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Determinants of vaccine hesitancy and interventions aimed at contrasting this issue in Europe: an overview of systematic reviews

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Abstract

Introduction. Vaccine hesitancy remains a major public health challenge in Europe, with declining confidence in vaccine safety and efficacy despite high overall acceptance. Evidence on its determinants and effective interventions is fragmented, underscoring the need for a comprehensive synthesis. This overview of systematic reviews aimed to describe the most recent determinants of vaccine acceptance, barriers to vaccination, and effective interventions to reduce hesitancy or increase uptake in Europe.

Methods. The search was conducted in PubMed, Embase, Epistemonikos. Reviews were eligible if they included European data.

Results. Of 3,363 papers, 88 reviews were included, classified into children, adolescents, and parents (n=29); pregnant women (n=11); healthcare workers (HCWs) (n=12); and the general population (n=36) reviews. Determinants of vaccine acceptance included high education, socioeconomic status, gender, trust in government/health authorities, and HCW recommendations, with associations that varied across populations, vaccines, and contexts. Emerging determinants such as health engagement and social media were reported. Main barriers included fear of side effects, safety concerns, preference for natural immunity, and logistical challenges. Interventions included educational campaigns, reminders, organizational changes, school-based programs, and digital tools. Active reminders, school-based programs, and organizational changes showed the most consistent effectiveness.

Conclusions. Vaccine hesitancy is multifaceted, requiring tailored, evidence-based strategies. Future research should prioritize rigorous study designs and underexamined factors.

Key words

- vaccination hesitancy
- Europe
- vaccine acceptance

INTRODUCTION

Vaccine hesitancy has been a recurring challenge since the advent of vaccinations [1]. Recognizing the global significance of this issue, the World Health Organization (WHO) identified vaccine hesitancy as one of the top ten threats to global health in 2019 [2]. In Europe, vaccine hesitancy has increased over the past two decades [3]. In particular, the most recent State of Vaccine Confidence in the European Union (EU) analyzed over 25,000 questionnaires across the 27 EU member states, highlighting fluctuations in public perceptions of vaccine importance, safety, and efficacy [4]. While overall confidence in vaccines remains high, perceptions of their safety and efficacy have diminished in most countries post-2020 [4]. As vaccination remains a cornerstone of public health, addressing vaccine hesitancy is essential to achieving high coverage rates, ensuring community protection, and preventing the resurgence of vaccine-preventable diseases. Despite the growing body of literature on vaccine hesitancy, evidence in the European context remains fragmented across different vaccines, population groups, and analytical approaches. While numerous primary studies and systematic reviews have explored specific determinants, barriers, or interventions, a comprehensive synthesis integrating these dimensions across populations and settings is still lacking.

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Within this context, the Addressing Vaccine Hesitancy in Europe (VAX-TRUST) study was funded by the European Union's Horizon 2020 research and innovation programme and was initiated in 2021. VAX-TRUST investigated vaccine hesitancy as a complex transnational, yet region- and context-specific phenomenon in Europe. With a specific focus on childhood vaccines, the study particularly emphasized interactions between healthcare workers (HCWs) and parents during vaccination visits, identifying these encounters as critical moments influencing vaccine hesitancy [5]. One of VAX-TRUST's objectives was to support HCWs in addressing hesitancy through tailored interventions [6]. To inform these interventions, a systematic review described existing strategies and interventions for HCWs [7], while complementary research, including the present work, focused on mapping the key determinants of vaccine hesitancy in Europe and identifying the strategies used to address it. Specifically, it intended to explore the factors influencing vaccine hesitancy, highlighting the differences in these determinants across various population groups that may attend vaccination centers, to better guide both research and patient interactions. Therefore, this overview of systematic reviews aimed to provide a comprehensive description of the most recent determinants of vaccine acceptance, barriers that hinder vaccinations, and potential effective interventions to reduce vaccine hesitancy or increase vaccine uptake in Europe.

MATERIALS AND METHODS

A systematic search was conducted across multiple databases, including PubMed, Embase, and Epistemonikos, to retrieve the most recent systematic reviews on the topic. The search was performed on March 22, 2022, and included only studies published from 2017 onward. The search strategy was structured using the population intervention comparison outcome (PICO) framework. The population included the European population, with a particular focus on the general population, pregnant women, parents, children and adolescents, as well as HCWs and healthcare students. The interventions/exposures analyzed were determinants of vaccine acceptance, barriers hindering vaccinations, and interventions designed to reduce hesitancy or increase vaccine uptake. Reviews that included studies with any control groups, as well as those without control groups, and any outcomes related to vaccine hesitancy and vaccine uptake were considered eligible. The search terms are available in the *Supplementary material available online* ("*List of search terms*"). The protocol was registered on the International prospective register of systematic reviews (PROSPERO) (CRD42022379111). This article is a revised and expanded version of a conference abstract presented at the 17th World Congress on Public Health (Rome, Italy, 2023) [8].

Eligible reviews had to meet the following criteria: systematic review or meta-analysis with the primary aim that includes exploring determinants of vaccine hesitancy and/or interventions aimed at reducing vaccine hesitancy or increasing vaccine uptake; published in peer-reviewed journals; focused on European populations. Studies were excluded if they: examined only non-European populations; were preprints; focused solely on specific subpopulations (e.g., individuals with diseases, minorities); addressed only vaccine efficacy, side effects, or vaccination coverage without discussing determinants, barriers, or interventions; analyzed pipeline vaccines, timely administration of the hepatitis B (HBV) vaccine birth dose, or were scoping reviews, narrative reviews, overviews, primary studies, editorials, letters, or conference papers. Exclusively qualitative systematic reviews were excluded because this overview aimed to compare determinants, barriers, and intervention types based on evidence allowing assessment of their recurrence and consistency across studies and populations.

The authors independently screened the titles and abstracts using the web application Rayyan [9]. Each article was evaluated by at least two authors. As training, 5% of the articles were independently screened by all authors, and disagreements were resolved through consensus before proceeding with the remaining papers. Then, full texts of potentially eligible studies were assessed against the inclusion and exclusion criteria by at least two authors, with decisions tracked in Excel. Reasons for exclusion were documented. Throughout the process, reviewers were blinded to each other's decisions, and disagreements were resolved through consensus.

Data were extracted into pre-designed Excel spreadsheets. The extracted information included: author and year of publication; vaccinations studied; target populations; search dates and databases; number, design, and years of included studies; continents and participants of included studies; determinants of vaccine acceptance and barriers hindering vaccinations in Europe; interventions targeting vaccine hesitancy or increasing vaccine uptake in Europe (with data on the results of interventions, if available). For each systematic review, at least one author extracted the data, and another author verified it. Discrepancies were resolved by discussion. When systematic reviews provided Europe-specific analyses or summaries, these were directly extracted and synthesized. When Europe-specific results were not reported, all primary studies included in the review were screened to identify those conducted in European countries, based on study setting and population. Data and conclusions from these European primary studies were then extracted and synthesized to generate a Europe-focused summary.

