State of the science review

Intention to COVID-19 vaccination and associated factors among health care workers: A systematic review and meta-analysis of cross-sectional studies

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Objectives: To gain insight into willingness and its influencing factors to vaccinate against COVID-19 among health care workers (HCWs), and provide a scientific basis for more reasonable epidemic prevention and control strategies.
Methods: A comprehensive literature search was conducted in 4 English databases (PubMed, EMBASE, Web of Science and the Cochrane Library) and 4 Chinese databases (Chinese National Knowledge Infrastructure (CNKI), the Chongqing VIP Chinese Science (VIP), Wanfang Database and China Biomedical Literature Database (CBM)) to collect the related studies. Quality evaluation was carried out for papers meeting the inclusion criteria using 6 items from the Downs and Black assessment checklist. The STATA statistical software version 15.1 was hired to perform meta-analysis.
Results: Nine records with a total of 24,952 subjects were included in this meta-analysis. The results of this meta-analysis revealed that the pooled effect value of COVID-19 vaccination willingness among HCWs using a random-effects model was 51% (95% confidence interval (CI) 0.41-0.62). Male, aged 30 years or older, having a history of prior influenza vaccination were facilitators for HCWs' intention to vaccinate against COVID-19 (odds ratio (OR) 1.82, 95% CI 1.37-2.41, $P = .000$, $I^2 = 59.4\%$; OR 1.32, 95% CI 1.16-1.51, $P = .000$, $I^2 = 31.7\%$; OR 2.97, 95% CI 1.82-4.84, $P = .000$, $I^2 = 88.1\%$). The impact of occupation on HCWs' intention to get vaccinated could not yet be definitively confirmed (OR 0.85, 95% CI 0.69-1.06, $P = .160$, $I^2 = 85.5\%$).
Conclusion: COVID-19 vaccination acceptance of HCWs was at moderate level. Strengthening awareness of COVID-19 vaccine among HCWs, particularly female HCWs under 30 years who have no history of prior influenza vaccination, is crucial to eliminate concerns about vaccination and promote the application of COVID-19 vaccine in this population.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a serious and lethal contagious disease caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is mainly transmitted from human to human through respiratory droplets.[1] The clinical picture of COVID-19 is dominated by the presence of fever, fatigue, cough, headache, diarrhea, hemoptysis and dyspnea.[2] COVID-19 is spreading across the world at an alarming rate, being formally declared as a pandemic and a public health emergency of international concern (PHEIC) by the World Health Organization (WHO).[3,4] As on 6th April 2021, the global prevalence data of COVID-19

collected from the WHO website revealed 131,309,792 confirmed cases and 2,854,276 deaths.[5] Of note, it is a pity that the availability of only limited symptomatic support therapy options and the absence of specific antiviral medicine for COVID-19 has led to the dependence of current disease control policies on active immunization.

HCWs were proposed to be given priority for vaccination by the Advisory Committee on Immunization Practices (ACIP) in December, 2020.[6] The rationales behind it are the followings. Firstly, health care workers (HCWs) have easier access to COVID-19 patients population in their daily diagnosis and treatment activities, and are at much greater risk of developing COVID-19 than other groups. In the United Kingdom and the United States, the COVID-19 test results showed that front-line HCWs have a 11-fold increased positive rates as compared to the general community.[7] Secondly, a previous study assessing the risk of infection transmission from physicians to patients through the hands, equipment and enclosing surfaces showed that physicians played an important role in spreading of nosocomial infections.[8] Therefore, the prevention and control of the infection among HCWs have protective effect both on patients and medical staff. Thirdly, results from a recent cross-sectional study have revealed that in addition to gender, marital status, perceived risk, history of prior influenza vaccination, the number of confirmed and suspected cases in local areas, vaccine efficacy, vaccination convenience and vaccine price, the recommendation from doctors is an independent predictor for the general population to receive COVID-19 vaccine.[9] Likewise, these results were verified in another cross-sectional study in Italy. The results of this survey demonstrated that recommendation from pediatricians to vaccinate their children is a significant factor in promoting the parental support for vaccine.[10] Last but not least, it is encouraging that COVID-19 vaccine have proven 95% efficacy in the prevention of COVID-19 infection in a multinational, large sample size randomized controlled trial.[11]

Accordingly, the principal objective of this meta-analysis was to investigate the intention to vaccinate against COVID-19 and its influencing factors among HCWs and provide the rationale for the promotion of COVID-19 vaccine.

METHOD

We prospectively registered key features on International Prospective Register of Systematic Reviews (PROSPERO) with unique
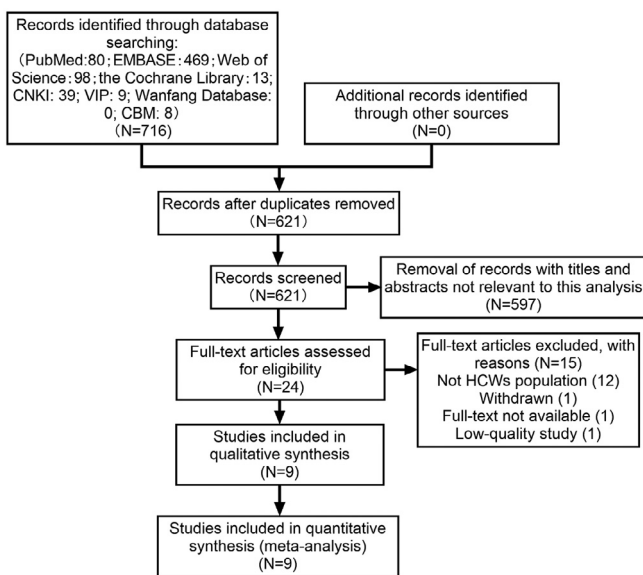

Fig 1. Flow chart depicting literature screening process.

