Effectiveness of Catch-up vaccination interventions versus standard or usual-care procedures in increase adherence to recommended vaccinations among different age groups: a systematic review and meta-analysis of randomized controlled trials and before-after studies.

Alessandra Fallucca, Walter Priano, Alessandro Carubia, Patrizia Ferro, Vincenzo Pisciotta, Alessandra Casuccio, Vincenzo Restivo

Submitted to: JMIR Public Health and Surveillance
on: September 19, 2023

Table of Contents

Effectiveness of Catch-up vaccination interventions versus standard or usual-care procedures in increase adherence to recommended vaccinations among different age groups: a systematic review and meta-analysis of randomized controlled trials and before-after studies.

Alessandra Fallucca[1]; Walter Priano[1]; Alessandro Carubia[1]; Patrizia Ferro[1]; Vincenzo Pisciotta[1]; Alessandra Casuccio[1]; Vincenzo Restivo[2]

[1]Department of Health Promotion, Mother and Child care, Internal Medicine and Medical Specialities, University of Palermo, 90127, Italy Palermo IT
[2]School of Medicine, University Kore of Enna Enna IT

Corresponding Author:
Alessandra Fallucca
Department of Health Promotion, Mother and Child care, Internal Medicine and Medical Specialities, University of Palermo, 90127, Italy
via del vespro 129
Palermo
IT

Abstract

Background: Within the worldwide challenge of tackling vaccine hesitancy, the Strategic Advisory Group of Experts on Immunization strongly promotes vaccination reminder and recall interventions which, together with the new opportunities offered by scientific progress, represent the key to successfully immunize the target population classes.

Objective: A systematic review with meta-analysis was conducted to provide an assessment of the effectiveness on increase in vaccination coverage for different interventions compared to the standard vaccination offer.

Methods: Two databases were consulted in February 2022, retrieving 1,850 studies. PRISMA statement guidelines were adopted and 80 manuscripts (47 trial/RCTs, and 33 before–after studies) were included after the assessment phase. Meta-analysis with random-effects model was performed by using STATA software (ver.14.1.2). The selected outcome was the relative risk (RR) of vaccination coverage improvement. Furthermore, meta-regression analyses and funnel plots were performed for the included manuscripts.

Results: The analyses showed, for the interventions considered cumulatively, an overall efficacy of RR=1.22 (95% CI: 1.18–1.25) for RCT and RR=1.70 (95% CI:1.54–1.87) for before – after studies. Subgroup analyses allowed to identify multicomponent interventions (RR=1.48; 95% CI:1.32–1.66) and recall clinical interventions (RR=1.25; 95% CI:1.17–1.34) as the most efficacious in increasing vaccination coverage for RCTs. On the other hand, educational (RR=2.13; 95% CI:1.60–2.83) and multicomponent (RR=1.61; 95% CI:1.43–1.82) interventions achieved the highest levels of increase for before-after studies. Meta-regression analyses showed that middle-aged adult population was associated with an higher increase (RCT: coefficient 0.51, 95% CI:0.09–0.61; before–after: coefficient= 1.27; 95% CI:0.70–1.84).

Conclusions: Community, family, and healthcare-based multidimensional interventions, as well as education-based catch-up strategies, effectively improve vaccination coverage. Therefore, their systematic implementation could be utmost relevant to target under-vaccinated population classes, thus aligning with nationally scheduled coverage levels and trying to eliminate or eradicate vaccine-preventable diseases. Clinical Trial: The review protocol was registered on PROSPERO with the number CRD42022307311 and it is available online.

(JMIR Preprints 19/09/2023:52926)
DOI: https://doi.org/10.2196/preprints.52926

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✔ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✔ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**
Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Systematic review and meta-analysis

Authors

Alessandra Fallucca[1]* - Walter Priano[1], Alessandro Carubia[1], Patrizia Ferro[1], Vincenzo Pisciotta[1], Alessandra Casuccio[1], Vincenzo Restivo[2].

[1]Department of Health Promotion, Mother and Child care, Internal Medicine and Medical Specialities, University of Palermo, 90127, Italy; [2] School of Medicine, University Kore of Enna, 94100, Italy. alessandra.fallucca@unipa.it; walter.priano@unipa.it; alessandro.carubia@unipa.it; patrizia.ferro@unipa.it; vincenzo.pisciotta@unipa.it; alessandra.casuccio@unipa.it; vincenzo.restivo@unikore.it

* Correspondence Alessandra Fallucca: alessandra.fallucca@unipa.it; Tel.: + 39 0916553630; +39 3804703272

Title

Effectiveness of Catch-up vaccination interventions versus standard or usual-care procedures in increase adherence to recommended vaccinations among different age groups: a systematic review and meta-analysis of randomized controlled trials and before-after studies.

Abstract

Background and objective: Within the worldwide challenge of tackling vaccine hesitancy, the Strategic Advisory Group of Experts on Immunization strongly promotes vaccination reminder and recall interventions which, together with the new opportunities offered by scientific progress, represent the key to successfully immunize the target population classes. A systematic review with meta-analysis was conducted to provide an assessment of the effectiveness on increase in vaccination coverage for different interventions compared to standard or usual care vaccination offer, regarding all vaccinations recommended for the different age groups.

Methods: Two databases were consulted in February 2022, retrieving 1,850 studies. PRISMA statement guidelines were adopted and 79 manuscripts (46 trial/RCTs, and 33 before–after studies) were included after the assessment phase. Meta-analysis with random-effects model was performed by using STATA software (ver.14.1.2). The selected outcome was the relative risk (RR) of vaccination coverage improvement. Furthermore, meta-regression analyses were performed for the included manuscripts.

Findings: The analyses showed, for the interventions considered cumulatively, an overall efficacy of RR=1.22 (95% CI: 1.19–1.26) for RCT and RR=1.70 (95% CI:1.54–1.87) for before – after studies. Subgroup analyses allowed to identify multicomponent interventions (RR=1.58; 95% CI:1.36–1.85) and recall clinical interventions (RR=1.24; 95% CI:1.17–1.32) as the most efficacious in increasing vaccination coverage for RCTs. On the other hand, educational (RR=2.13; 95% CI:1.60–2.83) and multicomponent (RR=1.61; 95% CI:1.43–1.82) interventions achieved the highest levels of increase for before-after studies. Meta-regression analyses showed that middle-aged adult population was associated with a higher increase (RCT: coefficient 0.54, 95% CI:0.12–0.95; before–after: coefficient= 1.27; 95% CI:0.70–1.84).

Conclusions: Community, family, and healthcare-based multidimensional interventions, as well as education-based catch-up strategies, effectively improve vaccination coverage. Therefore, their systematic implementation could be utmost relevant to target under-vaccinated population classes, thus aligning with nationally scheduled coverage levels and trying to eliminate or eradicate vaccine-

preventable diseases.

Keyword: vaccine strategies, catch–up interventions, recall intervention, vaccination coverage, multicomponent, education, remind, reward.

Introduction

The immunization programs are specifically designed to maximize health benefits of population by offering the most appropriate vaccinations for different age groups and type of patient [1]. The effectiveness of vaccination programs is based on a high uptake level, because in addition to direct protection for vaccinated individuals, there is also indirect protection for the community by decreasing the risk of infection [2].

Although vaccination is one of the most successful public health interventions, global immunization coverage rates are still at unsatisfactory levels with nearly 25 million children under 1 year of age missing routine diphtheria-tetanus-pertussis vaccination in 2021, and with only 15% HPV vaccination coverage among girls in least developed countries [3]. Under-vaccination can be related to lack of health services offered to the population, lower availability of vaccines for mass immunization programmes, difficulties in access to the services in term of space and time [4]. Insufficient budget is one of the main barriers for health governments to provide access to mass vaccination in low-income countries [5].

Although, the most developed countries health governments are strongly implementing national immunization programs, introducing new vaccines, and expanding the vaccination offer, coverage rates are far from the desirable targets, with outbreaks of vaccine-preventable diseases leading to hospitalizations and, in some cases, death [6] [7]. The literature examining the acceptance of routine vaccination for adolescents [HPV vaccine] and vaccines recommended for older people or people with chronic and disabling conditions [influenza, pneumococcal and herpes zoster vaccines] indicate critical issues with uptake [8] [9].

Vaccine hesitancy defined as ‘the reluctance or refusal to vaccinate despite vaccine availability, has gained recognition as a top threat to global health, as it could undermine successful and cost-effective vaccination programmes worldwide [10]. The main factors related to vaccine hesitancy were: the lack of awareness on benefits of vaccination, concerns regarding short- or long-term side effects of vaccines, general distrust of immunization practices and doubts regarding the high number of vaccines administered according to schedules [11]. Furthermore, the growing complexity of vaccination programs, with the introduction of new vaccines and the high number of recommended booster doses, could also represent an obstacle to the achievement of optimal coverage, causing difficulties in adherence and delays in vaccinating the target population [12].

Vaccinations declining threatens to strain health systems with outbreaks of vaccine-preventable diseases. Several attempts have been performed to identify approaches that increase immunization coverage: vaccine information campaigns, promotional and educational messages for patients and healthcare professionals, use of reminders and various mobile applications [12] [13]. Active vaccine catch-up interventions can represent an extremely useful tool for implementing adherence to vaccination practice. Experience and research can identify the most effective vaccination strategies.

The following systematic review and meta-analysis was conducted with the aim of assessing vaccine adherence to the different vaccine catch-up methods aimed at different age groups and selecting the

most relevant vaccination recall strategies in comparison to standard or usual care procedures based on the randomized controlled and before-after studies.

