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Review Paper

COVID-19 vaccine acceptance and hesitancy among patients with cancer: a systematic review and meta-analysis

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ARTICLE INFO

Article history:

Received 6 November 2021

Received in revised form

17 August 2022

Accepted 1 September 2022

Available online 8 September 2022

Keywords:

Acceptance

Attitudes

Cancer

COVID-19

Hesitancy

Vaccine

ABSTRACT

Objectives: Patients with cancer are more vulnerable to COVID-19 morbidity and mortality than the general population and have been prioritised in COVID-19 vaccination programmes. This study aims to investigate COVID-19 vaccine acceptance and hesitancy among patients with cancer.

Study design: This was a systematic review and meta-analysis.

Methods: PubMed, ScienceDirect and the Cochrane COVID-19 study registry were searched in addition to secondary literature using a predefined search method. Two authors independently performed the study identification, screening and eligibility assessment. This study followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses 2020 guidelines and Joanna Brades' Institute quality appraisal tools.

Results: A total of 29 studies and reports were selected for the final review. The pooled prevalence of vaccine acceptance was 59% (95% confidence interval 52–67%, I^2 : 99%). Concerns about vaccine-related side-effects, uncertainty about vaccine efficacy and safety, ongoing active anticancer therapies and scepticism about rapid vaccine development were the leading causes for vaccine hesitancy. Female gender and undergoing active anticancer treatments were significant factors associated with COVID-19 vaccine hesitancy. Early cancer stages (stages I and II) and good compliance with prior influenza vaccinations were significant factors associated with the acceptance of the COVID-19 vaccine.

Conclusions: Many patients with cancer are hesitant about COVID-19 vaccination. Well-designed problem-based educational interventions will increase compliance with COVID-19 vaccination.

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Introduction

The National Comprehensive Cancer Network has released COVID-19 vaccination guidelines and recommendations for patients with cancer.¹ Full COVID-19 vaccination is recommended for patients with cancer, their family members, caregivers and close contacts.² Patients with cancer are at an increased risk of COVID-19 due to anticancer treatments and compromised immune systems.³ These individuals are prioritised in COVID-19 vaccination programmes because of their high risk of mortality after COVID-19 infection.⁴

Patients with cancer are recommended COVID-19 vaccination,^{5–7} despite the lack of evidence on immunomodulation and safety and adverse events of the COVID-19 vaccines. A study by

Monin et al. showed a significant increase in immunogenicity after the booster dose.⁸ There are more reported benefits than adverse events for vaccinated patients with cancer.^{9,10}

Evidence on attitudes, perceptions, acceptance and hesitancy of COVID-19 vaccines among patients with cancer is limited. It is crucial to assess the perspectives of patients with cancer on COVID-19 vaccination, with the ultimate goal of implementing necessary actions to overcome vaccine hesitancy. This systematic review with meta-analysis aims to provide a comprehensive understanding of the factors associated with COVID-19 vaccine acceptance and hesitancy among patients with cancer.

Methods

The protocol for this study was registered in the International prospective register of systematic reviews (PROSPERO) on 6 September 2021 (CRD42021276950).

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Data sources, study selection and search strategy

The primary search was performed in PubMed, Science Direct and the Cochrane COVID-19 study register according to a pre-determined search method. The authors selected the keywords, databases and the exact search string during the pilot study. The electronic databases were searched from 25th April 2021 to 21st May 2022. Keywords were truncated and combined via Boolean operators to make the exact search string. In the secondary search, keywords were used in combination and alone in Google, Google Scholar and ResearchGate.¹¹ Used keywords were 'willingness', 'intention', 'hesitancy', 'acceptance', 'perception', 'attitudes', 'cancer', 'malignancy', 'neoplasm', 'tumour', 'COVID 19', 'coronavirus', 'SARS CoV 2', 'nCoV', 'vaccine', 'vaccination', 'immunisation' and 'injection'. The search strategy is shown in [Appendix 1 in the supplementary material](#). Only articles published in the English language were selected. When a potential study was identified, the full text was downloaded (note: when the free full text was unavailable online, an original paper or report was requested from the corresponding author or associated affiliations). The reference lists of selected studies were assessed to identify any additional relevant articles. This study followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses 2020 (PRISMA 2020) guidelines (see [Appendix 2 in the supplementary material](#)).¹²

Inclusion and exclusion criteria

Original studies published in the English language assessing attitudes, perceptions, willingness or hesitancy to COVID-19 vaccination in adult (aged ≥ 18 years) patients with cancer or cancer survivors who were being treated or followed up for cancers were included. Patients with recent cancer diagnoses who were waiting for treatment were also included.

'Vaccine acceptance' was defined as those patients who had been vaccinated, who were willing to get the vaccine or who were waiting to get the COVID-19 vaccine. 'Vaccine hesitancy' was defined as those patients who were reluctant to get the vaccine or refused to get vaccinated. Cross-sectional studies meeting the eligibility criteria were included; randomised controlled trials and case–control studies were excluded. Reports providing evidence relevant to the study objectives were included in the final review (latest PRISMA 2020 updates: 'report' could be a journal article, preprint, conference abstract, study register entry, clinical study report, dissertation, unpublished article, government report or any other document providing relevant information).¹²

