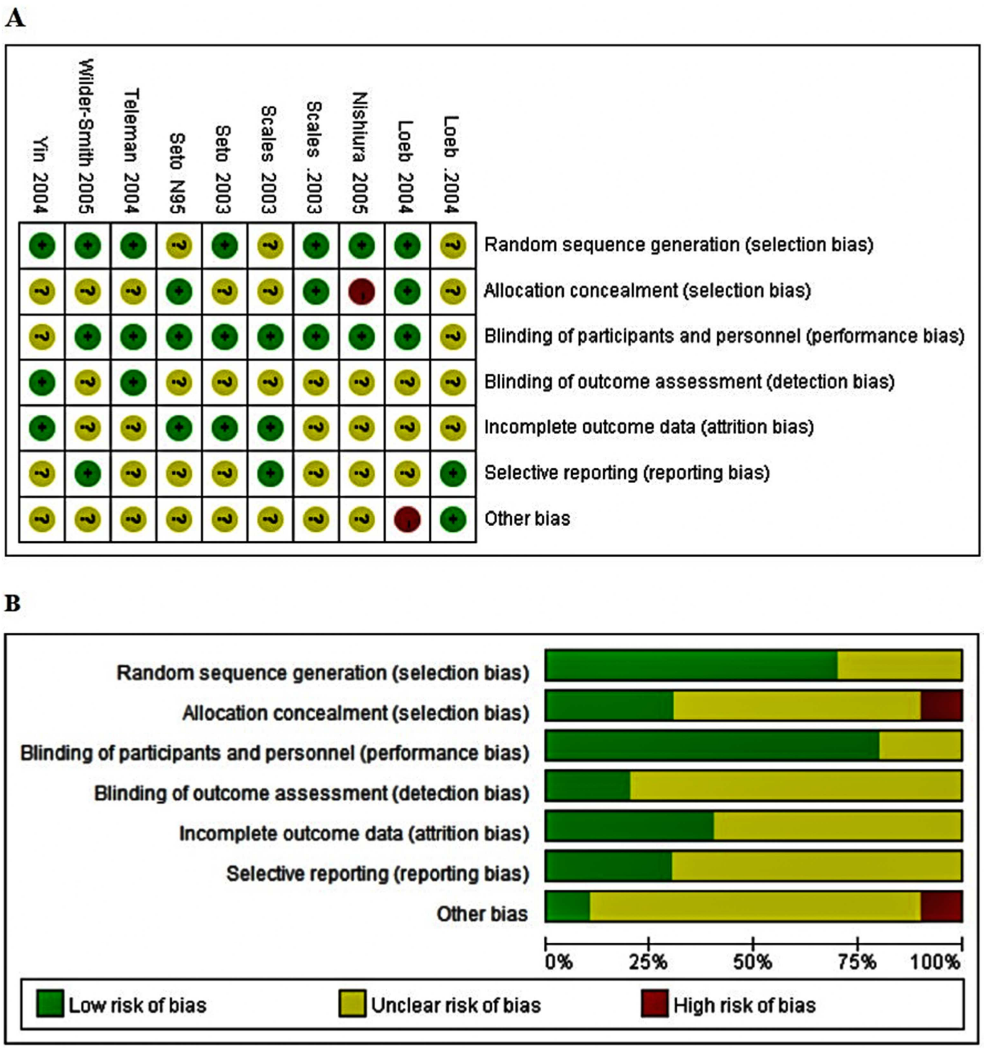
