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# Impact of COVID-19 pandemic on flu vaccine uptake in healthcare workers in Europe: a systematic review and meta-analysis

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## ABSTRACT

**Introduction:** Influenza immunization policies in Europe primarily target at-risk and vulnerable subjects. Healthcare workers (HCWs) are a key focus of vaccination campaigns. Our systematic review and meta-analysis aim to evaluate the role of the COVID-19 pandemic on influenza vaccine uptake among HCWs since the 2020/21 influenza season.

**Areas covered:** Fourteen studies were included in the meta-analysis and systematic review, selected from scientific articles available in MEDLINE/PubMed, ISI Web of Knowledge, and Scopus databases between 1 January 2021 and 15 January 2023. The analysis revealed a significant relationship between influenza vaccine uptake and COVID-19 related determinants, such as willingness to receive COVID-19 vaccination, fear of COVID-19, and differentiating between influenza and COVID-19 symptoms (OR = 5.70; 95%CI = 2.08–15.60). Several studies reported higher vaccination coverages in the 2020/21 season compared to previous seasons, with VC values ranging from +17% to +38% compared to the 2019/20 season. The included studies identified a shift in HCWs' attitudes toward influenza vaccination, attributed to increased awareness due to the COVID-19 pandemic.

**Expert opinion:** Vaccine hesitancy is common among HCWs in Europe, necessitating mutual strategies across all European countries. So far, mandatory vaccination policies have shown the most potential in achieving high and sustainable influenza vaccination rates among HCWs.

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## KEYWORDS

Healthcare workers; vaccine compliance; influenza; nosocomial infection; mandatory vaccination; SARS-CoV-2

## 1. Introduction



According to the official recommendations of the European Centre for Disease Prevention and Control (ECDC), influenza immunization policies in Europe are designed to protect the most at-risk and vulnerable individuals [1]. In this context, one of the primary objectives of vaccination campaigns is to improve vaccination coverage (VC) among healthcare workers (HCWs). Indeed, vaccination safeguards HCWs from occupational infectious diseases and reduces the risk of infection for patients within healthcare settings [2]. The influenza vaccine should be administered annually, typically from October to December in northern hemisphere, before the start of the upcoming influenza season.

Strategies for vaccinating HCWs in Europe vary from country to country. Maltezou HC et al. [3] reported that in 2018 most European countries recommended influenza immunization for all HCWs, while four countries had recommendation policies specific to certain settings or health personnel groups. Serbia had a mandatory policy for specific setting or health personnel groups, and Denmark had a not recommended – not mandatory policy. In 2017, Finland adopted a mandatory policy for all HCWs exposed to high infectious risk [4]. More recently, three Italian Regions implemented laws mandating a semi-mandatory regimen for influenza vaccination among HCWs, based on

occupational health assessments, with the possibility of salary suspension until immunization [5]. However, current VC data are generally unavailable in Europe due to the lack of national systems for collecting achieved coverage by Public Health institutions. Nevertheless, the literature reports sub-optimal VCs (on average less than 50%) in European HCWs [6–12].

The co-circulation of influenza virus and SARS-CoV-2 during the 2020/21 season has made the influenza vaccination campaign even more critical in minimizing influenza transmission within healthcare settings and to allocate healthcare resources effectively for managing COVID-19 patients. Notably, the literature indicates significantly higher VCs during the 2020/21 season compared to previous seasons [13–16], suggesting a more compliant behavior of healthcare personnel toward influenza immunization during the pandemic. This observation is further supported by the World Health Organization (WHO), which reported an average increase in vaccination coverage during the 2020/21 season in specific EU/EEA countries, including Hungary, Ireland, Lithuania, Norway, Romania, Slovenia, Spain, Croatia, and the UK [17]. This trend has also been observed in other high-risk populations, such as the elderly and patients with chronic diseases [18–20], as well as in the general population [21].