Evaluation process

After the removal of duplicate articles, two authors (K.I.P.P. and H.D.W.T.D.) independently screened the titles and abstracts of selected studies for their eligibility to be included in full text screening. The full texts of potential articles were retrieved, and an in-depth evaluation was undertaken (by K.I.P.P. and H.D.W.T.D.) to assess the eligibility to be included in the final analysis. Included studies were assessed for quality according to the Joanna Brines' Institute quality appraisal tool¹³ by the principal author (K.I.P.P.) and cross-checked by a co-author (H.D.W.T.D.). Any discrepancies in the screening process and risk of bias assessment were resolved by consensus. Article quality was considered to be 'fair' if the answer was 'no' or 'unclear' to two to three of eight questions in the Joanna Brines' Institute quality appraisal tool and 'high' if the answer was 'no' to only 1 or 'yes' for all questions.¹⁴

Data extraction, analysis and data synthesis

Data extraction was conducted according to a predefined data extraction table. Extracted data were cross-checked, and discrepancies were discussed. Authors, study year, study design and methodology, study location, sample collection dates, sample characteristics, study objectives, main findings (percentages, statistically significant and non-significant findings) and study limitations were extracted. Similarities and differences if the findings, sample-specific characteristics, trends and limitations were identified. The corresponding author was contacted in cases of any identified discrepancy.

Qualitative synthesis was carried out as a narrative summary, and meta-analyses were undertaken in Review manager 5.4.1 when the data were available to pool. People aged >65 years were considered as 'elderly', and people aged between 50 and 65 years were considered as 'advanced middle-aged adults' for the current systematic review.^{15,16} The heterogeneity among pooled studies was described as per the I^2 statistics.^{17,18} Heterogeneity among studies was not considered for the prevalence data during the meta-analysis. Study heterogeneity was categorised as low (0–40%), moderate (41–60%), substantial (61–80%) and considerable (81–100%).¹⁸ Heterogeneity was addressed; moderate heterogeneity was fixed with a random effects model to incorporate sample variation among pooled studies,¹⁹ and studies with low heterogeneity were analysed with a fixed effects model.¹⁹ Meta-analysis was not performed for the studies with significant heterogeneity.¹⁹ Pooled prevalence of patients with cancer were calculated for vaccine acceptance, vaccine hesitancy due to the fear of side-effects and uncertainty of effectiveness of the COVID-19 vaccines. The generic inverse variance method was used in pooled prevalence data analysis (95% confidence interval [CI], random effects model).¹⁷ Factors associated with vaccine acceptance and hesitancy were identified during the meta-analysis and described using odds ratios (ORs). Significant factors were identified and interpreted with the overall effect size (Z) and *P*-values. Studies that were not included in the pooled meta-analysis were narratively summarised.

Results

In total, 167 articles were identified during the initial search, and 101 in the secondary search. The study selection process is shown in [Fig. 1](#). Finally, 29 studies were selected for the review.^{20–48} The current systematic review reports studies from the following different geographical areas: Australia,⁴² Serbia,⁴⁷ Germany,^{25,26} Portugal,²⁸ Bosnia and Herzegovina,^{45,48} Italy,³⁷ France,^{27,35} Poland,^{31,40} Korea,³⁹ the US,^{23,38,41} Cyprus,²⁴ Mexico,³⁶ Tunisia,^{33,43} China,^{20,22,30,34,46} Turkey,²⁹ Ethiopia,⁴⁴ India³³ and Lebanon.²¹ Study characteristics are presented in [Table 1](#).

The pooled prevalence of COVID-19 vaccine acceptance was 59% (95% CI 52–67%), I^2 : 99% (see [Fig. 2\(a\)](#)).^{20–48} The pooled prevalence of vaccine hesitancy due to fear of vaccine-related side-effects was 53% (95% CI 40–67%), I^2 : 99% (see [Fig. 2\(b\)](#))^{21,34,35,37,38,40,42} and due to uncertainty about the vaccine effectiveness was 36% (95% CI 17–55%), I^2 : 99% (see [Fig. 2\(c\)](#)).^{21,34,37,40,49}

Study participants were sceptical about the rapid development of COVID-19 vaccines³¹ and reported low confidence in scientific results and the healthcare system.^{35,36} Frequently reported misconceptions included the potential of vaccines to cause infections (because they contain viruses), COVID-19 vaccines being contraindicated for patients with breast cancer, potential infertility and concern about a concealed chip within the vaccine to collect personal data.³⁶ Patients who were doubtful about COVID-19 vaccination perceived that there was insufficient knowledge of the side-effects and medical indications of the vaccines for patients with