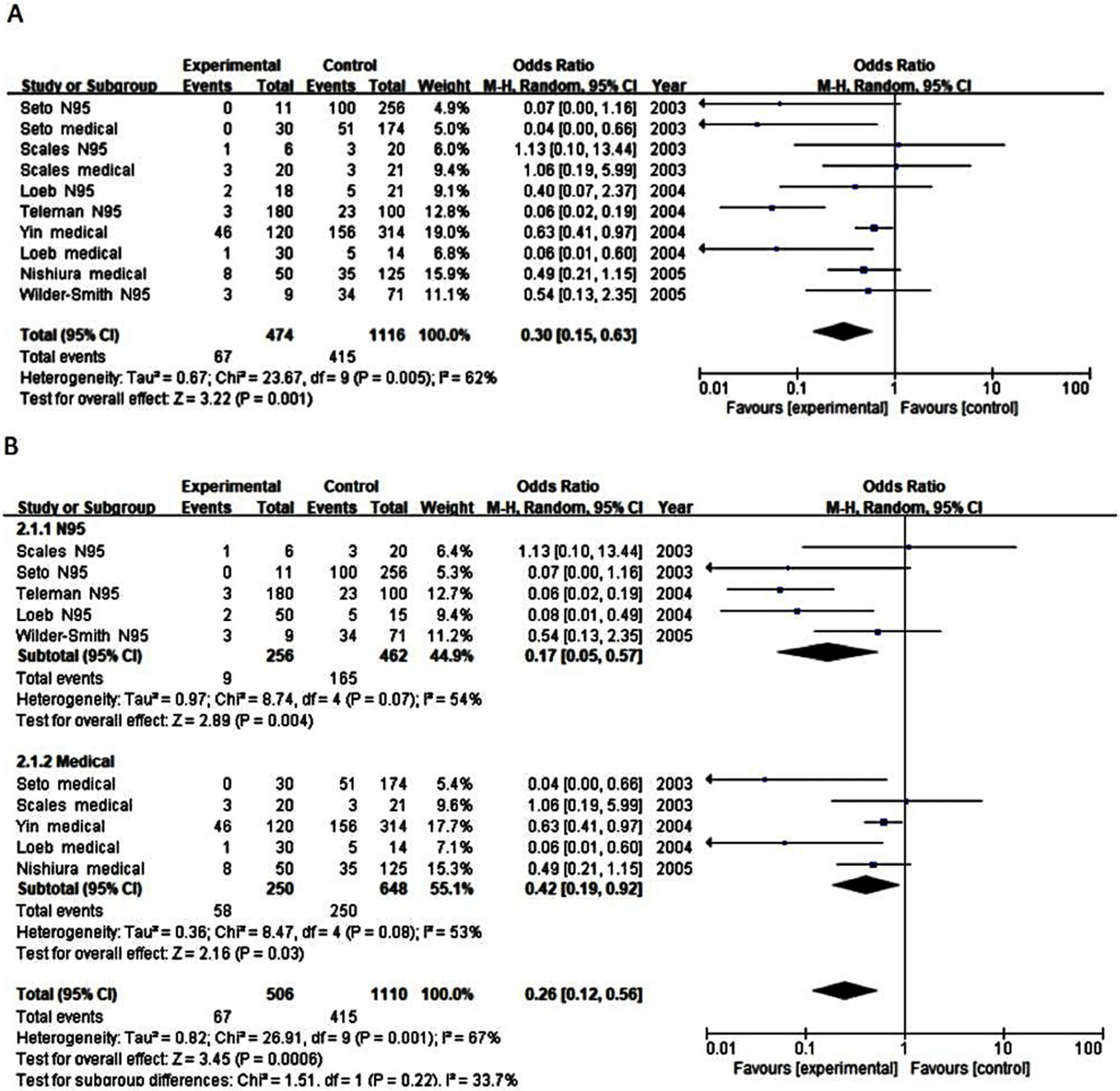


