SYSTEMATIC REVIEW

Effectiveness of interventions to increase healthcare workers' adherence to vaccination against vaccine-preventable diseases: a systematic review and meta-analysis, 1993 to 2022

Marco Clari[1,*] , Beatrice Albanesi[1,*] , Rosanna Irene Comoretto[1] , Alessio Conti[1] , Erika Renzi[2] , Michela Luciani[3] , Davide Ausili[3] , Azzurra Massimi[2] , Valerio Dimonte[1,4]
1. Department of Sciences of Public Health and Paediatrics, University of Turin, Turin, Italy
2. Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy
3. Department of Medicine and Surgery, University of Milano - Bicocca, Milan Italy
4. Azienda Ospedaliero-Universitaria Città della Salute e della Scienza, Turin, Italy

* These authors contributed equally to this work and shared first authorship

Correspondence: Rosanna Irene Comoretto (rosannairene.comoretto@unito.it)

Background: Vaccination adherence among healthcare workers (HCWs) is fundamental for the prevention of vaccine-preventable diseases (VPDs) in healthcare. This safeguards HCWs' well-being, prevents transmission of infections to vulnerable patients and contributes to public health. **Aim:** This systematic review and meta-analysis aimed to describe interventions meant to increase HCWs' adherence to vaccination and estimate the effectiveness of these interventions. **Methods:** We searched literature in eight databases and performed manual searches in relevant journals and the reference lists of retrieved articles. The study population included any HCW with potential occupational exposure to VPDs. We included experimental and quasi-experimental studies presenting interventions aimed at increasing HCWs' adherence to vaccination against VPDs. The post-intervention vaccination adherence rate was set as the main outcome. We included the effect of interventions in the random-effects and subgroup meta-analyses. **Results:** The systematic review considered 48 studies on influenza and Tdap vaccination from database and manual searches, and 43 were meta-analysed. A statistically significant, positive effect was seen in multi-component interventions in randomised controlled trials (relative risk (RR)=1.37; 95% CI: 1.13–1.66) and in observational studies (RR=1.43; 95% CI: 1.29–1.58). Vaccination adherence rate was higher in community care facilities (RR=1.58; 95% CI: 1.49–1.68) than in hospitals (RR = 1.24; 95% CI: 0.76-2.05). **Conclusion:** Interventions aimed at increasing HCWs' adherence to vaccination against VPDs are effective, especially multi-component ones. Future research should determine the most effective framework of interventions for each setting, using appropriate study design for their evaluation, and should compare intervention components to understand their contribution to the effectiveness.
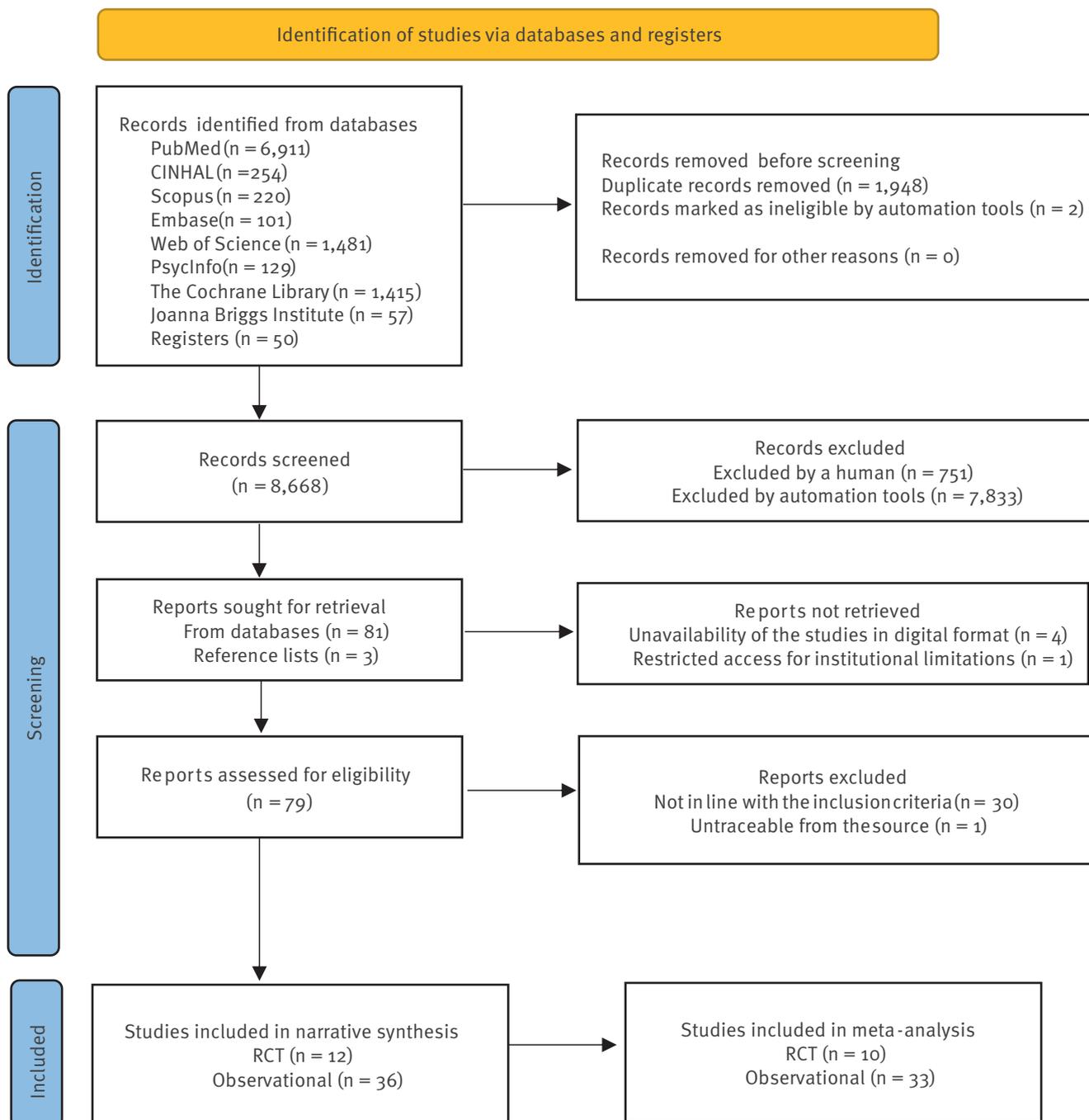
Introduction

Healthcare workers (HCWs) are at risk of contracting infectious disease at work and of transmitting infections to their patients, colleagues and families [1]. Indeed, HCWs are often sources of vaccine-preventable diseases (VPDs) in healthcare settings [1]. The World Health Organisation (WHO) estimates that ca 59 million HCWs worldwide are exposed to multiple occupational biohazards every day, through contact with infectious patients and with contaminated fluids and materials [2].

There are many benefits of vaccinating HCWs. Vaccination reduces the risk of infectious disease transmission within healthcare facilities and protect vulnerable patients [2]. Furthermore, vaccination can decrease illness and absenteeism among HCWs, which could lower the costs of healthcare services due to lost productivity [3]. Moreover, vaccinated HCWs are more likely to be knowledgeable about vaccinations and to be effective in improving confidence in vaccination among the general public [2,4]. Indeed, some studies have found that patients and their families consider vaccinated HCWs to be the most reliable sources of information regarding vaccinations, and a positive influence on their adherence to and trust in vaccinations [2,5,6]. During the COVID-19 pandemic,

FIGURE 1

PRISMA flowchart, systematic review on effectiveness of interventions to increase healthcare workers' adherence to vaccination

Identification of studies via databases and registers

Identification

Records identified from databases
PubMed (n = 6,911)
CINHAL (n =254)
Scopus (n = 220)
Embase(n = 101)
Web of Science (n = 1,481)
PsycInfo(n = 129)
The Cochrane Library (n = 1,415)
Joanna Briggs Institute (n = 57)
Registers (n = 50)

→ Records removed before screening
Duplicate records removed (n = 1,948)
Records marked as ineligible by automation tools (n = 2)

Records removed for other reasons (n = 0)

Screening

Records screened
(n = 8,668)

→ Records excluded
Excluded by a human (n = 751)
Excluded by automation tools (n = 7,833)

Reports sought for retrieval
From databases (n = 81)
Reference lists (n = 3)

→ Reports not retrieved
Unavailability of the studies in digital format (n = 4)
Restricted access for institutional limitations (n = 1)

Reports assessed for eligibility
(n = 79)

→ Reports excluded
Not in line with the inclusion criteria (n = 30)
Untraceable from the source (n = 1)

Included

Studies included in narrative synthesis
RCT (n = 12)
Observational (n = 36)

→ Studies included in meta-analysis
RCT (n = 10)
Observational (n = 33)

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the involvement of HCWs in establishing functional vaccination programmes played a key role in facilitating timely vaccination adherence and containing the spread of the virus [7].