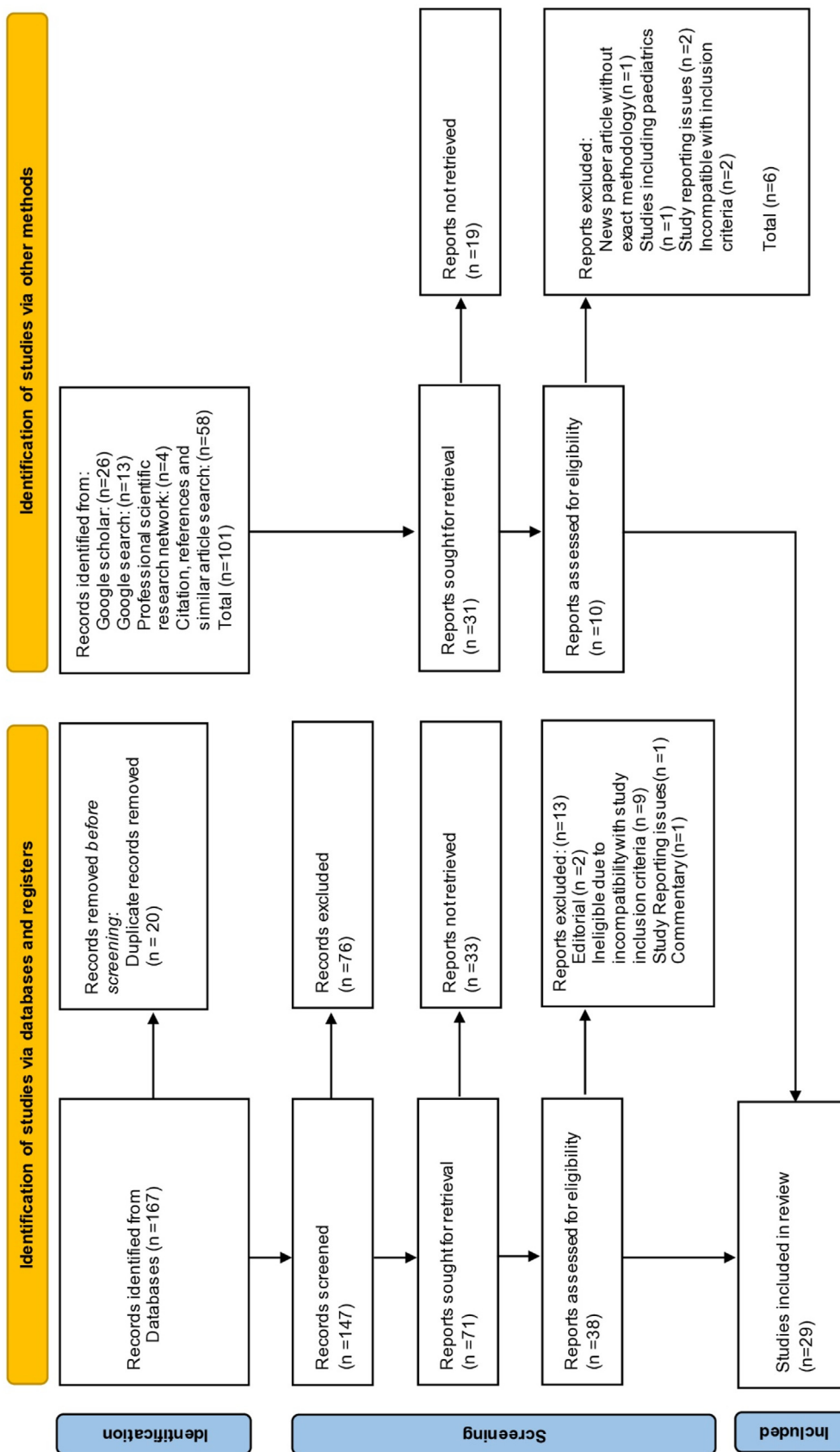
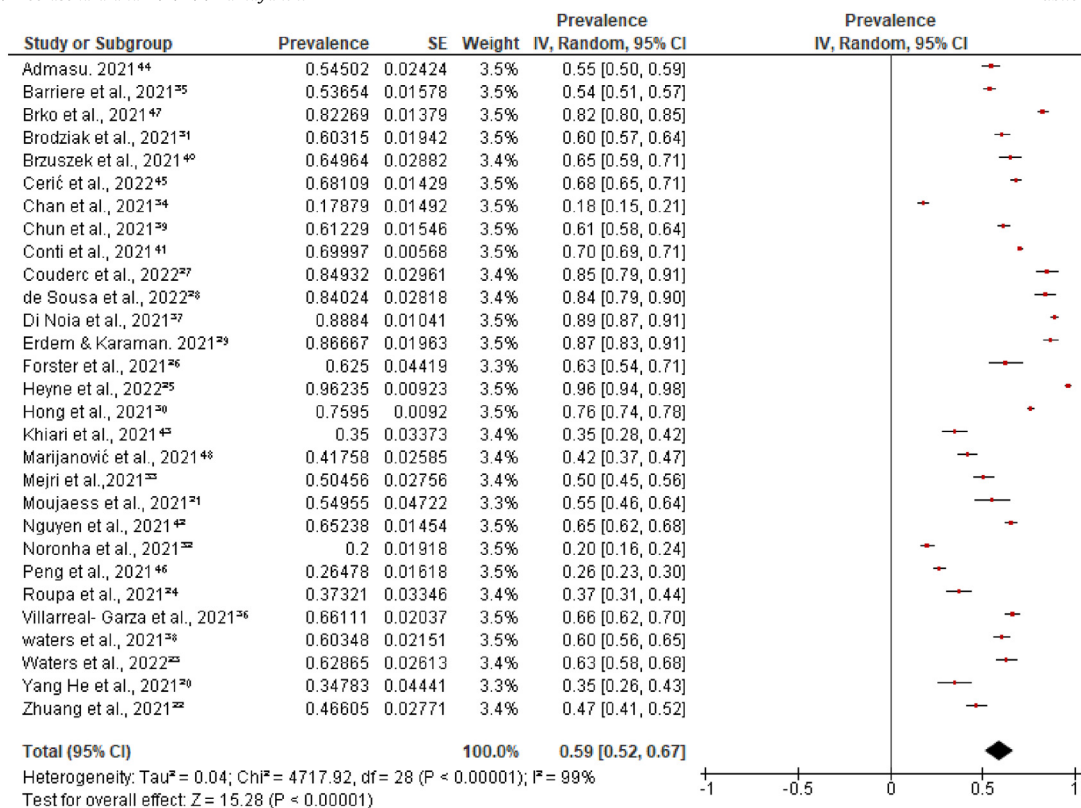