To investigate the role of the COVID-19 pandemic on influenza vaccine uptake since the 2020/21 influenza season, we

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### Article highlights

- HCWs are among the at-risk categories for whom influenza vaccination is strongly recommended
- vaccination protects HCWs from occupational infectious diseases and patients from the risk of infection
- Since the 2020/21 season, influenza seasons have been characterized by the co-circulation with SARS-CoV-2
- Our study evaluates the role of COVID-19 pandemic on influenza vaccine attitude.
- A significant relationship was evidenced between flu vaccine uptake and the COVID-19 related determinants [uptake or willingness to receive COVID-19 vaccination, fear of COVID-19, and differential diagnosis between influenza and COVID-19 symptoms].
- The scenario of management strategies for hesitant individuals is very difficult
- VCs reached in the 2020/21 season were higher than in previous seasons.
- None of the reported experiences proved to meet an optimal target
- Mandatory strategy seems to be necessary to deal with low uptake

conducted a systematic review of relevant literature and performed a meta-analysis. Our analysis focused on the association between influenza vaccine uptake and COVID-19 related determinants among HCWs in EU/EEA countries, including uptake or willingness to receive COVID-19 vaccination, fear of COVID-19, and the ability to differentiate between influenza and COVID-19 symptoms [22]. The choice of these determinants was based on existing literature, highlighting studies that targeted various high-risk populations, which indicated that the COVID-19 pandemic may have positively influenced influenza vaccine uptake among HCWs [23–27].

## 2. Body

### 2.1. Methods

The systematic review protocol was established following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [28]. The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the reference acknowledgment number CRD42023403169. The review question was formulated using the Population, Intervention, Comparison, and Outcome (PICO) framework, and it focused on the ‘relationship between the COVID-19 pandemic and influenza immunization among HCWs in Europe.’

#### 2.1.1. Search strategy, selection criteria, and data extraction

The Scopus, MEDLINE/PubMed, and ISI web of knowledge were systematically searched. Research articles, brief reports, letters, and editorials published between 1 January 2021 and 15 January 2023 were included in our search. The following terms were used for the search strategy: (adherence OR hesitan\* OR compliance OR attitude OR willingness) AND (influenza OR flu) AND (vaccin\* OR immun\*) AND (healthcare worker\* OR health personnel OR physician\* OR nurse\* OR doctor\* OR resident\* OR student\*) AND (EU OR EEA OR United Kingdom OR UK OR Italy OR France OR Spain OR Portugal OR Austria OR Belgium OR Bulgaria OR Croatia

OR Cyprus OR Czech Republic OR Denmark OR Estonia OR Finland OR Germany OR Greece OR Hungary OR Ireland OR Latvia OR Lithuania OR Luxembourg OR Malta OR Netherlands OR Poland OR Romania OR Slovakia OR Slovenia OR Sweden OR Iceland OR Norway OR Liechtenstein). Studies in English with full text were included. Abstracts without full-text, reviews, meta-analyses, papers not reporting epidemiological data, clinical trials, and studies unrelated to the purpose of this review (vaccine knowledge, seroprevalence, etc.) or not set in Europe were excluded. When necessary, we contacted study authors to obtain additional information. The list of papers was independently screened by two reviewers based on the title and/or abstract, following the predefined inclusion/exclusion criteria. Any discrepancies were recorded and resolved through consensus.

The extracted data included the year of publication, professional category of participants, European country, and the role of the COVID-19 pandemic on influenza vaccine attitude.

#### 2.1.2. Quality assessment

The methodological quality of the selected studies was assessed using the Newcastle – Ottawa Scale (NOS), adapted for cross-sectional studies [29]. The scale consists of seven categories, assessing three quality aspects (selection, comparability, and outcome/exposure), with scores ranging from 0 to 10. A high-quality study was defined with an NOS score between 7 and 10, intermediate with an NOS score between 4 and 6, and low between 0 and 3.

Two researchers independently assessed the risk of bias for each study; discrepancies were recorded and resolved by consensus.

#### 2.1.3. Main outcome and pooled analysis

The adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs), evaluated through multivariate regression models in the eligible studies, were selected as general outcome variables for the relationship between influenza vaccine uptake or willingness to get vaccinated in the following season and the role of the COVID-19 pandemic in their choice. A sub-analysis per professional category was performed.

The ORs and standard errors (SEs) data were calculated from the 95% CIs, and an additional logarithmic transformation was performed to stabilize the variance and normalize the distribution. The OR in the meta-analysis was calculated using the inverse variance and DerSimonian-Laird weights for random effects models. The heterogeneity estimate was obtained from the inverse-variance fixed-effects model. The OR and the 95% Wald confidence interval were plotted, and a forest plot was drawn. The  $I^2$  statistic was calculated as a measure of the proportion of the overall variance attributable to heterogeneity between studies rather than chance. A p-value <0.05 was considered an index of statistical significance of heterogeneity.