Vaccination adherence is generally defined as receiving a vaccination according to the vaccine's label-recommended dose schedule [8]; it is a behaviour resulting from a decision-making process influenced by various determinants [9]. Within healthcare settings and among HCWs, vaccination adherence can exhibit notable differences [10,11]. It can be influenced by contextual immunisation programmes as well as policies, legal requirements, workplace and patients' characteristics [2]. Despite long-standing recommendations that HCWs receive vaccinations against VPDs, their adherence to routine vaccination schedules is often suboptimal, leading to concern about preventing healthcare-associated infections [2,10,11]. European Union (EU) data about 2020/21 seasonal influenza vaccination showed that average vaccination coverage among HCWs is lower than the recommended vaccination coverage of 75% (median: 52%; range: 16–71) [2,10]. The hepatitis B vaccination rate in HCW in the EU is about 50% (update 2022), far lower than the recommended 80% [12]. The coverage with booster vaccinations for tetanus-diphtheria-acellular pertussis (Tdap) is variable worldwide, ranging from 6.1% to 63.9%, compared with the recommended 60% [13].

An HCW's decision to get vaccinated involves a series of individual and social determinants [6,14,15]. Underestimation of the severity of disease and limited access to vaccination are among the major reasons for non-adherence among HCWs [5,14]. Furthermore, fear of side effects and misinformation or doubts about the effectiveness of vaccines seem to affect HCWs' vaccination behaviours negatively [5,6,11]. Professional roles and work settings can also influence vaccination adherence in HCWs [15-17]. Low vaccination coverage is more frequent in healthcare assistants and nurses than in physicians, suggesting that vaccination adherence differs among HCWs professional categories. Those HCWs working in hospital settings generally have higher vaccination adherence [7,18]. Maybe vaccines are more easily accessible in hospitals than community settings. For instance, in contexts where vaccine shortages are prevalent, access to vaccinations in community settings can be more challenging [5,7,18].

Therefore, targeted interventions are needed to increase HCWs' adherence to vaccination against VPDs. While systematic reviews have investigated determinants of HCWs' adherence to vaccination against VPDs [19], there is little evidence on the effectiveness of interventions that aim to increase this adherence. Previous reviews or meta-analyses that assessed such interventions focused on seasonal influenza vaccination [20-23]; only one review evaluated Tdap vaccination among HCWs [24]. In particular, the systematic reviews by Rashid et al. [23], Hollmeyer et al. [20] and Lam et

al. [21], as well as the meta-regression by Lytras et al. [22], classified interventions that aimed to increase seasonal influenza vaccination coverage among HCWs and evaluated their effectiveness. However, to the best of our knowledge, no recent studies have performed an overall evaluation of interventions that meant to increase HCWs' adherence to vaccination against VPDs; instead, most existing reports cover the general population [25]. Also, no studies have tested the effectiveness of such interventions in subgroups of HCWs or healthcare settings. Furthermore, the literature is still fragmented and lacks a broad description of intervention characteristics, types, components, operational strategies and effectiveness. A better understanding of these could improve future vaccination campaigns and maximise healthcare resources.

The objective of this systematic review and meta-analysis was to describe interventions meant to increase HCWs' adherence to vaccination against VPDs and to estimate the effectiveness of these interventions. More specifically, this study will provide evidence to answer the following research questions: (i) What interventions have been designed to increase HCWs' adherence to vaccination against VPDs? (ii) What are the characteristics, types, components and operational strategies of these interventions? (iii) What was the effectiveness of each intervention? And (iv) are there any differences in effectiveness across subgroups of professional categories of HCWs or across healthcare settings?

Methods
A systematic literature review and meta-analysis was conducted according to the updated Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines [26]; the PRISMA checklist is appended in the Supplement. The review protocol was registered in PROSPERO (CRD42020212252). In line with the original protocol, we included studies that evaluated vaccination adherence against VPDs by all HCWs.

Search strategy
One investigator (BA) with experience carried out the literature searches under the supervision of a health librarian. To create an exhaustive search strategy and identify the most appropriate keywords, an explorative search of PubMed and CINAHL EBSCO was conducted in July 2022, followed by an analysis of the resultant titles and abstracts. Eight databases (PubMed, CINAHL EBSCO, Scopus, EMBASE, Web of Science, PsycInfo, The Cochrane Library and Joanna Briggs Institute) were searched from their beginning to 7 August 2022. Search strategies employed both thesaurus and free terms and were adapted for each database. The same author (BA) conducted manual searches in high-quality and relevant journals in the field – a list of which was taken from SCImago and Web of Science [27] – and on the reference lists of retrieved articles, to identify any additional relevant studies. A list of search terms is appended in the Supplement. No time limits were

Characteristics of included studies on effectiveness of interventions to increase healthcare workers' adherence to vaccination (n = 48)

Article (country, year)	Setting	Vaccination	Study period	Participants[a]	Sample size		Intervention
					Intervention	Control	
Randomised controlled trials (n = 12)							
Abramson [47] (Israel, 2010)	Community care	Seasonal influenza	2007–2008 (1 year)	Overall: 344 (physicians: 121; nurses: 68; other HCWs: 155)	163	181	Educational + promotional + policy
Borgey [49] (France, 2019)	Community care	Seasonal influenza	2014–2015 (1 year)	Overall: 1,336	496	840	Educational + promotional + policy
Chambers [52] (Canada, 2015)	Hospital and community	Seasonal influenza	2008–2012 (3 years)	Overall: 496,825[a]	165,079	331,746	Educational
Currat [55] (Switzerland, 2020)	Hospital	Seasonal influenza	2016 (2 weeks)	Overall: 357 (physicians: 116; nurses: 158; other HCWs: 83)	185	172	Educational
Dey [56] (UK, 2001)	Community care	Seasonal influenza	1999 (2 months)	Overall: 2,984 (physicians: 212; nurses: 1,531; healthcare assistants: 1,129; other HCWs: 112)	1,225	1,759	Educational + promotional
Golebiak [43][b] (Poland, 2020)	Hospital	Seasonal influenza	2017–2018 (1 year)	Overall: 327	245	82	Educational
Kimura [64] (US, 2007)	Community care	Seasonal influenza	2000–2002 (2 years)	Overall: 3,924 (nurses: 2,600; healthcare assistants: 1,000; other HCWs: 324)	2,407	1,517	Educational + promotional
Looijmans-van den Akker [67] (the Netherlands, 2010)	Community care	Seasonal influenza	2006 (1 year)	Overall: 6,608 (physicians: 733; nurses: 1,054; healthcare assistants: 4,821)	3,058	3,550	Educational + promotional
Rothan – Tondeur [75] (France, 2010)	Hospital	Seasonal influenza	2005–2006 (2 years)	Overall: 2,345 (physicians: 153; nurses: 586; healthcare assistants: 1,115: other HCWs: 491)	1,201	1,144	Educational
Rothan – Tondeur [76] (France, 2011)	Hospital	Seasonal influenza	2006–2007 (2 years)	Overall: 2,874 (physicians: 302; nurses: 686; healthcare assistants: 1,506: other HCWs: 380)	1,335	1,539	Educational
Saunier [77] (France, 2020)	Hospital	Seasonal influenza	2018–2019 (1 year)	Overall: 3,547	1,968	1,579	Informative

NS: not specified; Tdap: tetanus, diphtheria, pertussis; UK: United Kingdom; US: United States.

[a] Overall means overall sample of the study. For RCTs, 'Overall' is the sum of cases and controls. For observational studies, 'Overall' is the overall sample of the study (composed by both vaccinated and unvaccinated before and after intervention).

[b] Article not meta-analysed.

Characteristics of included studies on effectiveness of interventions to increase healthcare workers' adherence to vaccination (n = 48)

Article (country, year)	Setting	Vaccination	Study period	Participants[a]	Sample size		Intervention
Schmidtke [45][b] (UK, 2020)	Community care	Seasonal influenza	2019–2020 (1 year)	Overall: 8,438 (physicians: 1,440; nurses: 4,478; healthcare assistants: 2,520)	7,540	898	Educational + promotional + policy
Observational (n = 36)					Vaccinated after intervention	Vaccinated before intervention	
Babcock [42][b] (US, 2010)	Hospital and community	Seasonal influenza	2008–2009 (1 year)	Overall: NS	25,561	25,980	Educational + promotional + policy
Bert [48] (Italy, 2019)	Hospital	Seasonal influenza	2017–2018 (1 year)	Overall: 1,186	503	373	Educational + promotional
Boey [18] (Belgium, 2021)	Community care	Seasonal influenza	2016–2017 (1 year)	Overall: 828	368	378	Educational + promotional
Butteri [50] (US, 2010)	Hospital	Seasonal influenza	2007–2008 (1 year)	Overall: 106	77	69	Educational
Calderon [51] (US, 2008)	Hospital	Tdap	2007–2008 (1 year)	Overall: 1,281	484	447	Educational + promotional
Chittaro [53] (Italy, 2009)	Hospital	Seasonal influenza	2004–2006 (2 years)	Overall: 473 (physicians: 106; nurses: 254; healthcare assistants: 113)	283	49	Educational + promotional
Conte [84] (Italy, 2016)	Hospital	Seasonal influenza	2013–2014 (1 year)	Overall: 881 (physicians: 251; nurses: 423; healthcare assistants: 157; other HCWs: 50)	221	164	Educational + promotional
Cozza [54] (Italy, 2015)	Hospital	Seasonal influenza	2009–2013 (5 years)	Overall: 792	35	162	Educational + promotional
de Juanes [57] (Spain, 2007)	Hospital	Seasonal influenza	2002–2004 (2 years)	Overall: 5,654 (physicians: 1,177; nurses: 1,758; healthcare assistants: 2,719)	3,449	905	Educational + promotional
Frenzel [58] (US, 2016)	Hospital	Seasonal influenza	2006–2014 (8 years)	Overall: 34,807	17,927	8,762	Educational + promotional + policy

NS: not specified; Tdap: tetanus, diphtheria, pertussis; UK: United Kingdom; US: United States.