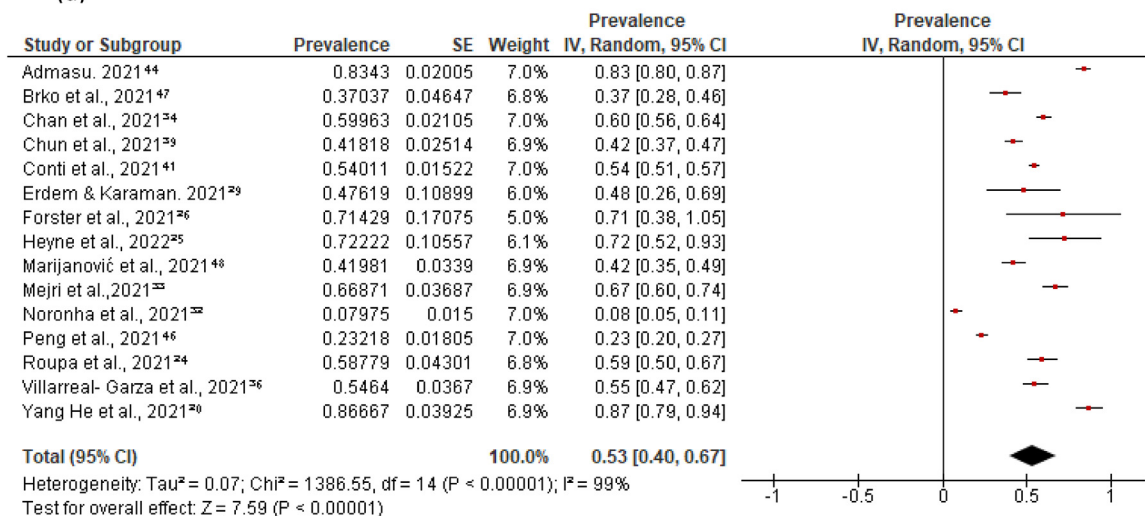


