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Strategies intended to address vaccine hesitancy: Review of published reviews



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ABSTRACT

When faced with vaccine hesitancy, public health authorities are looking for effective strategies to address this issue. In this paper, the findings of 15 published literature reviews or meta-analysis that have examined the effectiveness of different interventions to reduce vaccine hesitancy and/or to enhance vaccine acceptance are presented and discussed. From the literature, there is no strong evidence to recommend any specific intervention to address vaccine hesitancy/refusal. The reviewed studies included interventions with diverse content and approaches that were implemented in different settings and targeted various populations. Few interventions were directly targeted to vaccine hesitant individuals. Given the paucity of information on effective strategies to address vaccine hesitancy, when interventions are implemented, planning a rigorous evaluation of their impact on vaccine hesitancy/vaccine acceptance will be essential.

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1. Introduction

The high rate of childhood vaccination coverage in most countries indicates that vaccination remains a widely accepted public health measure [1]. However, national estimates of vaccination coverage do not reflect variability within the countries. Under-vaccinated individuals tend to cluster together, leading to increased transmission of vaccine-preventable diseases [2]. Sub-optimal vaccine coverage rates can, in part, be attributed to vaccine hesitancy. Many studies have also shown that even parents who have their children vaccinated can have doubts or even fears about immunisation [3–6]. Vaccine hesitancy is receiving increasing public health attention in developed and developing countries around the world. Evidence suggests that in North America, Europe, and in other parts of the world, public confidence in vaccines is decreasing and anti-vaccine movements are becoming stronger [7]. When faced with vaccine hesitancy, public health authorities are looking for effective strategies to address it.

Many public health interventions to promote vaccination have been based on a “knowledge-deficit” approach assuming that vaccine hesitant individuals would change their mind if given the proper information. However, research on vaccine acceptance has shown that individual decision-making regarding vaccination is far more complex and may involve emotional, cultural, social, spiritual or political factors as much as cognitive factors [8–10].

In this paper, a review of published reviews on strategies to address vaccine hesitancy and, more broadly, to enhance vaccine acceptance, is presented, and promising approaches on how to address vaccine hesitancy and its determinants are discussed. This review of published reviews aims to complement the systematic review on strategies to address vaccine hesitancy commissioned by the Working Group on Vaccine Hesitancy [11].

2. Methods

To identify relevant literature reviews or meta-analysis reviewing interventions to address vaccine hesitancy and/or to enhance vaccine uptake, a search was conducted in the electronic databases PubMed, EMBASE, Global Health, CINAHL, PsycINFO, SocINDEX with Full Text, ERIC for the period January 2008 to November 2014.

The search strategy was built using a combination of keywords (principal terms and synonyms) for four concepts: (1) interventions, (2) beliefs, attitudes and knowledge, (3) vaccination and (4)

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Table 1
Search strategy: keywords in free text terms.

Concepts	Keywords (free text terms)
Interventions	Intervention, social marketing, advertising, campaign, education, marketing, promotion, program
Beliefs, attitudes and knowledge	Knowledge, attitude, practice, behavior, behaviour, awareness, vaccine hesitancy, vaccine hesitant, vaccine-hesitant
Vaccination	Immunisation, immunization, vaccination
Review	Review, systematic review, meta-analysis

review (Table 1). Within each concept, keywords were combined with the Boolean search operators. The different concepts were also linked with the Boolean and Positional search operators. Keywords were searched in “titles, keywords and abstracts”. In each database, the use of free text terms was combined with controlled language by using the appropriate thesaurus (for instance, Medical Subject Heading terms in PubMed).

In addition, further studies were retrieved from reference listing of relevant articles and consultation with members of the WHO SAGE Working Group on Vaccine Hesitancy.

Abstracts of all identified papers were reviewed. Articles were included if they met the following criteria: were reviews or meta-analysis of interventions to address vaccine hesitancy and/or to improve vaccine acceptance (original studies, guidelines, letters or editorials were excluded); were reviewing interventions targeting parents and/or health-care providers; were published in books, journals or website from 1 January 2008 to 30 November 2014; were written in English. Because of the particularities in the delivery of the annual influenza vaccines, reviews that focused exclusively on strategies to increase influenza vaccine uptake were excluded.

3. Results

The search strategy yielded 15 literature reviews or meta-analysis that met the eligibility criteria [12–26]. The majority of these were published in the last 3 years (9/15). The number of studies included in each review ranged from 2 to 240 (median = 16 studies). Table 2 presents a summary of the purposes, settings and main conclusions of these reviews and meta-analysis.

Only two of the reviews identified directly targeted strategies to address vaccine hesitancy (defined as voluntary refusal or delay in acceptance of recommended childhood vaccines while vaccination services are available) [20,25]. Both of these reviews included almost exclusively studies conducted in the United States. Williams, after reviewing the effectiveness of 15 interventions to improve attitudes, vaccination intent or vaccine uptake, was unable to identify any type of intervention as being more effective than others [24]. She also noticed that few studies identified parents as vaccine-hesitant prior to participation [25]. Similarly, Sadaf et al. examined 30 studies that evaluated interventions to increase vaccine uptake; 17 of these were parent-centred information or education about vaccination. Although most of these studies reported a statistically significant improvement in parents' intentions to have their children vaccinated, the data were conflicting and thus offered only limited insights. These authors have concluded that their review did not identify any convincing

evidence on effective interventions to address parental vaccine hesitancy/refusal [20].