Three different sensitivity analyses were conducted to evaluate stability, as follows

- Sub-analysis considering only high-quality studies

- Sub-analysis per study sample (600+ vs. <600 HCWs; the median value of the sample of the included studies was calculated to define this cutoff)
- One study was excluded at a time, and the subsequent conclusions were reevaluated to evaluate significant distortions.

Statistical analysis was conducted using STATA MP17.

The impact of the COVID-19 pandemic on influenza vaccine attitude was gathered from all the available studies, and their respective findings were compared, with special attention given to the evidence presented in multiple included papers.

### 3. Results

#### 3.1. Identification of relevant studies

The flow-chart, constructed following the PRISMA guidance [28] (Figure 1), illustrates the article selection process. Based on the predefined inclusion criteria, a total of 28 articles were identified in ISI Web of Knowledge, 19 in Scopus, and 43 in MEDLINE/PubMed. After removing duplicate articles from the two databases, there were 48 eligible studies. Out of these, 15 were excluded as they did not evaluate the relationship

between COVID-19 and influenza vaccine uptake, 15 investigated influenza seasons outside the scope of this review, two were not in English language, one was a clinical trial, and one had unavailable full-text. Consequently, a total of 14 studies were deemed eligible [30–43], of which six were included in the quantitative analysis [30–43] (Table 1); all the included studies focused on the 2020/21 influenza season. Overall, 928 studies did not meet the inclusion criteria and were excluded.

#### 3.2. Quality assessment

The NOS was appropriately applied to the included studies, with 92.9% of them being classified as high quality (Table 1); all studies included in the quantitative analysis were of high quality.

#### 3.3. Pooled analysis

A significant relationship was evidenced between influenza vaccine uptake and COVID-19 related determinants (OR = 5.70; 95%CI = 2.08–15.60;  $I^2 = 95.0\%$ ;  $p < 0.0001$ ; Figure 2).

Sub-analysis by quality was unnecessary, as all included studies were of high quality. The exclusion of one study at