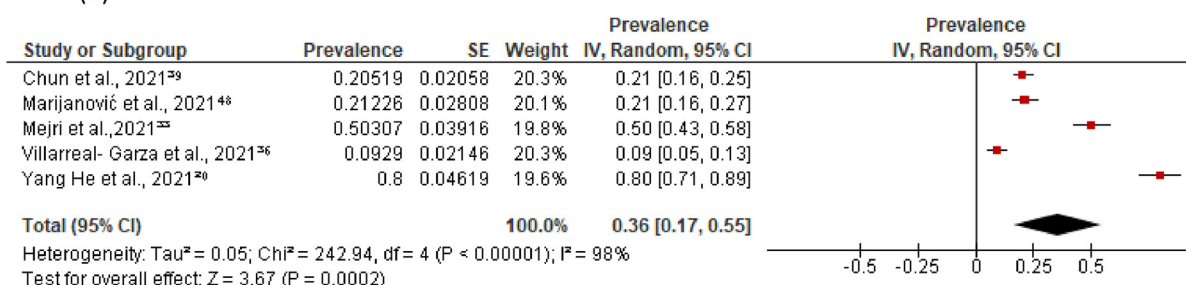
Fig. 1. Study selection process.



(a)

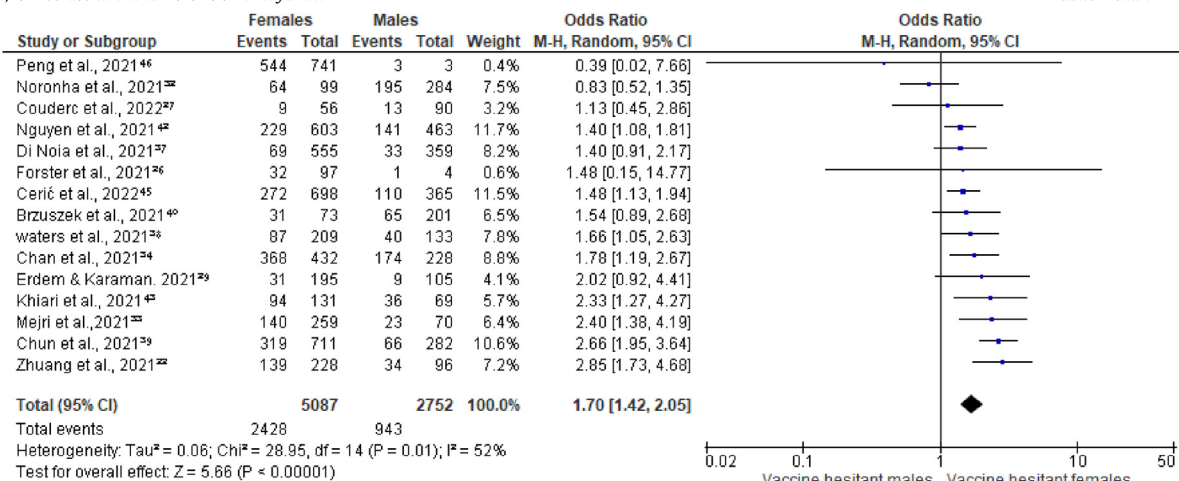


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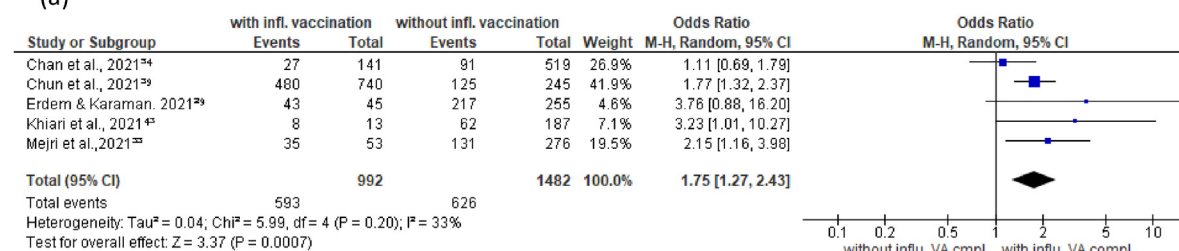


(c)

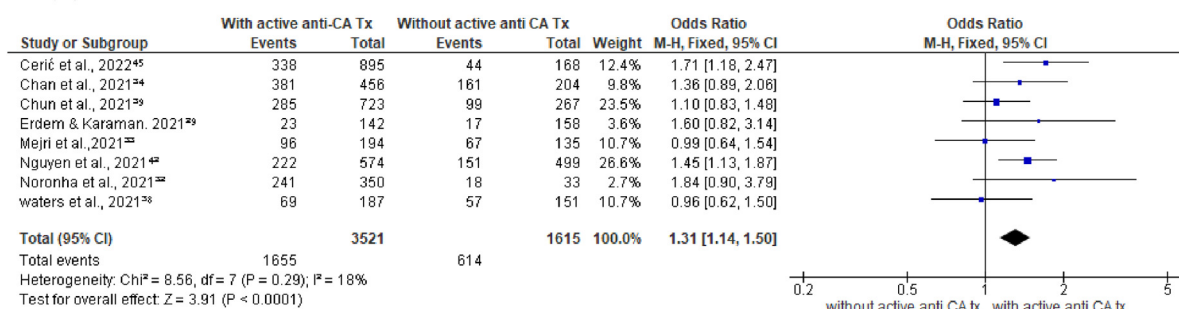
Fig. 2. Pooled prevalence of (a) vaccine acceptance, (b) vaccine hesitancy due to fear of side-effects and (c) vaccine hesitancy due to uncertainty of vaccine effectiveness. CI, confidence interval; SE, standard error.



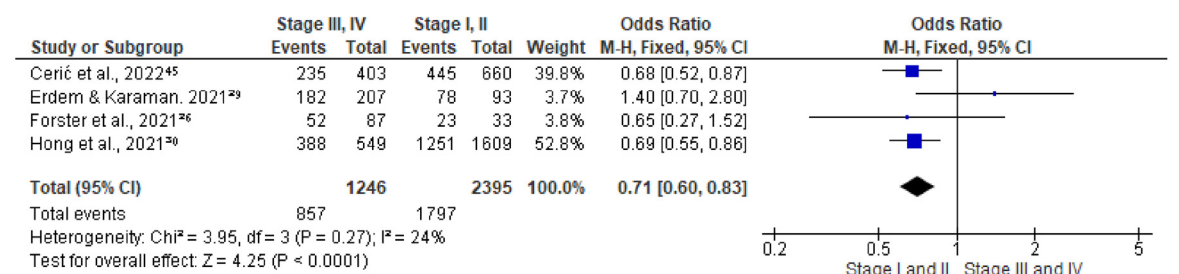
(a)



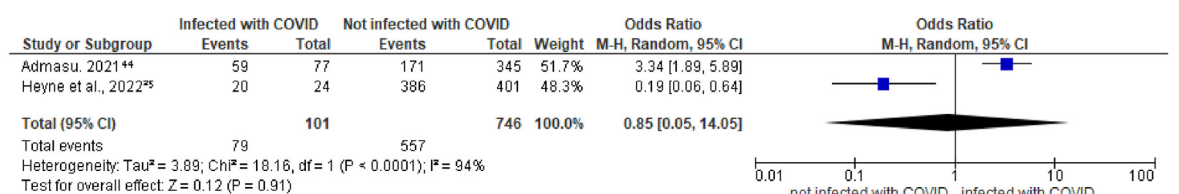
(b)



(c)



(d)



(e)

Fig. 3. Meta-analysis findings of factors associated with COVID-19 vaccine acceptance or hesitancy; (a) Gender, (b) compliance with previous influenza vaccination, (c) being with active anticancer treatments (d) advance stage of the cancer, and (e) history of COVID-19 infection.

Table 1
Key characteristics of included studies.