The risk of bias of the included systematic reviews was assessed using the "A MeaSurement Tool to Assess systematic Reviews 2" (AMSTAR 2) [10]. At least one author conducted the assessment, and another author verified it. Any disagreements were addressed through consensus-based discussions.

The narrative synthesis was organized by macro-categories of populations, summarizing how frequently data on determinants of vaccine acceptance, barriers hindering vaccinations, and interventions to address vaccine hesitancy or increase vaccine uptake were cited in the systematic reviews. For determinants and barriers, the synthesis followed the structure of the Vaccine Hesitancy Determinants Matrix, which categorizes fac-

tors influencing the decision to accept, delay, or reject vaccines into three domains: contextual influences, individual and group influences, and vaccine/vaccination-specific influences [11]. For interventions, the information on efficacy/effectiveness was summarized as "significant" if the systematic review reported significant improvements in any outcome, and "non-significant/conflicting" if no significant results were reported or if the studies included in the review showed mixed or conflicting findings.

RESULTS

Selection process

Out of 3,363 papers, 88 were selected. *Figure S1* (*Supplementary material available online*) shows the PRISMA flow diagram [12]. The included systematic reviews were classified, according to available European data, as primarily concerning children, adolescents, and parents (CAP) (n=29, 33% of the reviews); pregnant women (PW) (n=11, 12.5%), HCWs (n=12, 13.6%), and general population (GP) (n=36, 40.9%).

Characteristics of the systematic reviews

Included reviews were published between 2017 and 2022 considering all the subpopulations, except for PW (2018-2022). The year with the highest number of published articles was 2020 for CAP (n=8, 27.6% of CAP reviews) and 2021 for all the other categories (PW: n=5, 45.5%; HCWs: n=5, 41.7%; GP: n=12, 33.3%).

Search dates had no lower date limit in 24.1% of CAP reviews (n=7), 27.3% of PW reviews (n=3), 100% of HCWs reviews (n=12), and 16.7% of GP reviews (n=6). The most used lower limit in CAP reviews was 2006 (n=4, 13.8%), mostly related to the human papillomavirus (HPV) vaccination introduction. Considering the other populations, the most frequent range was around 2020-2021, due to the COVID-19 pandemic focus (PW: n=3, 27.3%; HCWs: n=3, 25.0%; GP: n=9, 25.0%).

Overall, the reviews used an average of 5 databases to conduct the search (databases mean: CAP 6; PW 4; HCWs 5; GP 5). The most used databases were: PubMed/MEDLINE (n=28, 96.6%), Embase (n=15, 51.7%), and Scopus (n=14, 48.3%) for CAP; PubMed/MEDLINE (n=11, 100.0%), Embase (n=5, 45.5%), and Web of Science (n=5, 54.5%) for PW; PubMed/MEDLINE (n=12, 100.0%), Embase (n=8, 66.7%), Web of Science (n=5, 50.0%) and CINAHL (n=5, 50.0%) for HCWs; PubMed/MEDLINE (n=36, 100.0%), CINAHL (n=16, 44.4%), and Embase (n=15, 41.7%) for GP.

The most frequent target populations of the CAP reviews were adolescents and young adults (n=10, 34.5%), parents of children (n=9, 31.0%), parents of children and adolescents (n=8, 27.6%). All PW reviews were on pregnant women. Few HCW reviews focused on a specific subgroup: 1 on midwives (8.3%), 1 on nurses (8.3%), and 1 on obstetrics/gynecologists (8.3%). Similarly, few GP reviews focused on some subgroups: 7 on elderly individuals or risk groups that included elderly (19.4%), 1 on women (2.8%), and 1 on university students (2.8%).

The most frequent target vaccinations of the CAP reviews were HPV (n=13, 44.8%), pediatric vaccines with no specific restriction (n=8, 27.6%), vaccines in adolescents (n=2, 10.3%), and COVID-19 (n=2, 10.3%). Considering PW reviews, the most frequent vaccinations were against COVID-19 (n=4, 36.4%) and flu (n=3, 27.3%). In HCW reviews, the most frequent vaccinations were against COVID-19 (n=3, 25.0%) and vaccinations with no specific restriction (n=3, 25.0%). Lastly, in GP reviews, the most frequent vaccinations were vaccines with no restrictions (n=13, 36.1%), COVID-19 (n=11, 30.6%), and flu (n=7, 19.4%).

Included studies within the reviews ranged between 6 and 103 for CAP (mean: 30 studies), 9 and 120 for PW (mean: 28), 6 and 96 for HCWs (mean: 27), and 5 and 470 for GP (mean: 45). Among these, studies conducted only in Europe per review ranged between 1 and 103 for CAP (mean: 11), 1 and 25 for PW (mean: 6), 1 and 82 for HCWs (mean: 14); 1 and 176 for GP (mean: 13). Only 5 reviews were exclusively based on European studies (3 CAP; 1 PW; 1 HCWs; 0 GP). Overall, the continent with the highest number of papers was America, with the following mean number of papers: 15 (CAP), 13 (PW), 10 (HCWs), and 19 (GP).

Details about the abovementioned characteristics are presented in the *Supplementary material available online* (*Table S1*).

European data

Considering the included European studies, most reviews (n=52) were focused only on determinants and/or barriers (CAP: n=14, 48.3%; PW: n=9, 81.8%, HCW: n=8, 66.7%; GP: n=21, 58.3%). Fewer reviews (n=27) were mostly focused on interventions (CAP: n=12, 41.4%; PW: n=2, 18.2%, HCW: n=2, 16.7%; GP: n=11, 30.6%). In some cases (n=9), the reviews included both papers on determinants/barriers and interventions due to their main aims (CAP: n=3, 10.3%; HCW: n=2, 16.7%; GP: n=4, 11.1%).

Studies on determinants/barriers included in the reviews were all observational studies (including quantitative, qualitative, and mixed methods designs). Considering the 27 reviews with European studies only on interventions, the percentage of randomized controlled trial (RCT) varied from 0% (PW: 0/3 primary articles), to 33.3% (CAP: 13/39 primary articles), 64.3% (GP: 27/42 primary articles), and 100.0% (HCW: 10/10 primary articles).

The publication year of the European primary papers included in the reviews ranged between 1980 and 2021 (CAP: 1980-2021; PW: 2010-2021; HCW: 1998-2021; GP: 1997-2022). The sample size ranged between 5 to 8,020,000 individuals (CAP: 5-1,204,588; PW: 14-247,316; HCW: 10-50,351; GP: 20-8,020,000) (*Supplementary material available online*, *Table S1*).