[a] Overall means overall sample of the study. For RCTs, 'Overall' is the sum of cases and controls. For observational studies, 'Overall' is the overall sample of the study (composed by both vaccinated and unvaccinated before and after intervention).

[b] Article not meta-analysed.

Table 1c

Characteristics of included studies on effectiveness of interventions to increase healthcare workers' adherence to vaccination (n = 48)

Article (country, year)	Setting	Vaccination	Study period	Participants[a]	Sample size		Intervention
Frisina [59] (US, 2019)	Hospital	Seasonal influenza	2014–2018 (4 years)	Overall: 102	92	72	Educational + promotional
Gilardi [60] (Italy, 2018)	Hospital	Seasonal influenza	2016–2018 (2 years)	Overall: 4,254 (physicians: 1,044; nurses: 2,133; healthcare assistants: 1,077)	369	278	Educational + promotional
Heinrich – Morrison [61] (Australia, 2015)	Hospital and community	Seasonal influenza	2013–2014 (1 year)	Overall: 14,359 (physicians: 2,188; nurses: 6,517; healthcare assistants: 2,646; other HCWs: 3,008)	6,009	3,866	Educational + promotional
Jiang [62] (US, 2018)	Hospital	Tdap	2014–2015 (1 year)	Overall: 1,997 (physicians: 747; nurses: 1,050; other HCWs: 200)	911	571	Educational + promotional
Kim [63] (US, 2018)	Hospital and community	Seasonal influenza	2011–2013 (3 years)	Overall: 690	301	240	Educational + promotional
Kuntz [65] (US, 2008)	Hospital	Seasonal influenza	2003–2006 (3 years)	Overall: 26,959	6,539	5,741	Educational + promotional
Leitmeyer [66] (Germany, 2006)	Hospital	Seasonal influenza	2002–2004 (2 years)	Overall: 792 (physicians: 306; nurses: 286; other HCWs: 200)	103	83	Educational + promotional + policy
Llupìa [83] (Spain, 2010)	Hospital	Seasonal influenza	2007–2009 (2 years)	Overall: 9,632 (physicians: 2,127; nurses: 2,867; healthcare assistants: 1,429; other HCWs: 3,209)	1,769	1,091	Educational + promotional + policy
Marwaha [68] (Canada, 2016)	Hospital	Seasonal influenza	2013 (1 year)	Overall: 19,398	2,062	2,439	Educational + promotional
Nace [69] (US, 2011)	Community care	Seasonal influenza	2002–2003 (1 year)	Overall: 2,550	485	432	Educational + promotional
Ofstead [85] (US, 2017)	Community care	Seasonal influenza	2014–2015 (1 year)	Overall: 2,732	640	726	Educational + promotional
Oguz [16] (Türkiye, 2019)	Hospital	Seasonal influenza	2016–2018 (2 years)	Overall: 1,144 (physicians: 403; nurses: 386; healthcare assistants: 355)	228	62	Policy

NS: not specified; Tdap: tetanus, diphtheria, pertussis; UK: United Kingdom; US: United States.

[a] Overall means overall sample of the study. For RCTs, 'Overall' is the sum of cases and controls. For observational studies, 'Overall' is the overall sample of the study (composed by both vaccinated and unvaccinated before and after intervention).

[b] Article not meta-analysed.

Characteristics of included studies on effectiveness of interventions to increase healthcare workers' adherence to vaccination (n = 48)

Article (country, year)	Setting	Vaccination	Study period	Participants[a]	Sample size		Intervention
Paranthaman [70] (UK, 2016)	Hospital	Tdap	2012 (1 year)	Overall: 553	121	389	Educational + promotional
Podczervinski [71] (US, 2015)	Hospital	Seasonal influenza	2010–2013 (3 years)	Overall: 3,087	1,583	1,264	educational + promotional + policy
Qureshi [44][b] (UK, 2004)	Hospital	Seasonal influenza	2000–2001 (1 year)	Overall: 530 (physicians: 31; nurses: 290; healthcare assistants: 35; other HCWs: 158; not specified: 16)	514	NS	Educational + promotional
Rakita [72] (US, 2010)	Hospital and community	Seasonal influenza	2005–2010 (5 years)	Overall: 9,727	4,967	4,588	Educational + promotional + policy
Ribner [73] (US, 2008)	Hospital and community	Seasonal influenza	2006–2007 (1 year)	Overall: 18,264	6,123	3,892	Educational + promotional + policy
Rodriguez-Fernandez [74] (Spain, 2016)	Hospital and community	Seasonal influenza	2012–2013 (1 year)	Overall: 685 (physicians: 190; nurses: 294; healthcare assistants: 201)	137	105	Educational
Sartor [17] (France, 2004)	Hospital	Seasonal influenza	2000–2002 (2 years)	Overall: 2,512 (physicians: 396; nurses: 707; other HCWs: 1,409)	654	587	Educational + promotional
Smedley [78] (UK, 2002)	Hospital	Seasonal influenza	1998–1999 (1 year)	Overall: 13,268 (physicians: 1,564; nurses: 5,947; healthcare assistants: 866; other HCWs: 4,891)	292	156	Educational + promotional
Smithers [79] (Australia, 2003)	Hospital	Seasonal influenza	2000–2001 (1 year)	Overall: 541 (physicians: 161; nurses: 283; other HCWs: 97)	65	51	Policy
Song [86] (Korea, 2006)	Hospital	Seasonal influenza	2013–2014 (1 year)	Overall: 2,227 (physicians: 1,020; nurses: 1,000; other HCWs: 207)	882	253	Educational + promotional
Tapiainen [80] (Switzerland, 2005)	Hospital	Seasonal influenza	2003–2005 (2 years)	Overall: 1,092 (physicians: 193; nurses: 643; other HCWs: 256)	133	100	Educational + promotional
Thomas [46][b] (US, 1993)	Community care	Seasonal influenza	1990–1991 (1 year)	Overall: 868 (physicians: 101; nurses: 200; other HCWs: 567)	54	46	Educational + promotional + policy
Walther [81] (Switzerland, 2015)	Hospital	Tdap	2012–2013 (1 year)	Overall: 854 (physicians: 186; nurses: 525; other HCWs: 143)	304	72	Educational + promotional
Zimmerman [82] (US, 2009)	Hospital and community	Seasonal influenza	2005–2007 (2 years)	Overall: 53,668	10,784	8,565	Educational + promotional

NS: not specified; Tdap: tetanus, diphtheria, pertussis; UK: United Kingdom; US: United States.

[a] Overall means overall sample of the study. For RCTs, 'Overall' is the sum of cases and controls. For observational studies, 'Overall' is the overall sample of the study (composed by both vaccinated and unvaccinated before and after intervention).

[b] Article not meta-analysed.

applied, and the search was limited to articles written in English and Italian.

Eligibility and exclusion criteria

Studies were evaluated based on PICOS criteria

Population
We used the lists of disciplines developed by the WHO [28,29] and the international classification of HCWs [29] to determine which HCWs to include. To be eligible for inclusion, studies had to report information on HCWs from the disciplines of medicine (e.g. physicians, resident physicians), nursing (e.g. registered nurses, licensed practical nurses) or healthcare assistants, (e.g. healthcare unit assistants, nurse aids) who worked in healthcare settings and had the potential to be exposed to patients and/or to infectious materials. If authors reported on other disciplines (e.g. physiotherapists, radiology technicians, midwives), these disciplines were also considered. However, in studies that reported results from both HCWs and general staff (people who did not provide direct care to patients, e.g. cleaners, drivers, administrative staff and other disciplines) [28], we included only the HCWs in the review and meta-analysis.