Methods

For the present systematic review purposes and to report both the review process and the results, the PRISMA statement guidelines were adopted [14]. The review protocol was registered on PROSPERO with the number CRD42022307311 and it is available online [15].

Search strategy and selection criteria

Two literature databases (PubMed/MEDLINE and Scopus) were consulted. The literature search was launched on 14th February 2022 by combining free text words and medical subject headings (MeSH). The search strategy consisted of a combination of general “vaccine”, “effectiveness”, “improvement” terms, and the condition of a catch/mop/keep-up intervention implementation. Search strings obtained are outlined in the appendix 1 (p 4).

PICOS criteria were adopted to select studies including population of all ages, without country and length of follow-up restriction, eligible for vaccination and receiving a catch/mop/keep – up remind or recall vaccination-based intervention. The objective was to assess intervention-dependent vaccination coverage improvement effectiveness (VCIE), a composite outcome created by cumulatively evaluating vaccination coverage improvement and series completion of vaccinations in comparison to standard vaccination offer. Both in the screening and the assessment phase, authors excluded research articles in according to the following criteria: topic or outcome out of review’s objective; non RCT or before – after study design; studies lacking vaccination coverage data; lack of data regarding the “before” or “control” group or description of catch – up/recall intervention. Furthermore, researchers proceeded to exclude non-English drafted manuscripts and full-text articles not available.

A total of six reviewers applied the inclusion criteria to screening as follows: three couples of two independent reviewers evaluated title and abstract of each identified article during the screening phase. Subsequently, the same couples performed the assessment phase evaluating the full text of the selected articles. In case of disagreements and doubts a final decision was achieved by undergoing a formal reconciliation process to reach consensus or resolved by the intervention of another reviewer.

Data analysis

A full-text review and data extraction using a standardized template for outcome measures and demographics of the study population were performed for studies that met the inclusion criteria [study design; country; study recruitment range; follow-up time; primary objective; outcome; intervention type; patients enrolled; females and age range; Gross National Income-GNI]. The variable “follow-up time since intervention” was arbitrarily categorized as follows: 0- to <6 (short), 6- to <12 (medium), more than 12 (long) months.

Moreover, since the study’s objective was to detail about the effectiveness of various type of catch/mop/keep – up remind or recall vaccination intervention on coverage rates, the variable “intervention type” was further classified based on an existing reference [16]. Intervention categories were settled as follows: “remind” studies divided into clinical, messaging, web, active calls, object;

"reward" studies; "educational" studies. Whenever multiple types of vaccination interventions were combined and thus, administered, they were classified in the category of "multicomponent" interventions.

According to GRADE classification, [17] bodies of evidence from RCTs are a priori regarded as "high" quality evidence, whereas those from observational studies start as "low" quality evidence. To further define and assess the risk of bias of each included study, two quality – assessment score tools specific for the study designs evaluated were used for RCTs, as shown in Table 2 [18] and for before – after studies, Table 5 [19]. Duval and Tweedie's non-parametric trim-and-fill method was used to adjust the effect of publication bias since it can make up for hypothetical small missing null or negative studies.

Study-level data were reported into Excel spreadsheets (Microsoft Excel v.2010). Risk ratios (RR) and corresponding 95% confidence intervals (95% Cis) of VCIE were directly calculated to assess the effect of different intervention types on receipt of immunizations. Separate analyses were performed on RCTs and before – after studies. Data were pooled if data about the main outcome (VCIE) was available from more than one study – using random-effects model meta-analysis. Focusing on stratifying results for the "intervention category" variable, pooled RRs and risk differences were computed for each intervention category. Analyses were performed through STATA (Stata software, version 14.2.1). Between-study variation was estimated by comparing each study's result with a Mantel-Haenszel fixed-effect meta-analysis. I-squared was used to quantify the extent of heterogeneity. Testing for publication bias was performed separately for RCTs and before – after studies for the main outcome. Furthermore, a meta-regression analyses with the following summary measures were performed: estimate of between-study variance [tau], proportion of between-study variance (adj-R^2), percentage of residual variation due to heterogeneity (I^2), joint test for all covariates (model F) with Knapp-Hartung modification (prob>F).

Results

A total of 1,869 research articles were identified from the literature databases, 1,784 (94%) from PubMed/MEDLINE platform and 85 (6%) from Scopus. After removing duplicates (n=22), 1,847 records were screened for the titles and abstracts. Of these, we assessed 239 full-text articles for eligibility and included 79 studies in the data extraction and qualitative synthesis, in detail 46 RCTs (58%) and 33 (42%) before – after studies were included in meta-analysis. The main reasons for excluding studies were: outcome out of review's interest (n=56), non-RCT or non-before – after study design (n=29). A summary of the screening process and exclusions is provided in a PRISMA flow diagram (Figure 1).

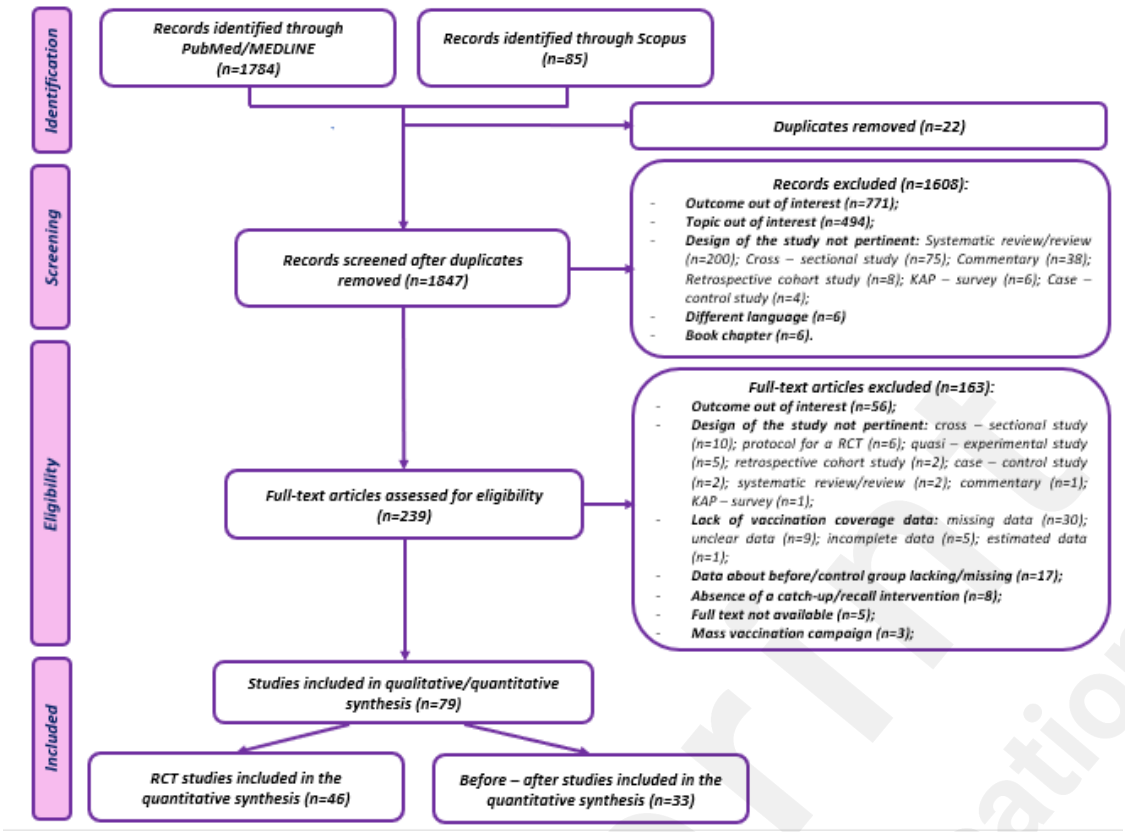


Figure 1. *PRISMA flow diagram of studies selection*

Characteristics, quality score and results of meta-analysis and meta-regression for RCT studies

Of the included RCTs 20 studies (43.5%) were conducted in the American continent (18 in the USA, 39.1%), 23.9% (n=11) were conducted in the Asia and 19.6% (n=9) in Europe. Only 5 studies (10.9%) were conducted in Africa and 1 in Australia. Based on the age groups to which the interventions were addressed, the studies were most frequently reported by: “infant-preschool” category in 45.6% of the studies (n=21); the "child-adolescent" category in 43.5% (n=20); the “middle-aged adult” category in 15.2% of studies (n=7). According to the classification of the type of intervention, “multi-component” studies were identified most frequently (47.8%, n=22), followed by “educational” studies (23.9%, n=11). The “reward” category was the least represented with 4.3% of the studies (n=2) and the “clinical” and “messaging” subcategories of the “reminder” interventions were the most populated with 21.7% (n= 10) and 28.3% (n=13) of the included studies (Table 1).