Determinants of vaccine acceptance

Figure 1 shows the determinants of vaccine acceptance that have been most frequently reported across multiple identified macro-categories. Considering contextual influences, the most frequently mentioned determinants of vaccine acceptance were higher educational attain-

	CAP review (n=29)	PW review (n=11)	HCW review (n=12)	GP review (n=36)
	Type of vaccine (n)	Type of vaccine (n)	Type of vaccine (n)	Type of vaccine (n)
CONTEXTUAL INFLUENCES				
Mothers'/Parents' higher education	HPV (3) Pediatric vaccines (2)	COVID-19 (4)	–	–
Higher socio-economic situation	HPV (2) Vaccines (1)	–	–	COVID-19 (4) Flu (2) HPV (1) Meningoc. (1) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1) Vaccines (1)
Higher educational level	–	–	COVID-19 (1)*	COVID-19 (4) HPV (1) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1) Vaccines (1)
Male gender	–	–	COVID-19 (1)*	COVID-19 (6) Flu (2) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1)
Being in favor of mandatory vaccinations	–	Pediatric vaccines (1)	Vaccines (1)*	–
INDIVIDUAL AND GROUP INFLUENCES				
Personal vaccination history (i.e., the participant or the parent has already been vaccinated for other vaccinations)	HPV (2)	Pregnancy vaccines (1) COVID-19 (4) Flu (1)	COVID-19 (3)* Flu (1)** Vaccines (1)**	COVID-19 (2) Flu (2) HPV (1) Vaccines (1) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1)
Perceiving VPDs as severe	–	Pregnancy vaccines (1)	COVID-19 (1)* Vaccines (1)*	COVID-19 (6) Flu (1) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1)
Awareness/knowledge regarding the specific vaccine or disease of focus	HPV (1) Vaccines (1)	Pregnancy vaccines (1)	Flu (1)* Flu (1)** Vaccine s (1)**	Flu (1) Meningoc. (1) Vaccines (1) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1)
Trust in government policies and health authorities	COVID-19 (1) HPV (1)	–	Vaccines (1)**	COVID-19 (4) Flu (1) Vaccines (1) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1)
Perceiving vaccines as important/ useful	COVID-19 (1) HPV (2) Pediatric vaccines (2)	Pregnancy vaccines (1) Pediatric vaccines (1)	Vaccines (1)**	COVID-19 (2) Flu (1) Meningoc. (1)
Perceiving the risk of contracting VPDs	–	–	COVID-19 (1)* Vaccines (1)* Flu (1)**	COVID-19 (2) Flu (1) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1)
Having a chronic disease	–	Flu (1)	–	COVID-19 3) Flu (3) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1)
Having received advice to get vaccinated (by other figures than physicians)	HPV (1)	–	–	Flu (1)
Older age	–	–	COVID-19 (1)* Vaccines (1)**	COVID-19 (6) HPV (1) Meningoc. (1) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1)
Younger age	–	–	HBV, measles, rubella, varicella, and flu (1)*	COVID-19 (1) Meningoc. (1)
VACCINE – AND VACCINATION – SPECIFIC ISSUES				
Healthcare professional recommendation	HPV (2) Pediatric vaccines (1)	Pregnancy vaccines (1)	–	COVID-19 (1) Flu (1) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1)

50%	40-49%	30-39%	20-29%	10-19%	1-9%	n.m.

Figure 1
Determinants of vaccine acceptance.

The figure shows the number of reviews that mention a determinant per type of vaccine. If the type is "vaccines", it means the review refers to vaccines without any restrictions. The color of the cells represents the percentage of reviews that mention a determinant relative to the total number of reviews in each column category (i.e., CAP: children, adolescents, and parents; GP: general population; HCWs: healthcare workers; PW: pregnant women). The darker the color, the higher the percentage of reviews that mention the determinant.
HPV: human papillomavirus; VPDs: vaccine-preventable diseases; Meningoc.: meningococcal disease; MERS: Middle East Respiratory Syndrome; n.m.: not mentioned; SARS: Severe Acute Respiratory Syndrome; *HCW: considered as vaccine (review: n=8); **HCW: considered as providers (review: n=4).

ment (of the parents or of the individual) and higher socioeconomic status, which represent structural determinants, as well as male gender, whose association with vaccine acceptance likely reflects context-specific social and cultural factors. A positive attitude towards mandatory vaccination policies was also mentioned both for pregnant women and HCWs.

Other contextual determinants were mentioned less frequently. Indeed, CAP reviews also mentioned being exposed to media and social media that promote vaccination (1 review on HPV) and having multiple options to access the vaccination (1 review on vaccines in general). Considering GP reviews, feeling close to radical parties or not feeling close to any party were also reported (1 review on COVID-19), as well as living in an urbanized area (1 review on vaccines in general) and being white (4 reviews on COVID-19, 2 on flu, and 1 on Severe Acute Respiratory Syndrome, Influenza A/H1N1, Middle East Respiratory Syndrome, Ebola Virus Disease, and COVID-19). Two GP reviews on COVID-19 and meningococcal vaccinations reported female gender as a positive determinant, in contrast with a higher number of abovementioned studies.

With regard to individual and group influences, the most frequently cited determinants across most macro-categories (HCW, GP and at least one between CAP and PW) were history of vaccination, perceiving vaccine-preventable diseases (VPDs) as severe, knowledge on VPDs or vaccines, trust in government and health authorities, perceiving vaccines as important and/or useful. For HCW and GP reviews, the perceived risk of contracting VPDs and age (with conflicting data) represented determinants that appeared in multiple reviews. Having received advice to get vaccinated (by other figures than physicians) and having a chronic disease were cited for GP and CAP/PW (*Figure 1*).

As for determinants specific for one macro-category, CAP reviews mentioned the perception of HPV vaccine benefits by parents (2 reviews on HPV), declaring willingness to protect own child (1 review on HPV and 1 on vaccines in general), parental perception about the importance of future partner protection (1 review on HPV), sexual habit (1 review on HPV), peer encouragement (1 review on HPV and 1 on vaccines in general), influence of grandparents (1 review on HPV), and child's older age (1 review on HPV). PW reviews highlighted in 4 reviews on COVID-19: maternal age higher than 30 years, proximity of childbirth/being in the third trimester, living with someone older than 65 years, having had COVID-19. The perception of responsibility and being physician or midwife were reported for both HCWs as vaccinees (1 review on vaccines in general and 2 reviews on COVID-19, respectively) and HCWs as providers (2 reviews on vaccines in general); while less years of work experience (1 review on COVID-19 and 1 review on HBV, measles, rubella, varicella and influenza) and working in intensive care units (1 review on HBV, measles, rubella, varicella and influenza) were reported for HCW as vaccinees. GP reviews mentioned health engagement (1 review on COVID-19) and having given up smoking (1 review on flu), perceiving vaccines as effective (4 reviews on COVID-19 and 1 on flu), considering side effects less risky than VPD (1 review on COVID-19 and 1 on flu), social norms/social pressure (2 reviews on COVID-19, 2 on flu, 1 on meningococcus, 1 on Severe Acute Respiratory Syndrome, Influenza A/H1N1, Middle East Respiratory Syndrome, Ebola Virus Disease, and COVID-19), perceived poor health (2 reviews on flu), being married (1 review on COVID-19 and 1 on flu), being a HCW (3 reviews on COVID-19), living with other people/having a large household (1 review on flu and 1 on vaccines in general).