Intervention
Studies of interventions aimed at increasing adherence, coverage, uptake or compliance to vaccination against VPDs among HCWs, in any setting or facility (i.e. public, private, teaching hospital, community care, home care) were eligible for inclusion. We excluded studies that described interventions that aimed to assess only HCWs' knowledge, attitudes, vaccination intentions or behaviours, or interventions acting on the determinants of vaccination.

Comparator
We used an inactive control (e.g. standard vaccination practice, none).

Outcomes
We defined as outcome the post-intervention vaccination adherence rate, i.e. the proportion of HCWs reporting vaccination divided by the total study sample participating in the interventions.

Study design
Studies with experimental (e.g. randomised and non-randomised controlled trials) and quasi-experimental (hereafter referred to as observational, e.g. pre–post evaluation studies) designs were eligible for inclusion. Qualitative studies, protocols, proceedings, guidelines, discussion/editorials and reviews were excluded, but the reference lists of relevant reviews were screened for additional relevant articles that could be included here.

Recommended vaccinations for HCWs were defined as those put forth by the WHO [30] and considered vaccinations against diseases such as: diphtheria, *Haemophilus influenzae* type b infection, hepatitis A and B, influenza (seasonal), measles, meningococcal infections, mumps, pertussis, pneumococcal infections, poliomyelitis, rubella, tetanus and varicella (we chose to not include other recommended vaccinations such as for example Japanese encephalitis as these are not frequently encountered in Western countries). Furthermore, we excluded COVID-19 and human papillomavirus vaccines because COVID-19 specifically referred to the pandemic context and human papillomavirus vaccines are mainly targeted at a younger age group. In the case of articles with limited or unclear information on the PICOS criteria, the first or corresponding author was contacted by email. If no response was received, the article was excluded.

Screening and data collection
The reference manager programme Endnote 20 [31] was used to collate articles identified in the databases and to identify duplicates. The titles and abstracts of remaining articles were then independently screened by two authors (BA and AC) using the automated tool Rayyan [32]. The full texts of studies that passed this screening were retrieved and assessed for eligibility. During this assessment, any disagreement or uncertainty regarding article inclusion was solved through consensus with a third author (MC). Data on study characteristics (design, setting, vaccination type and study period), participants, sample size, intervention type, components and operational strategies were extracted from included articles using a specifically designed data collection form; narrative descriptions for the meta-analysis were independently extracted by two authors (BA and AC). Disagreements and uncertainties were solved by consensus with a third researcher who is an expert in meta-analyses (MC). The data collection form was piloted on five studies, and appropriate adjustments were made before definitive data aggregation.

Assessment of methodological quality and risk of bias
The methodological quality of included articles was independently assessed by two authors (BA, AC) using the Quality Assessment Tool for Controlled Intervention Studies and the Quality Assessment Tool for Before–After (Pre–Post) Studies with No Control Group developed by the National Heart, Lung, and Blood Institute [33]. The use of these two distinct tools ensured a comprehensive evaluation of study quality and allowed us to appropriately assess the quality of studies with different designs and methodologies. Each criterion was evaluated according to the tool's questions, assigning cannot determine (CD), no (N), not reported (NR) or yes (Y). Based on this evaluation, the quality of included studies was rated as good (with only one CD, N, NR), fair (with two CD, N, NR) or poor (with more than two CD, N, NR). Any disagreement in the assessment of quality was solved through discussion with a third author (AC). Furthermore, two authors (BA, MC) assessed the risk

Study quality and risk of bias of publications on effectiveness of interventions to increase healthcare workers' adherence to vaccination (n = 48)

A. Randomised controlled trials

B. Observational studies

Domains:
D1: Bias arising from the randomisation process
D2: Bias due to deviations from intended intervention
D3: Bias due to missing outcome data
D4: Bias in measurement of the outcome
D5: Bias in selection of the reported result

Judgement
✕ High
– Some concerns
+ Low

Domains:
D1: Bias due to confounding
D2: Bias due to selection of participants
D3: Bias in classification of interventions
D4: Bias due to deviations from intended interventions
D5: Bias due to missing data
D6: Bias in measurement of outcomes
D7: Bias in selection of the reported result

Judgement
● Critical
✕ Serious
– Moderate
+ Low

of bias of included studies, using the Cochrane Risk-of-Bias tool for Randomised Trials (RoB 2) for randomised controlled trials (RCTs) [34] and the Risk of Bias In Non-Randomised Studies of Interventions (ROBINS-I) tool for observational studies [35]. These two instruments assessed the risk of bias in terms of randomness and concealment of subject allocation, blinding of subjects and outcome assessors, proportion of missing data, selective reporting and other sources of bias. The risk of bias for each domain was then categorised as low, some concerns or high for the RoB 2, and as low, moderate or high for ROBINS-I.

Data overview and meta-analysis

The summary relative risk (RR) for the experimental group (or post-intervention timing in observational studies) as compared with the control group (or pre-intervention timing) was estimated using both the fixed-effects model and the random-effects model

proposed by DerSimonian and Laird [36]. We estimated both 95% confidence intervals (CIs) and 95% prediction intervals [37]. When significant heterogeneity was found, we present the results from the random-effects model. The heterogeneity between study-specific estimates was measured with the I^2 statistic [38]. Statistical significance level was set at a p value < 0.05.

We performed subgroup analyses to assess the effect that different intervention types (mono-component vs multi-component), professional categories (physicians, nurses, healthcare assistants and other HCWs) and healthcare settings (hospital, community care and facilities providing both hospital and community care services) had on post-intervention vaccination adherence rate. Sensitivity analyses were performed using the leave-one-out technique to control between-study heterogeneity [39]. A separate sensitivity analysis that excluded studies with a poor quality rating was also

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performed. Publication bias was evaluated through funnel plot inspection and the Egger's test [40]. Analyses were performed using the statistical programme R with *metafor* and *meta* packages [39,41]. We performed a systematic narrative synthesis to present available data for all studies that could not be included in the meta-analyses.

Results

Search strategies identified a total of 10,618 articles (Figure 1). After the removal of duplicates, the title and abstract of 8,668 articles were screened, leading to the exclusion of 8,584 articles. This left 84 articles to be retrieved and their full texts assessed for eligibility. Five of these could not be retrieved and the authors could not be contacted, so 79 articles were finally assessed for eligibility. Of these 79 articles, 31 were excluded: thirty did not meet the inclusion criteria, and one was untraceable from any sources (Figure 1). After the full-text evaluation, 48 articles were included in the systematic review. Five of those articles [42-46] were not eligible for the meta-analysis, which finally included 43 articles [16-18,47-86].

Study characteristics

The characteristics of the included studies are summarised in Table 1. The earliest study was reported in 1993 [46], with a peak in publication from 2014 to 2019 (n = 16). The studies were conducted in the EU (n = 25), mainly in France (n = 5) and Italy (n = 5), and in the US (n = 16), Canada (n = 2), Israel (n = 1), South Korea (n = 1) and Türkiye (n = 1). Twelve studies were RCTs [43,45,47,49,52,55,56,64,67,75-77], while 36 had an observational design [16-18,42,44,46,48,50,51,53,54,57-63,65,66,68-74,78-86]. Among the RCTs, three were cluster-randomised trials [49,67,77] and three had a 2 × 2 factorial design [43,45,64]. Randomisation in the RCTs was performed at the individual level [45,47,49,52,56,64,67] and at the unit (hospital/hospital ward) level [43,55,75-77]. Forty-four articles provided interventions for seasonal influenza vaccination [16-18,42-50,52-61,63-69,71-80,82-86], and four were on Tdap vaccination [51,62,70,81]. Studies recruited participants mainly in hospital settings (n = 30) [16,17,43,44,48,50,51,53-55,57-60,62,65,66,68,70,71,75-81,83,84,86] but 10 enrolled participants from community care [18,45-47,49,56,64,67,69,85]. The remaining studies were performed in facilities that provided both hospital and community care services (n = 8) [42,52,61,63,72-74,82]. Study periods ranged from 2 weeks [55] to 8 years [58].

Participants

A total of 768,402 HCWs were included in the 48 studies. Sample sizes ranged from 327 [43] to 496,825 [52] in RCTs, and from 102 [59] to 51,541 [42] in observational studies. Twenty-six studies [16,17,44-47,53,55-57,60-62,64,66,67,74-76,78-81,83,84,86] specified the number of participating HCWs: physicians accounted for 15,268 participants, nurses for 36,724 and healthcare assistants for 21,689. There were 15,940

participants who fell into the category of other HCWs, including rehabilitation technicians, pharmacists and laboratory staff. Twenty-two articles did not specify the number or professional category of HCWs [14,42,43,48-52,54,58,59,63,65,68-73,77,82,85]. The age of participants ranged from 18 to 66 years. The majority of HCWs were female (n = 55,310); males accounted for 4,202 participants. Only four articles [43,54,60,86] considered HCWs' duration of employment, with a minimum of 2 years [60] and a maximum over 40 years [43].