Study no.	Author, year and country	Study period	Sample characteristics				Quality appraisal
			Sample size	Median/mean age in years	Gender		
					Male	Female	
1.	Di Noia et al., 2021, ³⁷ Italy	1/03/2021 to 20/03/2021	914	62 (21–97)	39%	61%	Fair
2.	Barrière et al., 2021, ³⁵ France	1/11/2020 to 12/12/2020	999	67 (18–97)	43.9%	56.1%	Fair
3.	Brodziak A et al., 2021, ³¹ Poland	26/01/2021 to 18/02/2021	635	53 (18–89)	19.8%	80.2%	Good
4.	Conti et al., 2021 ⁴¹	1/12/2020 to 21/12/2020	6516	63.93 ± 12.28	40.2%	59.8%	Fair
5.	Villarreal-Garza et al., 2021, ³⁶ Mexico	12/03/2021 to 26/03/2021	540	49 (23–85)	–	100%	Fair
6.	Waters et al., 2021, ³⁸ USA	10/2020– to 01/2021	342	29.5 ± 6.5	38.9%	61.1%	Fair
7.	Mejri et al., 2021, ³³ Tunisia	02/2021 to 05/2021	329	54 ± 13.4	21.3%	78.7%	Good
8.	Yang He et al., 2021, ²⁰ China - Hubei	Not indicated	115	–	–	–	Fair
9.	Moujaess et al., 2021, ²¹ Lebanon	25/01/2021– to 12/02/2021	111	61 (23–85)	33.3%	66.7%	Fair
10.	Brzuszek et al., 2021, ⁴⁰ Poland	Not indicated	280	–	73%	27%	Fair
11.	Chun et al., 2021, ³¹ Korea	02/2021– to 04/2021	993	57.4 ± 12.0	28.3%	71.7%	Fair
12.	Chan et al., 2021, ³⁴ China–Hong Kong	31/01/2021– to 15/02/2021	660	–	34.5%	65.5%	Good
13.	Brko et al., 2021, ⁴⁷ Serbia	1/07/2021– to 15/08/2021	767	–	–	–	Fair
14.	Heyne et al., 2022, ²⁵ Germany	09/2021– to 11/2021	438	61.4 ± 12.3	39.5%	60.5%	Fair
15.	De Sousa et al., 2022, ²⁸ Portugal	08/03/2021– to 02/04/2021	169	61 (29–82)	35.5%	64.5%	Good
16.	Cerić et al., 2022, ⁴⁵ Bosnia and Herzegovina	22/10/2021– to 30/11/2021	1063	61.9 ± 11.5	34.3%	65.7%	Fair
17.	Waters et al., 2022, ²³ USA	10/2020– to 01/2021	341	–	39.3%	60.7%	Fair
18.	Roupa et al., 2021, ²⁴ Cyprus	22/01/2021– to 12/02/2021	211	52.6 ± 12.4	34.6%	64.9%	Fair
19.	Khiari et al., 2021, ⁴³ Tunisia	02/2021	200	54.4 ± 12.7	34.5%	65.5%	Good
20.	Nguyen et al., 2021, ⁴² Australia	30/07/2021– to 07/08/2021	1073	62 ± 11.97	43.2%	56.2%	Good
21.	Peng et al., 2021, ⁴⁶ China	05/06/2021– to 12/06/2021	744	48 (40–54)	0.4%	99.6%	Good
22.	Erdem and Karaman, 2021, ²⁹ Turkey	05/2021– to 06/2021	300	55.16 ± 12.91	35%	65%	Fair
23.	Admasu, 2021, ⁴⁴ Ethiopia	05/2021– to 08/2021	422	35.7 ± 6.86	42.8%	57.2%	Good
24.	Zhuang et al., 2021, ²² China	03/2021– to 05/2021	324	–	–	–	Good
25.	Foster et al., 2021, Germany	15/03/2021– to 28/07/2021	120	Breast cancer: 57 (23–85) Gynaecological cancer: 56 (34–78)	3.33%	96.67%	Fair
26.	Hong et al., 2021, ³⁰ China	17/06/2021– to 03/09/2021	2158	–	48.89%	51.11%	Good
27.	Marijanović et al., 2021, ⁴⁸ Bosnia and Herzegovina	02/2021	364	61.6 ± 11.2	38.5%	61.5%	Good
28.	Couderc et al., 2021, ²⁷ France	18/01/2021– to 07/05/2021	150	81 ± 0.5	61.3%	38.7%	Fair
29.	Noronha et al., 2021, ³² India	07/05/2021– to 10/06/2021	435	58 (52–65)	73.8%	26.2%	Fair

cancer.³¹ Patients who had a neutral view on COVID-19 vaccination were more likely to get vaccinated after receiving sufficient information on vaccine efficacy and safety.^{35,36} A meta-analysis for age-wise comparison was not performed due to inconsistency within the data.^{31,33,35,39–41} However, several studies reported that elderly individuals were more likely to get vaccinated and less likely to refuse the vaccine.^{31,33,35} Patients aged <50 years were more likely to be hesitant about receiving the COVID-19 vaccine.^{33,40} According to the eight included studies, education level was not significantly associated with vaccination status.^{22,29,30,33,34,39,42,46} According to Barrière et al., the vaccine-hesitant population relied on their own opinions on COVID-19 vaccination, whereas those who accepted the COVID-19 vaccine followed their oncologist's opinion.³⁵ Brodziak et al. showed that most people depend on their healthcare professionals' opinions (i.e. oncologist or general practitioner) on COVID-19 vaccination.^{22,24,29,31,36,46}

Factors associated with vaccine acceptance and hesitancy

A meta-analysis was undertaken for the following variables: gender, compliance with previous influenza vaccination, active anticancer treatments, stage of cancer, and history of COVID-19 infection. Fig. 3 presented the analysis results and Fig. 4 shows publication bias in the pooled studies in each analysis.