Last, considering vaccine and vaccination-specific issue, the recommendation by HCWs was frequently mentioned for all categories (except HCW reviews) (*Figure 1*). CAP reviews specifically reported health insurance coverage (2 reviews on HPV) and PW reviews the presence of an obstetrician following the pregnancy (4 reviews on COVID-19). HCW reviews that considered HCW as providers reported 1 review on vaccine in general that described as determinant: general positive attitude towards vaccination, not having false beliefs about vaccines (reported also in another review on flu), having seen VPDs, patients' clinical status, willingness to vaccinate own child, routine recommendation of vaccinations, working alone, and being ready to discuss sexuality with patients for the HPV vaccine. For HCW as vaccinee, 1 review on HBV, measles, rubella, varicella and influenza reported receiving the proposal by an occupational health physician and a general practitioner or from the vaccination service as determinant.

The *Supplementary material available online* (*Table S1* and *Table S2*) shows further details considering each review.

Barriers hindering vaccinations

Figure 2 shows the barriers hindering vaccinations that have been most frequently reported across multiple identified macro-categories. Most of such barriers were the opposite of abovementioned determinants of vaccine acceptance, i.e., belonging to an ethnic minority, perceiving VPDs as not severe, lack of knowledge, distrust of information received by government and health authorities, and perceiving vaccines as not important/useful. Similarly, the role of HCWs was also highlighted by barriers such as lack of recommendation by HCWs (*Figure 2*) and receiving recommendations against the vaccination (also by healthcare professionals) (3 CAP reviews, 2 on HPV and 1 on pediatric vaccines). Although they were reported in only one macro-category, other variables that were quite the opposite of the aforementioned determinants were noted as barriers: having a low education level (4 PW reviews, 3 on COVID-19 and 1 on flu) or parents' low education level (4 CAP reviews, 1 on COVID-19, 2 on HPV and 1 on pediatric vaccines), female gender (6 GP reviews, 4 on COVID-19 and 2 on flu), socioeconomic barriers such as low income and living in poor areas (9 GP reviews, 5 on COVID-19, 2 on flu, 1 on Severe Acute Respiratory Syndrome, Influenza A/H1N1, Middle East Respiratory Syndrome, Ebola Virus Disease, and COVID-19, and 1 on vaccines in general), being against mandatory vaccination policies (2 CAP reviews on COVID-19) and

	CAP review (n=29)	PW review (n=11)	HCW review (n=12)	GP review (n=36)
	Type of vaccine (n)	Type of vaccine (n)	Type of vaccine (n)	Type of vaccine (n)
CONTEXTUAL INFLUENCES				
Religious beliefs	HPV (2) MMR (1)	–	–	COVID-19 (1)
Being immigrant/ethnic minority	HPV (1) Adolescent vaccines (1)	–	–	COVID-19 (5) Flu (1)
INDIVIDUAL AND GROUP INFLUENCES				
Perceiving VPDs as not severe/poor risk perception	HPV (1)	Flu (1)	Flu (1)**	COVID-19 (2) Meningoc. (1) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1) Vaccines (1)
Previous negative experience with vaccinations	HPV (1)	–	–	Flu (1)
Lack of knowledge or lack of information	HPV (6) MMR (1) Pediatric vaccines (2) Adolescent vaccines (1)	Flu (1) Pediatric vaccines (1)	Flu (1)** Measles, mumps, and rubella (1)** Pediatric vaccines (1)** Vaccines (1)**	COVID-19 (5) Flu (2) Meningoc.(1)SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1)
Distrust of information received by government and health authorities	HPV (1) MMR (1)	Pediatric vaccines (1)	Vaccines (1)*	COVID-19 (5) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1)
Fear of side effects	HPV (5) MMR (1) Pediatric vaccines (2) Adolescent vaccines (1)	Flu (1) Pediatric vaccines (1)	–	–
Perceiving vaccines as not important/useful	COVID-19 (1) HPV (4) Pediatric vaccines (2) Vaccines (1)	Flu (1)	–	–
Perceiving vaccines as unsafe/harmful	COVID-19 (1) HPV (4) Pediatric vaccines (2) Vaccines (1)	Pregnancy vaccines (1) Flu (1)	COVID-19 (2)* Vaccines (1)* Flu (1)** Measles, mumps, and rubella (1)** Vaccines (1)**	–
Thinking that children are too young/preferring to wait when children are older	HPV (2) MMR (1)	Pediatric vaccines (1)	–	–
Preference for natural immunity	MMR (1)	Flu (1) Pediatric vaccines (1)	–	–
Perceiving vaccines as not effective	HPV (1)	–	COVID-19 (2)* Vaccines (1)* Flu (1)** Measles, mumps, and rubella (1)** Vaccines (1)**	COVID-19 (6) Flu (2) SARS, Flu A/H1N1, MERS, Ebola, and COVID-19 (1) Vaccines (1)
Too busy schedule	HPV (1)	–	–	Meningoc. (1)
Unemployment	–	COVID-19 (3)	–	COVID-19 (1)
VACCINE – AND VACCINATION – SPECIFIC ISSUES				
Physical barriers to vaccination (e.g., economic reasons such as costs; access to clinic etc)	HPV (5) COVID-19 (1) Adolescent vaccines (1)	–	–	COVID-19 (1) Flu (1) Meningoc. (1) Vaccines (1)
Lack of recommendation by healthcare providers	–	Flu (1)	–	Flu (1)

50%	40-49%	30-39%	20-29%	10-19%	1-9%	n.m.

Figure 2
Barriers hindering vaccinations.