Globally, most of the interventions analysed in the reviews that were examined for the present study were primarily to inform or to educate about vaccination [13,14,16,17,20,21,25]. Brief written educational interventions (e.g. pamphlets) were one of the most tested interventions included in the reviews. Although some studies reported a statistically significant improvement in vaccine uptake, the data were very inconsistent and, in most cases, the evidence was of low or moderate quality. None of the reviews included any recommendation for a particular type of informational or educational intervention as an effective strategy to increase vaccine uptake or to reduce vaccine hesitancy. For instance, Odone et al. reviewed interventions that apply new media (Internet and social media) to promote vaccine uptake and increase vaccination coverage [16]. These authors concluded that text messaging, accessing vaccination campaign websites, using patient-held web-based portals and computerised reminders may increase vaccine uptake, whereas there was insufficient evidence to determine effectiveness of use of social networks, email communication and smartphone applications [17]. Cairns et al. examined the effectiveness of promotional communications in the European context and also concluded that there is good evidence that a range of promotional communications can positively change knowledge, attitudes and behaviours. However, because many communication interventions were part of multi-component strategies, the net contribution of communication in improving vaccine uptake was difficult to assess [13]. The conclusions of two Cochrane reviews examining interventions to inform and educate about early childhood vaccination also indicate that the evidence that this type of interventions may increase vaccine uptake is of low quality [16,21].

In collaboration with the US Centers for Disease Control and Prevention, the Community Guide³ also has regularly published evidence-based recommendations on interventions intended to improve routine delivery of universally recommended vaccinations in the United States [12]. This work is based on a logic framework that stratified population-based interventions to improve vaccination coverage by the outcomes that they attempted to influence, and divided them into three categories: (1) interventions to increase community demand for vaccinations; (2) interventions that enhance access to vaccinations and (3) provider-based interventions [27]. Interventions to increase community demand for vaccination recommended by the Community Preventive Services Task Force based on sufficient evidence of effectiveness in increasing vaccination rates in children and adults are: client or family incentive rewards (e.g. food vouchers, gift cards, lottery prizes, baby products, the provision of transportation or child care, provision of vaccination at no cost, etc.); reminder and recall interventions; multi-component interventions that also enhance access to vaccination services and reduce missed opportunities by vaccination providers and vaccine requirements for daycare or school entry [12]. Similar conclusions were reached by Ward et al. who reviewed strategies to increase vaccination uptake in Australia and by Williams et al. who looked at strategies to optimise vaccine uptake among preschool children in high-income countries [23,26].

Wigham et al. reviewed the effectiveness, acceptability and economic costs of financial incentives and quasi-mandatory schemes, defined as “interventions that increase demand for vaccinations by offering contingent rewards or penalties with real material value; or that restrict access to universal goods or services,” on uptake of preschool vaccinations [23]. Studies examined in this review

⁴ Organisation for Economic Co-operation and Development.

⁵ Interventions aimed at communities were defined as those directed at a geographic area, and/or interventions directed to groups of people who share at least one common social or cultural characteristic.

³ The Community Guide is a website that houses the official collection of all Community Preventive Services Task Force findings and the systematic reviews on which they are based (Online: <http://www.thecommunityguide.org/>).

Table 2
Summary of published literature reviews and meta-analysis on strategies to address vaccine hesitancy (2006–2014).

First author/year of publication/title	Description of the reviews			Number of studies included	Quality assessment of studies	Main conclusions
	General Purpose and setting	Inclusion/Exclusion criteria	Main outcome measure			
The Community Guide, <i>Increasing Appropriate Vaccination</i> [12]	To present the results of systematic reviews of the effectiveness, applicability, other effects, economic impact, and barriers to use of selected population-based interventions intended to improve vaccination coverage in HIC	<p>Inclusion:</p> <p>Interventions addressing universally recommended adult, adolescent, or childhood vaccinations</p> <p>Primary study</p> <p>Take place in HIC</p> <p>Written in English</p> <p>Meet the evidence review and <i>Guide</i> chapter development team's definition of the interventions</p> <p>Provide information on one or more outcomes related to the analytic frameworks</p> <p>Compare a group of persons who had been exposed to the intervention with a group who had not been exposed or who had been less exposed</p>	Vaccine uptake	From 2 to 240 depending on the type of interventions	Reported	<p>Interventions to increase community demand for vaccinations</p> <p>The Community Preventive Services Task Force recommends:</p> <p>Client or family incentive rewards based on sufficient evidence of effectiveness in increasing vaccination rates in children and adults (based on results from 6 studies that evaluated incentive awards alone or in combination with additional interventions).</p> <p>Reminder and recall interventions based on strong evidence of effectiveness in improving vaccination coverage in children and adults, in a range of settings and populations, when applied at different levels of scale from individual practice settings to entire communities, across a range of intervention characteristics, when used alone or with additional components (62 studies).</p> <p>Community-based interventions implemented in combination (to enhance access to vaccination services, increase community demand, and reduce missed opportunities by vaccination providers) to increase vaccinations in targeted populations, on the basis of strong evidence of effectiveness in increasing vaccination rates (17 studies).</p> <p>Vaccination requirements for child care, school, and college attendance based on strong evidence of effectiveness in increasing vaccination rates and in decreasing rates of vaccine-preventable disease and associated morbidity and mortality, based on findings from 27 studies demonstrating effectiveness of vaccination requirements: for attendance in a variety of settings; for an array of recommended vaccines; in populations ranging in age from early childhood to late adolescence.</p> <p>There is insufficient evidence to determine the effectiveness of:</p> <p>Client-held paper immunisation records (7 studies)</p> <p>Clinic-based education when used alone (4 studies)</p> <p>Community-wide education when used alone (6 studies)</p> <p>Monetary Sanction Policies (2 studies)</p> <p>Provider- or system-based interventions</p> <p>The Community Preventive Services Task Force recommends:</p> <p>Health-care system-based interventions implemented in combination on the basis of strong evidence of effectiveness in increasing vaccination rates in targeted client populations (62 studies).</p> <p>Immunisation information systems on the basis of strong evidence of effectiveness in increasing vaccination rates (240 studies)</p> <p>Assessment and feedback for vaccination providers based on strong evidence of their effectiveness in improving vaccination coverage in children and adults, alone or in combination with additional interventions, in a variety of settings and populations (33 studies)</p> <p>Provider reminders based on strong evidence of effectiveness in improving vaccination coverage in adults, adolescents, and children; when used alone or with additional components; across a range of intervention characteristics; and in a range of settings and populations (48 studies)</p> <p>Standing Orders based on strong evidence of effectiveness in improving vaccination rates in children and adults, alone or in combination with additional interventions, in a variety of settings and populations (40 studies).</p> <p>There is insufficient evidence to determine the effectiveness of:</p> <p>Provider education when used alone (5 studies)</p>