Figure 6. *Assessment of the risk bias of 9 OSs.*

(A) OSs received a high (red), low (green) or uncertain (yellow) risk of bias score for each of the domains.
(B) Percentage of OSs with high, low or uncertain risk of bias in each domain.

Ten OSs compared respiratory infectious diseases risk in medical staff wearing masks with that of convenience-selected controls wearing no masks. Wearing medical masks or N95 respirators conferred significantly greater protection against respiratory infectious diseases (OR = 0.30; 95% CI: 0.15–0.63; $P < 0.05$) (Figure 7A). Because of heterogeneity, the data were divided for subgroup analysis according to the following: medical masks and N95 respirators; virus types; geographic locations. Subgroup analysis showed that heterogeneity of the data for medical mask use was $I^2 = 53\%$ ($P = 0.08$), and the heterogeneity for N95 respirator use was $I^2 = 54\%$ ($P = 0.07$). The heterogeneity of the data for coronaviruses was $I^2 = 66\%$ ($P = 0.005$) and the heterogeneity for influenza virus was $I^2 = 38\%$ ($P = 0.21$). The heterogeneity of the data for Asia was $I^2 = 85\%$ ($P = 0.0002$) and the heterogeneity for North America was $I^2 = 0\%$ ($P = 0.72$), showing that the heterogeneity of the data for medical mask and N95 respirator use, coronaviruses and influenza virus were very small. Therefore, the heterogeneity of the data in the included studies has little relationship with difference in the use of medical masks or N95 respirators and coronaviruses or influenza virus and may be caused by other factors (Figure 7B and 7C). The heterogeneity of the data for Asia was very large, while the heterogeneity of the data for North America was very small. Therefore, the possibility that the heterogeneity of the data in the included studies was related to the geographic locations could not be excluded (Figure 7D).