Table 1
Characteristics of included studies

Study and year published	Country	Study period	Population studied	Total N	Intended to accept N (%)	Administration channel	Evaluation Tool	Type of questions	Response rate %
Gagneux-Brunon 2021	France	March to July 2020	HCWs at university hospital and center for COVID-19 diagnosis	2047	1574 (76.9)	On-line and paper-based	Questionnaire developed by Dominique et al[25]	Closed	-
Kwok 2021	China	March to April 2020	Nurses	1205	759 (63.0)	On-line	Questionnaire developed by Betsch et al[26]	Likert-type scale	-
Papagiannis 2020	Greece	February 2020	HCWs in 5 public hospitals	461	200 (43.4)	Personal interviews	Self-designed questionnaire	Likert-type scale	92.2%
Shaw 2021	US	November to December 2020	HCWs at an academic medical center	5277	3032 (57.5)	E-mail	Questionnaire developed by Opel et al[27]	Closed	55%
Shekhar 2021	US	October to November 2020	HCWs at 5 major hospital systems	3479	1247 (35.8)	On-line	Self-designed questionnaire	Closed	-
Unroe 2021	US	November 2020	Nursing home staff	8243	3704 (44.9)	Text message	Self-designed questionnaire	Closed	33%
Verger 2021	France, Belgium, Canada	October to November 2020	General practitioners and nurses	2678	1939 (72.4)	On-line and telephone	Self-designed questionnaire	Likert-type scale	-
Wang 2020	China	February to March 2020	Nurses	806	322 (40.0)	E-mail	Self-designed questionnaire	Closed	5.2%
Zhang 2021	China	September to October 2020	Hospital staff and CDC's staff	756	209 (27.6)	On-line	Self-designed questionnaire and net promoter score	Likert-type scale	-

CDC, centers for disease control and prevention; HCW, health care worker; US, United States; -, missing data.

Table 2
Characteristics of included studies

Study and year published	Clearly stated aim	Clearly defined study population	Study sample representative of the source population	Attempt made to adjust for confounding	Attempt made to validate survey responses to institutional records where possible	Discussion of study limitations	Quality grading
Gagneux-Brunon 2021	Yes	Yes	Unable to determine	Unable to determine	No	Yes	3
Kwok 2021	Yes	Yes	Yes	Unable to determine	No	Yes	4
Papagiannis 2020	Yes	Yes	Unable to determine	Unable to determine	No	Yes	3
Shaw 2021	Yes	Yes	Yes	Unable to determine	No	Yes	4
Shekhar 2021	Yes	Yes	Unable to determine	Unable to determine	No	Yes	3
Unroe 2021	Yes	Yes	Yes	Yes	No	Yes	5
Verger 2021	Yes	Yes	Yes	Unable to determine	No	Yes	4
Wang 2020	Yes	Yes	Yes	Unable to determine	No	Yes	4
Zhang 2021	YesUS,	Yes	Unable to determine	Unable to determine	No	Yes	3

identifying number (CRD42021237987) and performed this meta-analysis in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[12]

Search strategy

Four English databases (PubMed, EMBASE, Web of Science and the Cochrane Library) and 4 Chinese databases (Chinese National Knowledge Infrastructure (CNKI), the Chongqing VIP Chinese Science (VIP), Wanfang Database and China Biomedical Literature Database (CBM)) were comprehensively retrieved for relevant literature published from their date of inception to February 19, 2021. The following Medical Subject Heading (MeSH) terms and MeSH-derived topical terms were utilized as key phrases in various combinations: "COVID-19," "SARS-CoV-2," "2019-nCoV," "vaccination," "immunization," "medical staff," "medical staff, hospital," "health personnel," "physicians" and "nurses." We did not use any explicit language restriction, although we used only English and Chinese search terms in this meta-analysis. Manual search of reference lists were conducted to find potential relevant articles. Two investigators independently performed the literature screening and the detailed steps of selection process is presented in Figure 1. Any divergences in screening results were resolved by discussion between reviewers and, if necessary, consulting a senior reviewer to reach a consensus. The software Endnote (version X9.1) was used for reference management.
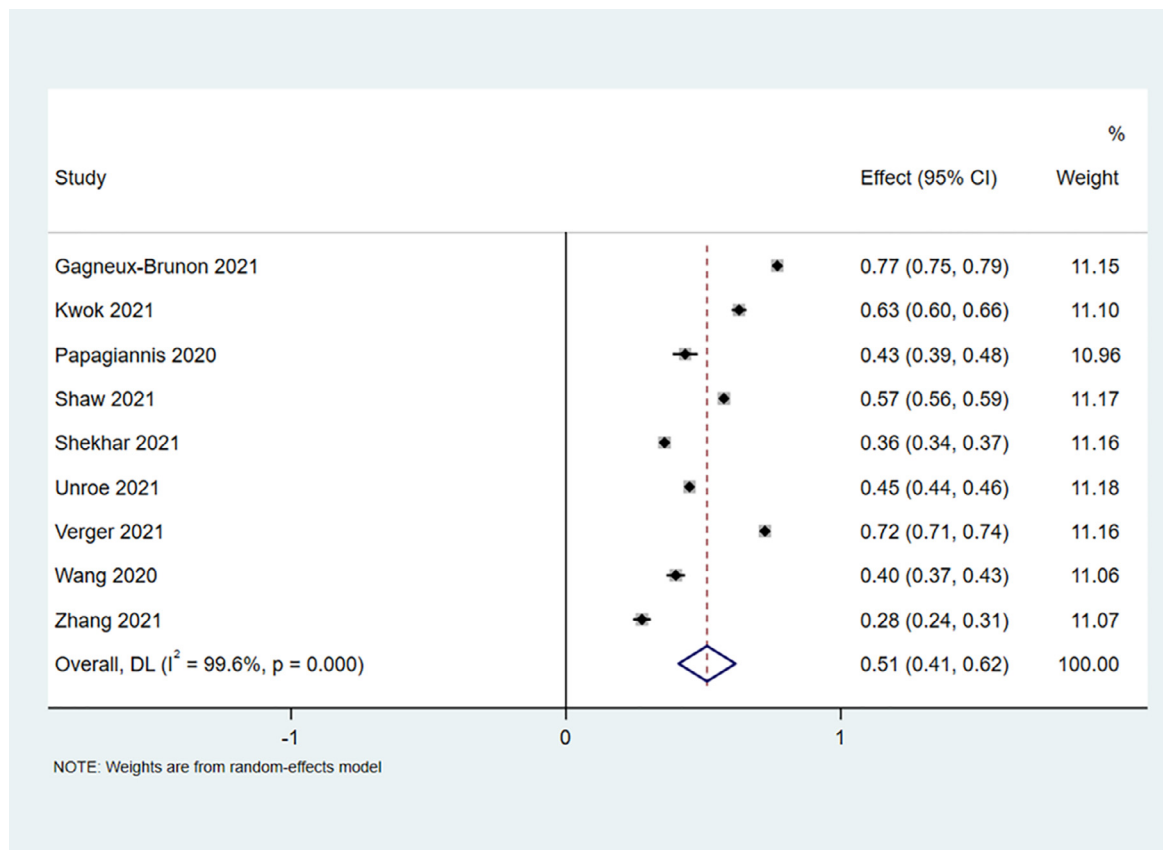