Interventions

The components of interventions were classified as informational when they involved the distribution of instructive or decision-aid tools such as leaflets or booklets which provided essential evidence-based information about VPDs and vaccines or facilitated well-informed decision making of HCWs. They were defined as promotional when the interventions included active promotion of information or education on vaccines and vaccinations through broad campaigns that included operational strategies such as communicational or promotional activities. Components were defined as educational when the intervention aimed to change HCWs' knowledge and/or attitudes, or applied specific educational methodologies or strategies such as role playing or video-modelling. Lastly, components were classified as policy when the interventions proposed programmes, activities or mandated actions by regulatory authorities or healthcare organisations.

Based on the number of components, interventions were organised into two overarching types: mono-component (containing one component, e.g. an educational component only) and multi-component interventions (containing two or more components, e.g. an educational and a promotional component). The majority of studies investigated multi-component interventions (n = 38) [17,18,42,44-49,51,53,54,56-73,78,80-86]. Among these, 27 used a combination of educational and promotional components, and 11 used a combination of educational, promotional and policy components. Ten studies [16,43,50,52,55,74-77,79] used mono-component interventions such as an educational component (n = 7), a policy component (n = 2) or an informational component (n = 1) alone. The operational strategies applied for each component were organised by contents, modalities of intervention delivering, tools employed and the frequency and number of sessions that the intervention comprised (all components and interventions for each study are detailed in the Supplement).
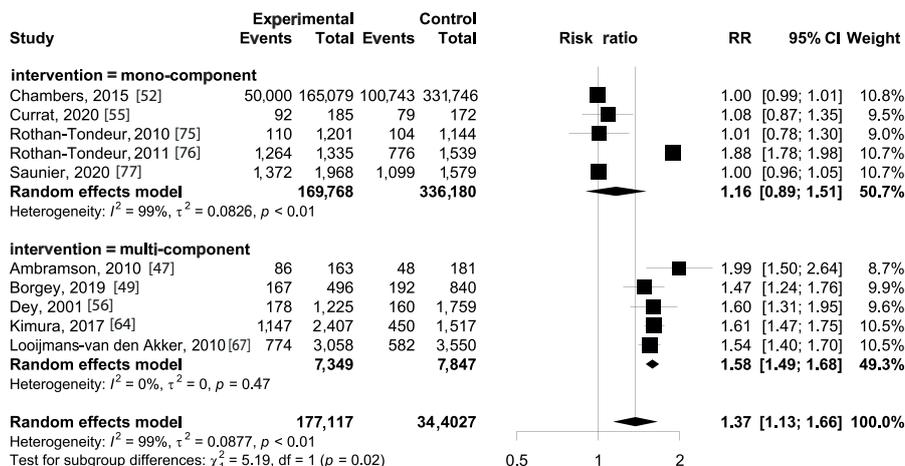
Mono-component interventions

Informational
Saunier et al. [77] investigated an intervention with an informational component in which an informative leaflet and a decision aid tool on seasonal influenza vaccination was distributed to HCWs. The leaflet listed five bullet points which contained information on seasonal
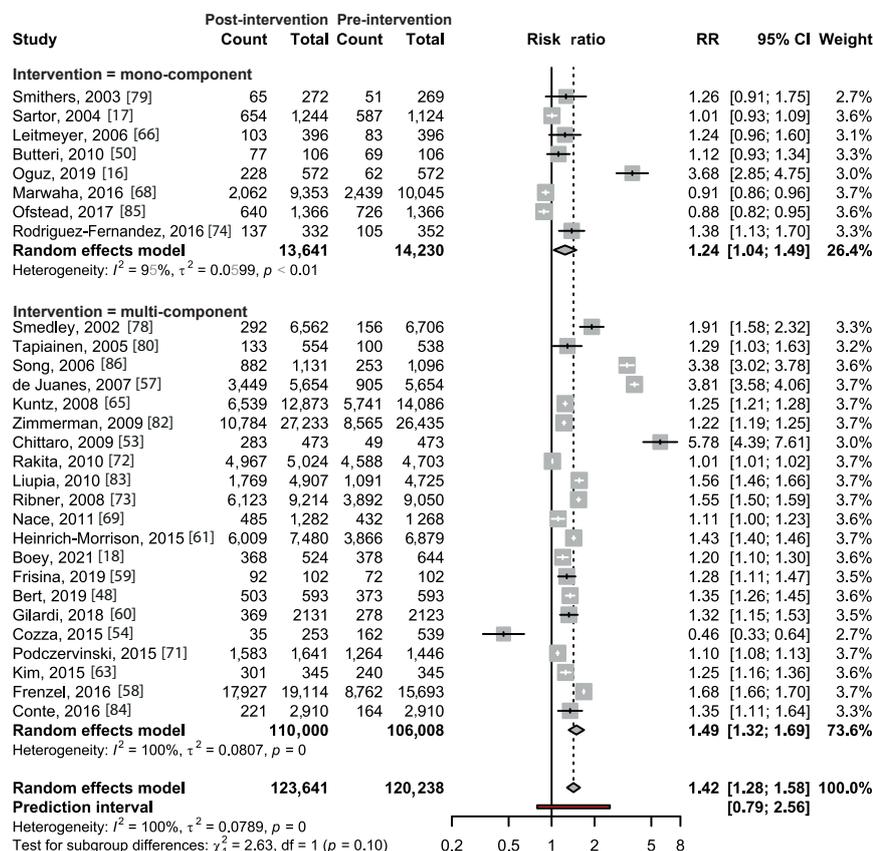
Plots of random-effects meta-analysis stratified by vaccination and type of intervention for publications on effectiveness of interventions to increase healthcare workers' adherence to vaccination (n = 43)
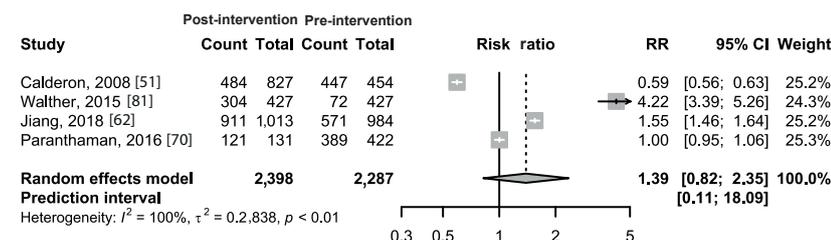
A. Randomised controlled trials

Study	Experimental Events	Total	Control Events	Total	Risk ratio	RR	95% CI	Weight
intervention = mono-component								
Chambers, 2015 [52]	50,000	165,079	100,743	331,746		1.00	[0.99; 1.01]	10.8%
Currat, 2020 [55]	92	185	79	172		1.08	[0.87; 1.35]	9.5%
Rothan-Tondeur, 2010 [75]	110	1,201	104	1,144		1.01	[0.78; 1.30]	9.0%
Rothan-Tondeur, 2011 [76]	1,264	1,335	776	1,539		1.88	[1.78; 1.98]	10.7%
Saunier, 2020 [77]	1,372	1,968	1,099	1,579		1.00	[0.96; 1.05]	10.7%
Random effects model		**169,768**		**336,180**		**1.16**	**[0.89; 1.51]**	**50.7%**
Heterogeneity: $I^2 = 99\%$, $\tau^2 = 0.0826$, $p < 0.01$								
intervention = multi-component								
Ambramson, 2010 [47]	86	163	48	181		1.99	[1.50; 2.64]	8.7%
Borgey, 2019 [49]	167	496	192	840		1.47	[1.24; 1.76]	9.9%
Dey, 2001 [56]	178	1,225	160	1,759		1.60	[1.31; 1.95]	9.6%
Kimura, 2017 [64]	1,147	2,407	450	1,517		1.61	[1.47; 1.75]	10.5%
Looijmans-van den Akker, 2010 [67]	774	3,058	582	3,550		1.54	[1.40; 1.70]	10.5%
Random effects model		**7,349**		**7,847**		**1.58**	**[1.49; 1.68]**	**49.3%**
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.47$								
Random effects model		**177,117**		**34,4027**		**1.37**	**[1.13; 1.66]**	**100.0%**
Heterogeneity: $I^2 = 99\%$, $\tau^2 = 0.0877$, $p < 0.01$								
Test for subgroup differences: $\chi_1^2 = 5.19$, df = 1 ($p = 0.02$)								