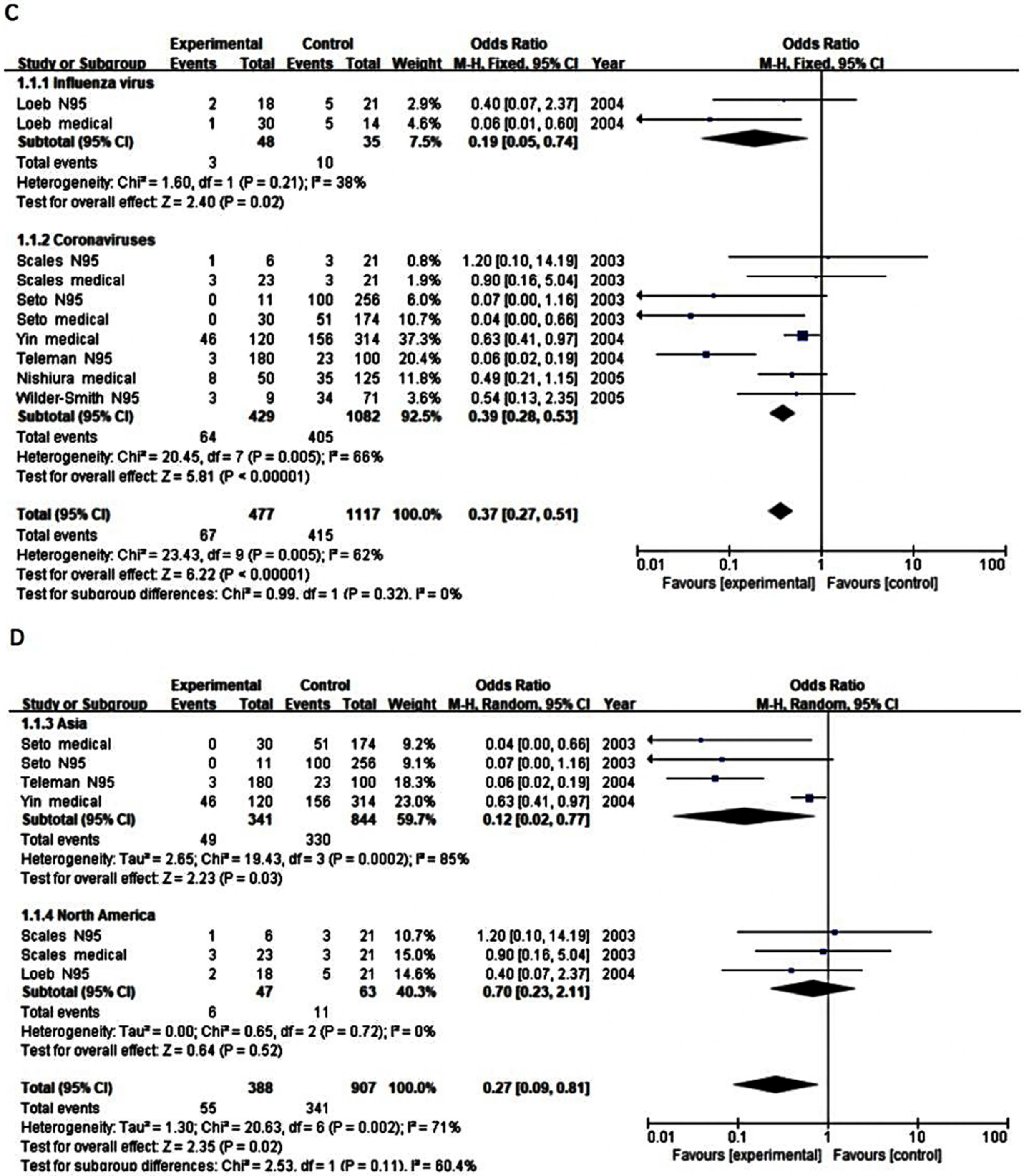


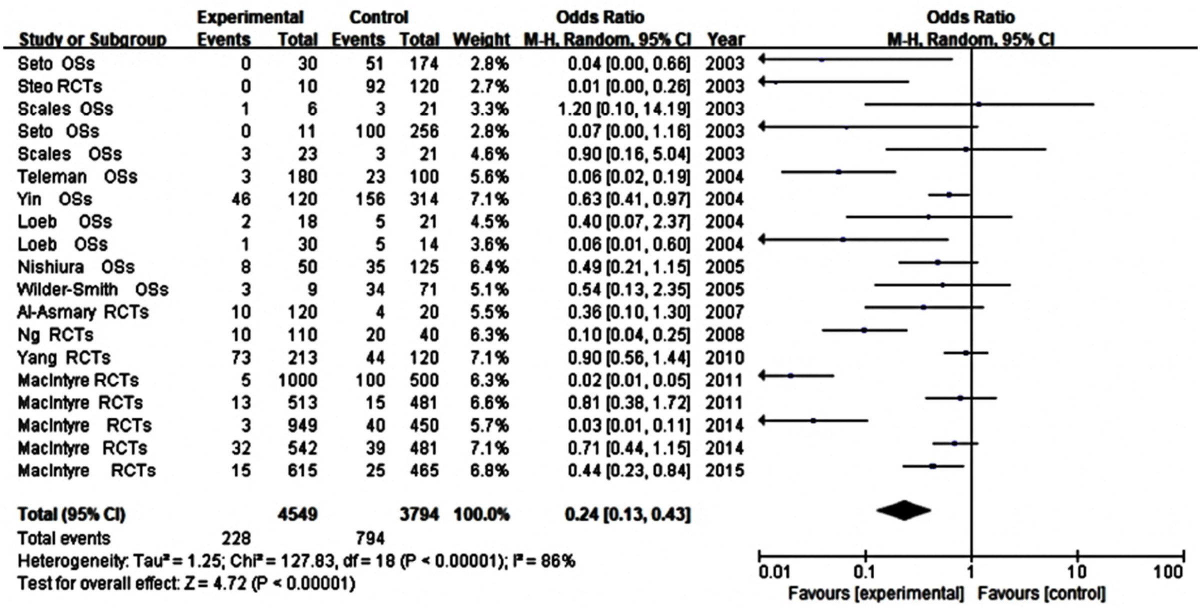
Figure 7. *Meta-analysis of OSs assessing the protective effects of N95 respirators and medical masks against respiratory infectious diseases.*

(A) Meta-analysis of the effect of wearing N95 respirators and medical masks for protection against respiratory infectious diseases.
(B) Subgroup analysis of the effect of wearing N95 respirators and medical masks for protection against respiratory infectious diseases.
(C) Subgroup analysis of the effect of wearing masks for protection against different types of viruses.
(D) Subgroup analysis of the effect of wearing N95 respirators and medical masks for protection against respiratory infectious diseases in different geographic locations.