Publication	*Country*	*Study year range*	*Follow-up time since intervention*	*Main outcome [vaccination rate/coverage]*	*Intervention type*	*Mean age among intervention and controls*	*Number of patients enrolled*	*Quality Score assigned*
Rodewald LE et al. 1999 [20]	USA	1994-1995	18 months	All vaccines full series completion	**education** [outreach educational campaign]	0 to 12 months	2741	5
LeBaron CW et al. 2004 [21]	USA	1996-1998	36 months	dTPa, polio, MMR, Hib series completion	**education** [in person telephone call]	1 to 14 months	3050	3
Kimura AC et al. 2007 [22]	USA	May - Oct. 2002	3 months	Influenza	**education** [educational campaign for health care workers]	18 to 65 years	2338	1
Gilkey MB et al. 2014 [23]	USA	2011	12 months	dTPa, Meningococcal	**education** [in person and webinar delivered AFIX [assessment, feedback, incentives, exchange] educational sessions]	11 to 12 years [n°=32676]; 13 to 18 years [n°74767]	107443	1
Brewer NT et al. 2016 [24]	USA	2015	6 months	HPV 9 full series completion	**education** informative announcements vs face to face conversation	11 to 12 years	17173	3
Wong VWY et al. 2016 [25]	China	2013 - 2015	0.5 months	Influenza [adherence to self-reported vaccination]	**education** [face to face short individual educational session for	33 to 34 years	321	3

					pregnant women]			
Brown VB et al. 2016 [26]	Nigeria	2012 - 2013	12 months	All vaccines	**education** [nurse led educational sessions in primary health care centers]	0 to 12 weeks [intervention on parents]	300	1
Hu Y et al. 2017 [27]	China	2014	12 months [from birth to 1st year of life]	All vaccines full series completion	**education** [educational sessions for pregnant women	adults [women of 20-30y]; infants up to 1st year of life	1252	3
Esposito S et al. 2018 [28]	Italy	2015 - 2016	8 months	dTPa, Men ACWY	**education** [multiple web-based educational programs]	adolescents	615	2
Lemaitre T et al. 2019 [29]	Canada	2014	24 months	All vaccines full series completion	**education** [motivational interview-based educational strategy]	adults [mothers]; children at 2 years of age	2717	1
Miralles Munoz R et al. 2021 [30]	Spain	Oct. 2017 - Mar. 2018	6 months	Influenza	**education** [face to face educational intervention]	middle aged to aged >80 [≥60 healthy [99]; ≥60 with risk factors [132]; <60 with risk factors [31]; others [11]]	524	1
Rodewald LE et al. 1999 [20]	USA	1994 -1995	18 months	All vaccines full series completion	**multicomponent** [combined: tracking + outreach with prompting]	0-12 months	2741	5
LeBaron CW et al. 2004 [21]	USA	1996 -1998	36 months	dTPa, polio, MMR, HIB full series completion	**multicomponent** [autodialer with outreach backup]	1 to 14 months	3050	3
Szilagyi PG et al. 2006 [31]	USA	1998 - 2000	18 months	dTPa, HBV	**multicomponent** [audiotaped telephone reminders and active calls]	11 to 14 years	3006	5
Kimura AC et al. 2007 [22]	USA	May - Oct. 2002	3 months	Influenza	**multicomponent** [educational campaign and vaccination day for health care workers]	18 - 65 years	2271	1
Schwarz K et al. 2008 [32]	USA	1995	3 months	HBV	**multicomponent** [video on HBV, gift packages for children and cash gifts for caregiver]	2 to 18 years	328	1
Humiston SG et al. 2011 [33]	USA	2002 - 2004	0 months	Influenza	**multicomponent** [patient tracking, recall, outreach and provider prompts]	<65 years	3752	3
	UK	Feb. 2010 - Mar.	6 months	HPV series initiation and	**multicomponent** [first time invitees: letter,	16 to 18 years	1000	2

Mantzari E et al. 2015 [34]		2010		completion	voucher [financial incentive], text messages] vs [previous non-attenders: letter, voucher [financial incentive], text messages]			
Chamberlain AT et al. 2015 [35]	USA	2012 - 2013	3 months after giving birth	dTPa, Influenza	**multicomponent** [multilevel intervention involving clinic, provider and patient]	26.9 to 27.5 years [perinatal vaccination]	325	1
Richman A et al. 2016 [36]	USA	Aug. 2011- Dec. 2013	7 months	HPV full series completion	**multicomponent** [sms + e-mail]	18 to 26 years	283	1
Zimmerman RN et al. 2016 [37]	USA	2014 - 2015	9 months	HPV 9 full series completion	**multicomponent** [multimodal intervention: facilitations for access to vaccination services, communications with patients, messages, calls, training sessions]	11 to 17 YEARS	10861	3
Brown VB et al. 2016 [26]	Nigeria	2012 - 2013	12 months	All vaccines completion	**multicomponent** [reminder intervention + providers training]	0 to 3 months [intervention on parents]	297	1
Grace X Ma et al. 2017 [38]	USA		12 months	HBV	**multicomponent** [training of providers and involvement of church through messaging]	≥18 [mean age 51.6]	2212	2
Nagar R et al. 2018 [39]	India	Aug. - Dec. 2015	6 months	dTPa full series completion [within 180 days from birth]	**multicomponent** [necklace with pendant that records immunity data, voice reminder]	0 to 3 months	137	2
Esposito S et al. 2018 [28]	Italy	2015 - 2016	8 months	dTPa, Men ACWY, Men B	**multicomponent** [educational program on the website + face to face lessons]	11.6 to 16.4 years	636	2
Wallace AS et al. 2019 [40]	Indonesia	Jan. 2016 - Jul. 2016	7 months	dTPa full series completion [3rd dose]	**multicomponent** [home-based records + sticker]	0 to 12 months	3616	3
Borgey F et al. 2019 [41]	France	Nov. 2014 - Mar. 2015	0 months	Influenza	**multicomponent** [multilevel intervention approach]	18 to 65 years [health care professionals]	4069	3
Currat M et al. 2020 [42]	Switzerland	Apr. 2016 - Oct. 2016	5 months	Influenza	**multicomponent** [pre-employment health test check: face to face intervention + reminder: information leaflet]	31 to 33 years	379	1

Menzies R et al. 2020 [43]	Australia	Feb. 2015 - Dec. 2015	36 months	All vaccines timeliness vaccination	**multicomponent** [sms through VaxSMS app, calendar reminder]	2 to 8 months [intervention on parents]	1594	1
Liao Q et al. 2020 [44]	China	Oct. 2017 - Dec. 2017	5 months	Influenza	**multicomponent** [vaccination reminders + pressure component, whats app discussion group]	6 months to 6 years	365	1
Yunusa U et al. 2021 [45]	Nigeria	Nov. 2019	6 months	dTPa, HBV, Hib full series completion [3rd dose]	**multicomponent** [sms, calls]	20.2 to 33 years	554	1
Levine G et al. 2021 [46]	Ghana	Mar. 2019 - Apr. 2019	3 months	All vaccines timeliness vaccination	**multicomponent** [mobilel phone-based reminders + incentives to health workers and caregivers]	28.5 to 29,8 years [mothers interviewed]; outcome for neonatal vaccination	467	3
Kagucia WE et al. 2021 [47]	Kenya	Dec. 2016 - Mar. 2017	6 months	MMR 1 timeliness vaccination	**multicomponent** [sms, financial incentive]	6 to 8 months	537	3
Brown VB et al. 2017 [48]	Nigeria	2012 - 2013	13 months	dTPa full series completion	**remind active call**	3 weeks	614	1
Levine G et al. 2021 [46]	Ghana	Mar. 2019 - Apr. 2019	3 months	All vaccines timeliness vaccination	**remind active call** [phone call with health care worker reminder]	28.5 to 29,8 years [mothers interviewed]; outcome for neonatal vaccination	479	3
Kimura AC et al. 2007 [22]	USA	May - Oct. 2002	3 months	Influenza	**remind clinical** [vaccination day for health care workers]	18 to 65 years [health care workers]	2349	1
Fiks AG et al. 2007 [49]	USA	Sep. 2004 - Aug. 2005	check at 2 years of age	All vaccines captured immunization	**remind clinical** [electronic health record [EHR] based clinical reminder]	0 to 2 years	3217	0
Andersson N et al. 2009 [50]	Pakistan	2005 - 2007	24 months	MMR, dTPa full series completion	**remind clinical** [informed discussion about vaccination]	12 to 23 months [intervention on parents]	904	3
Gilkey MB et al. 2014 [23]	USA	2011	12 months	dTPa, Meningococcal	**remind clinical** [in person consultations]	11 to 12 years [n°=32676]; 13 to 18 years [n°=74767]	69051	1
Yoo BK et al. 2015 [51]	USA	2009 - 2011	12 months	Influenza	**remind clinical** [SLV: school located vaccination	6 months to 18 years	13561	0

					against flu in 2009-2010 and 2010-2011]			
Brown VB et al. 2016 [26]	Nigeria	2012 - 2013	12 months	All vaccines full series completion	**remind clinical**	0 to 3 months	298	1
Kriss JL et al. 2017 [54]	USA	2013	2 months after giving birth	dTPa	**remind clinical** [messaging iBook]	25.4 to 27.5 years [women in perinatal period]	73	3
Hu Y et al. 2018 [44]	China	2014	24 months	Varicella	**remind clinical** [messaging iBook]	25 to 26 years [parents]; outcome for children at 2 years of age	136	1
Wallace AS et al. 2019 [40]	Indonesia	Jan. 2016 - Jul. 2016	7 months	dTPa full series completion	**remind clinical** [home-based records]	0 to 12 months	3616	3
Blanchi S et al. 2020 [54]	France	May 2018 - May 2019		dTPa-IPV	**remind clinical** [catch-up strategy during hospitalization]	65 to 97 years [hospitalized patients]	162	3
Rodewald LE et al. 1999 [20]	USA	1994 - 1995	18 months	All vaccines series completion	**remind messaging** [prompting]	0 to 12 months	2741	5
Quinley JC et al. 2004 [55]	USA	1999 - 2000	3 months	Pneumococcal [african-american vs american	**remind messaging** [telephone call reminder]	<65 years	218 [african-american]; 732 [american]	3
LeBaron CW et al. 2004 [21]	USA	1996 - 1998	36 months	dTPa, polio, MMR, Hib full series completion	**remind messaging** [autodialer: automated telephone or mail reminder]	1 to 14 months	3050	3
Irigoyen MM et al. 2006 [56]	USA	2001 [Jul. - Dec.]	6 months	dTPa	**remind messaging** [continuos messaging reminders]	6 weeks to 15 months [outcome at 6 months post intervention]	1662	3
Muehleisen B et al. 2007 [57]	Switzerland	2003	9 months	All vaccines completion	**remind messaging** [written letter reminders]	2 months to 17 years; intervention on parents [post-discharge catch-up immunization]	532	3
Rand CM et al. 2015 [58]	USA	2013 - 2014	9 months [July 2013- March	HPV 9 full series completion	**remind messaging** [reminder text messages]	11 to 16 years	3812	2