The figure shows the number of reviews that mention a barrier per type of vaccine. If the type is "vaccines", it means the review refers to vaccines without any restrictions. The color of the cells represents the percentage of reviews that mention a barrier relative to the total number of reviews in each column category (i.e., CAP: children, adolescents, and parents; GP: general population; HCWs: healthcare workers; PW: pregnant women). The darker the color, the higher the percentage of reviews that mention the barrier.
HPV: human papillomavirus; VPDs: vaccine-preventable diseases; Meningoc.: meningococcal disease; MERS: Middle East Respiratory Syndrome; n.m.: not mentioned; SARS: Severe Acute Respiratory Syndrome; *HCW: considered as vaccine (review: n=8); **HCW: considered as providers (review: n=4).

general negative attitude towards vaccinations (1 PW review on flu), not living in an urbanized area (2 CAP reviews, 1 on HPV and 1 on vaccines in adolescents), parents' age less than 30 years (1 CAP review on COVID-19), being not married (2 GP reviews, 1 on flu and 1 on vaccines in general), living alone (2 CAP reviews on flu), unhealthy behaviors such as alcohol consumption (1 CAP review on flu), perceived good health (4 GP reviews, 1 on COVID-19, 2 on flu and 1 on Severe Acute Respiratory Syndrome, Influenza A/H1N1, Middle East Respiratory Syndrome, Ebola Virus Disease, and COVID-19). Instead, some variables described as determinants in some reviews were reported as barriers in other: working as HCW (3 PW reviews on COVID-19) complications from other diseases or poor health (1 GP review on COVID-19), and age, both young age (4 GP reviews, 3 on COVID-19 and 1 on flu) and older age (1 HCW review on vaccines in general, with HCWs as providers).

However, additional variables were reported.

As for contextual influences, religious beliefs were reported both in CAP and GP reviews (*Figure 2*). Moreover, relying on information found in the web/social media (3 reviews on COVID-19 and 1 review on measles, mumps, and rubella, MMR) and disagreement between experts on the safety of vaccines (1 review on pediatric vaccines) were described in CAP reviews. Not having a regular source of care was reported in 1 GP review on flu.

Considering individual and group influences, previous negative experience with vaccinations, fear of side effects, perceiving vaccines as unsafe/harmful, thinking that children are too young/preferring to wait when children are older, preference for natural immunity, perceiving vaccines as not effective, too busy schedule, and unemployment were reported across multiple macro-categories (*Figure 2*). In addition, other variables were reported in only one macro-area: having never experienced VPD (2 GP reviews on flu), false beliefs about vaccines (6 GP reviews, 4 on COVID-19 and 2 on flu), parental concerns about children sexual activity (1 CAP review on HPV), fear of harming the fetus (2 PW reviews, 1 on pregnancy vaccinations and 1 on flu), perceiving that vaccines are too many (1 CAP review on HPV), anxiety status (3 PW reviews on COVID-19), having had previous pregnancies (4 PW reviews, 2 on COVID-19 and 2 on flu) and being pregnant (3 PW reviews on COVID-19), and living with children (1 GP review on vaccines in general). Regarding HCW as providers 1 review on vaccines in general highlighted practicing alternative medicine as a barrier. When considering HCWs as vaccinees, another general review reported the perception that vaccination should be an autonomous decision.

Lastly, physical barriers to vaccination (e.g., costs) were considered as additional variables related to vaccine and vaccination-specific issue reported both in CAP and GP reviews (*Figure 2*). Focusing on variables presented only in one macro-area, there were: fear of injection (2 CAP reviews on HPV) and administrative errors (1 CAP review on pediatric vaccines). Specific barriers were related to HCW as providers: being uncomfortable administering more injections during the same consultation (1 review on pediatric vaccines), lack of guidelines/clear official recommendations (3 reviews: 1 pediatric vaccines, 1 vaccines in general, 1 flu; 1 review on flu also considering HCW as vaccinees), lack of training (3 reviews: 1 flu, 1 pediatric vaccines, and 1 vaccines in general), having a role less involved in vaccination (1 review on pediatric vaccines), and workload and organizational issues (3 reviews: 1 pediatric vaccines, 1 vaccines in general, 1 flu).

The *Supplementary material available online* (*Table S1* and *Table S2*) shows further details considering each review.

Interventions

A total of 15 CAP reviews considered interventions aimed at improving vaccinations intentions or rates. Most of them were on HPV (n=7) or about pediatric or adolescents' vaccines in general (n=6). Only one review specifically focused on pertussis and one on MMR. Considering PW, 2 reviews reported interventions, one on pertussis and one on flu and pertussis. As for GP reviews (n=15), most works were about vaccines with no particular restrictions (n=10), 3 on flu, 1 on COVID-19, and 1 on HPV. Last, 4 HCW reviews containing interventions were about HBV, measles, rubella, varicella and flu (n=1), flu (n=1), respiratory diseases (n=1), and vaccines in general (n=1).

Seven areas of interventions have been identified. *Figure 3* shows the interventions that have been most frequently reported across multiple macro-categories.

The most discussed intervention across all reviews involved the provision of educational materials and campaigns targeting populations (17 reviews). The distribution of printed materials, such as leaflets, and social media educational campaigns were the most frequently mentioned interventions, with conflicting results for both (*Figure 3*). Additionally, one CAP review on MMR reported positive results for in-person educational campaigns, while a CAP review on HPV highlighted the effectiveness of television and magazine communication campaigns. One GP review (vaccines in general) showed non-significant results for mailed educational programs.

A total of 12 reviews mentioned interventions based on active invitations and reminders for the population. Reminders via phone, text, or email were the most cited across all macro-categories and consistently yielded significant results (*Figure 3*). Similarly, nurses' calls to parents showed positive results in a CAP review on adolescent vaccines. Letters and postcards were effective in 4 GP reviews (2 on vaccines in general, 2 on flu), while reminder postcards for motivating the elderly did not show significant results (1 GP review on vaccines in general). Active invitations with significant results included invitation letters in one CAP review on HPV and telephone appointments in 2 GP reviews (1 on flu and 1 on vaccines in general).

Twelve reviews discussed organizational changes. The most frequently mentioned interventions across macro-categories were increased involvement of general practitioners (e.g., in patient management or com-

Intervention	CAP review (n=15)	PW review (n=2)	HCW review (n=4)	GP review (n=15)
	Type of vaccine (n)	Type of vaccine (n)	Type of vaccine (n)	Type of vaccine (n)
Financial incentives for general practice	Pediatric vaccines (1)+	Flu/pertussis (1)-	–	–
Printed materials (e.g., leaflets)	HPV (1)+ Pediatric vaccines (1)-	Flu/pertussis (1)-	–	Vaccines (7)+ COVID-19 (1)+ Flu (1)+
Social media education campaign	Pediatric and adolescent vaccines (1)+ HPV (2)+-	Flu/pertussis (1)-	–	Vaccines (1)+
Reminder call/text/email for the population	MMR (1)+ Pediatric and adolescent vaccines (1)+ Pediatric vaccines (1)+ HPV (1)+	–	–	Flu (4)+
GP patients management/GP communications	MMR (1)+	Flu/pertussis (1)-	–	Vaccines (1)+
Community pharmacy programme	–	Flu/pertussis (1)-	–	Flu (1)-
Opt-out approach	–	–	Vaccines (1)- Respiratory diseases (1)-	Vaccines (1)-
Communication tools and engagement of HCWs	–	Pertussis (1)+	.	Vaccines (1)+
Training sessions and materials for HCW	–	–	Respiratory diseases (1)+	Flu (1)+
Reminders and feedback for HCW (e.g., periodic messages and coverage updates)	Pediatric vaccines (1)+	–	Respiratory diseases (1)+	–

50%	40-49%	30-39%	20-29%	10-19%	1-9%	n.m.