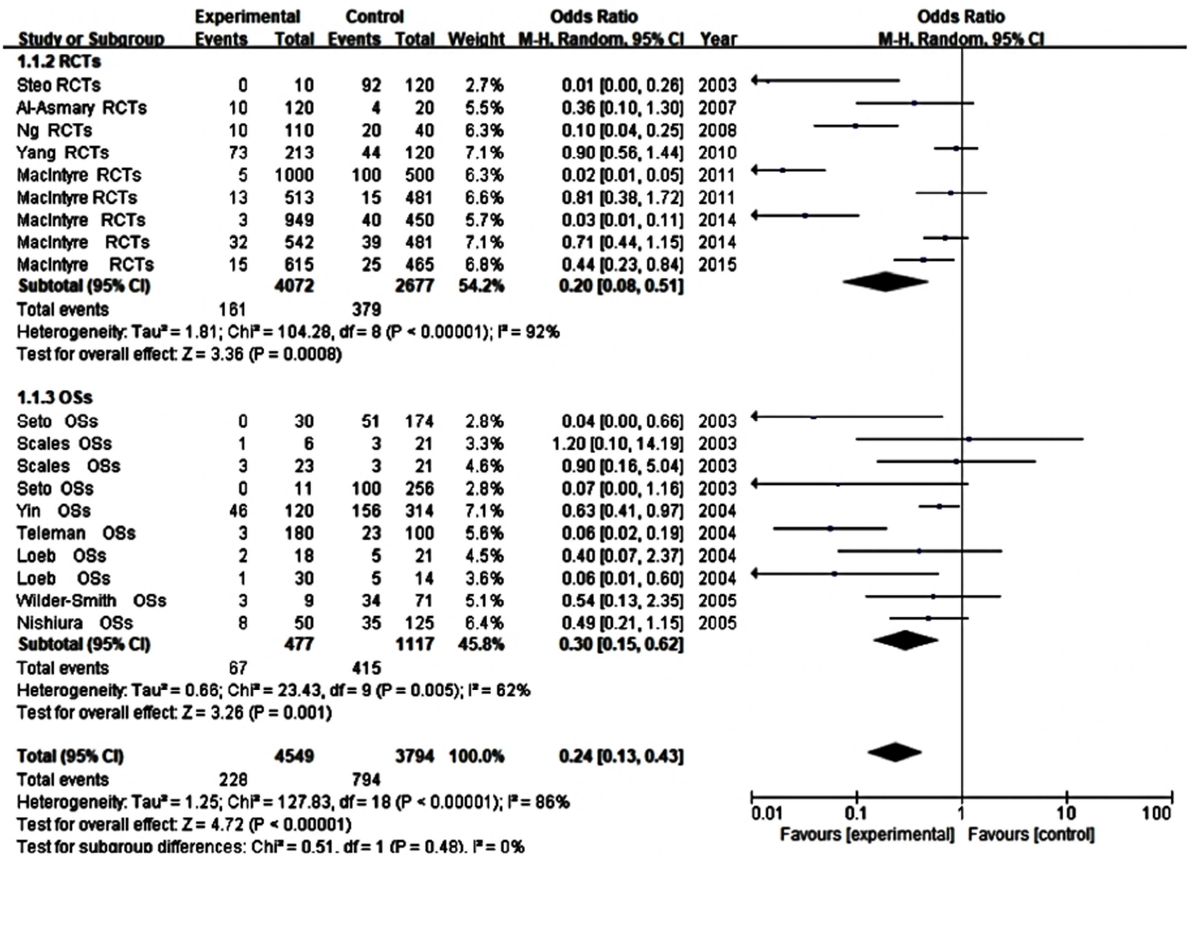
3.4. Mask Use Versus No Mask Use for Protection Against Respiratory Infectious Diseases in RCTs and OSs

A total of nineteen reports compared respiratory infectious diseases risk in medical staff wearing masks to that of convenience-selected controls wearing no masks. Wearing N95 respirators or medical masks conferred significantly greater protection against respiratory infectious diseases (OR = 0.24; 95% CI: 0.13–0.43; $P < 0.05$) (Figure 8A). Because of heterogeneity, the data were divided for subgroup analysis according to the following: RCTs and OSs; N95 respirators and medical masks. Subgroup analysis showed that the heterogeneity of the data for RCTs was I^2 = 92% (P < 0.00001) and the heterogeneity for OSs was I^2 = 62% (P = 0.005). The heterogeneity of the data for N95 respirators was I^2 = 93% (P < 0.00001) and the heterogeneity for medical masks was I^2 = 89% (P < 0.00001). These results showed that the heterogeneity of the data for RCTs and OSs, N95 respirators and medical masks was very large. Therefore, the heterogeneity of the data in the included studies has little relationship with the differences in the RCTs or OSs or N95 respirators or medical masks and may be caused by other factors (Figure 8B and 8C).