B. Observational studies

Study	Post-intervention Count	Total	Pre-intervention Count	Total	Risk ratio	RR	95% CI	Weight
Intervention = mono-component								
Smithers, 2003 [79]	65	272	51	269		1.26	[0.91; 1.75]	2.7%
Sartor, 2004 [17]	654	1,244	587	1,124		1.01	[0.93; 1.09]	3.6%
Leitmeyer, 2006 [66]	103	396	83	396		1.24	[0.96; 1.60]	3.1%
Butteri, 2010 [50]	77	106	69	106		1.12	[0.93; 1.34]	3.3%
Oguz, 2019 [16]	228	572	62	572		3.68	[2.85; 4.75]	3.0%
Marwaha, 2016 [68]	2,062	9,353	2,439	10,045		0.91	[0.86; 0.96]	3.7%
Ofstead, 2017 [85]	640	1,366	726	1,366		0.88	[0.82; 0.95]	3.6%
Rodriguez-Fernandez, 2016 [74]	137	332	105	352		1.38	[1.13; 1.70]	3.3%
Random effects model		**13,641**		**14,230**		**1.24**	**[1.04; 1.49]**	**26.4%**
Heterogeneity: $I^2 = 95\%$, $\tau^2 = 0.0599$, $p < 0.01$								
Intervention = multi-component								
Smedley, 2002 [78]	292	6,562	156	6,706		1.91	[1.58; 2.32]	3.3%
Tapiainen, 2005 [80]	133	554	100	538		1.29	[1.03; 1.63]	3.2%
Song, 2006 [86]	882	1,131	253	1,096		3.38	[3.02; 3.78]	3.6%
de Juanes, 2007 [57]	3,449	5,654	905	5,654		3.81	[3.58; 4.06]	3.7%
Kuntz, 2008 [65]	6,539	12,873	5,741	14,086		1.25	[1.21; 1.28]	3.7%
Zimmerman, 2009 [82]	10,784	27,233	8,565	26,435		1.22	[1.19; 1.25]	3.7%
Chittaro, 2009 [53]	283	473	49	473		5.78	[4.39; 7.61]	3.0%
Rakita, 2010 [72]	4,967	5,024	4,588	4,703		1.01	[1.01; 1.02]	3.7%
Liupia, 2010 [83]	1,769	4,907	1,091	4,725		1.56	[1.46; 1.66]	3.7%
Ribner, 2008 [73]	6,123	9,214	3,892	9,050		1.55	[1.50; 1.59]	3.7%
Nace, 2011 [69]	485	1,282	432	1 268		1.11	[1.00; 1.23]	3.6%
Heinrich-Morrison, 2015 [61]	6,009	7,480	3,866	6,879		1.43	[1.40; 1.46]	3.7%
Boey, 2021 [18]	368	524	378	644		1.20	[1.10; 1.30]	3.6%
Frisina, 2019 [59]	92	102	72	102		1.28	[1.11; 1.47]	3.5%
Bert, 2019 [48]	503	593	373	593		1.35	[1.26; 1.45]	3.6%
Gilardi, 2018 [60]	369	2131	278	2123		1.32	[1.15; 1.53]	3.5%
Cozza, 2015 [54]	35	253	162	539		0.46	[0.33; 0.64]	2.7%
Podczervinski, 2015 [71]	1,583	1,641	1,264	1,446		1.10	[1.08; 1.13]	3.7%
Kim, 2015 [63]	301	345	240	345		1.25	[1.16; 1.36]	3.6%
Frenzel, 2016 [58]	17,927	19,114	8,762	15,693		1.68	[1.66; 1.70]	3.7%
Conte, 2016 [84]	221	2,910	164	2,910		1.35	[1.11; 1.64]	3.3%
Random effects model		**110,000**		**106,008**		**1.49**	**[1.32; 1.69]**	**73.6%**
Heterogeneity: $I^2 = 100\%$, $\tau^2 = 0.0807$, $p = 0$								
Random effects model		**123,641**		**120,238**		**1.42**	**[1.28; 1.58]**	**100.0%**
Prediction interval							**[0.79; 2.56]**	
Heterogeneity: $I^2 = 100\%$, $\tau^2 = 0.0789$, $p = 0$								
Test for subgroup differences: $\chi_1^2 = 2.63$, df = 1 ($p = 0.10$)								

C. Tdap vaccination

Study	Post-intervention Count	Total	Pre-intervention Count	Total	Risk ratio	RR	95% CI	Weight
Calderon, 2008 [51]	484	827	447	454		0.59	[0.56; 0.63]	25.2%
Walther, 2015 [81]	304	427	72	427		4.22	[3.39; 5.26]	24.3%
Jiang, 2018 [62]	911	1,013	571	984		1.55	[1.46; 1.64]	25.2%
Paranthaman, 2016 [70]	121	131	389	422		1.00	[0.95; 1.06]	25.3%
Random effects model	**2,398**		**2,287**			**1.39**	**[0.82; 2.35]**	**100.0%**
Prediction interval							**[0.11; 18.09]**	
Heterogeneity: $I^2 = 100\%$, $\tau^2 = 0.2,838$, $p < 0.01$								

CI: confidence interval; RR: relative risk; Tdap: tetanus-diphtheria-acellular pertussis.

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TABLE 2

Sub-group meta-analyses of interventions to increase healthcare workers' adherence to vaccination, by category of work and setting (n = 43 interventions)

	Number of studies	RR	95% CI
Randomised controlled trials			
HCW category			
Physicians	4	1.37	1.13–1.66
Nurses	4	1.59	1.06–2.40
Healthcare assistants	3	1.41	1.06–1.87
Others	2	1.29	1.02–1.62
Random effects		1.43	1.25–1.64
I^2	79% (p < 0.01)		
x^2	0.84 (p = 0.84)		
Settings			
Hospital	3	1.24	0.76–2.05
Community care	5	1.58	1.49–1.68
Hospital and community care	2	1.00	0.99–1.01
Random effects		1.37	1.25–1.64
I^2	99% (p < 0.01)		
x^2	246.05 (p < 0.01)		
Observational studies			
HCW category			
Physicians	13	1.40	1.20–1.63
Nurses	13	1.38	1.16–1.64
Healthcare assistants	8	1.64	1.22–2.19
Others	7	1.43	1.07–1.90
Random effects		1.43	1.31–1.56
I^2	94% (p < 0.01)		
x^2	1.07 (p = 0.79)		
Settings			
Hospital	22	1.50	1.32–1.70
Community care	3	1.05	0.87–1.28
Hospital and community care	4	1.40	1.29–1.51
Random effects		1.43	1.29–1.58
I^2	100% (p < 0.01)		
x^2	9.11 (p = 0.01)		

CI: confidence interval; HCW: healthcare worker; RR: relative risk.

influenza virus, its principal transmission route, the possible option to decrease the risk of getting seasonal influenza, and the possible benefits of vaccinations. One thousand leaflets were distributed during an in-service information session.

Educational

The contents of interventions with an educational component varied across studies [43,50,52,55,74-76]. Most contents were related to virus transmission channels, immunology and virology, and misconceptions about vaccination. The modalities principally included in-service workshops or theoretical lessons about vaccines and vaccinations. For example, Chambers et al. [52] and Rothan-Tondeour [75,76] proposed active educational

in-service learning, while Golebiak et al. [43] proposed a training on influenza and a follow-up meeting after 2 weeks with educators. PowerPoint presentations and leaflets were the most frequently used educational tools. The duration of the educational sessions varied from 5 min per week [55] to 2 h per week [75,76]

Policy

Interventions with a policy component provided operational strategies to increase HCWs adherence to vaccination against VPDs [16,79]. No details were provided on the content of these interventions. The interventions were delivered following the policies on seasonal influenza immunisation implementation in their local contexts. Specifically, we have chosen to categorise as policy interventions those improving vaccine accessibility for HCWs and providing data for the ongoing evaluation and enhancement of vaccination policies. In particular, the intervention provided by Oguz et al. [16] used a mobile immunisation team to visit and immunise on-site HCWs in a hospital setting, and collected information about previous vaccination uptake.

Multi-component interventions

Educational and promotional

Two of the multi-component interventions were based on conceptual or mapping models [67,85]. In particular, the included educational components offered a variety of theoretical contents mainly related to immunology, misconceptions on immunisation, and infectious preventive measures. The modalities of delivery for the educational components were in-service lectures, discussions, and online learning. The teaching tools used were videos featuring role models, video recordings of lectures, and slideshows. The educational components included sessions that lasted anywhere from 2 min (e.g. online educational videos) to 6 h (e.g. lectures or plenary discussions) with intervals of 3 weeks to 2 months between sessions. Furthermore, the promotional components described in Chittaro et al. [53], Kuntz et al. [65] and Dey et al. [56] included free immunisation and activities that promoted vaccination. The most used promotional tools were informational websites, leaflets and posters. The promotional components in the intervention reported by Podczervinski et al. [71] used in-service coordinators to distribute materials and monitor promotional activities. Ribner et al. [73] used a task force to constantly verify vaccination trends and ensure consistent timely communication. The duration, frequency and sessions of these promotional activities were not specified.