			2014]					
Chen L et al. 2016 [59]	China	2013 - 2015	14 months [December 2013 - January 2015]	BCG, HBV, dTPa-IPV, MMR full series completion	**remind messaging** [smartphone application: reminder vaccination messages]	0 to 13 months [children]; intervention on parents	214	3
Domek GJ et al. 2016 [60]	Guatemala	2013	6 months	All vaccines [pentavalent, Rotavirus, Polio, pneumococcal] series completion	**remind messaging** [sms reminders]	2 to 4 months [infants]; intervention on parents	321	3
Hu Y et al. 2018 [53]	China	2014	24 months	Varicella	**remind messaging** [video messaging]	25 to 26 years [parents]; outcome for children at 2 years of age	136	1
Menzies R et al. 2020 [43]	Australia	Feb. 2015 - Dec. 2015	36 months	All vaccines timeliness vaccination	**remind messaging** [sms reminders through VaxSMS app]	2 to 8 months [mean age 4 months] : intervention on parents	1594	1
Liao Q et al. 2020 [44]	China	Oct. 2017 - Dec. 2017	5 months	Influenza	**remind messaging** [vaccination reminders through Whatsapp]	6 months to 6 years	365	1
Qin W et al. 2021 [61]	China	2019 - 2020	10 months	Varicella	**remind messaging:** telephone notification vs written notification	Telephone notification: 2.1 to 12.2 years [mean age 4.0 years]; Written notification: 2.1 to 7.3 years [mean age 3.8 years]	800	1
Kagucia WE et al. 2021 [47]	Kenya	Dec. 2016 - Mar. 2017	6 months	MPRV 1 timeliness vaccination	**remind messaging** [sms]	6 to 8 months	537	3
Nagar R et al. 2018 [39]	India	Aug. - Dec. 2015	6 months	dTPa full series completion [3rd dose]	**remind object** [pendant recording the vaccination history of the child]	0 to 6 months [outcome assessed within 180 days from birth]	123	2
Siddiqi DA et al. 2020 [62]	Pakistan	Jul. 2017 - Oct. 2017	Until administration of Measles-1 vaccine or till 12 months of	dTPa, HBV, Hib full series completion [3rd dose]; MMR 1	**remind object** [alma sana bracelet vs star bracelet]	Infants: 0.2 to 5 weeks [mean age 2.5]; Mothers: 20.8 to	2497	3

			age			31.4 years [mean age 26.6; Fathers: 26.1 to 37.7 years [mean age 31.8]		
Irigoyen MM et al. 2006 [56]	USA	2001 [Jul. - Dec.]	6 months	dTPa vaccination rate at 6 months post intervention in infants	**remind web**	6 weeks-15 months	1662	3
Kriss JL et al. 2017 [52]	USA	2013	2 months after giving birth	dTPa [prenatal period]	**remind web** [messaging video]	25.3 to 25.8 years	73	3
Menzies R et al. 2020 [43]	Australia	Feb. 2015 - Dec. 2015	36 months	All vaccines timeliness vaccination	**remind web** [e-mail calendar reminder]	2 to 8 months [mean age 4 months]	1594	1
Saaksvuoril L et al. 2022 [63]	Finland	Jun. 2018 - Oct. 2018	5 months	Influenza, All vaccines [in western region [low coverage]]	**remind web** [e-mail: individual benefits reminder vs individual and social benefit reminder]	>65 years [mean age 75.5]	7398	3
Chandir S et al. 2010 [64]	Pakistan	2006 - 2007	16 months	dTPa full series completion	**reward** [food/medicine coupon incentives]	0 - 6 months	3059	1
Alessandrini V et al. 2019 [65]	France	Oct. 2016 - Jan. 2017	4 months	Influenza	**reward** [free vaccination at prenatal consultation ward]	27.1-38.2 years	248	1

Table1. Characteristics of RCT included studies*: Variables reported: author first name, publication year, country, recruitment study year range, follow- up time period since intervention, outcome/s, intervention type and category, mean age range among controls/interventions, number of enrolled patients*

The quality score evaluation of the included RCT studies showed the maximum result assigned (score=5) for two studies [20] [31]. A score of 1 point was assigned to several studies, including eight "multicomponent" studies [22] [32] [35] [36] [42] [43] [44] [45], five "educational" [22] [23] [26] [29] [30], three "remind" [48] [53] [61], and two “reward” studies [64] [65]. Only two studies were assessed with the minimum score assigned (score=0) [49] [51]. Adequacy of randomization and blinding was found for twenty-seven (58.7%) and two (4.3%) of the forty-six included studies, respectively (Table 2).

	Randomization			*Blinding*			*An account of all patients*	
	Mentioned	*Appropriate*	*Inappropriate or not mentioned*	*Mentioned*	*Appropriate*	*Inappropriate or not mentioned*	*Fate of all patients known*	*Total score*
Quinley JC et al. 2004 [55]	+	+	?	?	?	−	+	3
Le Baron CW et al. 2004 [21]	+	+	?	?	?	−	+	3
Irigoyen MM et al. 2006 [56]	+	+	?	?	?	−	+	3
Szilagi P et al. 2006 [31]	+	+	?	+	+	?	+	5
Fiks A et al. 2007 [49]	?	?	−	?	?	−	?	0
Muehleisen B et al. 2007 [57]	+	+	?	?	?	−	+	3
Kimura AC et al. 2007 [22]	+	?	−	?	?	−	+	1
Schwarz K et al. 2008 [32]	+	?	−	?	?	−	+	1
Andersson N et al. 2009 [50]	+	+	?	+	?	−	+	3
Chandir S et al. 2010 [64]	?	?	−	?	?	−	+	1
Humiston SG et al. 2011 [33]	+	+	?	+	?	−	+	3
Rand CM et al. 2014 [58]	+	+	?	+	?	−	?	2
Gikey MB et al. 2014 [23]	+	?	−	?	?	−	+	1
Mantzari E et al. 2015 [34]	+	+	?	?	?	−	?	2
Yoo BK et al. 2015 [51]	+	?	−	?	?	−	?	0
Chamberlain AT et al. 2015 [35]	+	?	−	?	?	−	+	1
Richman RA et al. 2016 [36]	+	?	−	+	?	−	+	1
Brewer NT et al. 2016 [24]	+	+	?	+	?	−	+	3
Zimmerman RK et al. 2016 [37]	+	+	?	?	?	−	+	3

Wong WVY et al. 2016 [25]	+	+	?	?	?	−	+	3
Chen L et al. 2016 [59]	+	+	?	?	?	−	+	3
Domek GJ et al. 2016 [60]	+	+	?	?	?	−	+	3
Brown VB et al. 2016 [26]	+	?	−	?	?	−	+	1
Brown VB et al. 2017 [48]	+	?	−	+	?	−	+	1
Ma GX et al. 2017 [38]	+	+	?	?	?	−	+	2
Hu Y et al. 2017 [27]	+	+	?	+	?	−	+	3
Kriss JL et al. 2017 [52]	+	+	?	?	?	−	+	3
Hu Y et al. 2018 [53]	+	?	−	?	?	−	+	1
Nagar R et al. 2018 [39]	+	+	?	?	?	−	+	2
Esposito S et al. 2018 [28]	+	+	?	?	?	−	+	2
Rodewald LE et al. 1991 [20]	+	+	?	+	+	?	+	5
Aaron S et al. 2019 [40]	+	+	?	?	?	−	+	3
Alessandrini V et al. 2019 [65]	?	?	−	?	?	−	+	1
Borgey F et al. 2019 [41]	+	+	?	+	?	−	+	3
Lemaitre T et al. 2019 [29]	+	?	−	?	?	−	+	1
Currat M et al. 2020 [42]	+	?	−	?	?	−	+	1
Danya AS et al. 2020 [62]	+	+	?	?	?	−	+	3
Blanchi S et al. 2020 [54]	+	+	?	?	?	−	+	3
Menzies R et al. 2020 [43]	+	?	−	?	?	−	+	1
Liao Q et al. 2020 [44]	+	?	−	+	?	−	+	1
Yunusa U et al. 2021 [45]	?	?	−	?	?	−	+	1
Qin W et al. 2021 [61]	+	?	−	?	?	−	+	1
Levine G et al. 2021 [46]	+	+	?	+	?	−	+	3
Miralles-Munoz R et al. 2021 [30]	+	?	−	?	?	−	+	1
Kagucia WE et al. [47]	+	+	?	+	?	−	+	3
Saaksvuoril L et al. 2022 [63]	+	+	?	?	?	−	+	3

Table 2. The scoring system used for RCTs*: 1 additional point for appropriate item, 0 points if not appropriate , -1 point for not mentioned or not appropriate method. Minimum score of at least 0 per single analysed section.*

Overall results of meta-analyses for all RCTs studies showed a RR of 1.22 (p<0.001) demonstrating an increase of the VCIE for all types of interventions included in RCTs sample (heterogeneity and significance tests for all intervention categories are reported in Supplementary material, appendix 2, p. 5). The most effective interventions are fully illustrated in Supplementary material, appendix 4, p. 7 (Forest plot of RCTs included studies). The highest efficacy was reported for “multicomponent” interventions with a RR of 1.58 (p<0.001) (appendix 4a; p.7), followed by “remind clinical” studies with a RR= 1.24 (p<0.001) (appendix 4b; p. 7). Also “educational” (RR:1.15; p<0.001) and “remind messaging” (RR 1.14; p<0.001) studies showed a positive effect on VCIE. Forest plots, summarising results for other types of recall interventions, are reported in Supplementary material, appendix 4c-4d; p. 8.