A



B



C

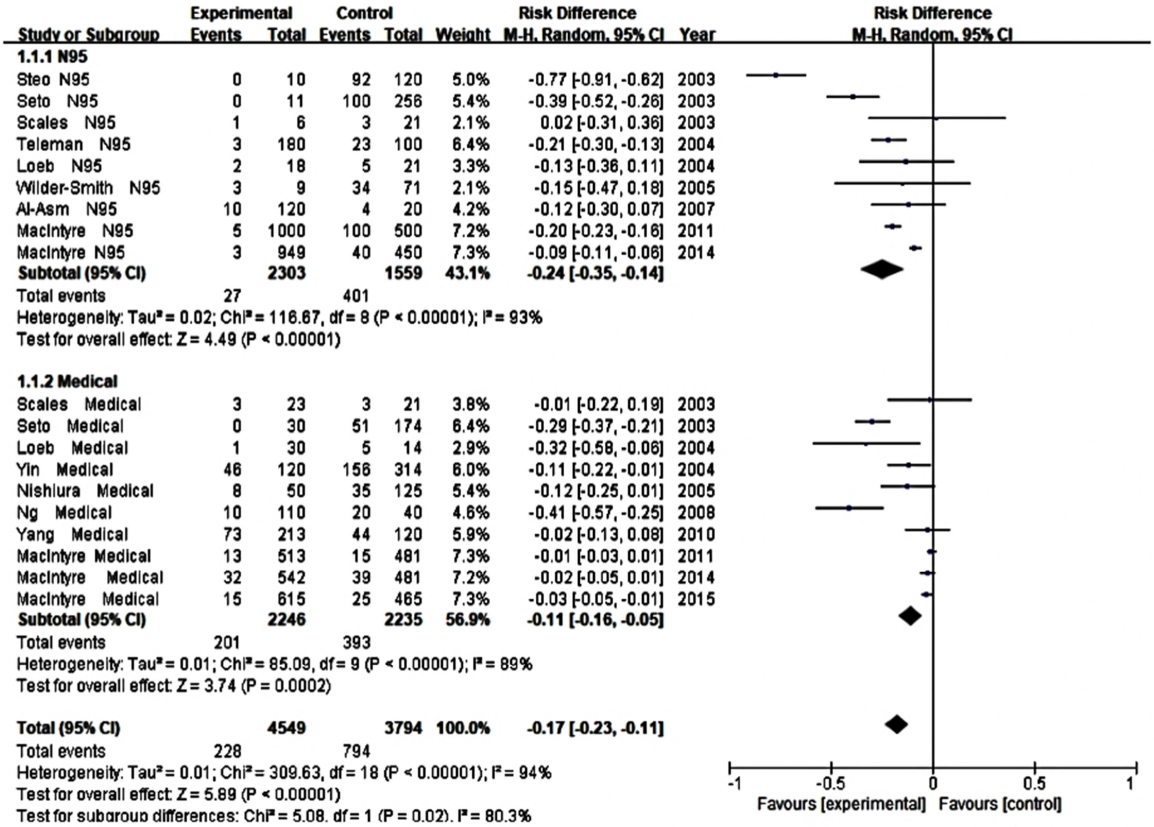


Figure 8. Meta-analysis of OSs and RCTs assessing the protective effects of N95 respirators and medical masks against respiratory infectious diseases.

(A) Meta-analysis of RCTs and OSs comparing the protective effects of mask use versus no mask use for protection against respiratory infectious diseases.
(B) Subgroup analysis of the effect of RCTs and OSs for protection against respiratory infectious diseases.
(C) Subgroup analysis of the effect of N95 respirators and medical masks for protection against respiratory infectious diseases.