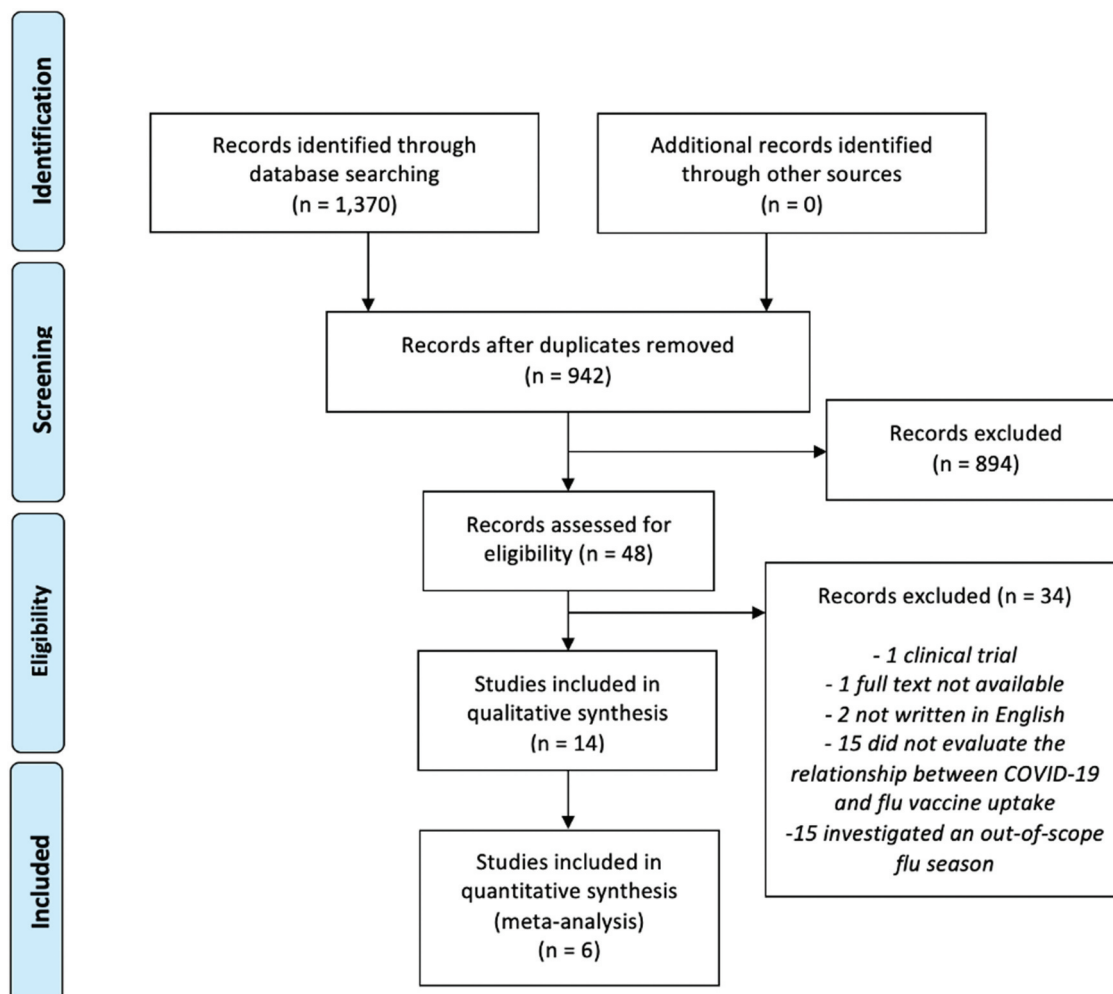
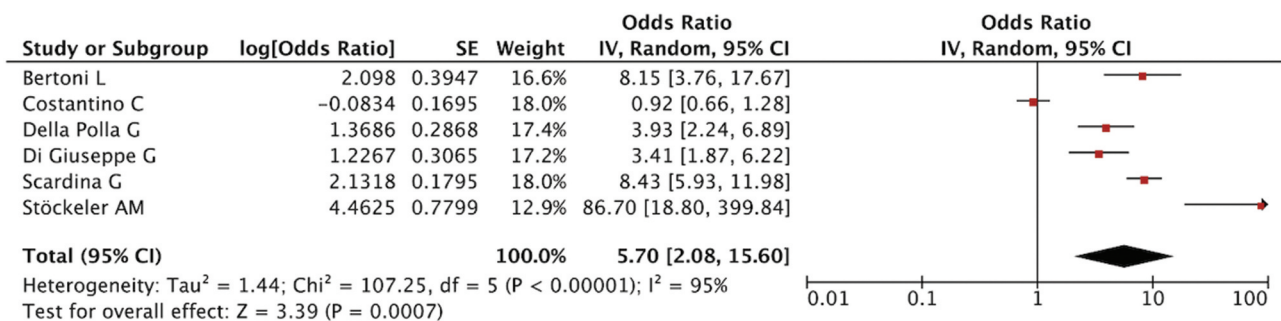


Figure 1. Flow-chart of the bibliographic research.