For RCTs studies, meta-regression analyses to obtain the best fitting model were performed including the following variables: publication year, continent, GNI, age category, follow-up time since intervention. In according to this analysis interventions conducted in the European continent (coefficient= 1.001; p=0.029) and involving adult-middle age” people (coefficient=0.537; p=0.012) were the most effective in increasing vaccination coverage (Table 3).

Variable	***Coeff***	***s.e.***	***t***	***p-value***	***95% C.I.***
Publication year	*0.001*	*0.017*	*0.05*	*0.960*	*-0.034 – 0.036*
Continent					
Africa	*0.449*	*0.594*	*0.76*	*0.452*	*-0.736 – 1.635*
America	*0.084*	*0.426*	*0.20*	*0.843*	*-0.766 - 0.935*
Europa	*1.003*	*0.448*	*2.24*	***0.029***	***0.108 – 1.898***
Asia	*0.192*	*0.485*	*0.40*	*0.694*	*-0.775 – 1.158*
GNI	*0.013*	*0.163*	*0.08*	*0.937*	*-0.312 – 0.338*
Age					
Infant – Preschool	*0.069*	*0.209*	*0.33*	*0.743*	*-0.349 – 0.487*
Children – Adolescent	*0.280*	*0.182*	*1.54*	*0.127*	*-0.082 – 0.643*
Adult – Middle age	*0.537*	*0.208*	*2.57*	***0.012***	***0.121 - 0.954***
Aged	*-0.075*	*0.234*	*-0.32*	*0.749*	*-0.542 – 0.392*
Follow-up					
6 months	*-0.238*	*0.669*	*-0.36*	*0.732*	*-1.573 – 1.097*
12 months	*0.277*	*0.685*	*0.40*	*0.687*	*-1.089 – 1.644*
>12 months	*0.173*	*0.694*	*0.25*	*0.803*	*-1.210 – 1.558*

Table 3. *Meta-regression of RCT studies, * = statistically significant results*

Characteristics, quality score and results of meta-analysis and meta-regression for before-after studies

Of the 33 before after studies included, 42.5% [n=14] were conducted in the American continent, mainly in the USA (n=13, 39.3%), followed by Europe with 30.3% (n=10) studies, and Asia with 15.2% (n=5) studies. Other 9% (n=3) of studies were carried out in the African continent (Egypt, Kenya and Nigeria) and only 3% (n=1) in Australia.

The most prevalent “age categories” were the “child-adolescent” (57.6%, n=19) and the “adult-middle age” (39.4%, n=13) categories.

The most frequent “intervention category” was “multicomponent” (n=16) followed by “educational” studies (n=9). Within “remind” studies, 4 were classified as “clinical”, 2 as “messaging” and the other 2 respectively as “active call” and “reward” studies. Further informations are provided in Table 4.

Publication	*Country*	*Recruitment/ study year range*	*Follow up time since interventio n*	*Outcome*	*Type of intervention*	*Age range*	*N° patients enrolled*	*Quality-Score assigned*
Gargano LM et al. 2011 [66]	USA	2008-2009	12 months	Influenza [2008-2009 and 2009-2010]	**education** [school-based educational intervention in rural Georgia]	12- to 18 years	3916	8
Chen J et al. 2012 [67]	China	2006-2007	< 6 months	HBV	**education** [a pilot program for HBV education in rural China]	5- to 12 years	2833	6
Suryadevara M et al. 2013 [68]	USA	2011-2012	9 months	All vaccines full series completion	**education** [educational intervention for resource poor families]	0- to 18 years	1531	8
Toleman MS et al. 2015 [69]	UK	2012-2014	24 months	Influenza, Pneumococcal [cancer ill patients]	**education** [implementation of clinical guidelines to educate health care workers; outcome for vaccination rates in chemotherapy patients]	Adults to aged > 80	200	6

Sengupta P et al. 2017 [70]	India	2013-2014	14 months	dTPa, OPV, HBV full series completion	**education** [educational intervention on migrant population]	9- to 12 months	647	5
Costantino C et al. 2019 [71]	Italy	Oct. 2016 - Nov. 2016	6 months	Influenza [health care workers]	**education** [educational intervention on influenza vaccination conducted at “Paolo Giaccone” University Hospital of Palermo, for the 2016/2017 seasonal influenza vaccination campaign]	18- to 65 years	125	7
Wallace-Brodeur R et al. 2020 [72]	USA	2016	36 months	HPV full series completion	**education** [quality improvement and educational training of partecipants]	13- to 17 years	26763	8
Glanternik JR et al. 2020 [73]	USA	May 2015-Jul. 2015	7 months	All vaccines	**education** [training intervention of physicians to help improve communication and provide education to vaccine hesitant parents. Outcome for infants vaccinated]	Physicians: 24 to 65 years; Infants: 0 to 6 months	13425	7
Costantino C et al. 2021 [74]	Italy	Oct. 2019-Oct. 2020	13 months	Influenza, dTPa, Influenza + dTPa	**education** [educational intervention in childbirth classes]	18- to 40 years [pregnant women]	326	8
Paunio M et al. 1991 [75]	Finland	1982	75 months	MMR	**multicomponent** [mass media and individual approach]	14 months to 6 years	562932	6
Abd Elaziz KM et al. 2010 [76]	Egypt	2008	1 month	MMR	**multicomponent** [posters, flyers, messages]	16- to 23 years [medical and non-medical students]	651	6
	Spain	2008 - 2009 influenza season	6 months	Influenza [health care workers]	**multicomponent** [messages sent by e-mail, 2 prize drawings and a	>18 years	9632	7

Llupià A et al. 2010 [77]					Web page]			
Cushon A. et al. 2012 [78]	Canada	2007-2009	10 months	MMR	**multicomponent** [phone calls; letter, reminder home visit]	14- to 20 months	24540	8
Aspesi AV et al. 2013 [79]	USA	2010-2011	9 months	Pneumococcal	**multicomponent** [checklist, educational pocket cards, handout]	all ages [hospitalized patients]	2258	6
Hu Y et al. 2015 [80]	China	2011-2014	32 months	All vaccines	**multicomponent** [training program for vaccinators, screening tool to identify vaccination demands among migrant clinic attendants, social mobilization for immunization]	Infants: 1288 Preschool: 260	1548	6
Baker DB et al. 2016 [81]	USA	2013-2014	12 months	PCV 13 + PPV23	**multicomponent** [system-level intervention at an academic rheumatology clinic that included electronic reminders with linked order sets, physician auditing and feedback, patient outreach]	Mean age: 57 years [rheumatoid arthritis patients]	1255	6
Mazzoni SE et al. 2016 [82]	USA	2010 -2014	24 months	dTPa, Influenza, HPV 9 [perinatal period]	**multicomponent** [stocking of immunizations in clinics, revision and expansion of standing orders, creation of a reminder/recall program, identification of an immunization champion to give direct provider feedback, expansion of a payment assistance program, and staff education]	dTPa: 20.7- to 33.4 years [mean age 27.4]; Influenza: 19.1- to 40.8 years [mean age 29.9 years]; HPV 9: 19- to 25.1 years [mean age 22.3 years]	dTPa:2710; Influenza 19409; HPV 12443	5
Mustafa M et al. 2017 [83]	Qatar	2014-2015	4 months	Influenza [health care workers, hospital B]	**multicomponent** [promotional, educational and vaccine delivery interventions; a dedicated influenza vaccination [IV] team; telephone hotline; free IV with improved access, leadership involvement; incentives; group educational sessions; and reporting/tracking activities]	18- to 65 years	Hospital A: 15341; Hospital B: 16357	6
Nzioki JM et al. 2017 [84]	Kenya	2012 - 2014	18 months	All vaccines	**multicomponent** [Community	0- to 1 years	833	5

					mobilization, identification and training of volunteer community health workers; enumeration, mapping of households and creating Community Units [CUs]; recruitment and training of Community Health Extension Workers [CHEWs]			
Varman M et al. 2018 [85]	USA	2015-2016	8 months	HPV 9 full series completion	**multicomponent** [clinic discussion and introduction of a multilevel interventionaiming at avoiding missed opportunities, send reminder mailings, educate patients]	13- to 17 years [intervention on parents]	3393	6
Poscia A et al. 2019 [86]	Italy	2015	8 months	All vaccines	**multicomponent** [90 minutes health promotion intervention, which includes theoretical introduction and an interactive role-play technique. Parents received informed consent and invitation to a meeting with the project team]	11.3- to 13.3 years [mean age 12.3 years]	801	7
Kaufman J et al. 2020 [87]	Australia	Oct. 2018- Dec. 2018	3 months	Influenza, Pertussis	**multicomponent** [the intervention targets all three levels of the healthcare encounter - the practice, provider and parent-levels [P3]: it includes midwife prompts and vaccine communication training, website, fact sheets, and parent SMS reminders]	21- to 40 years [mean age 32 years]; outcome for infants	62	8
Podraza L et al. 2021 [88]	USA	Jul. 2020	5 months	Men ACWY, Men B	**multicomponent** [multicomponent intervention]	16- to 19 years	335	7
Akwataghibe, NN et al. 2021 [89]	Nigeria	May 2016-Dec. 2016	4 months	All vaccines	**multicomponent** [cycles of dialogue and action between community members, frontline health workers and local government officials in two wards of Remo North, facilitated by the research team]	>9 months [more than half of child sample was >2 years of age]	340	7
Perkins RB et al. 2021 [90]	USA	Jan. 2017-Dec. 2017	12 months	HPV 9 full series completion	**multicomponent** [multilevel intervention : provider training and ≥1 other evidence-based systems improvement]	13 years	3283	7