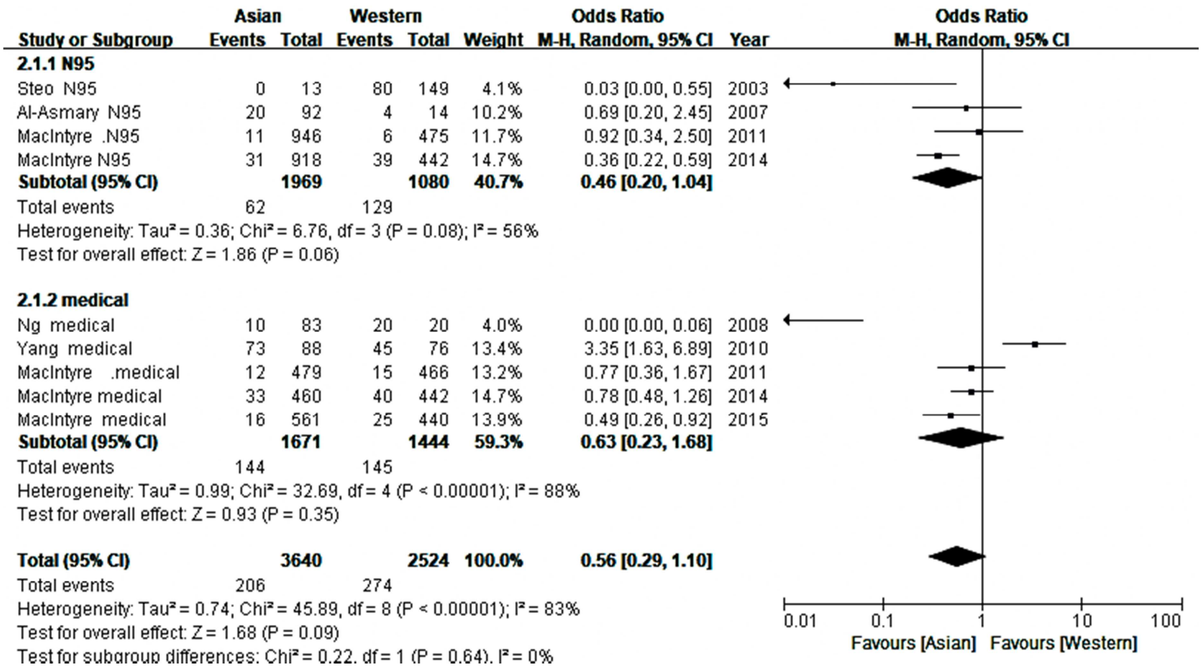


Figure 9. Meta-analysis of Asian and Western studies assessing the protective effects of N95 respirators and medical masks against respiratory infectious diseases.

3.5. Asian Versus Western Studies of Protection Against Respiratory Infectious Diseases Using N95 Respirators or Medical Masks

Four reports compared the use of N95 respirators for protection against respiratory infectious diseases in Asian and Western locations. There was no difference between the Asian and Western studies in terms of wearing N95 respirators to prevent respiratory infectious diseases (OR = 0.46; 95% CI: 0.20–1.04; $P > 0.05$). Five reports compared the use of medical masks for protection against respiratory infectious diseases in Asian and Western locations. There was no difference between Asian and Western studies in terms of wearing medical masks to prevent respiratory infectious diseases (OR = 0.63; 95% CI: 0.23–1.68; $P > 0.05$) (Figure 9).

4. Discussion

Both the RCTs and OSs included in this meta-analysis showed that the use of N95 respirators or medical masks has a significantly greater protective effect against respiratory infectious diseases among medical workers compared with those who did not use these types of PPE. Furthermore, although our meta-analysis showed that N95 respirators provide better protection against respiratory infectious diseases than medical masks, there is no convincing evidence that medical masks are inferior to N95 respirators, especially in routine care and during non-aerosol-generating procedures. Medical masks have also been reported to be similarly effective to N95 respirators in preventing influenza infection [18]. For a few respiratory infectious diseases, our meta-analysis suggested that N95 respirators were more protective than medical masks; however, the confidence intervals were wide and there was considerable heterogeneity ($P = 0.0008$, $I^2 = 76\%$). This heterogeneity may have been due to differences in the inclusion and exclusion criteria among the studies (Figure 5). In the results, the N95 and regular mask subgroup, virus types subgroup and geographic locations subgroup all showed a significant protective effect of using masks (Figure 4B and Figure 7B), which this is consistent with previous publications [6, 24]. However, there was no difference between Asian and Western locations in terms of the use of N95 respirators to prevent respiratory infectious diseases (Figure 9). It should be noted that we have not yet searched for RCTs comparing the use of medical masks with N95 respirators for protection against SARS-CoV-2 infection and this issue is worthy of consideration.