Figure 3
Interventions to reduce vaccine hesitancy and/or increase vaccine uptake.

The figure shows the number of reviews that mention an intervention per type of vaccine. If the type is "vaccines", it means the review refers to vaccines without any restrictions. The color of the cells represents the percentage of reviews that mention an intervention relative to the total number of reviews in each column category (i.e., CAP: children, adolescents, and parents; GP: general population; HCWs: healthcare workers; PW: pregnant women). The darker the color, the higher the percentage of reviews that mention the intervention. When a plus sign (+) is present, it indicates a significant improvement in outcomes according to the review; a minus sign (-) means no significant results or conflicting findings.
HPV: human papillomavirus; MMR: measles, mumps, and rubella; n.m.: not mentioned.

munication), community pharmacy programs, and opt-out approaches (*Figure 3*). However, except for general practitioner involvement, most interventions did not show significant improvements. Other reviews reported effective interventions that included promoting and administering vaccines for newborn parents in maternity wards (1 CAP review on pertussis), midwives providing vaccines (1 PW review on flu and pertussis), offering free vaccines at the workplace (1 HCW review on flu), providing free vaccinations (3 GP reviews on vaccines in general and flu), and facilitating easier access to vaccinations (1 GP review on HPV).

Seven reviews (only CAP reviews) mentioned school-based interventions, primarily focusing on school-based educational programs (7 reviews, with 4 on HPV and 3 on pediatric and adolescent vaccines). Additionally, 2 reviews (1 on HPV and 1 on pediatric vaccines) involved school nurses, and 1 review on pediatric vaccines described vaccine administration in schools. All these interventions were reported as effective.

Six reviews addressed digital interventions. Three CAP reviews showed positive results with computer- and web-based tailored interventions (2 on HPV) and mobile apps for vaccination promotion and reminders (1 on pediatric vaccines). However, three other reviews reported non-significant results for websites using storytelling (1 CAP review on pediatric vaccines), web-based interventions with virtual assistants (1 GP review on vaccines in general), and digital game-based interactive simulations (1 GP review on vaccines in general).

Six reviews reported interventions specific for HCWs. Communication tools and engagement of HCWs, training sessions and materials for HCWs, and reminder and feedback (e.g., periodic messages and coverage updates) for HCWs were mentioned across multiple macro-categories (*Figure 3*), all showing significant positive results. Programs that involved the training of leaders (2 HCW reviews, 1 on flu and 1 on respiratory diseases) and the implementation of policies emphasizing staff vaccinations (1 HCW review on flu) reported as well good results. One HCW review on respiratory disease vaccines revealed that reminders based on social norms were not effective. Additionally, 1 HCW review reported successful multifaceted interventions based on education, active promotion, and easy access to influenza vaccination.

Five reviews described financial incentives. Financial incentives for general practice were reported across multiple macro-categories (*Figure 3*), showing conflicting results. Financial incentives for the population were addressed in three CAP reviews: 2 reviews (1 on HPV

and 1 on adolescent vaccines) showed positive results and 1 review on HPV reported non-significant results.

The *Supplementary material available online* (*Table S1* and *Table S2*) shows further details considering each review.

Risk of bias

Details of the AMSTAR 2 evaluation for each review are reported in *Supplementary material available online* (*Table S3*). Overall, the most frequent issues were common across the reviews with the different targets populations: lack of a clear and complete explanation about the reasons of the selection of study designs (CAP: n=26; PW: n=5; HCW: n=11; GP: n=34); lack of a complete list of excluded studies with reasons (CAP: n=26; PW: n=10; HCW: n=10; GP: n=30); lack of reporting about funding of the included studies (CAP: n=21; PW: n=9; HCW: n=11; GP: n=23); lack of an interpretation of risk of bias assessment in the discussion (CAP: n=21; PW: n=7; HCW: n=8; GP: n=27).

DISCUSSION

The aim of this overview was to describe potential determinants of vaccine hesitancy that should be considered in both research and clinical practice in Europe and explore potential interventions.

First, the distribution of reviews showed that CAP and GP received the most attention, likely because they are the largest population groups. Their importance in public health vaccination strategies also makes them a key focus. The publication peak in 2020-2021 reflected the possible dual impact of the COVID-19 pandemic: it increased research specifically on COVID-19 vaccines while also intensifying the broader public debate around vaccinations [13]. Among specific vaccines, those against HPV, COVID-19, and influenza received the most attention. This emphasis highlighted their significance in public health priorities. While COVID-19 naturally gained substantial attention due to the timing of the overview, the focus on HPV and influenza vaccines may stem from the fact that their coverage rates in Europe [14] remain well below the established targets [15, 16], necessitating an in-depth understanding of underlying reasons and possible strategies.

While observational studies dominated research on determinants and barriers, the limited inclusion of RCTs in intervention-focused reviews highlighted a significant evidence gap, restricting the possibility to plan effective strategies to enhance vaccine uptake. The HCW category exhibited the highest percentage of RCTs, likely due to the relative ease of conducting such studies among healthcare professionals. However, the scarcity of RCTs in vaccine research may also reflect broader challenges, including complex regulatory and ethical systems, patient recruitment difficulties, insufficient funding, and limited access to skilled staff and infrastructure [17, 18]. Addressing these barriers is essential to enable more robust trials and advance evidence-based approaches.

Considering determinants and barriers, one key finding is the consistent influence of contextual determinants, particularly education level and socioeconomic status on vaccine acceptance. These factors appeared across various macro-categories, suggesting their broad utility as predictors of vaccination behavior. A high level of education, whether that of the individual or their parents, emerged as a significant determinant in most reviews. Socioeconomic status also reflected the ongoing disparities in vaccine uptake. This finding highlighted the ongoing need for more targeted interventions to overcome these barriers. Interestingly, Sacre *et al*. suggested that key mechanisms linking socioeconomic status to vaccine uptake include knowledge (access to or understanding of information) and confidence (in vaccines or decision-making) [19]. Social and political contexts are also commonly cited as influencing vaccine acceptance. For instance, for certain populations, such as HCWs and PW, support for mandatory vaccination emerged as a positive determinant. This support may reflect a broader dynamic, where individuals are more willing to accept stricter measures for themselves and others when they perceive the promoted behaviors, such as vaccination, as highly effective in achieving health benefits [20], highlighting the importance of clear and evidence-based communication from policymakers to build trust and demonstrate the impact of such measures.