**Table 1.** Characteristics of the selected studies included in the meta-analysis and systematic review.

First author	Year	Quality	sample	Flu season	Country	Professional category	Multivariate model
<i>Quantitative study</i>							
Bertoni L*	2022	h	579	2020/21	Italy	Cancer center HCWs	Multivariate regression model of flu vaccine uptake; determinants: COVID-19 vaccine uptake, age, sex, profession
Costantino C	2022	h	1450	2020/21	Italy	community Pharmacists	Multivariate regression model of flu vaccine uptake; determinants: fear of contracting SARS-CoV-2, vaccine confidence in preventing influenza, comorbidity, vaccination as the best strategy to prevent COVID-19
Della Polla G	2021	h	615	2020/21	Italy	General and University hospitals' HCWs	Multivariate regression model of flu vaccine uptake; determinants: having indicated that influenza and COVID-19 share similar symptoms as a reason to be vaccinated, not having underlying chronic medical conditions, not having been vaccinated regardless of COVID-19, the belief that an infected HCW cannot pass the influenza virus on to their patients, the belief that influenza is not a severe illness, age, length of practice in years, no perceived risk of getting infected with influenza
Di Giuseppe G	2021	h	490	2020/21	Italy	General hospitals' HCWs	Multivariate regression model of willingness to receive flu vaccination; determinants: willingness to receive COVID-19 vaccination, influenza vaccination uptake in the previous influenza seasons, believing that influenza vaccination is helpful in distinguishing influenza symptoms from COVID-19 symptoms, believing that influenza vaccine is helpful in preventing influenza in hospital settings, concern about the possibility to transmit influenza to hospitalized patients, concern about influenza vaccine side effects, sex, profession
Scardina G	2021	h	6323	2020/21	Italy	University hospital HCWs	Multivariate regression model of flu vaccine uptake; determinants: the importance of flu vaccine during COVID-19 pandemic, risk perception, profession
Stöckeler AM	2021	h	190	2020/21	Germany	emergency department HCWs	Multivariate regression model of flu vaccine uptake; determinants: intention to be vaccinated because of COVID-19, on-site clinic, more than two doses received in the previous seasons, profession
<i>Qualitative study</i>							
Albanesi B	2022	h	11446	2020/21	Italy	University hospital HCWs	-
Kearns EC	2022	h	728	2020/21	Ireland	University hospital HCWs	-
Papageorgiou C	2022	h	962	2020/21	Cyprus	General hospital HCWs	-
Sani T	2022	h	2021	2020/21	Italy	General hospital HCWs	-
Di Pumpo M*	2021	m	11857	2020/21	Italy	University hospital HCWs	-
Grochowska M	2021	h	419	2020/21	Poland	University hospital HCWs	-
Perrone PM	2021	h	2103	2020/21	Italy	University hospital HCWs	-
Štěpánek L	2021	h	603	2020/21	Czech Republic	General hospital HCWs	-

**Figure 2.** Forest plot of the association between vaccine uptake and COVID-19 related determinants.

a time showed no significant distortions from any specific paper. However, a significant distortion was evident when considering sub-analysis by sample size, with an OR of 11.4 (95%CI = 2.70–46.79;  $I^2 = 87\%$ ;  $p$ -value  $< 0.0001$ ) in studies with a sample size of  $< 600$  subjects and an OR of 3.11 (95%CI = 0.71–13.68;  $I^2 = 98\%$ ;  $p$ -value  $< 0.0001$ ) in studies with a sample size of 600+ subjects.

Sub-analysis was performed based on professional category, but since only one study [31] focused on community pharmacists, the following analysis is based only on HCWs working in hospital facilities. A significant relationship was evidenced between influenza vaccine uptake and COVID-19 related determinants in this population (OR = 7.45; 95%CI = 3.88–14.30;  $I^2 = 81.0\%$ ;  $p < 0.0001$ ). Sub-analysis by quality was unnecessary, considering all included studies were high quality. The exclusion of Stöckeler AM et al. [35] reduced heterogeneity to 69% (OR = 5.56; 95%CI = 3.39–9.12;  $I^2 = 69\%$ ;  $p$ -value = 0.020). Additionally, sub-analysis by sample size showed a non-significant difference with an OR of 11.4 (95%CI = 2.70–46.79%;  $I^2 = 87\%$ ;  $p$ -value  $< 0.0001$ ) in studies with a sample size of  $< 600$  subjects and an OR of 5.95 (95%CI = 2.82–12.53;  $I^2 = 80\%$ ;  $p$ -value = 0.020) in studies with a sample size of 600+ subjects.

### 3.4. Role of COVID-19 pandemic on influenza vaccine attitude

Several studies have highlighted that the VCs during the 2020/21 season were higher than in previous seasons, with VC values ranging from +17% to +38% compared to the 2019/20 season [30,32–34,36,39–42]. Di Pumpo M et al. [40] developed a linear regression model based on the data from 2016/17 to the 2019/20 influenza season, predicting a 30.4% influenza VC in the 2020/21 season. Epidemiological data, however, reported a 54.5% coverage among health personnel, indicating a significant increase in vaccine uptake.