Gender

Seventeen studies were initially pooled for the gender meta-analysis and revealed to have a substantial statistical heterogeneity (I^2 : 87%). Two sources of statistical heterogeneity were identified^{30,44} due to extreme narrow values for the CIs with considerable weight on both studies (Admasu: weight: 6.8%, $n = 422$, OR: 0.24

[95% CI 0.16–0.36];⁴⁴ and Hong et al.: weight: 7.6%, $n = 2158$, OR: 0.94 [95% CI 0.77–1.14]).³⁰ Fifteen studies were finally pooled for the gender variable (see Fig. 3a). Because of the moderate statistical heterogeneity among the 15 pooled studies, the random effects model was used to analyse the data.^{24,38,40,41,43,27,30–32,35–37} Meta-analysis of the pooled studies indicated that female gender is significantly associated with vaccine hesitancy (pooled OR: 1.70 [95% CI 1.42–2.05], I^2 : 52%, overall effect: $Z = 5.67$, $P < 0.00001$).

Prior compliance with previous influenza vaccination

Five studies were grouped to assess the effect of influenza vaccination and COVID-19 vaccine hesitancy (see Fig. 3b).^{29,33,34,39,43} Patients with prior influenza vaccination were more likely to accept COVID-19 vaccination (pooled OR: 1.75 [95% CI 1.27–2.43], I^2 : 33%, overall effect: $Z = 3.37$, $P = 0.0007$).

Undergoing active anticancer treatments

Nine studies were pooled to investigate the association between undergoing active anticancer treatments and vaccine hesitancy (Fig: 3c).^{29,30,32,33,38,39,42,45,47} Brko et al. and Hong et al. showed significantly high heterogeneity (I^2 : 79%), which can be explained by inappropriate data reporting.^{30,47} A total of seven studies were pooled for the final analysis. Meta-analysis of the pooled studies indicated that patients undergoing active anticancer treatments were more likely to be hesitant about COVID-19 vaccination (pooled OR: 1.31 [95% CI 1.14–1.50], I^2 : 18%, overall effect: $Z = 3.91$, $P < 0.0001$).

Cancer stage

Four studies were pooled to identify the effect of cancer stage on COVID-19 vaccine acceptance (see Fig. 3d).^{26,29,30,45} Patients with advanced stages of cancer (stages III and IV) showed low

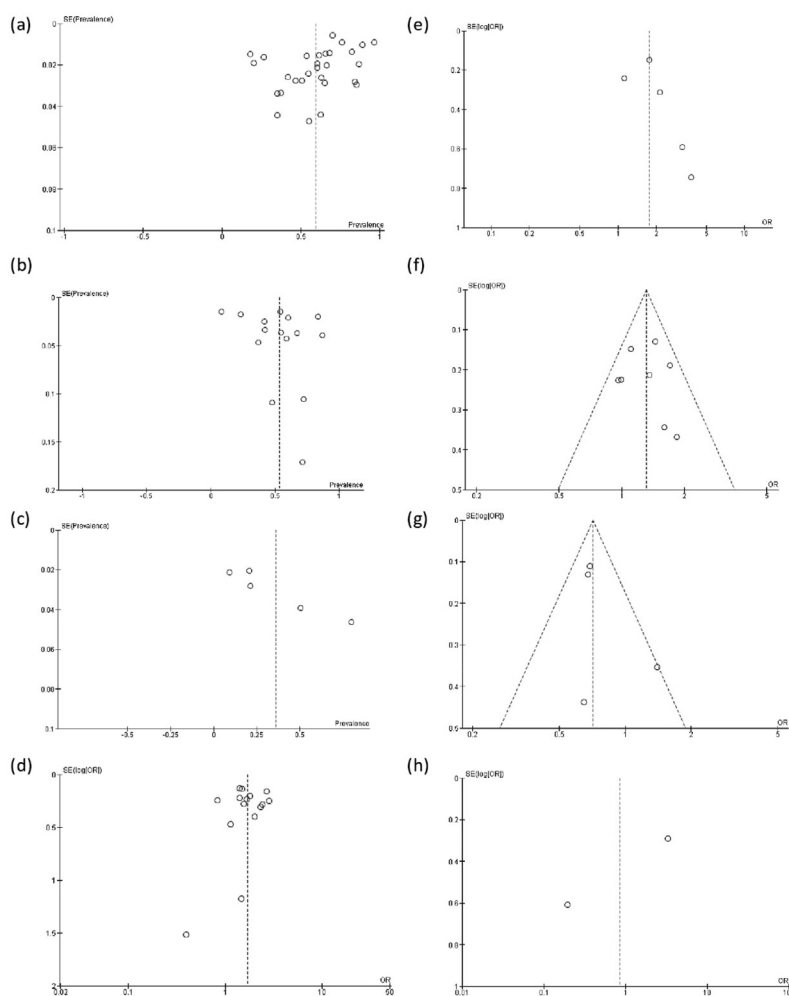


Fig. 4. Funnel plots of the analysis. (a) Pooled prevalence of vaccine acceptance; (b) pooled prevalence of vaccine hesitancy due to fear of side-effects; (c) pooled prevalence of vaccine hesitancy due to the uncertainty of vaccine efficacy; (d) effect of gender on COVID-19 vaccine hesitancy; (e) effect of previous influenza vaccination on vaccine acceptance; (f) effect of active anticancer treatments on vaccine hesitancy; (g) effect of cancer stage on vaccine hesitancy; and (h) effect of history of COVID-19 infection on vaccine acceptance. CI, confidence interval.

acceptance of the COVID-19 vaccination (pooled OR: 0.71 [95% CI 0.60–0.83], I^2 : 24%, overall effect: $Z = 4.25, P < 0.0001$).