Fig 2. Forest plot depicting COVID-19 vaccine acceptance among health care workers (HCWs).
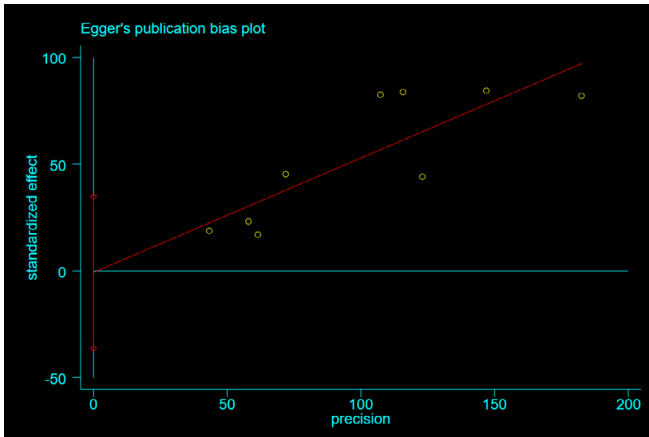
Fig 3. Egger regression plot of COVID-19 vaccine acceptance among HCWs.

*Inclusion and exclusion criteria*

Inclusion criteria were as follows: (1) published cross-sectional studies on acceptance of COVID-19 vaccination among HCWs employed in inpatient or outpatient medical settings or long-term care centers; (2) the outcome measures of interest were vaccination acceptance and its influencing factors. We defined vaccination acceptance as the percentage of HCWs who are willing to undergo vaccination once it is available, which was assessed through self-report; (3) provided raw data or odds ratios (ORs) for the outcome measures of interest, with confidence intervals; (4) cross-sectional designs.

Exclusion criteria were as follows: (1) not relevant articles; (2) reviews, commentaries, editorials, letters, case reports, protocols, conference abstracts and animal experiments; (3) duplicated articles; (4) full text not available; (5) low-quality studies.

Quality assessment and data extraction

The methodological quality of the literature was evaluated with reference to the following 6 items from the Downs and Black assessment checklist reported in literature[13,14]: (1) clearly stated aim; (2) clearly defined study population; (3) study sample representative of the source population; (4) attempt made to adjust for confounding; (5) attempt made to validate survey responses to institutional records where possible; and (6) discussion of study limitations. One point for items rated as yes, and zero for items rated as no or unable to determine. We classified a total score of 5-6 as high-quality studies, 3-4 as moderate-quality studies and 1-2 as low-quality studies, respectively. After independently assessing the quality of the documents, 2 reviewers carried out a quality discussion on each of the included
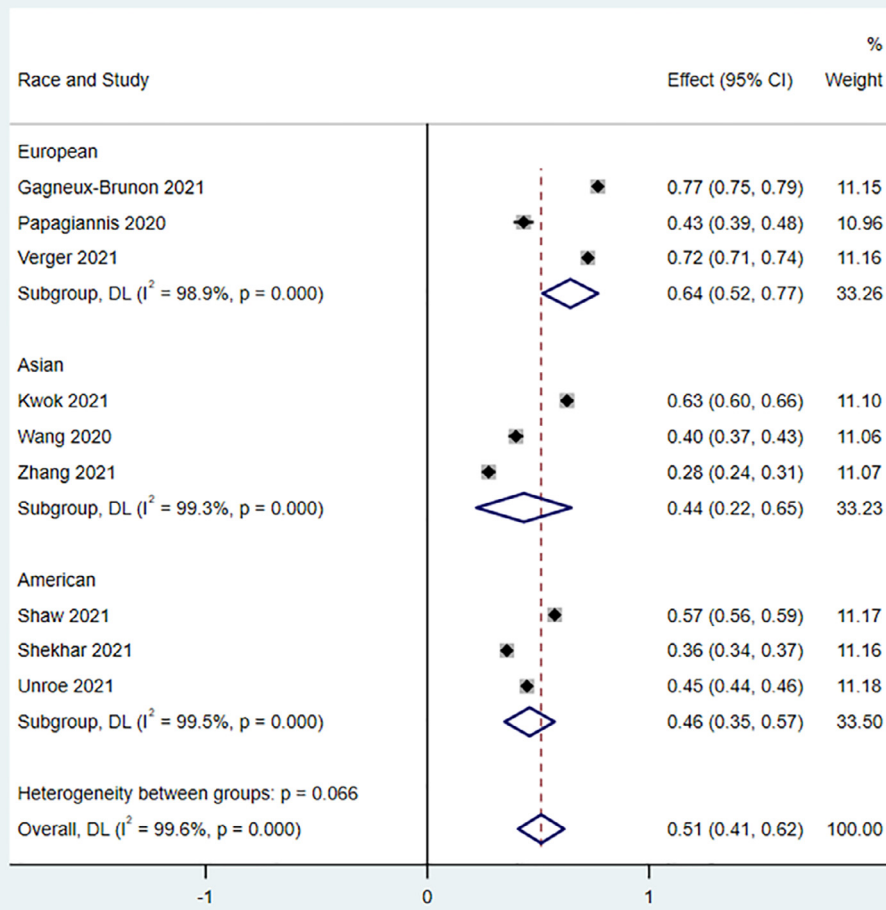
Fig 4. Forest plot depicting COVID-19 vaccine acceptance among HCWs after subgroup analysis according to race.