The authors identified a shift in HCWs' attitudes toward influenza vaccination, attributing it to heightened awareness due to the COVID-19 pandemic [32–39,41,43], particularly among subjects who had not been vaccinated in previous seasons [37–39,41]; concerns about contracting both influenza and COVID-19 were significant motivators, especially in this sub-group [32,33,43]. Among the never vaccinated subjects, two studies [30,33] reported that younger employees and females were more likely to change their attitudes due to the COVID-19 pandemic. Other primary reasons for influenza vaccine uptake included the desire to protect family members (as predominantly expressed by female HCWs), belonging to a high-risk category, and the intention to safeguard both patients and themselves [31,33,36,37,39,43]. Sani T et al. [39] reported that HCWs were aware that influenza vaccination for the 2020/21 season could help reduce the number of influenza cases among HCWs and facilitate the differential diagnosis and management of suspected COVID-19 cases. Scardina G et al. [34] reported that working in a COVID-19 ward did not influence influenza vaccination compliance, whereas strong promotion of vaccination by healthcare administration among personnel in close contact with patients was a determinant of a more favorable attitude.

Overall, one of the main determinants of vaccination compliance was having been vaccinated in previous influenza seasons and being willing to receive or having received the COVID-19 vaccine [33–35].

A better attitude toward the vaccine uptake was recorded in males [30,33,36,41,42] and physicians/medical residents [30,32–35,41,43]; indeed, Bertoni L et al. [30] reported that males and physicians were more compliant with vaccination campaigns over time, being more than twice and three times more likely to get vaccinated when compared with their counterparts. Albanesi B et al. [36] reported that during the 2020/21 influenza season, the median age of the vaccinated population increased compared to the previous one. Vaccinated HCWs primarily relied on scientific and institutional sources [32,33,36], although they expressed a desire for additional information from experts and Public Health institutions [32,33].

## 4. Conclusion

Our meta-analysis revealed that the COVID-19 pandemic had a significant influence on influenza vaccine uptake among HCWs (OR = 5.70; 95%CI = 2.08–15.60), particularly among health personnel working in nosocomial facilities (OR = 7.45; 95%CI = 3.88–14.30). This could be attributed to the added distress and challenges faced by HCWs in hospitals settings during the pandemic, such as hospital management issues, reformation of wards, increased awareness of being at higher risk of infection, and the complications of COVID-19. In contrast, community pharmacists, who have less close contact with patients, did not show the same level of influence from the pandemic. The systematic review supported the findings from the meta-analysis, reporting an increase in VC during the 2020/21 influenza season compared to the previous season (ranging from +17% to +38%).

Particularly, HCWs who had not been vaccinated in previous seasons were motivated by their concerns about COVID-19, leading them to choose to get the influenza shot in the 2020/21 season [37–39,41]. A longitudinal study published in 2022 [44] evaluated 938 non-HCWs subjects on the role of fear of COVID-19 in vaccination willingness, showing its relevance in predicting and possibly influencing vaccination willingness.

Several pieces of evidence highlight that health personnel can transmit influenza to patients at high risk of complications [45]. Our review emphasizes that protecting frailer individuals is a crucial determinant of a positive attitude among health personnel, especially considering the co-circulation of both viruses. Agreeing with Orr P [46], an HCW's duty of care includes helping patients, doing no harm, and obtaining informed consent; in this light, the seasonal influenza vaccination is part of this duty of care.

It is crucial to highlight that the 2020/21 influenza season was characterized by an unusually low circulation of the virus. The World Health Organization European Region reported a remarkable 99.8% reduction in sentinel influenza virus positive detections, with only 33 out of 25,606 tests showing positive results (0.1%), compared to an average of 14,966 out of 39,407 (38.0%;  $p < 0.001$ ) over the same period in the