Table 2 (Continued)

First author/year of publication/title	Description of the reviews			Number of studies included	Quality assessment of studies	Main conclusions
	General Purpose and setting	Inclusion/Exclusion criteria	Main outcome measure			
Cairns (2012), <i>Systematic literature review of the evidence for effective NIS promotional communications</i> [13]	To examine the effectiveness of national immunisation schedule promotional communications in European context	<p>Inclusion: All included studies reported evaluation, experimental, quasi-experimental, or interrupted time series (ITS) data on vaccine-uptake or likely behavioural precursors Experimental and pilot studies of communications promoting nationally scheduled vaccination were also eligible for inclusion European countries and their territories English and non-English language Academic and grey literature Published from 2000 to 2011</p> <p>Exclusion: Off topic Not a primary study</p>	<p>Change in measured immunisation uptake rates</p> <p>Secondary outcomes included measured changes in the target audience's knowledge, attitudes and other behavioural determinants</p>	33 (22 on interventions promoting influenza vaccination, 11 on childhood vaccines)	Reported	Of the 33 evaluation studies 15 captured in the review were rated as high validity studies on the basis of the quality, validity and applicability appraisal process; 7 high scoring studies reported convincing evidence of positive effect and 8 reported no evidence of effectiveness. Interventions that included an aim to promote more favourable attitudes to immunisation did not yield any evidence of more pro-immunisation attitudes. The review found that interventions aiming to improve knowledge levels were usually successful, but did not demonstrate any positive effects on vaccine uptake or intention to be vaccinated Some interventions that aimed to improve knowledge levels of health-care workers through education and training did report evidence of improved rates of vaccine uptake There is good evidence that a range of promotional communications can positively change knowledge, attitudes and behaviours. The evidence for increased vaccine uptake is particularly promising for health-care workers, patient risk groups (including the elderly), and seasonal influenza vaccine promotions. However many of the interventions captured by the review combined communication channels and methods, so it is not possible to identify which types of communication initiatives are most effective, or to estimate their contribution to overall intervention effect. In addition, many interventions included structural change to make vaccinations more accessible (e.g. reduced cost, more accessible clinics), further complicating attempts to determine the net contribution of communications
Fu (2014), <i>Educational interventions to increase HPV vaccination acceptance: a systematic review</i> [14]	To summarise and evaluate the evidence for educational interventions to increase HPV vaccination acceptance	<p>Inclusion: Randomised controlled trials (RCTs), Non-randomised controlled trials (NRCTs) as well as quasi-experimental designs HPV vaccine acceptance in patients eligible to receive the vaccine, or their parents Presented educational interventions and measured the following outcomes: (1) receipt of HPV vaccine (any dose or completion of the 3-dose series), (2) intention to receive HPV vaccine, or (3) attitude towards HPV vaccine Published from 1946 to 20 August 2013 English language</p> <p>Exclusion: Pilot or descriptive projects which reported only qualitative or anecdotal results Studies that did not focus primarily on populations eligible to receive HPV vaccine or their parents, or that did not subset results in a way that would allow the authors to extract information on these target groups</p>	Receipt of HPV vaccine, intention to receive HPV vaccine, attitude towards HPV vaccine	33	Reported	Most studies involved populations with higher educational attainment and most interventions required participants to be literate. The minority of studies used HPV vaccine uptake as the outcome. Well-designed studies adequately powered to detect change in vaccine uptake were rare and generally did not demonstrate effectiveness of the tested interventions. There is no strong evidence to recommend any specific educational intervention for widespread implementation.