studies on the basis of the above evaluation criteria and reached an agreement to form a ultimate literature quality evaluation.

Statistical analysis

The data analysis and statistical software STATA version 15.1 (StataCorp, College Station, TX) was applied to perform meta-analytical calculations. Egger's test with a level of significance set at P<0.05 were further applied to examine possible publication bias.

RESULTS

Screening process

Electronic search and additional evaluation of reference lists yielded a total of 716 potentially relevant articles, which were reduced to 621 after omitting duplicates. There were only 24 remaining papers found to be relevant after a preliminary screening of titles and abstracts, and full-text review were further conducted for confirmation of each study's eligibility. In the full-text investigation phrase, twelve records were removed as subjects did not meet the inclusion criteria. One record was removed as full-text not available. One was removed as withdrawn. In the quality assessment phrase, one was removed as low quality.[15] Eventually, nine studies[16-24] with an aggregate sample size of 24,952 individuals published from 2020 to 2021 conformed to our inclusion criteria, of which eight in English[16-23] and one in Chinese.[24]

Study characteristics

All of the literatures involved in this meta-analysis were cross-sectional designs. Of nine papers included, 3 were from Europe,[16,18,22] 3 were from Asia[17,23,24] and 3 were from America.[19-21] All studies were published between 2020 and 2021. The sample size ranged from 461 to 8243 subjects interviewed. The proportion of HCWs who were willing to undergo vaccination reported in the selected literature varied from 28% to 77% (median 0.45, mean 0.51). As for the evaluation of vaccine hesitancy, all study instruments were administered by a questionnaire of various types (online, e-mail, telephone, text message, personal interview and paper-based). Six of the included studies utilized self-designed questionnaires,[18,20-24] and the other 3 adopted questionnaires previously reported in the literature.[16,17,19] The characteristics of included studies are listed in Table 1. The average quality score was 3.7 points, with a maximum score of 5 points and a minimum score of 3 points. One study were judged to be of high-quality[21] and eight of moderate quality.[16-20,22-24] The detailed quality appraisal results for each study are provided in Table 2.

Meta-analysis of vaccination acceptance

Nine accounts[16-24] reported the acceptance of COVID-19 vaccine in a total of 24,952 HCWs. Since the Cochrane Q test for heterogeneity demonstrated high heterogeneity among the included studies (I^2 = 99.6%, Cochrane Q test P = .000), random-effect model was

Sample size and Study	Effect (95% CI)	% Weight
≥1000		
Gagneux-Brunon 2021	0.77 (0.75, 0.79)	11.15
Kwok 2021	0.63 (0.60, 0.66)	11.10
Shaw 2021	0.57 (0.56, 0.59)	11.17
Shekhar 2021	0.36 (0.34, 0.37)	11.16
Unroe 2021	0.45 (0.44, 0.46)	11.18
Verger 2021	0.72 (0.71, 0.74)	11.16
Subgroup, DL (I^2 = 99.7%, p = 0.000)	0.58 (0.46, 0.71)	66.91
<1000		
Papagiannis 2020	0.43 (0.39, 0.48)	10.96
Wang 2020	0.40 (0.37, 0.43)	11.06
Zhang 2021	0.28 (0.24, 0.31)	11.07
Subgroup, DL (I^2 = 95.2%, p = 0.000)	0.37 (0.27, 0.47)	33.09
Heterogeneity between groups: p = 0.007		
Overall, DL (I^2 = 99.6%, p = 0.000)	0.51 (0.41, 0.62)	100.00