previous six seasons [47]. This substantial decline in influenza cases can be attributed to the public health and physical distancing measures implemented during the COVID-19 pandemic; a correlation between the adoption of additional containment measures and a further decrease in Influenza-like Illness incidence has been observed [48]. Unfortunately, in the 2021/22 influenza season, a decrease in VC was reported by many authors in the literature [13,49,50] and by Public Health Institutions [17], returning to values similar to those achieved in the seasons before the COVID-19 pandemic; this evidence suggests that once the acute phase of the emergency was over, HCWs' attitude worsened, possibly due to the lack of a robust preventive culture [13]. Thus, achieving high VC among HCWs is once again a concern; evidence in the European scientific literature shows that a mandatory policy seems to be the fastest and most effective strategy for achieving high levels of immunity among healthcare personnel. Finland was the first European country to introduce a national mandatory seasonal influenza vaccination policy for HCWs in 2017; a survey investigating the application of this law on the health personnel of Kuopio University Hospital showed that VC increased from 59.5% to 99.6%, according to the hospital's records [4]. Another Finnish study [51] described the influenza VC among HCWs during seasons 2017/18, 2018/19, and 2019/20, reporting VC of 83.7% in the 2017/18 season, 90.8% in the 2018/19 season, and 87.6% in 2019/20 season. Di Lorenzo A et al. [52] described the Apulian Regional Law 19 June 2018 n. 27, which promoted the influenza vaccination as mandatory for health personnel working in high-risk wards; the VC reached among HCWs of Bari Policlinico University-General Hospital working in high-risk wards after the mandatory provision was 77.8% (+179% compared to the previous season). The opinion of European HCWs on this policy is generally favorable [4,53–55], even if, in some cases, health personnel think that it should be used as a last resort [56].

The main limitation of this meta-analysis was the small number of included studies and their high heterogeneity, as indicated by the  $I^2$  values; however, the use of random-effects analysis in the statistical analysis helped to minimize this bias, making it less critical. It is important to acknowledge that most of the included studies were from Italy, which might limit the generalizability of our results to other European countries and hinder performing a sub-analysis per geographic area. In Italy, there is a notable trend of publishing numerous scientific studies on vaccinology, particularly focusing on vaccination among healthcare workers. This phenomenon can be attributed to several factors: a strong tradition of scientific research and a well-established healthcare system, the emphasis on public health and disease prevention, a proactive approach to healthcare policy and its commitment to evidence-based medicine drive the generation of scientific evidence, and the collaboration between Italian researchers and healthcare professionals. While other European countries also conduct vaccination research, the specific focus on healthcare workers and the volume of studies in Italy may be a result of the convergence of these factors. Nonetheless, the systematic review included contributions from multiple European countries, providing a broader perspective. One strength of our meta-

analysis was the estimation of the OR regarding the association between influenza vaccine uptake and the COVID-19 pandemic, which had not been previously reported in the literature. Additionally, the systematic review focused on the main determinants of vaccination uptake during the pandemic in Europe, shedding light on essential factors influencing healthcare workers' vaccination decisions.

## 5. Expert opinion

The literature suggests that achieving better compliance in this sub-group population requires a multifactorial approach [57]. This approach should include active measures, such as offering on-site immunization clinics [58], conducting effective promotion campaigns [59], providing education and training for health personnel [60], and implementing communication campaigns by Public Health and Governmental institutions [61]. By protecting healthcare professionals and vulnerable patients, these measures ensure the safety of nosocomial structures, reduce absenteeism, and maintain efficient services for people. However, as reported in a 2022 review [6], no single intervention other than mandatory vaccination policies can consistently achieve high and sustainable influenza vaccination rates among HCWs; mandatory vaccination policies offer several advantages, such as easier and less costly implementation than voluntary programs, achieving high and sustainable vaccination rates within a few years, and promoting a culture of safety over health personnel's autonomy. Therefore, considering the common issue of vaccine hesitancy among HCWs in Europe, a mutual strategy must be implemented in all European countries [62]; however, reaching a common strategy may prove to be challenging. In light of the current epidemiological framework, hospital administrations must work diligently to overcome vaccine hesitancy among health personnel. Public Health institutions should also legislate policies to secure hospital wards and protect frailer subjects.

In recent times, the authors emphasize the urgency of implementing short-term mandatory vaccination policies targeting healthcare workers. These measures are considered a critical step in safeguarding public health and mitigating the risks posed by infectious diseases like COVID-19. The evidence reported in the literature shows that this strategy can lead to high VC among HCWs [4,51,52]. Simultaneously, the authors advocate for the development of medium-to-long-term strategies aimed at addressing vaccine hesitancy among HCWs and promoting a culture of prevention.

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## Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or material discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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## Author contributions

FPB and ST conceived the study. NS and DR did the literature research. FPB did the meta analysis. EC and AD participated in the design of the meta analysis. GM supervised the meta analysis. FPB and ST codrafted the first version of the article.

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