Exposure to media, particularly social media, promoting vaccination has emerged as a determinant of vaccine acceptance, especially for the HPV vaccine. This highlighted the dual role of media as both a potential barrier (e.g., misinformation) and a facilitator in promoting vaccine uptake. The growing influence of social media in shaping public opinion highlights the need for deeper exploration of its impact on vaccine hesitancy. While social media provides opportunities for wider engagement and diverse viewpoints, it also demands literacy skills to help users to understand the complexities of digital information and discern credible sources effectively [21].

This overview also described how determinants and barriers can differ across populations. For example, parents' decisions to vaccinate (especially regarding HPV) were influenced by perceptions of the vaccine's benefits, peer encouragement, and the influence of grandparents. These factors may be key in shaping vaccine acceptance within family dynamics. Pregnant women showed unique vaccine hesitancy or acceptance patterns influenced by maternal age, proximity to childbirth, and household demographics. This highlights the importance of tailoring strategies to address the specific social and familial contexts that shape individual decision-making. Interestingly, while HCWs may have greater knowledge of vaccine-preventable diseases and vaccines due to their profession, their vaccine uptake can still be influenced by personal experiences, attitudes toward health behaviors, and perceived risks. This suggests that while HCWs are likely to be better informed about vaccines, addressing individual health perceptions, social influences, and emotional barriers is important to improve uptake. HCWs as vaccine providers face additional challenges, such as the perceived responsibility to recommend vaccines and the organizational constraints related to workload, lack of clear guidelines, and insufficient training. Furthermore,

HCWs' personal beliefs and practices, such as alternative medicine preferences, were found to be barriers, suggesting that providers' attitudes may affect their vaccine recommendations and practices, which in turn influence vaccine uptake among the general population. Thus, it is essential to develop targeted interventions that address both personal attitudes and professional responsibilities to strengthen HCWs' roles as vaccine promoters.

An underexplored factor was health engagement, which was found to be a relevant determinant in some GP reviews. Individuals with higher health engagement or those who gave up smoking appeared more likely to accept vaccines, in line with broader behavioral models that link health literacy and proactive health behaviors. This is consistent with findings from Nudelman *et al*. [22], who reported that higher engagement in healthy lifestyle behaviors prior to the pandemic correlated significantly with greater adherence to coronavirus protective measures. Similarly, the framework of Multiple Health Behavior Change [23] suggests that health behaviors are interrelated, with perceived health status mediating their impact on overall health outcomes. However, the relationship between health engagement and vaccine hesitancy remains relatively unexplored in the existing literature and warrants further investigation. Unhealthy behaviors, such as alcohol consumption, noted as barriers in some studies, further highlighted the complexity of these relationships. Havigerová [24] found that health behaviors, including nutrition, substance use, and physical activity, may be influenced by multiple factors like attitudes and economic status, rather than a single latent factor. Understanding how these behaviors interact and influence vaccine hesitancy could provide essential information.

Interestingly, some variables were reported as both determinants and barriers depending on the study. For example, being an HCW was identified as both a positive determinant in some populations and a barrier in others. This contradictory finding could reflect the complexity of HCWs' attitudes toward vaccination, where professional responsibilities might promote a sense of duty to vaccinate, while personal experiences, such as burnout or lack of institutional support, may contribute to vaccine hesitancy. These mixed results highlight the need for nuanced strategies to address vaccine hesitancy in healthcare professionals. Further contrasting variables include age, which was a determinant in some reviews (particularly among younger populations) but a barrier in others. Similarly, complications from other diseases or poor health were identified as barriers in some studies, particularly regarding COVID-19 vaccines for GP reviews. These contrasting results indicate the complexity of vaccine hesitancy, whereby the same variables may act as determinants or barriers depending on contextual, population-specific, and vaccine-related factors, underscoring the need for tailored approaches that consider the specific circumstances of different groups.

Considering interventions, one of the most common strategies identified across multiple macro-categories was the provision of educational materials and campaigns. Although widely implemented, the results were inconsistent. Printed materials and social media campaigns were often mentioned, but their effectiveness varied across reviews. For instance, while in-person educational campaigns for MMR and television-based campaigns for HPV were deemed successful in some CAP reviews, other types of campaigns, such as mailed educational materials in GP reviews, showed no significant impact. This variability aligns with findings from Zhao *et al*. [25], who highlight that health communication campaigns often have modest effects on behavior change. The heterogeneous effectiveness of educational interventions may partly reflect differences in delivery modalities. Passive approaches, such as mailed materials, were more often associated with no effects, whereas more interactive strategies, including in-person campaigns, appeared more likely to be effective. This suggests that information provision alone may be insufficient to address vaccine hesitancy. Despite this, even small impacts can lead to substantial public health benefits at the population level. Furthermore, the effectiveness of campaigns is highly context-dependent, with stronger results reported in areas like road safety or tobacco control compared to sexual health or mammography [25]. These findings suggest that the impact of educational campaigns targeting vaccinations warrants further exploration, particularly in relation to specific contexts and delivery modalities. When it comes to social media campaigns, the challenges in evaluating their effectiveness become even more pronounced. In social media campaigns, evaluating effectiveness is more complex, with many studies unable to determine whether objectives were met [26]. Engagement has become a central metric for success; however, not all engagement is beneficial, as negative engagement, such as misinformation, remains a challenge [26]. This is in line with the earlier observation that media, especially social media, can act as both a facilitator and a barrier in promoting vaccine uptake, suggesting that improving digital literacy and critical engagement with online content could be essential components in improving the effectiveness of social media-based interventions.

Active reminders, including phone calls, text messages, and emails, emerged as one of the most consistently effective interventions across all groups. These findings showed the importance of proactive communication and the role of personalized, direct engagement with individuals. Overall, the consistent effectiveness of active reminders across multiple populations and settings highlights their potential as scalable, low-cost interventions that can be readily integrated into routine vaccination programs. However, while reminders were generally effective, reminder postcards for elderly individuals in GP reviews did not show significant results, indicating that targeted approaches based on the population's specific needs are crucial. Given these insights, it would be worth to compare different reminder methods in more robust studies, as seen in other prevention areas [27] and emerging research on vaccination interventions [28].