<p>Glenton (2011), <i>Can lay health workers increase the uptake of childhood immunisation?</i> Systematic review and typology [15]</p>	<p>To assess the effects of lay health workers' (LHWs) interventions on childhood vaccination uptake</p>	<p>Inclusion: RCTs, NRCTs, ITS studies, controlled before–after (CBA) studies and studies where the intervention's aim was to increase vaccination coverage among children <5 years of age Any intervention delivered by LHWs which aimed to increase childhood vaccination coverage Studies where LHWs were used as a substitute for trained health professionals or in addition to health professionals Published up to February 2009</p>	<p>Vaccination coverage</p>	<p>12 (7 in HIC)</p>	<p>Reported</p>	<p>In 6× studies, LHWs promoted vaccine uptake among economically disadvantaged families in high-income countries. The LHW programmes increased the number of children whose vaccinations were up to date. This evidence was of moderate quality Evidence was of low quality for LHWs promoting vaccine uptake among families in LMICs (However, the LHW programme increased the number of children whose DPT and measles vaccinations were up to date) The quality of the evidence was very low for the impact of vaccines given by the LHWs. In 2 studies, LHWs increased the number of children whose vaccinations were up to date compared with standard care. However, it is unclear whether these differences were statistically significant</p>
<p>Kaufman (2012), <i>Face to face interventions for informing or educating parents about early childhood vaccination</i> [16]</p>	<p>To assess the effects of face-to-face interventions for informing or educating parents about early childhood vaccination on vaccine uptake and parental knowledge</p>	<p>Inclusion: RCTs and cluster RCTs This review focuses on face-to-face single or combined interventions to inform or educate (oral presentations, one-on-one or group classes or seminars, information sessions, or home outreach visits). Published up to 2012</p> <p>Exclusion: Interventions directed to communities</p>	<p>Primary outcomes are vaccination status of child and parents' knowledge or understanding of vaccination</p>	<p>7 (6 RCTs and 1 cluster RCT – 3 LMIC, 4 HIC)</p>	<p>Reported</p>	<p>The overall result is uncertain because the individual study results ranged from no evidence of effect to a significant increase in vaccination Three studies reported vaccination status measured 3 months after a single-session intervention. Effect of the intervention remains uncertain. Four comparisons from these studies showed inconsistent results (studies with higher risk of bias were associated with greater increase in vaccination, compared with controls, while study with lower risk of bias showed no or little evidence of effect. The quality of evidence was low Results for interventions where vaccination status was measured at the conclusion of a multi-session intervention indicated a very uncertain effect, with statistically insignificant effect ranging from reduced to no evidence of effect, and had wide confidence intervals. The quality of evidence was very low Effect was also very uncertain for studies measuring knowledge or understanding of vaccination. The two multi-session interventions showed non-significant increases in knowledge scores compared with controls. The quality of evidence was very low</p>

Table 2 (Continued)

First author/year of publication/title	Description of the reviews			Number of studies included	Quality assessment of studies	Main conclusions
	General Purpose and setting	Inclusion/Exclusion criteria	Main outcome measure			
Odone (2014), <i>Effectiveness of interventions that apply new media to improve vaccine uptake and vaccine coverage</i> [17]	To systematically collect and summarise the available evidence on the effectiveness of interventions that apply new media to promote vaccine uptake and increase vaccination coverage for children, adolescents and adults in high-income settings	Inclusion: Studies conducted in countries members of the OECD ⁴ Interventions that applied mobile phones and internet-based tools Original studies using an observational or experimental study design Published from 1 January 1999 to 30 September 2013 English language Exclusion: Guidelines, review, letters or editorial Interventions targeting vaccines recommended for people with specific medical conditions, vaccines for international travellers or health-care professionals	Primary outcomes are vaccine coverage or vaccine uptake	19	Reported	The majority of the studies were conducted in the USA (74%, $n = 14$) 13 (68%) of the studies were experimental, the rest having an observational study design. 11 studies (58%) reported results on the primary outcome. Retrieved studies explored the role of: text messaging ($n = 7$, 37%), smartphone applications ($n = 1$, 5%), Youtube videos ($n = 1$, 5%), Facebook ($n = 1$, 5%), targeted websites and portals ($n = 4$, 21%), software for physicians and health professionals ($n = 4$, 21%), and email communication ($n = 1$, 5%) There is some evidence that text messaging, accessing immunisation campaign websites, using patient-held web-based portals and computerised reminders increase vaccination coverage rates Insufficient evidence is available on the use of social networks, email communication and smartphone applications Due to high degree of heterogeneity between studies no quantitative assessment could be performed More research is needed to assess the effectiveness and cost-effectiveness of interventions applying new media and on how to successfully market constructive public health messages in the new communication era Moderate quality evidence: Evidence-based discussions probably improve DPT3 and measles coverage Information campaigns probably increase uptake of at least one dose of a vaccine Low quality evidence: Facility-based health education alone or in combination with redesigned vaccination cards may improve the uptake of combined vaccine against diphtheria, pertussis, and tetanus (DPT3) coverage One study suggests that this monetary incentive may lead to little or no difference in the uptake of MMR or DPT1 Training of immunisation managers to provide supportive supervision for health providers was assessed by one study and may improve the uptake for DPT3, OPV3, and hepatitis B3 Home visits may improve OPV3 and measles vaccine coverage A combination of monetary incentives (patient oriented); quality assurance (provider oriented); and provision of equipment, drugs and materials (health system oriented) interventions was evaluated in another arm of a study. The study suggests that this intervention may lead to little or no difference in MMR coverage
Oyo-Ita (2011), <i>Interventions for improving coverage of child immunization in low- and middle-income countries</i> [18]	To evaluate the effectiveness of intervention strategies to boost and sustain high childhood vaccination coverage in LMIC	Inclusion: RCTs, NRCTs, and ITS studies Interventions targeting children aged 0–4 years, caregivers, and health providers Comparisons with routine immunisation practices in the study setting or with different interventions or similar interventions implemented with different degrees of intensity Published up to 2010 except 2011 in the case of the MEDLINE search Exclusion: Patient reminder and recall as this is covered in an existing review [73] Controlled before-and-after studies that had only two study locations	Proportion of target population fully immunised with recommended vaccines, by age Number of children aged two years fully immunised per vaccine	6 (5 cluster RCTs)	Reported (4 studies at high risk of bias)	Few papers were identified; few papers were of strong scientific quality The strategies to “bring immunizations closer to the community” (including non-health workers to encourage people to seek immunisation services, bringing immunisation services to communities, and increasing demand through educating communities) could improve the percentage of FVC Use of home visits for education and/or immunisation service delivery may increase in the percentage of FVC Conflict areas are generally difficult to reach because of security concerns. Three papers evaluated strategies that provided vaccinations in conflict areas. Strategies involved using bush planes to gain access to populations, providing incentives to attract people to immunisation sites, going house-to-house to motivate parents to bring their children for vaccination, and working with communities to coordinate provision of services
Ryman (2008), <i>Too little but not too late: Results of a literature review to improve routine immunization programs in developing countries</i> [19]	To identify strategies used to increase routine immunisation programmes	Inclusion: Studies published in English, French, or Spanish from 1975 through 2004 Primary data on effectiveness of the strategy were not required for inclusion, as the goal was to identify all possible strategies Exclusion: Studies with low quality scores	Percentage change in fully vaccinated children (FVC), percentage change in vaccination coverage for specific antigens, dropout from routine vaccinations, or timeliness of vaccination	25	Reported (studies with a score <60 were excluded)	