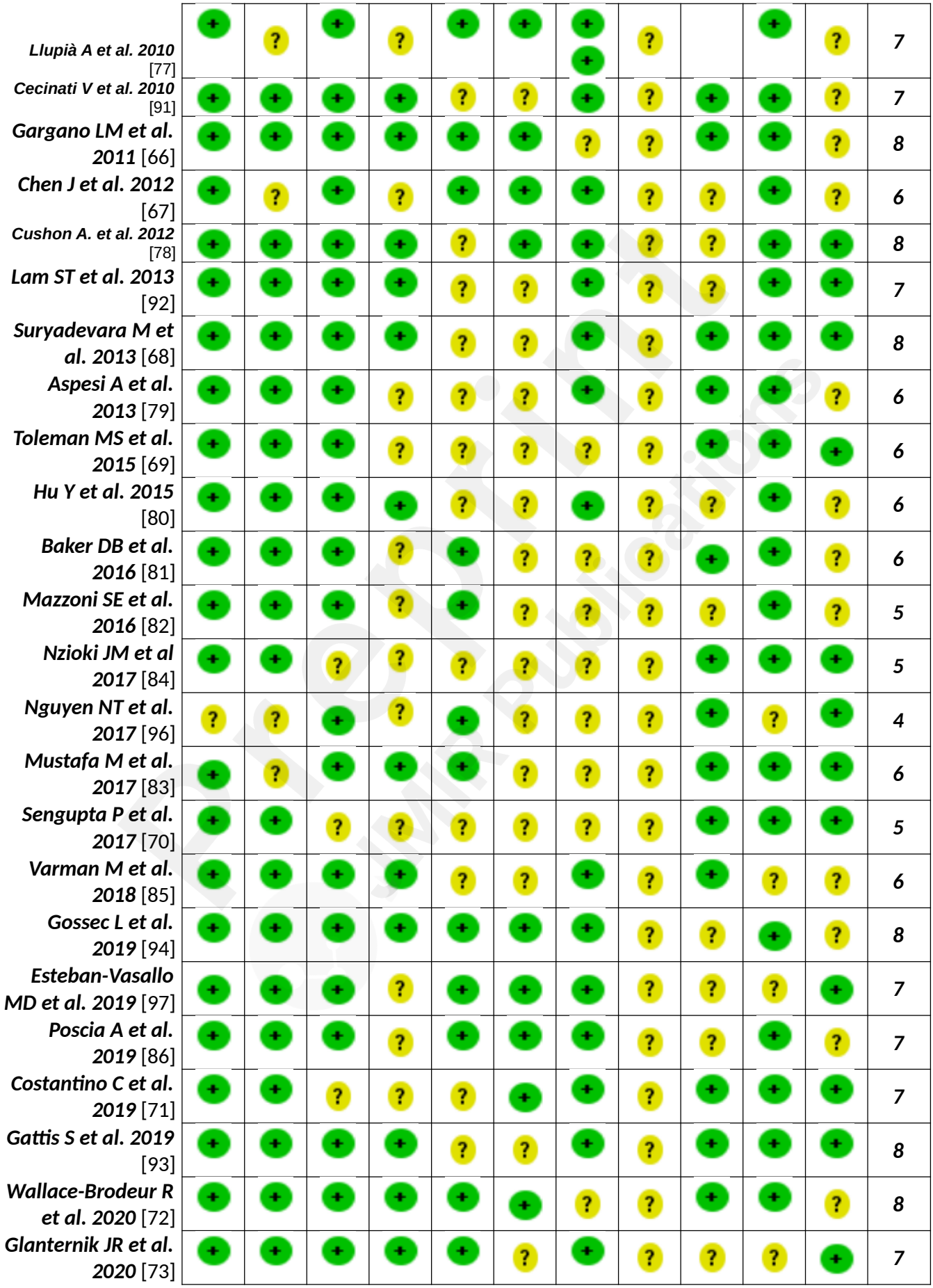
Cecinati V et al. 2010 [91]	Italy	2006-2007	< 6 months	Influenza [cancer ill patients]	**remind active call** [telephone recall system managed by pediatricians who usually follow up cancer ill children]	10 years [intervention on parents]	205	7
Lam ST et al. 2013 [92]	USA	2010-2011	1 month	dTPa	**remind clinical** [face to face reminder at the gynecological visit]	Adult to aged > 80 women [child-bearing age or with frequent exposure to children]	2309	7
Gattis S et al. 2019 [93]	USA	2011- 2016	36 months	Influenza [transplanted patients]	**remind clinical** [face to face remind for transplanted patients with the implementation of the transplant pharmacy vaccine program]	10.8- to 11.3 years	3044	8
Gossec L et al. 2019 [94]	France	May 2014-Oct. 2015	36 months	Influenza, Pneumococcal	**remind clinical** [nurse visit for comorbidity counselling and for vaccination execution]	Rheumatoid arthritis patients: 18- to 80 years [mean age 58.0 years]	970	8
Hernàndez-Garcia I et al. 2021 [95]	Spain	Nov. 2014-Jun. 2018		PCV 13 + PPV23	**remind clinical** [hospital vaccine consultation]	Adult to aged > 80 [cronic kidney disease patients]	101	4
Nguyen NT et al. 2017 [96]	Vietnam	2013 - 2015	12 months	All vaccines timeliness vaccination	**remind messaging** [sms reminders]	Children	7371	4
Esteban-Vasallo MD et al. 2019 [97]	Spain	2016 [influenza vaccination campaign]	.4 months	Influenza [rare disease patients]	**remind messaging** [sms reminders]	47- to 68 years	106987	7
Fairbrother G et al. 1997 [98]	USA	1993-1996		dTPa, OPV, HBV, Hib, MMR	**reward** [distribution of free vaccines to health care providers]	3 months to 3 years	3211	7

Table 4. Characteristics of before – after included studies*: Variables reported: author first name, publication year, country, recruitment study year range, follow- up time period*

since intervention, outcome/s, intervention type and category, mean age range among controls/interventions, number of enrolled patients

The scoring system used to assess bias for before-after studies investigated several items and 1 additional point was assigned each time the item in question was present. The items in question included: clearly stated study question or objective (32/33 studies, 97%); prespecified and clearly described eligibility/selection criteria for the study population (28/33, 85%); study participants representative of those who would be eligible for the test/service/intervention in the general/clinical population of interest (28/33, 88%); whether all eligible participants who met prespecified entry criteria were enrolled (15/33, 45%); sample size large enough to provide confidence (18/33, 55%); test/service/intervention clearly described and delivered consistently across study population (17/33, 52%); prespecified, clearly defined, valid, reliable, and consistently assessed outcome measures across all study participants (19/33, 58%); people who assessed outcomes blinded to participant exposures/interventions (0/33, 0%); losses to follow-up after baseline 20% or less and whether those lost to follow-up were considered in the analysis (19/33, 58%); presence of changes in outcome measures from pre- to post-intervention with p-values statistically examined for pre-post changes (27/33, 82%); outcome measures taken several times before the intervention/after the intervention (15/33, 45%).The evaluation of the quality score of the before-after studies included showed the maximum score assigned (score=8) for eight studies, four of which were "educational" [66] [68] [72] [74]; two "multicomponent" [78] [87], and two "remind clinical" [93] [94]. The lowest score (score=4) was assigned to two studies, a "remind clinical" [95] and a "remind messaging" [96] (Table 5).