Educational, promotional and policy

Two of the multi-component interventions were based on conceptual multi-phase models: the intervention of Borgey et al. [49] was based on the Five Keys WHO model, and that of Schmidtke et al. [45] was based on the nudge theory. In particular, the nudge theory involves influencing behaviour through subtle suggestions or environmental modifications without coercion

[87]. The contents of the educational components were mostly related to HCWs' misconceptions about vaccination against VPDs and strategies to prevent infection; only two interventions [42,72] had educational components based on theoretical content that referred to immunology and virology. Teaching methods included in-service education and training, and the most common educational tools were slideshows, role-playing and clinical case discussions. Some interventions created a multidisciplinary team (e.g. nurses, physicians, psychologists and managers) to achieve a more effective management of information and communication channels. In particular, the intervention reported by Babcock [42] organised 'town hall meetings' during a vaccination campaign, during which HCWs received vaccination training. The duration of educational activities varied from 1 h (e.g. on-site training) [61] to 6 h per session (e.g. lectures or discussions) [53]; the intervention of Looijmans-van den Akker et al. [67] offered two sessions of 1 h each.

The most frequently used tools for promotional components were posters, leaflets, internal newspapers, email newsletters and websites. Babcock et al. [42] created a dedicated question and answer blog concerning vaccinations. The policy components included recommendations and guidelines for vaccination monitoring, which generally referred to other institutional sites (e.g. WHO). Some interventions used mandatory vaccination or financial compensation to increase HCWs' interest in getting vaccinations. In particular, Frenzel et al. [58], Ribner et al. [73] and Walther et al. [81] each implemented distinct mandatory activities within their prevention programmes. Frenzel et al. [58] employed mandatory vaccinations, Walther et al. [81] organised mandatory appointments for administering vaccinations, and Ribner et al. [73] introduced a mandatory declination form for those opting to refuse vaccination, while Calderon et al. [51], Leitmeyer et al. [66] and Llupià et al. [83] used monetary compensation or gifts as a part of their intervention to increase HCWs' vaccination adherence. However, none of the studies specified the duration of the promotional or policy components of interventions.

Study quality and risk of bias
The overall quality of evidence was evenly distributed for RCTs: four articles had a rating of good quality [49,55,67,77], four had a rating of fair quality [47,52,64,75] and four had a rating of poor quality [43,45,56,76]. None of the observational studies had a rating of good quality. Instead, 24 had a rating of fair quality [16-18,42,48,53,54,57-60,62,69-71,73,74,78-80,83-86] and 11 had a rating of poor quality [44,46,50,51,58,65,66,68,72,81,82]. All details about quality assessment are appended in the Supplement.

The risk of bias was high for the half of the RCTs (n = 6) [43,45,47,56,75,76] (Figure 2); four RCTs presented some concerns of bias [49,52,55,64]; and only two had a low risk of bias [67,77]. All the observational studies were found to have a low or moderate risk of bias. The most problematic issues were confounding, measurement of outcomes bias and bias in the selection of reported results. Moderate bias due to confounding was found in all the included observational studies. Twenty-five had moderate bias in the measurement of outcomes [16,17,42,48,50,53,54,57-63,66,68,70,73,74,78,79,83-86], and 25 showed moderate bias in the selection of reported results [16-18,42,48,51,53,54,57-62,66,70,73,74,78-80,83-86] (Figure 2).

Random-effects meta-analysis stratified by vaccination and type of intervention

Vaccine-preventable diseases
Figure 3 shows the effect of mono-component and multi-component interventions on HCWs' adherence to vaccination against VPDs in RCTs and observational studies. In RCTs, the implementation of multi-component interventions yielded a higher, statistically significant, positive effect (RR = 1.58; 95% CI: 1.49–1.68) on HCWs' post-intervention adherence to seasonal influenza vaccination than did mono-component interventions (RR = 1.16; 95% CI: 0.89–1.51). Moreover, in observational studies, multi-component interventions showed a higher, statistically significant, positive effect on post-intervention adherence to seasonal influenza vaccination (RR = 1.49; 95% CI: 1.32–1.69) when compared with mono-component interventions (RR = 1.24; 95% CI: 1.04–1.49). Multi-component interventions also showed a positive effect on post-intervention adherence to Tdap vaccinations (RR = 1.39; 95% CI: 0.82–2.35), but this increase was not statistically significant (Figure 3, Panel C).

Subgroup meta-analysis by professional category
The interventions described in RCTs led to a statistically significant increase in post-intervention adherence to seasonal influenza vaccination in all professional categories, with a larger increase among nurses (RR = 1.59; 95% CI: 1.06–2.40) than healthcare assistants (RR = 1.41; 95% CI: 1.06–1.87) and physicians (RR = 1.37; 95% CI: 1.13–1.66). Nevertheless, the difference between professional categories was not statistically significant (p = 0.84).

In observational studies, all professional categories presented a statistically significant increase in post-intervention vaccination adherence rate, with a higher increase among healthcare assistants (RR = 1.64; 95% CI: 1.22–2.19) than other professional categories (RR = 1.43; 95% CI: 1.07–1.90), but the differences between groups were not statistically significant (p = 0.79) (Table 2).

Subgroup meta-analysis by healthcare setting
In the RCTs carried out in community care settings, interventions had a positive effect and were followed by a statistically significant increase in post-intervention adherence to vaccination against seasonal

influenza (RR=1.58; 95% CI: 1.49–1.68). We found no relation in HCWs' post-intervention adherence to vaccination against seasonal influenza in hospital settings (RR=1.24; 95% CI: 0.76–2.05) (Table 2).

In observational studies set in hospitals, interventions had a positive effect on HCWs' post-intervention vaccination adherence rate (RR=1.50; 95% CI: 1.32–1.70). In studies set in facilities providing both hospital and community care (RR=1.40; 95% CI: 1.29–1.51), we found a not statistically significant effect in community care (RR=1.05; 95% CI: 0.87–1.28) (Table 2).

Publication bias and sensitivity analysis

No publication bias was seen for RCTs or observational studies on seasonal influenza (p=0.150 and p=0.057, respectively) and for Tdap vaccination (p=0.570).

For seasonal influenza, the leave-one-out sensitivity analysis did not modify the results, neither for RCTs nor for observational studies. However, for Tdap vaccination, the removal of the studies with extreme results [51,81] did modify the results of the pooled random effects model. We also performed a sensitivity analysis after removing studies with poor quality; it did not reveal any differences in the results for seasonal influenza vaccination in RCTs or observational studies, but made the pooled RR statistically significant for observational studies on Tdap vaccination (RR=1.84; 95% CI: 1.14–2.97). All details about publication bias and sensitivity analysis are appended in the Supplement.

Discussion

This systematic review and meta-analysis proved that interventions aimed at increasing vaccination adherence for influenza and Tdap vaccines among HCWs are effective, especially multi-component ones. Unlike a previous work [22], this review performed meta-analyses stratified by type of intervention and performed subgroup meta-analyses by professional category and healthcare setting. Interventions were more effective in nurses and healthcare assistants than in other HCW groups. According to the observational studies, interventions in community care settings were less effective than those performed in hospital settings and in facilities including both hospital and community services. Conversely, RCTs showed that interventions in hospital settings were not significantly different from those carried out in community care settings.

Our results show that most studies on the effectiveness of interventions are observational; observational or descriptive methodologies are generally preferred to RCTs to measure the effects of vaccination programmes or to increase vaccination coverage on a population level [88]. Indeed, observational studies can include much larger populations than RCTs [89]. Although observational studies are less precise (e.g. wider CIs) and more prone to bias, they may be more practical (e.g. shorter duration), and they ensure external validity and generalisability of the data [89].

The interventions that met the inclusion criteria of this systematic review related to influenza and Tdap vaccinations. In the US, the latest data on the rate of seasonal influenza vaccination among HCWs showed that the COVID-19 pandemic increased HCWs' adherence to seasonal influenza vaccination, but uptake was still limited [90]. However, this result is not entirely generalisable worldwide. Recent data [91] showed a significant increase in seasonal influenza vaccination rates among HCWs during and immediately after the COVID-19 pandemic. Therefore, the pandemic seemed a major factor in HCWs' adherence to vaccination, to protect families and patients, and demonstrated moral and civic responsibility. Our meta-analysis suggested that interventions do affect HCWs' adherence to influenza vaccination, with vaccination adherence increased by 43% in observational studies and 37% in RCTs. An increase in vaccination adherence by at least 35% is recognised as the minimum required to yield a potential protective impact on acquired influenza infection [3,92].

Tetanus and diphtheria are rare diseases in high-income countries, and Tdap vaccination policies during childhood vary globally [13]. In many high-income countries, Tdap vaccination is mandatory during childhood, but this is not the case in all regions. Despite these differences, Tdap vaccinations are strongly recommended for HCWs across various settings [92]. The US Centers for Disease Control and Prevention recommended that HCWs receive a Tdap booster every 10 years [12], but a recent review [93] showed that HCWs' adherence to Tdap boosters was under 40% and pertussis outbreaks are increasing, especially in neonatology, paediatrics and obstetrics units. Results from our meta-analysis are in line with previous evidence, as it seemed that interventions were not significantly effective in increasing HCWs' adherence to Tdap boosters.