Sadaf (2013), <i>A systematic review of interventions for reducing parental vaccine refusal and vaccine hesitancy</i> [20]	To evaluate the literature on interventions to decrease parental refusal of and hesitancy towards recommended childhood and adolescent vaccines	<p>Inclusion: Primary reports of intervention studies Quantitative outcome measures (vaccine refusal, behaviour, attitudes and/or intent to vaccinate) Published between 1990 and July 2012 English language</p> <p>Exclusion: Non-intervention studies, reviews, historical articles, case reports, commentaries, clinical guidelines and recommendations</p>	Parental vaccine refusal behaviour, attitudes towards immunisation, and/or intent to vaccinate	30 (25 from USA)	Reported (most studies scored low on GRADE criteria)	<p>Most studies (13) used a before-after intervention design and the remaining were RCTs (3), NRCTs (7) and evaluation studies (6) The review did not reveal any convincing evidence on effective interventions to address parental vaccine hesitancy/refusal Large number of studies evaluated interventions for increasing vaccination coverage rates such as the use of reminder/recall systems, parent, community-wide, and provider-based education and incentives as well as the effect of government and school vaccination policies Few intervention studies measured outcomes linked to vaccine refusal such as vaccination rates in refusing parents, intent to vaccinate, or change in attitudes towards vaccines</p>
Saeterdal (2014), <i>Interventions aimed at communities to inform and/or educate about early childhood vaccination (review)</i> [21]	To assess the effects of interventions aimed at communities to inform and/or educate people about vaccination in children aged 6 years and younger	<p>Inclusion: Individual or cluster-randomised and quasi-randomised controlled trials, ITS and repeated measures studies and controlled before-and-after studies Interventions aimed at communities⁵ and intended to inform and/or educate about vaccination in children aged 6 years and younger Interventions conducted in any setting</p>	Knowledge among participants of vaccines or vaccine-preventable diseases and of vaccine service delivery; child immunisation status; and unintended adverse effects	2	Reported (evidence of low or moderate certainty on GRADE criteria)	<p>Two cluster-randomised trials were included that compared interventions aimed at communities to routine immunisation practices (one in India and another in Pakistan) The trials show low certainty evidence that interventions aimed at communities to inform and educate about childhood vaccination may improve knowledge of vaccines or vaccine-preventable diseases among intervention participants (adjusted mean difference 0.121, 95% CI: 0.055–0.189) These interventions probably increase the number of children who are vaccinated. The study from India showed that the intervention probably increased the number of children who received vaccinations (RR 1.67, 95% CI: 1.21–2.31; moderate certainty evidence). The study from Pakistan showed that there is probably an increase in the uptake of both measles (RR 1.63, 95% CI: 1.03–2.58) and DPT vaccines (RR 2.17, 95% CI: 1.43–3.29) vaccines, but there may be little or no difference in the number of children who received polio vaccine (RR 1.01, 95% CI: 0.97–1.05) There is also low certainty evidence that these interventions may change attitudes in favour of vaccination among parents with young children (adjusted mean difference 0.054, 95% CI: 0.013–0.105), but they may make little or no difference to the involvement of mothers in decision-making regarding childhood vaccination (adjusted mean difference 0.043, 95% CI -0.009–0.097).</p>
Shea (2009), <i>Increasing the demand for childhood vaccination in developing countries: a systematic review</i> [22]	To review literature on efforts to stimulate demand for routine childhood vaccination	<p>Inclusion: Studies providing a description of activities that seemed designed to increase demand for childhood vaccination Studies that provided quantitative estimates of the impact of interventions Published up to September 2008 and searched for primary studies published since 2004</p> <p>Exclusion: Studies of exclusively supply side initiatives Studies from developed countries</p>	Uptake of routine childhood vaccines	8	Reported	<p>Most studies reviewed represented a low level of evidence Interventions with an impact on vaccine uptake included knowledge translation (KT) (mass media, village resource rooms and community discussions) and non-KT initiatives (incentives, economic empowerment, household visits by extension workers) Most claimed to increase vaccine coverage by 20% to 30%. Estimates of the cost per vaccinated child varied considerably with several in the range of US\$10–20 per vaccinated child Mass media campaigns may be effective, but the impact depends on access to media and may be costly if run at a local level. The persistence of positive effects has not been evaluated</p>