Organizational changes emerged as a common theme in the interventions, particularly across the GP and

HCW categories. Among these, the increased involvement of general practitioners in patient management and communication was one of the most frequently cited interventions, consistently showing positive results. While organizational changes can be beneficial, their success may depend on how they are integrated into existing healthcare infrastructures and whether they address the specific needs of the population being targeted. For example, offering free vaccinations in maternity wards and workplaces showed promising results in some reviews, highlighting the importance of making vaccines easily accessible within familiar settings. However, other organizational changes, such as community pharmacy programs and opt-out approaches, did not always lead to significant improvements. Interestingly, opt-out approaches generally increased participation in other contexts, e.g., in colorectal cancer screening [29] and HIV testing [30]. However, challenges arise when communication is unclear, as shown by resistance to opt-out flu vaccination policies in the English National Health Service [31]. Therefore, an effective implementation may require clear communication and engagement with the target population. Overall, approaches building on existing healthcare structures, such as greater involvement of general practitioners, may appear more broadly transferable, whereas setting-specific strategies (e.g., workplace- or maternity ward-based vaccination and opt-out policies) may be more context-sensitive and dependent on local organizational and communication conditions. Accordingly, organizational interventions should be interpreted in light of their implementation context, with transferable strategies being more suitable for large-scale programs and context-sensitive approaches requiring local adaptation.

School-based interventions were found to be consistently effective in CAP reviews. This reinforces the value of using schools as settings for vaccination campaigns, particularly in reaching adolescents and young children. As noted in previous research, schools provide one of the most accessible avenues for implementing health promotion and preventive measures for school-aged children [32], emphasizing their important role not only in vaccination initiatives but also in advancing comprehensive public health efforts for younger populations.

The effectiveness of digital interventions was more variable. While some CAP reviews found positive results with web-based tailored interventions and mobile apps, other digital strategies, such as storytelling websites or game-based simulations in GP reviews, showed no significant impact. These mixed results suggest that while digital tools hold promise, their success may depend on various factors that require further examination. Jakob *et al*. [33] highlighted that adherence to tools such as mobile apps may depend on factors like personalization, ease of use, and addressing barriers such as low technical competence and privacy concerns, which should be addressed in the development of such interventions. These findings further indicate that usability, personalization, and users' digital literacy should be clearly reported and systematically evaluated in future studies, as they are likely key determinants of the effectiveness of digital vaccination interventions.

In terms of interventions specific to HCWs, communication tools, training, and feedback mechanisms consistently yielded positive results. Training healthcare leaders and implementing policies emphasizing staff vaccinations were also shown to be effective. These findings highlight the importance of engaging HCWs in vaccination promotion and ensuring they are well-equipped with the necessary information and resources. Complementing these results, our other work within the VAX-TRUST project, a systematic review aimed at identifying interventions targeted at HCWs, with few categories of interventions showing consistently positive findings. Nevertheless, it highlighted that newer strategies, such as apps, gaming, and simulations, could offer promising avenues to support HCWs [7]. Thus, while digital interventions could represent an innovative approach, the mixed results in both our works suggest that the characteristics of successful interventions need further exploration.

Last, financial incentives demonstrated mixed results. While some CAP reviews, particularly on HPV and adolescent vaccines, showed positive impacts of financial incentives, others reported non-significant results. Similarly, financial incentives aimed at general practices showed conflicting outcomes. According to Miranda *et al*. [34], it is worth noting that many studies on incentives fail to report details such as the rationale, magnitude, and design of incentive strategies. Addressing these aspects could help refine financial incentives and improve their effectiveness in promoting healthy behaviors.

This work had several limitations that should be acknowledged. The overview was constrained by the specific needs of the VAX-TRUST project, posing time and geographical restrictions. Search windows varied across the included systematic reviews, which may have affected comparability of findings. This is particularly relevant given that vaccine hesitancy is a complex and dynamic phenomenon that evolves over time and across contexts [11]. Determinants and barriers identified in this overview are based predominantly on observational evidence; therefore, causal relationships cannot be inferred and residual confounding cannot be excluded. Determinants and barriers were reported as framed in the included systematic reviews, with some reviews describing factors associated with vaccine acceptance and others reporting opposite characteristics as barriers. This overview cannot determine whether these reflect symmetric or distinct underlying mechanisms. The reliance on systematic reviews as the primary unit of analysis may have introduced biases related to the quality and scope of the included reviews. A further limitation relates to the extraction of Europe-specific evidence from global systematic reviews. When European results were not explicitly reported, primary studies conducted in European countries were identified and synthesized based on their reported setting. While this approach enabled the inclusion of relevant European evidence, it depends on the quality of reporting in the original reviews and primary studies and may have introduced selection bias or incompletely

captured contextual heterogeneity across Europe. The quality of the included reviews posed challenges. Common issues across the reviews included insufficient explanation of the reasons for selecting study designs, incomplete reporting of excluded studies with reasons, lack of transparency regarding funding sources, and inadequate interpretation of the risk of bias assessments. Therefore, while the overview provides valuable insights, it must be interpreted with these quality concerns in mind. In addition, the exclusion of exclusively qualitative systematic reviews may have resulted in the loss of rich contextual and experiential insights into vaccine hesitancy Last, the binary classification of intervention effectiveness as "significant" *versus* "non-significant or conflicting" was adopted to enable synthesis across highly heterogeneous systematic reviews; however, this necessary simplification may not fully capture variations in effect size, outcome relevance, and contextual factors, and the findings should therefore be interpreted with caution.

CONCLUSIONS

This overview highlights vaccine hesitancy as a multifaceted, dynamic, and context-dependent phenomenon, characterized by the coexistence of determinants and barriers that may vary across populations, vaccines, and settings, underscoring the need for tailored, evidence-based strategies.

Key gaps, including the limited use of RCTs, hinder the development of effective interventions. Among the most novel and underexplored determinants, health engagement is reported as a relevant factor, reflecting the need for a holistic approach that integrates broader health behaviors. Similarly, social media's dual role as both a facilitator and a barrier emerged with its growing influence, requiring deeper investigation and targeted strategies to improve its impact. Our findings suggest prioritizing interventions with more consistent effectiveness and higher scalability, such as active reminders, school-based programs, and organizational changes embedded within existing healthcare structures. Strengthening the role of primary care providers and reducing structural and logistical barriers appear particularly suitable for large-scale implementation, whereas more context-sensitive strategies require careful local adaptation and stakeholder engagement. In contrast, digital interventions and financial incentives warrant further evaluation to clarify the conditions under which they are effective. Overall, future research should prioritize rigorous study designs and implementation-focused studies to support evidence-informed vaccination policies across Europe.

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Conflicts of interest statement

The Authors declare no conflicts of interest.

Authors' contributions

Conceptualization: GLM, MF, EL, ME, EDV, RS; methodology: GLM, MF, EL, ME, EDV, RS; investigation: GLM, AD, SP, AP, CGS, EC, CL; data curation: GLM, AD, SP, AP, CGS, EC, CL; writing – original draft preparation: GLM, AD, SP, AP, CGS, EC, CL; writing – review and editing, visualization: GLM; supervision: MF, EL, ME, EDV, RS; project administration: GLM, MF. All Authors have read and agreed to the published version of the manuscript.

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