NOTE: Weights and between-subgroup heterogeneity test are from random-effects model
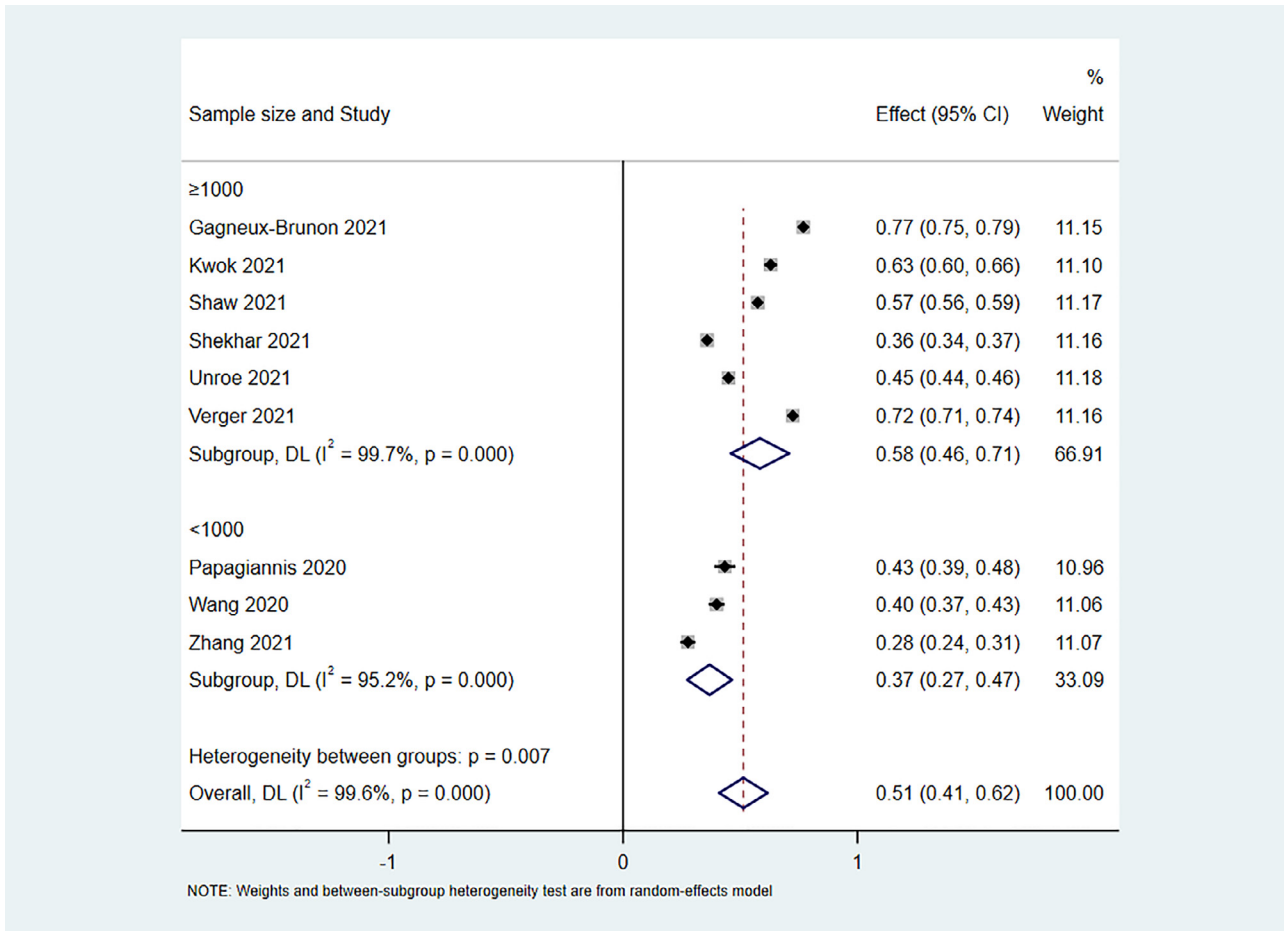
Fig 5. Forest plot depicting COVID-19 vaccine acceptance among HCWs after subgroup analysis according to sample size.

applied. As is shown in Fig 2, the pooled effect value of vaccination willingness was 51%, with a 95% CI of 0.41-0.62. No significant publication bias was noted on Egger's test (t = -0.05, Egger's test P = .961, Fig 3).

Subgroup analysis of vaccination acceptance

Due to severe heterogeneity observed among selected studies, additional subgroup analyses for the meta-analysis was implemented to clarify the source of heterogeneity. Nevertheless, no apparent difference between overall heterogeneity and subgroup heterogeneity occurred in subgroup analyses, indicating that the heterogeneity was not correlated with race, sample size and publication year (Fig 4, Fig 5, Fig 6).

Meta-analysis of factors associated with COVID-19 vaccine acceptance

Meta-analysis was carried out for the 4 potentially determinants involved in the selected studies. As there were statistically significant heterogeneities present for occupation and history of prior influenza vaccination, a random-effects model was adopted for the meta-analysis (I^2 = 85.5%, Cochrane Q test P = .000; I^2 = 88.1%, Cochrane Q test P = .000). In contrast, a fixed-effects model was adopted given no obvious heterogeneity for gender and age (I^2 = 0.0%, Cochrane Q test P = .369; I^2 = 31.7%, Cochrane Q test P = .222). The meta-analysis results showed that male, aged 30 years or older, having a history of prior influenza vaccination were facilitating factors affecting the

HCWs' intention of COVID-19 vaccination (OR 1.99, 95% confidence interval (CI) 1.65-2.41, P = .000, Fig 7; OR 1.32, 95% CI 1.16-1.51, P = .000, Fig 8; OR 2.97, 95% CI 1.82-4.84, P = .000, Fig 9). Whereas, the relationship between occupation and the willingness of COVID-19 vaccination cannot be determined (OR 0.85, 95% CI 0.69-1.06, P = .160, Fig 10). Also, there were too few studies reported outcomes of interest to permit sensitivity analysis and Egger's test.

DISCUSSION

We found in the present study that the overall acceptance of COVID-19 vaccine in HCWs population was 51%, which was somewhat lower than that of the general population reported by Robinson et al.[28] One possible contributor for this finding is that HCWs are exposed to more professional information, and therefore has more concerns about the effectiveness and safety of COVID-19 vaccine, which may affect their decision to get vaccinated and hinder their recommendation of vaccination to patients.