Table 2 (Continued)

First author/year of publication/title	Description of the reviews			Number of studies included	Quality assessment of studies	Main conclusions
	General Purpose and setting	Inclusion/Exclusion criteria	Main outcome measure			
Ward (2012), <i>Strategies to improve vaccination uptake in Australia, a systematic review of types and effectiveness</i> ^[23]	To profile and critique available evidence of strategies to improve vaccine uptake in Australia and evaluate their effectiveness	Inclusion: Published from 1997 through to May 2011 English language Studies must have reported original research about, or evaluation of, one or more interventions to improve uptake of one or more vaccines available in Australia Studies must have included a quantitative measure of uptake as a primary outcome Exclusion: Studies describing uptake in the absence of an intervention or reporting only other outcomes (i.e. descriptive or qualitative)	Vaccine uptake	49	Reported	The most effective and common strategies for increasing community demand and provider-based interventions were patient reminder/recalls and provider reminders. Education for the public and providers (either alone or as part of a multicomponent strategy) had variable impact on uptake, with increases less substantial or direct when compared with reminder/recalls Also effective were integration of vaccination status checks into routine health assessments, individual provider support, and targeted promotion campaigns in the mass media, although studies of these interventions were minimal and confined to particular target groups and vaccines For enhancing access, catch-up plans for those overdue for vaccination were particularly effective, often reducing the percentage of those overdue by more than 50%. The two studies involving an accelerated vaccination schedule for hepatitis B showed an increase in the overall completion rate compared with the standard schedule Results from the few studies of home visits for routine childhood vaccination highlighted their effectiveness, particularly when targeting Aboriginal and Torres Strait Islander children. The same effectiveness was observed for expanding access in hospitals and vaccination clinics in public settings There were several effective regulatory interventions that were beyond 'baseline practice' of funding vaccines on the NIP and school-based vaccination programmes. These included national parental incentives; the maternity immunisation allowance (MIA) and linking vaccination to the child care benefit as well as a jurisdictional hepatitis B vaccination policy for high-risk infants, then subsequently for all newborns. All other regulatory interventions primarily focused on provision of funded vaccine coupled with mandatory vaccination policies for health-care workers (HCWs) and were implemented at a jurisdictional and/or organisational level. The small number of studies showed limited effectiveness of this strategy
Wigham (2014), <i>Parental Financial Incentives for Increasing Preschool Vaccination Uptake: Systematic Review</i> [24]	To determine the effectiveness, acceptability, and economic costs and consequences of parental financial incentives and quasi-mandatory schemes for increasing the uptake of preschool vaccinations in high-income countries	Inclusion: RCTs and cluster RCTs, CBA studies, time series analyses examining the effectiveness of parental financial incentives and quasi-mandatory schemes or any empirical studies exploring acceptability Parents of preschool-aged children (effectiveness component) Members of any relevant stakeholder group (acceptability component) Studies in high-income countries	Uptake of preschool vaccinations (effectiveness component) Acceptability of the intervention (acceptability component)	10 (4 on effectiveness, 6 on acceptability)	Reported	There was substantial heterogeneity across studies in terms of both interventions and methods There is not sufficient evidence to conclude whether parental incentives and quasi-mandatory interventions are effective for increasing uptake of preschool vaccinations. One study with low risk of bias did find short-term effects of quasi-mandatory interventions linking vaccinations to education, but effects were extinguished within 6 years There was some evidence that quasi-mandatory interventions linking vaccination to education were also the most acceptable interventions considered, although the risk of bias in these studies was high, and this finding may be specific to contexts where such interventions are widespread