National and international guidelines unanimously recommend the use of N95 respirators for protection against aerosols; however, this is inconsistent with the current recommendations for non-aerosol prophylaxis and routine care for COVID-19 patients [25-28]. Although medical masks are cheaper, the European Centers for Disease Control and Prevention and the Centers for Disease Control and Prevention still recommend N95 respirators for non-aerosol-generating procedures [29]. Indeed, Kobayashi et al. argued that long-term use and reuse of N95 respirators during the COVID-19 pandemic could effectively protect volunteer workers [30]. In contrast, the WHO and the Public Health Agency of Canada recommend the use of medical masks during the care of patients with COVID-19 [29]. Ng et al. published a case report on the use of respiratory devices for protection against COVID-19 [31]. Thirty-five of the 41 medical workers wore medical masks. Despite exposure to a patient with severe pneumonia who tested positive for SARS-CoV-2 nucleic acids, all of these medical staff tested negative for SARS-CoV-2 nucleic acids 14 days later [31]. Thus, among the studies included in our analysis, this case report provides the only direct evidence of the protective effects of medical masks against SARS-CoV-2 infection. Therefore, the effectiveness of mask use for protection against COVID-19 remains to be fully clarified.

There are some limitations to this meta-analysis. First, the number of included studies is small, and therefore, may result in distribution bias. Analysis of a greater number of studies is required to reduce the risk of distribution bias. Second, there may be measurement bias, publication bias and selection bias in the included articles. Third, the limitations of the underlying studies, beyond just the biases, For instance, the Radonovich et al. (2019) RCT did not really control for consistency of use between its medical mask and N95 groups [18], so its conclusions about non-inferiority may be swayed by differential consistency in use among healthcare personnel assigned to the various groups within the study. Further studies with high-quality methodology and strictly defined inclusion and exclusion criteria are required. Fourth, heterogeneity among the data in the included studies was identified, which may be related to the research population, region, and virus species. Although the subgroup analysis of the use of N95 respirators and medical masks was conducted for some indicators in this study, it was not conducted for different populations, virus species and other types of masks. Therefore, more detailed subgroup analysis is required to provide a more convincing basis for our conclusions. Fifth, the source of infection was not identified in all trials and some medical staff may have been infected before the trial. Finally, at present, the protective effects of N95 respirators and medical masks against SARS-CoV-2 infection have not been studied specifically; therefore, therefore, it is not possible to extend our conclusion to the situation for SARS-CoV-2.

5. Conclusions

Here, we conducted a literature review and meta-analysis of RCTs and OSs of the protective effects of N95 respirators and medical masks against respiratory infectious diseases, including COVID-19. Both the RCTs and OSs included in this meta-analysis showed that the use of N95 respirators or medical masks has a significantly greater protective effect against respiratory infectious diseases among medical workers compared with those who did not use these types of PPE. However, only one case report showed the effectiveness of medical masks for preventing COVID-19. Although our analysis provides evidence to support the universal use of N95 respirators and medical masks in the medical and healthcare environment, the effectiveness of masks for protection against COVID-19 remains to be established. Moreover, in the absence of sufficient resources during an epidemic, medical masks and N95 respirators should be reserved for high-risk, aerosol-generating producing procedures.

Author Contributions

GHW participated in the study design and writing of the manuscript; QYJ participated in the English grammar correction and writing of the manuscript; XPZ, HWH participated in analysis and writing of the manuscript. All authors read and approved the final manuscript.

Conflict of Interest Statement

All the authors declare no conflict of interest.

Acknowledgements

This study was supported by the General Program of National Natural Science Foundation of China (No. 81771626; 81971423); The Jiangsu Provincial Maternal and Child Health Key Talents Project (No. FRC201731); Social Development project of Jiangsu Province (BE2020658); COVID-19 Infection emergency Technology project (SYS2020030).

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