The results of this meta-analysis found that COVID-19 vaccination acceptance among HCWs were influenced by the following factors. Firstly, we found that vaccination intention did vary with gender. Male participants were more likely to receive the COVID-19 vaccine compared to females when it was available. This result is in agreement with those of several other studies.[29-31] Possible explanations for this phenomenon could be because of the high morality rates in males than females.[32] Secondly, age-based differences in vaccination intention especially merit attention, with more participants aged
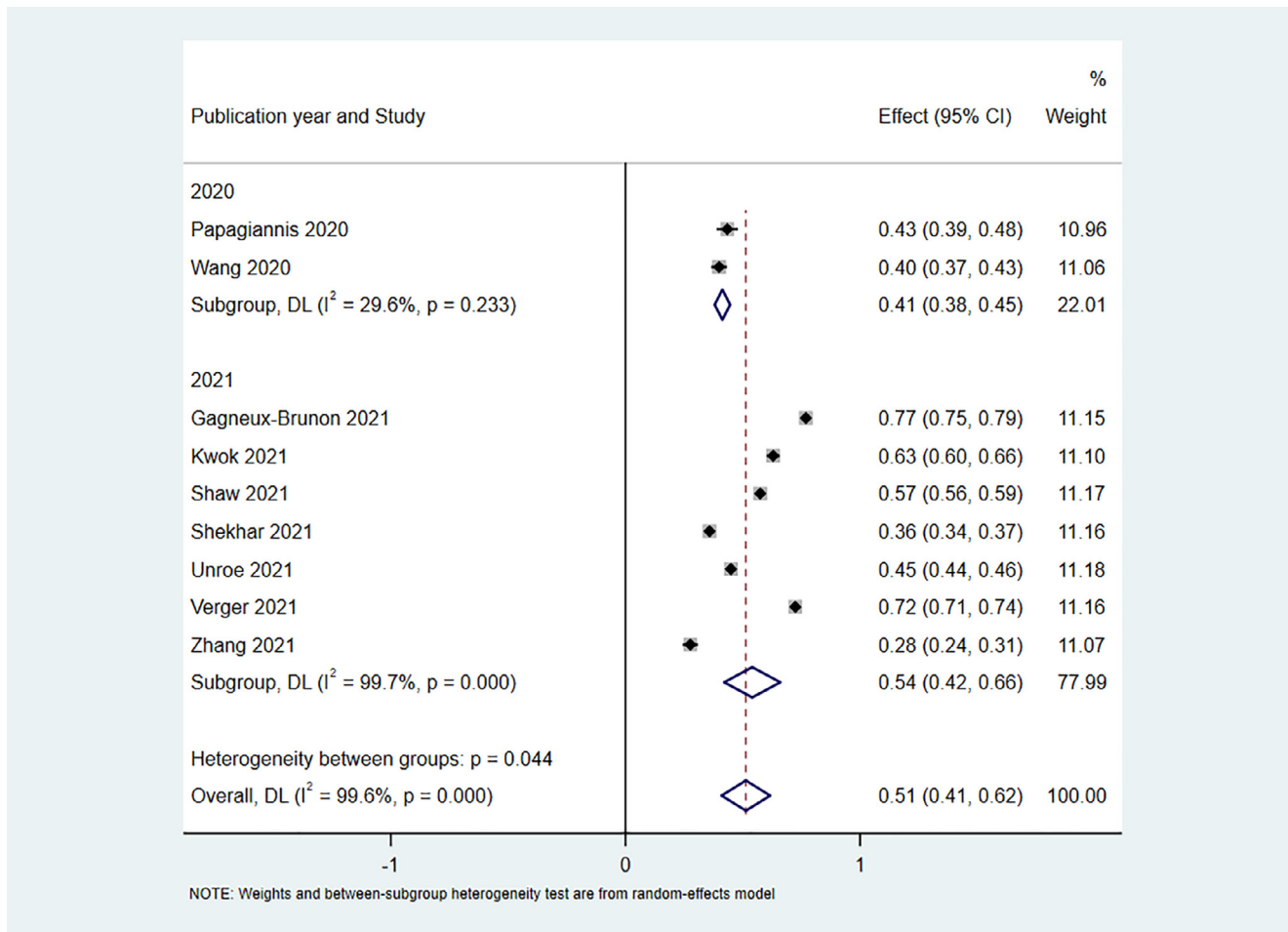

Fig 6. Forest plot depicting COVID-19 vaccine acceptance among HCWs after subgroup analysis according to publication year.
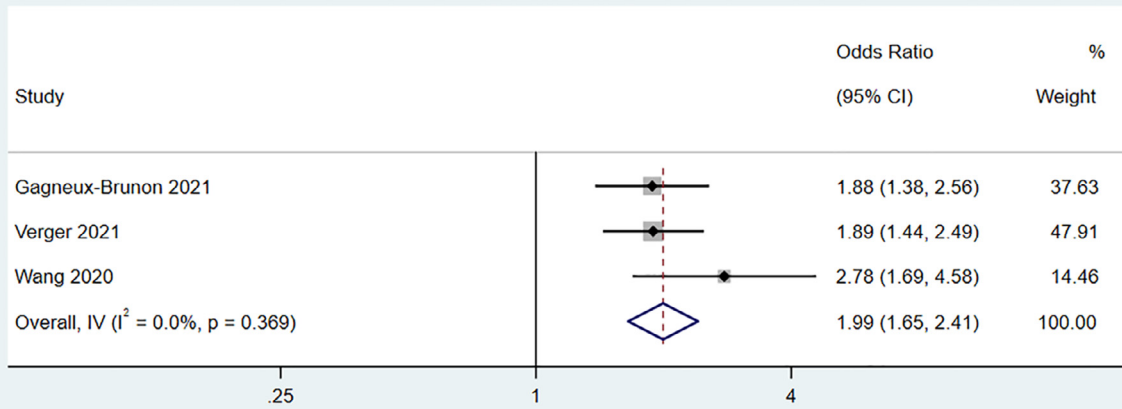
Fig 7. Forest plot depicting the relationship between gender and COVID-19 vaccine acceptance among HCWs.
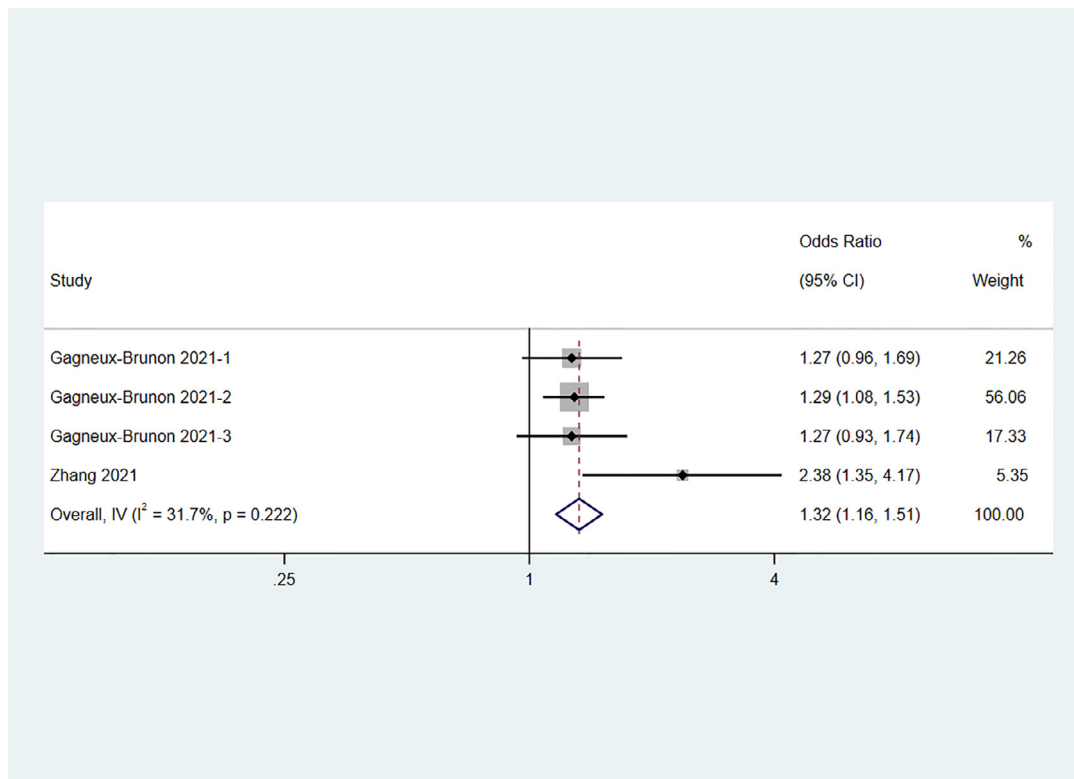