Previous COVID-19 infection

Two studies were pooled to assess the effect of previous COVID-19 infection and vaccine acceptance (see Fig. 3e).^{25,44} The results showed no statistically significant association between prior COVID-19 infection and COVID-19 vaccine acceptance (pooled OR: 0.85 [95% CI 0.05–14.05], $I_2 = 94%$ overall effect: $Z = 3.19, P = 0.91$).

Discussion

The current systematic review and meta-analysis investigated whether gender, compliance with previous influenza vaccination, active anticancer treatments, stage of the cancer and history of COVID-19 infection were related to COVID-19 vaccine acceptance.

Pooled prevalence statistics found that approximately half of the patients with cancer accepted COVID-19 vaccines.^{20–48} In total, 58% of the pooled population were willing to be vaccinated against COVID-19. Patients with cancer who received the COVID-19

vaccination reported mild reactions, such as a sore arm, fatigue and headache; however, concerns about vaccine safety may cause considerable COVID-19 vaccination hesitancy.⁷ Studies recommend all doses of COVID-19 vaccines for patients with cancer, as this significantly reduces COVID-19–related morbidity and mortality.⁴⁹ National Comprehensive Cancer Network guidelines recommend COVID-19 vaccination for all patients with cancer unless there is a clinical contraindication.¹

A meta-analysis of this systematic review found that the female gender and undergoing active anticancer treatments are associated with vaccine hesitancy. Good compliance with previous influenza vaccination and being in the early stages of cancer (stages I and II) are associated with COVID-19 vaccine acceptance. According to the results of the narrative synthesis, elderly individuals (aged >65 years) are more likely to accept the vaccine (note: a meta-analysis on the age variable could not be performed because of significant heterogeneity among studies). This result is supported by previous literature showing that older and middle-aged adults are more likely to accept the COVID-19 vaccine than the younger population.^{50,51} Females in the general population have been shown to be

more hesitant about COVID-19 vaccines^{52,53} and are significantly concerned about the side-effects of COVID-19 vaccination.^{33,54}

Concerns about COVID-19 vaccine-related side-effects and effectiveness were highly prevalent among patients with cancer. Fear of unknown future COVID-19 vaccine-related side-effects and doubt about vaccine benefits were common factors associated with vaccine hesitancy in the community.⁵⁵ Specific educational programmes on COVID-19 vaccine safety and efficacy for patients with cancer are essential for increasing vaccine acceptance and reducing mortality associated with COVID-19.⁵⁶ These findings are important when implementing educational interventions, which need to be tailored according to sociodemographic characteristics.⁵⁷ Personal mobile communications, such as text messages emphasising the basic information on COVID-19 vaccines, social benefits and their contribution to herd immunity, have been shown to enhance vaccine acceptance.^{58–60} In addition, personal reminders of COVID-19 vaccine doses increases vaccine acceptance.^{59,60}

According to the narrative synthesis, education level is not likely to impact vaccine acceptance or hesitancy. However, previous studies suggest that people with a higher education level are more likely to accept the vaccine than those with a low education level in the general population.^{52,61} This is supported by the study of Matsuyama et al. that showed educational attainment is significantly associated with health information needs.⁶² Patients with cancer with poor health literacy levels poorly adhere to their treatments, have ineffective communication and have high anxiety levels.⁶³ Therefore, patients with cancer may require more information regarding COVID-19 vaccines from a trusted source.

A history of receiving the influenza vaccination was compatible with the willingness to be vaccinated against COVID-19 in general and cancer populations.^{52,61} Some believe that influenza vaccines prevent the spread of COVID-19.⁶⁴ Trust in health interventions and scientific findings may enhance vaccine compliance in the community.⁶⁵

Strengths and limitations

This systematic review is the first attempt to collate evidence on COVID-19 vaccine acceptance or hesitancy in patients with cancer. An extensive literature search, independent screening and adherence to the PRISMA guidelines strengthened the methodological quality of this study. The small number of databases searched was a limitation of this study; however, this could not be avoided due to the lack of free databases available in the country of the present publication. This study presents information from 18 countries, and therefore, results can be generalised globally; however, it should be noted that this review included online surveys and single-centre studies, which is a limitation to the results.

Conclusions

The findings from the present study highlight the requirement of problem-based educational interventions to address vaccine hesitancy of patients with cancer and their caregivers. Knowledge on vaccine efficiency, side-effects and oncological indications for vaccinating against COVID-19 should be disseminated effectively. According to the current study, oncologists were the most favourable means of delivering information about COVID-19 vaccines for patients with cancer. Motivational interviewing is important to enhance vaccine compliance⁶⁶ and responding to individual concerns about specific reasons for their vaccine hesitancy is essential.⁶⁶ Moreover, trust in healthcare providers significantly improves vaccine acceptance.⁶⁷ Kelkar et al. stated that patient education programmes delivered by oncologists enhance COVID-19 vaccine enthusiasm.⁶⁸ When restrictions are in place and face-to-

face meeting are prohibited, online education interventions can be used. Kelkar et al. reported the effectiveness of webinars in reducing COVID-19 vaccine hesitancy of patients with cancer, caregivers, and other people who engage with patients with cancer and cancer care.⁶⁹ Provision of information via positive framing enhances vaccine acceptance.⁶⁸ Moreover, the current review highlights the need for well-designed qualitative studies to provide in-depth analyses of cancer patients' attitudes, perceptions, willingness or hesitancy towards COVID-19 vaccines.

Author statements

Ethical approval

Not applicable.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

The authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.puhe.2022.09.001>.

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