Williams (2014), <i>What are the factors that contribute to parental vaccine-hesitancy and what can we do about it?</i> [25]	To review the known barriers to vaccination reported by vaccine-hesitant parents and the current evidence on strategies to address parental vaccine hesitancy/HIC	<p>Inclusion: Intervention specifically targeting vaccine-hesitant (VH) parents or health-care providers working with VH parents Quantitative evaluation of improvement Published between 2003 and 2013 English language</p> <p>Exclusion: Qualitative studies Interventions not focusing on vaccines recommended by ACIP</p>	Attitudes, vaccination intent or vaccine uptake of children	15 (7 on childhood vaccines and 8 on HPV vaccine)	Not reported	<p>Current data do not support one method for intervention as having superior effect over others Few interventions have evaluated the ultimate outcome: on-time vaccination of infants or children Most reported interventions are primarily educational in nature, yet the decision-making process for vaccine-hesitant families is likely very complex and influenced by factors which are difficult to measure, such as influences by social networks. This complexity probably contributes to the lack of evidence for effective interventions Cultural tailoring and message framing of interventions have been used successfully in conjunction with educational material for VHPs Use of a theoretical model to provide a framework for development of interventions is often recommended; however, few of the studies identified in this review did use a theoretical model</p>
Williams (2011), <i>Primary care strategies to improve childhood immunisation uptake in developed countries: systematic review</i> [26]	To conduct a systematic review of strategies to optimise vaccine uptake within preschool children in developed countries	<p>Inclusion: Experimental studies reporting original research including RCTs, NRCTs, before and after studies and ITS studies Targeting populations of children under 5 years of age living in developed countries Published from inception to 1 June 2010 English language</p> <p>Exclusion: Studies for which the full article was not available, and studies that did not contain any original data</p>	Increase in the proportion of the target population up to date with standard recommended universal vaccinations	46	Reported	<p>Parental reminders have been shown to have an overall positive effect on vaccine uptake. These effects have been reported with both generic and specific reminders and with all methods of reminders and recall The limited number of studies precludes reaching an evidenced-based conclusion on the effect of parental education interventions on parental behaviour Only one study concerned patient-held records and did not demonstrate a significant difference between usual care and a home-based record booklet Provider reminder/recall strategies, provider education and provider feedback shown to have a positive effect on vaccination rates Multicomponent interventions shown to have a positive effect on vaccination rates. It is not possible to identify which component of the intervention has had the greatest effect on vaccination rates</p>

were all from high-income countries. These authors concluded that there was not sufficient evidence to show whether parental incentives and quasi-mandatory interventions were effective for increasing uptake of preschool vaccinations. Studies reviewed by these authors have also indicated that quasi-mandatory interventions linking vaccination to education were acceptable, although the risk of bias in the relevant studies was high, and they were conducted in contexts where such interventions were widespread [24].

Glenton et al. have examined the effects of lay health workers on childhood vaccine uptake [14]. These authors concluded that, both among disadvantaged families in high-income countries and among families in low- and middle-income countries, lay health worker programmes may increase the number of children whose vaccinations are up-to-date, but the evidence was of very low to moderate quality [15].

Finally, three reviews focused exclusively on interventions implemented in low- and middle-income countries [18,19,22]. Few articles describing the effectiveness of interventions to increase vaccine uptake were included in these reviews (from 6 to 25). Moreover, most of these studies represented a low level of evidence. The conclusions of these reviews indicate that face-to-face education, information campaigns, household visits, incentives or training of health-providers may increase childhood vaccine uptake in low- or middle-income countries settings, but many of the studies reviewed were at high risk of bias [18,19,22].

4. Discussion

From the reviews, there is no strong evidence on which to recommend any specific intervention to address vaccine hesitancy/refusal. The reviewed studies included interventions with diverse content and approaches that were implemented in different settings and targeted various populations. The number of interventions similar enough to be grouped was often low and insufficient to demonstrate effectiveness using recognised validation criteria [28]. In addition, many of the reviewed studies were conducted in the United States and few were from low- and middle-income countries, further limiting the generalisability of the findings. The studies at low risk of bias were mostly single-component interventions (often educational interventions), which are less challenging to evaluate than multi-component interventions or interventions aiming to change determinants that are difficult to measure (such as social norms). Finally, few studies included in the reviews used vaccine uptake or on-time vaccination as the outcome and even fewer studies were directly targeting vaccine-hesitant individuals. While acknowledging these caveats, the findings indicate that reminders and recall for patients and health-care providers are effective tools to improve vaccine uptake among various groups and in different settings [12,23,26]. However, there is limited evidence on the effectiveness of reminders and recalls for vaccine-hesitant individuals [29,30].

There is mixed evidence on the effectiveness of interventions involving face-to-face communication interventions, health-care provider training, community-based actions, and communication using mass media. Vaccination requirements or mandates for school admittance are viewed as effective in increasing vaccine uptake in high-income countries [2,12,20,24,31]. However, these strategies do not adequately address the underlying causes of vaccine hesitancy and refusal [24]. In addition, such policies can raise concerns about civil liberties [32] that may heighten mistrust in the vaccine programme. Moreover, there are high-income countries where such policies are not in place, such as Canada, yet uptake rates are comparable. Concerns have also been raised that in low-income countries, mandatory vaccination for school

entry may add another barrier to access to primary education. Thus, mandating vaccination as a strategy to address vaccine hesitancy must be approached with great care and caution. The impact of potential negative consequences (e.g. distrust in the immunisation programme, decrease in school access) may outweigh potential benefits such as the increase in vaccination coverage in some settings.

Many traditional educational tools (e.g. information pamphlets) had little or no impact on vaccine hesitancy [13,14,16,17,20,21,25]. Furthermore, some communication interventions could even reinforce vaccine hesitancy, as shown by a recent study by Nyhan et al. [33]. These researchers conducted a randomised controlled trial in the United States using four interventions to refute claims of a link between the measles, mumps and rubella (MMR) vaccine and autism, based on current public health communication. The study showed that none of the interventions significantly increased parental intention to vaccinate although it did reinforce the decision of those who were already intending to do so. Most importantly, these interventions decreased the intention to vaccinate among parents who had the least favourable attitudes towards vaccines [33]. This highlights the importance of carefully designed public health messages, and that messages need to be tailored for the specific target group, because messaging that too strongly advocates vaccination may be counterproductive, reinforcing the hesitancy of those already hesitant [34].