Fig 8. Forest plot depicting the relationship between age and COVID-19 vaccine acceptance among HCWs.
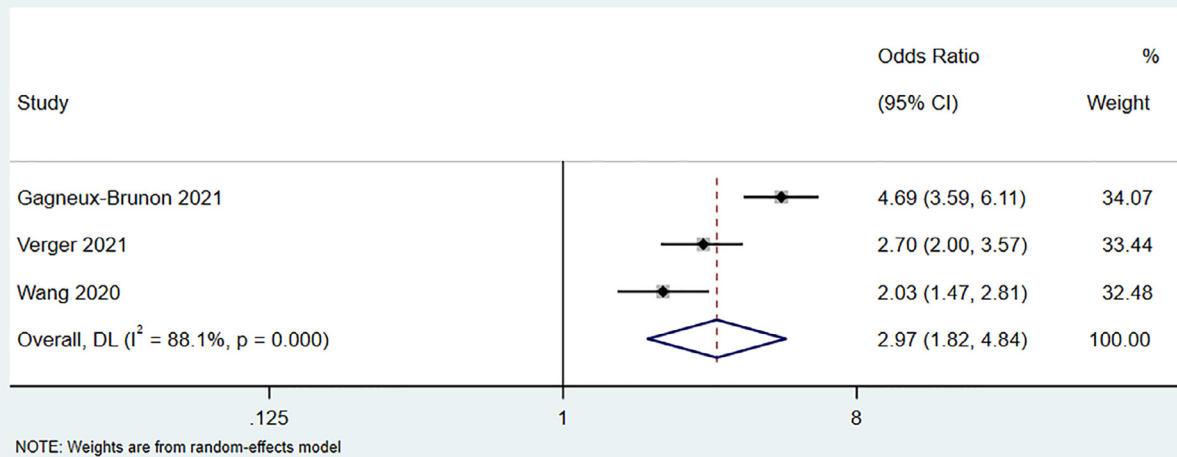
Fig 9. Forest plot depicting the relationship between history of prior influenza vaccination and COVID-19 vaccine acceptance among HCWs.

30 years or older than those under 30 years being vaccinated. Some of reasons can possibly relate to the relatively high prevalence and morality rates of COVID-19 in the elderly people.[32] Thirdly, as foreseen, the results revealed that those with a history of prior influenza vaccination also had significantly greater intention to get vaccinated against COVID-19. This may be attributed to the fact that those who have received influenza vaccination tend to pay more attention to the prevention of respiratory diseases and have more knowledge regarding vaccines. Fourthly, Clinicians seem to be less likely to take the COVID-19 vaccine but no significant relationship was found between occupation and intention to take the COVID-19 vaccine. Taken together, targeted strategies of COVID-19 vaccination need to be formulated and implemented for female health care workers under the age of 30 years who have no history of influenza vaccination in order to address the issue of vaccine hesitancy among HCWs.

Given the moderate level of intention to COVID-19 vaccination among HCWs, there is a need to increase vaccine acceptance in this population. Currently, most countries recommend that HCWs be vaccinated against COVID-19. Italy has become the first country in Europe to introduce a mandatory vaccination policy for HCWs, requiring those who refuse to be vaccinated to transfer to jobs without the risk of spreading the virus or suspend their work without pay for more than a year, after suffering from the most severe effects of COVID-19 among European countries. A recent report revealed that only about one in 10,000 health workers refused to be vaccinated in Italy.[33] Serbia are considering doing the same.[34] Moreover, a previous meta-analysis showed that the majority of HCWs could accept a mandatory vaccination policy, suggesting that it could be accepted if necessary.[35] Furthermore, free vaccination policy may also contribute to

increase vaccination rates and the result has been validated by a study conducted in China.[36]