	1. Was the study question or objective clearly stated?	2. Were eligibility/selection criteria for the study population prespecified and clearly described?	ion of interest? 3. Were the participants in the study representative of those who would be eligible for the	4. Were all eligible participants that met the prespecified entry criteria enrolled?	5. Was the sample size sufficiently large to provide confidence in the findings?	ulation? 6. Was the test/service/intervention clearly described and delivered consistently across the study	nts? 7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently	8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?	? 9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the	: changes? 10. Did the statistical methods examine changes in outcome measures from before to after the	]? 11. Were outcome measures of interest taken multiple times before the intervention and multiple times	Total
Paunio M et al. 1991 [75]	+	+	?	?	+	+	+	?	?	+	?	**6**
Fairbrother G et al. 1997 [98]	+	+	+	+	+	+	?	?	?	+	?	**7**
Abd Elaziz KM et al. 2010 [76]	+	+	+	+	?	+	?	?	?	+	?	**6**



Kaufman J et al. 2020 [87]	+	+	+	?	?	+	+	?	+	+	+	***8***
Costantino C et al. 2021 [74]	+	+	+	+	+	+	+	?	?	+	?	***8***
Podraza L et al. 2021 [88]	+	+	+	?	+	+	?	?	+	?	+	***7***
Akwataghibe NN et al. 2021 [89]	+	+	+	?	+	+	?	?	+	+	?	***7***
Perkins R et al. 2021 [90]	+	?	+	?	+	+	+	?	?	+	+	***7***
Hernàndez-Garcia I et al. 2021 [95]	+	+	+	?	?	?	?	?	+	?	?	***4***

Table 5. The scoring system used for before-after studies*: 1 additional point for appropriate item, 0 points if inappropriate. Negative score not expected.*

Meta-analyses results for before – after showed statistically significant RR=1.70 (p<0.001. Subgroup analyses (appendix 7; p. 11) displayed that the most efficacy intervention reported was "remind active call" intervention (RR: 2.19, p<0.001), followed by "educational" (RR: 2.16, p<0.001) and "multicomponent" (RR:1.61, p<0.001). Heterogeneity and significance tests for type of intervention are shown in Supplementary material, appendix 5, p. 9.

Meta-regression analyses were also performed for before – after studies by using the following variables: quality-score, publication year, continent, GNI, age category, intervention type, follow-up time since intervention. The variable associated with a statistically significant increase in vaccination coverage was "age category adult-middle age" (coefficient=1.27 p=0.01; Table 6).

Variable	***Coeff***	***s.e.***	***t***	***p-value***	***95% C.I.***
Quality-score	*0.21*	*0.18*	*1.20*	*0.24*	*-0.15 – 0.57*
Publication year	*-0.002*	*0.03*	*-0.08*	*0.94*	*-0.06 – 0.05*
Continent					
Africa	*-0.06*	*0.66*	*-0.09*	*0.93*	*-1.43 – 1.31*
America	*-0.14*	*0.33*	*-0.44*	*0.67*	*-0.82 – 0.53*
Australia	*-0.32*	*0.64*	*-0.51*	*0.62*	*-0.98 – 1.63*
Asia	*-0.08*	*0.54*	*-0.14*	*0.89*	*-1.20 – 1.04*
GNI					
Low income	*0.06*	*0.36*	*0.17*	*0.87*	*-0.68 – 0.80*
Low-middle income	*0.51*	*0.56*	*0.92*	*0.37*	*-0.63 – 1.66*
Upper-high income	*0.51*	*0.73*	*0.70*	*0.49*	*-0.99 – 2.02*
Intervention type					
Education	*-0.16*	*0.75*	*-0.21*	*0.84*	*-1.70 – 1.39*
Multicomponent	*-0.38*	*0.70*	*-0.54*	*0.60*	*-1.84 – 1.08*
Active call	*0.25*	*0.98*	*0.25*	*0.80*	*-1.77 – 2.26*
Clinical remind	*-0.67*	*0.84*	*-0.80*	*0.43*	*-2.40 – 1.05*
Remind messaging	*-0.45*	*0.86*	*-0.52*	*0.61*	*-2.23 – 1.33*
Age					
Infant – Preschool	*-0.19*	*0.31*	*-0.61*	*0.55*	*-0.83 – 0.45*
Children – Adolescent	*-0.05*	*0.29*	*-0.17*	*0.87*	*-0.65 – 0.55*
Adult – Middle age	*1.27*	*0.28*	*4.54*	***0.00****	***0.70 – 1.84***
Aged	*-0.75*	*0.38*	*-1.95*	*0.06*	*-1.54 – 0.04*
Follow-up					
12 months	*0.37*	*0.32*	*1.17*	*0.25*	*-0.29 – 1.03*
>12 months	*0.05*	*0.32*	*0.14*	*0.89*	*-0.62 – 0.71*

Table 6. *Meta-regression of before-after studies, * = statistically significant results*

Discussion

Principal results

Catch-up vaccination strategies are an essential topic of a high-quality national immunization program and should be implemented on an ongoing basis (99). It is useful to know the effectiveness of vaccination intervention in order to select the ones that work best based on the different socio-

demographic realities. Randomized controlled trials and before-after studies were included for this research as the most effective catch-up strategies.
Overall, catch-up interventions identified in the studies and classified into four categories ("multicomponent", "educational", "remind" and "reward-studies"), proved to be effective in promoting adherence to vaccination, except for practices linked to some type of "reward" which did not show statistical significance [64] [65]. Reminder and recall interventions are used to remind members of a target population that vaccinations are due [recall] or late [reminder]. Reminders and recalls strategies differ in content, according to vaccination and according to the target category, and are implemented by various methods: telephone with active calls; messaging by SMS, email, or letter; through a face-to-face comparison in a clinical setting; through the using of a physical object and via web pages. In detail, active calls interventions can greatly improve the percentage of adherence to vaccination: probably because telephone contact offers direct consultation with healthcare professionals able to answer patients' doubts and questions. Furthermore, active calls represent a reminder tool that is easily accessible and adaptable even in a context with few resources; as demonstrated by a study conducted in Nigeria in which vaccination uptake was doubled for new-borns belonging to mothers who had been called by vaccination centre healthcare workers [48].

Vaccination reminder interventions carried out by sending messages (SMS, email, letters, notifications) are also effective, but have less impact than “active calls” [61]. Probably the "messaging remind" is limited by the lack of possibility of an immediate [question and answer] discussion with the healthcare workers and by the difficulty of personalizing the text of the message, often predefined and sent by automatic software [21]. However, the huge spread of mobile technologies can allow for quick and easy communication with a very large community of people. Moreover, given the low cost and omnipresence of mobile phones, "messaging reminds" could be an excellent strategy to implement even in low- and middle-income countries [47] [60].

Another highly effective strategy for the implementation of vaccination coverage was the “clinical-remind” in which all the vaccination promotion interventions took place directly in the hospital or primary care settings. Offering the vaccination to the patient who is in hospital for an examination, consultation or treatment is a strategy promoted by WHO to reduce all “missed opportunities” for vaccination with the aim of improving the delivery of health services and promoting full synergy among healthcare professionals [101]. A demonstration is provided by a randomized study carried out in Georgia in 2018 in which the Tdap vaccine was offered to pregnant women during the gynecological visit in antenatal clinics; there was a greater predisposition to receive vaccination in pregnant women involved with the intervention compared to the control arm [52]. The Advisory Committee on Immunization Practices [ACIP] currently recommends that pregnant women will be vaccinated with Tdap during every pregnancy, regardless of immunization history [102]. Despite recommendations, maternal Tdap vaccination coverage remains low, in the United States as in many other parts of the world; evidence shows that vaccination strategies based on patient involvement in a clinical setting can effectively increase their coverage [52].

The results also show how effective “educational interventions” in vaccine catch-up should be. Health education is one of the main tools for a population to ensure that its citizens have access to health services. Already in 1983, the WHO considered health education a universal right of a community to be achieved through combined information and education courses aimed, on the one hand, at increasing the population's desire to be in good health and, on the other, to increase the

ability to discern the validity of the information received [104]. However, lack of knowledge and misinformation represent the main barriers that hinder mass access to vaccination [12]. Given that sustained and conscious attitude, a change is required in the context of vaccination with a more appropriate educational message. In particular, among the educational interventions selected, the most effective ones appear to be based on face-to-face dialogue between patients and healthcare professionals. A randomized control trial conducted in Italy to evaluate the impact of different types of educational programs, aimed at adolescent population, showed that face-to-face lessons are more effective in determining an increase in vaccination coverage than lessons held on the web [28].

A very effective strategy to increase vaccination coverage is the multidimensional approach, which was the most frequently used in the studies included in this review. This defines the interventions that combine vaccination reminder tools with awareness sessions and vaccination education of patients, carried out in several steps and in different ways. According to Strategic Advisory Group of Experts on Immunization [SAGE], “multicomponent” interventions work better than those with a single component, because, by acting on different aspects, they are more successful in increasing knowledge and awareness and in encouraging psychological shifts and attitudes changes towards vaccinations [104]. A high-impact example comes from a before-after study in which a multifaceted intervention, conducted at a rheumatology clinic in Illinois [USA], including electronic reminders with linked order sets, physician auditing and patient outreach, improved patient vaccination rates [81].

The meta-regression analysis revealed greater effectiveness of vaccination interventions in the European continent than other territorial realities. This result is probably a consequence of the gap that exists between high-income and low-middle-income countries in terms of the availability of economic resources and accessibility to health services [4]. There is no universal vaccine catch-up approach that works well for every reality and context and this is particularly true for developing countries for which scientific evidence remains limited. Most of the vaccine interventions in the WHO African Region reviewed by SAGE, to derive guidelines to address vaccine hesitancy, are found in the grey literature, which was not included in our review work [104]. However, this research has shown findings that may be globally relevant. For example, health strategies based on the reminder are effective and inexpensive and could be very appropriate for countries with limited resources [47]. On the other hand, the finding of a marked success of some vaccination programs carried out in the European continent, highlights the need for an evaluation of the performances of the vaccination services in these countries [28][71][77][97]. To date, there is a lack of standards for immunization services based on monitoring the quality improvement of the offered services. No further progress has been made since the National Vaccine Advisory Committee's standard draft for vaccination services produced in the 1980s [105]. However, some authors have suggested models to develop accreditation manual for vaccination services, with a minimum set of quality standards providing high-quality preventive healthcare services, useful for maximizing the effectiveness of the service and adequately use the economic resources addressed to public health [106] [107].