Subgroup meta-analyses showed the positive effect of multi-component interventions on HCWs' adherence to vaccination against VPD such as influenza and Tdap. There is consensus that mono-component interventions are not effective in increasing vaccination adherence among HCWs rapidly and substantially [22]. Indeed, contextual, psychological and social factors and determinants act on an individual's interest and behaviour towards vaccination [19,94]. Therefore, multi-component interventions, by better addressing these underlying behavioural complexities, would effectively encourage vaccination adherence among HCWs [19,95]. The literature states that successful interventions should contain as many components as possible [20,22]. However, in resource-limited settings, interventions could focus on at least two components to rapidly increase vaccination rates, such as educational and promotional components [21,22]. The combination of educational and promotional components in particular seemed to increase HCWs' vaccination adherence [21]. Moreover, interventions delivered as in-ward training combined with promotional campaigns

had a positive effect on HCWs' vaccination adherence, increasing it by almost 20% [20,95]. Furthermore, educational initiatives delivered as in-practice training in parallel with the distribution of informative materials increased HCWs' adherence, their level of knowledge, and led to positive attitudes towards vaccination [96]. The Strategic Advisory Group of Experts on Immunization (SAGE) highlighted the importance of finding a balance in planning vaccination interventions and advises that before tailoring specific interventions, it is essential to first assess the root causes affecting vaccine uptake [97,98]. The diverse needs and contexts of HCWs must be considered when designing effective strategies. When promotional strategies are poorly implemented, HCWs may be more reluctant to vaccinate, while clear, accurate and strong promotional or communicational activities improve HCWs' awareness of vaccination [97,98]. The review by Jarret et al. [19] reported that theoretical education combined with strong promotional activities increased HCWs' adherence to vaccination by more than 25%. Furthermore, a strong promotional campaign improved HCWs' trust in vaccinations [99].

Policy amendments (e.g. free vaccination), were effective in increasing adherence to seasonal influenza vaccination [22,23] and multi-component interventions that included free access to vaccination increased HCWs' post-intervention vaccination adherence by 30% [19,22]. However, the effectiveness of such interventions depends on the type of policy. Mandatory or financial policy strategies could be quite effective on their own, but the diffusion of recommendations or guidelines on vaccination did not achieve the same positive results [21,22], especially when they were not applied continuously and for a long time. Educational materials or guidelines on vaccination need to be distributed continuously for at least 1 year, and the intervention should be based on an implementation protocol of ca 2 years, to ensure continuity in vaccination adherence among HCWs [2]. Indeed, prolonged interventions seem to increase HCWs' vaccination adherence by more than 90% [100]. Previous studies have shown that mandatory workplace vaccination policies or financial incentives also increase HCWs' vaccination uptake, especially during the COVID-19 pandemic [101] or for seasonal vaccinations [22]. However, there are ethical issues to these policies, as they can be seen as morally coercive [102]. Multi-component interventions which applied soft policy strategies that consider the local context and facilitate access to vaccination have been more effective than strong, mandatory policies [99].

It is of the utmost importance that interventions be based on a conceptual model or framework that supports the effectiveness of the interventions [3,21,89]. Despite the availability of taxonomies or classification models such as the SAGE model [98], behavioural models, situational behavioural theories and health belief models that are common in the public health literature

on vaccination, such as during the recent COVID-19 pandemic [103], conceptual models and frameworks are still infrequently used in the construction of interventions. Conceptual models or theories allow researchers to identify predictors of individual vaccination behaviour and the barriers or facilitators on which they can intervene to promote vaccination [103]. The WHO recommends the use of conceptual models when planning interventions on vaccination, and the five-factors model [104] was recommended by the European Centre for Disease Prevention and Control during the COVID-19 pandemic. This model groups vaccination determinants to facilitate vaccination acceptance and has been adopted as the standard for implementing interventions to promote vaccines [105]. Further models exist to facilitate vaccination readiness and acceptance, such as the 7C model [106,107] or the ProVac-ce model [108], useful in assessing HCWs' psychosocial determinants towards vaccination. Recently, the WHO has adopted the COM-B model as a framework for implementing targeted vaccination interventions [109,110]. It could be a possible solution in designing targeted interventions for HCWs, as it provides a comprehensive approach to understanding and influencing behaviour in the context of vaccination. Surprisingly, the interventions found in our systematic review rarely used this conceptual model, and none of the studies applied it to plan their interventions.

Our meta-analysis showed the positive effects of interventions on vaccination adherence by professional category, especially in HCWs commonly defined as more hesitant, such as nurses and healthcare assistants [111]. Indeed, vaccination coverage is lower among nurses and healthcare assistants than physicians, and healthcare assistants tend to have a more negative attitude towards vaccination than nurses and physicians [112]. Nurses' or healthcare assistants' hesitancy may be stem from a lack of knowledge on vaccines (e.g. different types of vaccines or recommendations), or from a belief that VPDs are minor illnesses [112,113].

Contrasting evidence emerged from the subgroup meta-analysis by healthcare setting. Interventions proposed in observational studies were more effective in increasing vaccination adherence in hospital settings than in community care settings. In contrast, interventions proposed in RCTs obtained a more positive effect in community care settings. It is likely that the characteristics of community care settings (e.g. smaller or more balanced populations) allowed researchers to have better study control, avoid bias or pay greater attention to inclusion and exclusion criteria [114]. It is plausible to assume that conducting a hospital RCT on a topic related to patient safety (and not only to operator safety) could be difficult, especially with regard to the ethical requirements of trials, so in this setting, observational studies are probably easier to do than RCT [114,115]. However, further high-quality RCTs are needed in both settings to prevent methodological

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biases, a point that has been underlined in earlier reviews [116].

The results of this meta-analysis are affected by a large amount of heterogeneity, which could be caused by the clinical, methodological and statistical differences in the primary studies [117]. Firstly, the individual components of interventions were often very different, and the samples of HCWs were not homogenous: some studies interviewed staff from a single professional category, whereas the majority pooled different HCWs of different professional categories using a convenience-based sampling method. Furthermore, the different healthcare settings, countries (culture may affect intervention effectiveness), the specific details of each intervention, and the way these interventions were implemented could not be homogeneous.

When the methodological quality of studies included in a meta-analysis is good, it is expected to confer a lower risk of bias and yield reliable results [34,35]. It is well known that when small (and underpowered) studies are included in a meta-analysis, this tends to render more extreme treatment effects than when larger studies are included [118]. In our meta-analysis, this issue was evident in the assessment of adherence to Tdap vaccination, as the poor quality of the included studies affected and reduced the pooled effect of the interventions. It is possible that individual quality measures (e.g. anonymisation or allocation concealment) were not consistently considered in the included studies.

The main limitation of this systematic review and meta-analysis lies in the overrepresentation of influenza vaccination, with only few studies addressing Tdap and none addressing other vaccines such as measles, mumps, rubella. This limits both the generalisability of our findings to other VPDs and the possibility of conducting more in-depth analyses. Therefore, future research should provide a more comprehensive understanding of interventions on HCWs' adherence to specific vaccinations. The poor quality of some of the included studies negatively affected the power of the meta-analytic results. The different demographic characteristics of participants and the various HCW groups and settings considered led to high heterogeneity across results. Furthermore, no assessment was possible about the mandatory nature of vaccinations according to different settings or about the possible choice of getting the vaccine, as this information was not available for all studies. Almost none of the participants in RCTs were masked in terms of treatment allocation, given the nature of the intervention itself. Although search syntaxes were conducted with the assistance of an expert librarian, the sensitivity of the search was highly dependent on the specific database used, which might have led to missing some studies. It is important to note that updates in the literature were carefully monitored, with the latest screening conducted in 2022.

Conclusions

Multi-component interventions had a greater positive effect than mono-component interventions, and we saw the effectiveness of interventions on several categories of HCWs. This meta-analysis pointed out which interventions could be useful to promote higher vaccination adherence (for influenza and Tdap vaccinations) in this population. In particular, multi-component interventions using suitable components and operational strategies could increase and promote vaccination adherence among HCWs and support vaccination policies. Therefore, our results could enhance evidence-based policymaking and maximise healthcare resources. Future research should guide decision-makers in determining the most effective frameworks for the implementation of interventions, the most reliable study design in specific settings (e.g. RCTs for community care vs observational for hospital settings), and in comparing different components to determine how they contribute to the effectiveness of interventions.

Conflict of interest

None declared.

Authors' contributions

MC and BA were involved in funding acquisition, study conceptualisation, study selection, data extraction and curation, formal analysis, writing – original draft, writing – review and editing and quality assessment. RIC and AC were involved in study selection, data extraction and curation, formal analysis, writing – original draft, writing – review and editing and quality assessment. VD was involved in Writing –review and editing. ER, ML, DA and AM were involved in study formal analysis, quality assessment and reviewing of the manuscript.

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