The strength of the present study lies in its rapid analysis about willingness and its influencing factors of COVID-19 vaccination among HCWs to provide useful insight for the implementation of COVID-19 vaccination in the future. In the meantime, we must acknowledge that our study was subject to certain limitations that warrant mention. Firstly, owing to the limited data available, this meta-analysis assessed vaccination intention rather than actual vaccination. Even though intention was believed to be the most immediate antecedent of subsequent behaviour,[37] previous investigation suggested that intention did not necessarily translate into behaviour.[38] As a result, measuring vaccine completion appears more important especially for COVID-19 vaccine that need several doses.[39] Further researches are required to examine vaccine uptake and completion. Secondly, although we scanned systematically for published peer-reviewed journal articles in this meta-analysis, whereas possibly valuable unpublished data, gray literature and non-peer-reviewed papers was excluded to ensure quality, which may inevitably cause some publication bias. However, Egger's test suggested that there was no evidence for publication bias. Thirdly, apparent heterogeneity was detected in this meta-analysis. Apart from using the random-effect model, we tried to perform subgroup analyses by race, sample size and publication year in order to compensate for this deficiency to some extent, however, the source of heterogeneity was not found through subgroup analyses based on the above confounding factors. Therefore, a broader range of potential confounders should be considered in the future analyses which incorporate more original studies. Besides, a measurement bias exists due to different resources
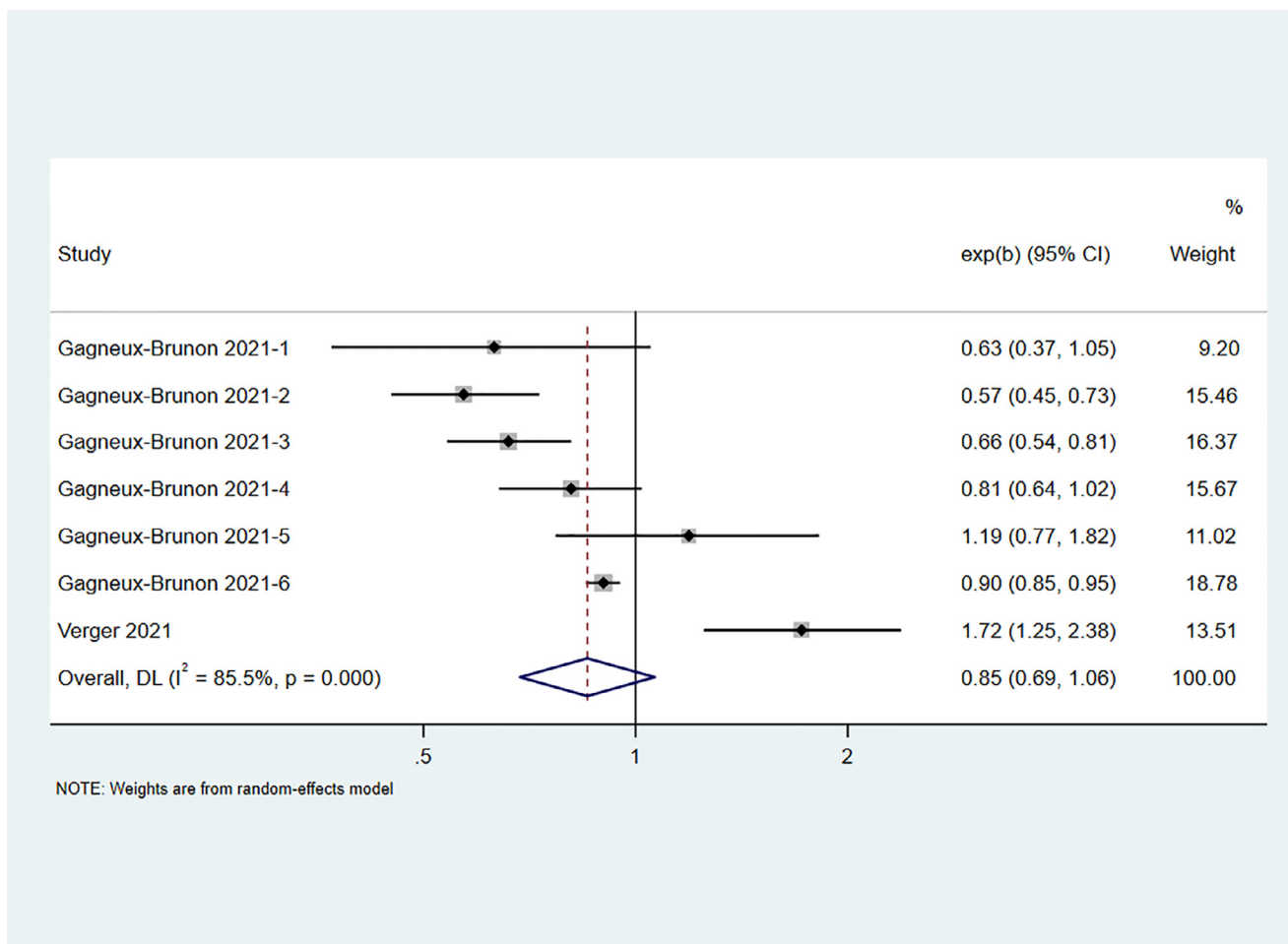
Fig 10. Forest plot depicting the relationship between occupation and COVID-19 vaccine acceptance among HCWs.

for assessing vaccine hesitancy among studies. Consequently, we recommend that further studies employ well-validated and uniform questionnaires to enhance inter-study comparability.[40] Last but not least, population studied were primarily in economically developed areas, which reduce the generalizability of the study results.

CONCLUSION

In conclusion, COVID-19 vaccination acceptance of HCWs was at moderate level. In the case of newly-available COVID-19 vaccine, little is known regarding its efficacy and safety at this moment for most individuals. Thus, global governments should expand and intensify their health education efforts urgently to improve knowledge, attitude and practice regarding COVID-19 vaccination that are beneficial to promotion of COVID-19 vaccination.

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