Finally, the meta-regression results also showed that various interventions aimed at vaccination catch-up work well on a target population: middle-aged adults. The possible reasons are to be found in the ways in which the vaccination service is organized by age group. Most vaccines developed to date are targeted at the pediatric population and mass immunization of the youngest is strongly supported, even in developed countries, by extensive national and international collaborative efforts to ensure adequate access to life-saving vaccines. Furthermore, childhood vaccination programs are

homogeneous, clearly defined and supported by annual monitoring of vaccine diffusion and impact in terms of reducing morbidity and mortality. On the other hand, the adult population is more difficult to reach with the most common methods of offering scheduled vaccines but catch-up vaccination and recall interventions could be very effective in increasing coverage.

The elderly population, aged 65 and over, suffers from the lack of specific vaccination programs for this age group, being the population most susceptible to risks and complications related to infectious diseases[108]. In 2009, two geriatric societies, EUGMS and IAGGER, formulated guidelines for recommended vaccinations in the geriatric population. Despite this implementation, the vaccination offer for elderly patients still remains heterogeneous among the various European countries [109]. The current challenge that remains is to develop vaccination programs for older adults that are as far-reaching and effective as programs for children.

Furthermore, several vaccination catch-up interventions are based on "reminder" and involve sending messages or emails and information via dedicated web pages [36] [53] [97]. Although the use of mobile technologies can represent a great strength of vaccination strategies aimed at adolescents and adults, on the contrary, for the elderly population, it could represent an obstacle. Other intervention modalities may be more appropriate. A study conducted in France with the aim of offering recommended vaccinations to hospitalized patients showed a significant increase in vaccination coverage [54]. Vaccination counseling provided in hospital or outpatient settings may be the most effective strategy to achieve adequate diffusion of vaccination among the elderly population.

Comparison with prior works

We identified some previous meta-analyses, published between 2017 and 2018, reporting the effect of vaccine interventions targeting certain population groups or focused on specific types of intervention [3]. Patient reminder and recall systems have been examined in many cases, but the available literature does not present data on the potential effect of other vaccine catch-up interventions [110]. Furthermore, the search strategy for this systematic review was not restricted to any geographical context, time limit, nor was set up to identify a specific type of vaccination. Our study provides an analysis of multiple vaccination strategies that could allow the implementation of the most appropriate interventions for each population and vaccination category and for different socio-demographic contexts.

Limitations

The search strategy for this systematic review did not include grey literature documents and reports. Although the field of investigation was extended to every geographical context, most of the studies selected and included were carried out in developed countries, probably because some studies on vaccinations and recall interventions carried out in developing countries are found in grey literature. Furthermore, no vaccination catch-up intervention related to the COVID-19 vaccine was included. The COVID-19 vaccination is not part of the scheduled vaccinations and was launched during an emergency pandemic situation. Despite these limitations, this study is one of the first that has investigated a wide range of vaccine catch-up strategies for scheduled vaccines, including recent studies targeting all age groups of the population.

Conclusions

Vaccination reminder interventions based on educational sessions of the population, on the use of reminders of different types (messages, calls) and multifaceted interventions, that combine multiple strategies, have been shown to be effective in increasing vaccination coverage. There is not a universal catch-up strategy that works well for every reality and context. It is necessary to adopt the most appropriate intervention strategy based on the category of patients, the availability of resources and the socio-economic level of the population to be vaccinated.

Funding

This study did not receive any funding.

Contributors

AF and WP contributed equally to this study. AF, WP, AC and VR were responsible for the conceptualisation and were actively involved in planning the methodology. AF, WP, AC, PF, VP and AC contributed equally to the investigation and project administration. AF and WP drafted the original manuscript. VR and AC provided critical advice. VR verified the underlying data reported in the manuscript. All authors reviewed, edited, and approved the final version of the manuscript. All authors had full access to all the data in the study and responsibility for the decision to submit for publication.

References

1. WHO - Global immunization policies and guidelines. WHO recommendations for routine immunization - summary tables 2021. available online: https://www.who.int/teams/immunization-vaccines-and-biologicals/policies. (last accessed on 10th june 2023)

Supplementary Files

Characteristics of RCT included studies.
URL: http://asset.jmir.pub/assets/d7c8e17edd5917863f23f0457faac872.docx

The scoring system used for RCTs.
URL: http://asset.jmir.pub/assets/def3f05d8a0c15eb24f1433bec3c3a88.docx

Meta-regression of RCT studies.
URL: http://asset.jmir.pub/assets/1f623f0fb8a6088d782eca320b184c89.docx

Characteristics of before – after included studies.
URL: http://asset.jmir.pub/assets/6a71b22f639ad51551ca8dd2569a30e2.docx

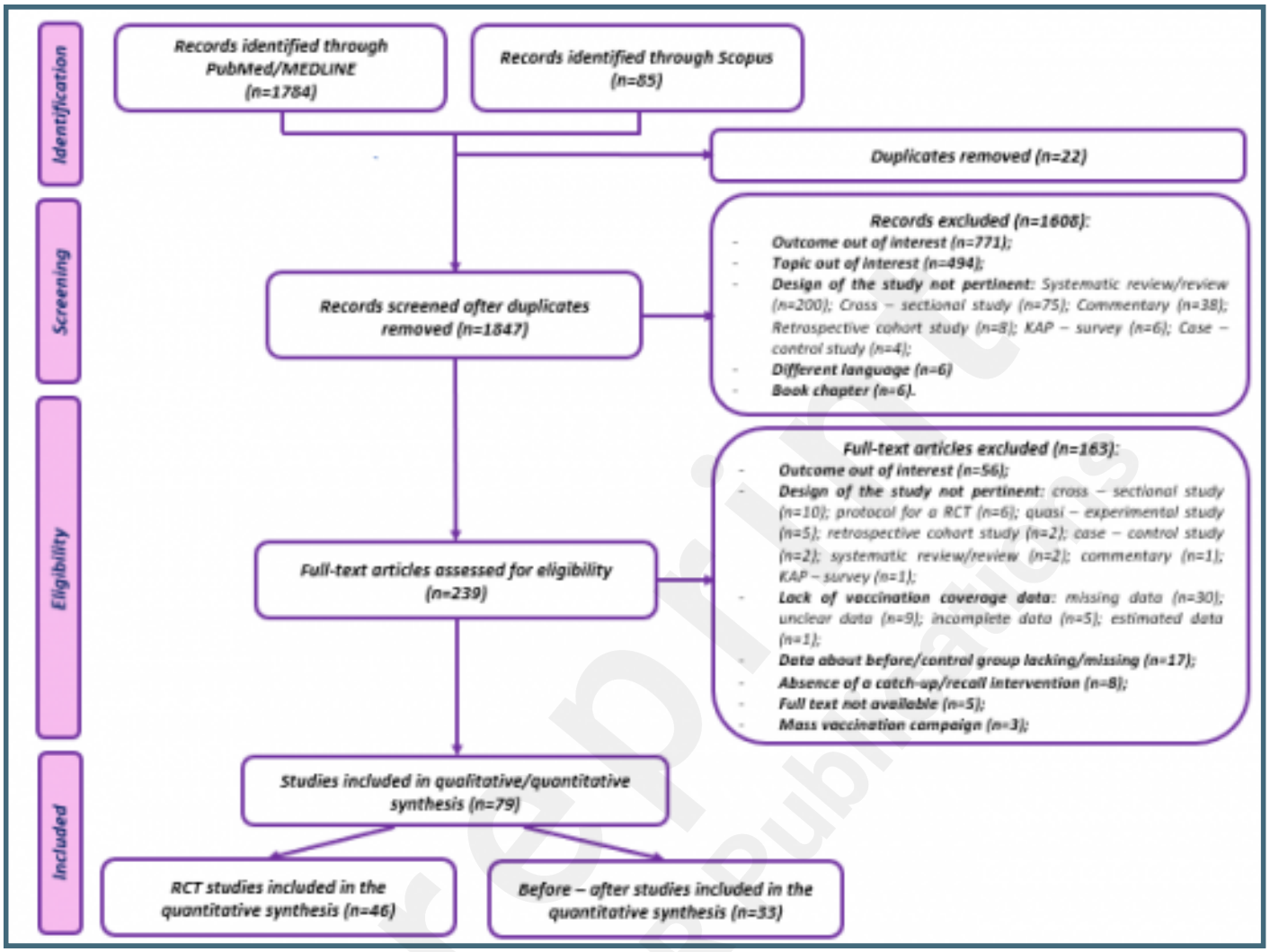
The scoring system used for before-after studies.
URL: http://asset.jmir.pub/assets/f65a02e0c17e274d76612c3495bb4175.docx

Meta-regression of before-after studies.
URL: http://asset.jmir.pub/assets/e0381df54bbb709f2b614b3429895fc8.docx

PRISMA Checklist.
URL: http://asset.jmir.pub/assets/7042eb287d7a4d11250548b140c2d570.pdf

Figures

PRISMA flow diagram of studies selection.



Multimedia Appendixes

Supplementary appendix.
URL: http://asset.jmir.pub/assets/6894bb5f115ad0e4048bb3a43e7eec13.docx