The conclusion from some of the reviews indicates that mass vaccine promotion campaigns may enhance positive attitudes towards vaccination and, ultimately, increase coverage rates [13,18,22]. However, interventions using mass media are difficult to evaluate and are not well-suited to experimental design; other types of evaluation are subject to various forms of bias due to the many potential confounding factors which limits the quality of the evidence available. When communication interventions are part of multi-component strategies, it becomes almost impossible to evaluate their direct impact on vaccine uptake [13]. In developing communication interventions to address vaccine hesitancy, the use of Internet and social media is often recommended, but few web-based strategies have been evaluated [17,35]. Limitations of this type of strategy include difficulties in “attracting” vaccine-hesitant individuals and exclusion of individuals without Internet access or with low literacy levels, while advantages include low cost and high potential to adapt and personalise messages [36,37]. The emergence of social media as a source of online health information combined with decreasing rates of vaccination mean that it is critical to understand how social media can influence parents’ decision-making processes, and to develop communication strategies about vaccination [38].

Mitigation of pain associated with vaccination was not addressed in the reviews, yet injection pain has been shown to cause distress for recipients, parents, and adults, as well as those giving the injection. Fear of injection can lead to hesitancy. Evidence-based guidelines on pain mitigation during vaccination have been published [39]. Early research in high-income countries has shown that parents are more comfortable with infant vaccination when pain is mitigated, [40] but pain mitigation has not been specifically tested among those whose vaccine hesitancy is related to fear of pain.

The SAGE Working Group on Vaccine Hesitancy also discussed the role of childhood beliefs about vaccination in shaping adult vaccination acceptance. Historically, children have not been systematically educated in schools about vaccines, so that some of the adult population may not appreciate their benefits for health and societal value for their children and for themselves. While other opportunities to learn about vaccines exist (e.g. from media, information pamphlets, health-care professionals), these routes may be missed by many in the population. In contrast, older generations

understood the value of vaccines within the context of personal experience with vaccine-preventable diseases and/or the disease impact on other children and therefore as adults they did not need to be taught about the risks of these diseases and the benefit of the vaccines. Now many vaccine-preventable diseases have declined or disappeared as a result of high vaccine uptake, thereby negating the personal experience route for education about the benefits of vaccination. Ensuring education and knowledge about vaccines in younger individuals (children, adolescents, young adults), possibly through school-based programmes, may provide a good opportunity to encourage future vaccine acceptance by parents and adults and minimise the potential for development of hesitancy, although research is needed to evaluate this strategy in the short and longer term. Evidence of the impact of education on behaviour change is available in areas such as bullying [41], exercise behaviour change initiatives [42] or environmental activism. An interesting model that could be used to integrate vaccination science in education is the Earth Science Literacy Initiative (ESLI), funded by the National Science Foundation in the United States [43]. The ESLI has gathered and codified the underlying understanding of Earth sciences into a succinct document [44] with the explicit intent of influencing educational standards, as a means to improve curricula, teaching, assessment, and ultimately learning, throughout the United States.

As stressed by Leask et al., when the literature is considered more broadly, two major influences on vaccine hesitancy emerge: the influence of social norms and the interactions with health-care providers [45]. The role of social norms is developed through social networks, through which parents gather information and form opinions about vaccination [46,47]. The influence of social networks on parents' decisions to delay vaccination or to refuse vaccines has been identified [46,48]. However, people who are opposed to vaccination often take disproportionately more space in the discussions about vaccination in the public forum and too often the voices of parents who are in favour of vaccination are not heard. Some interventions capitalising on the influences of social norms and social networks have been implemented to address vaccine hesitancy (e.g. peer-to-peer communication valuing fully vaccinated communities or vaccine "champion" parents to talk with vaccine-hesitant parents, development via social media of a community of parents who vaccinate or of a community of parents whose children were affected by a vaccine-preventable disease, etc.) [49–51]. However, the effectiveness of these interventions remains to be evaluated. From another standpoint, the interaction between patients and health-care providers is the cornerstone of maintaining confidence in vaccination [6,52,53]. A study conducted by Gust et al. in the United States concluded that information or reassurance from a health-care provider was the main factor in changing the decision of parents who had planned to delay or refuse a vaccine for their child [54]. In recent years, many communication tools to help health-care providers to discuss with vaccine-hesitant parents have been published, [53,55–58] but their effectiveness has still not been evaluated. Whereas communication frameworks often suggest discussing vaccines in a participatory and open manner, recent research by Opel et al. found that more firm, presumptive discussion styles might be more effective in improving vaccine acceptance [48].

Vaccine hesitancy can be seen not only towards routine vaccination but also in mass vaccination campaigns in high-, middle- and low-income countries [59–61]. Determinants of hesitancy in mass campaigns vary and include convenience, confidence and complacency factors, as also seen with routine programmes [62]. While neither the systematic review of strategies [63] nor the reviews examined in this article have focused on interventional research in the context of mass campaigns, the Working Group did note that *successful* mass campaigns had a number of common features; these include the polio elimination campaign in India [64] (although the

reaction to the mass polio campaign approach has also provoked distrust in some countries), [65] polio virus containment in Israel in 2013, [66] meningococcal A campaigns in several countries in the African meningitis belt [67,68] and meningococcal C outbreak control campaigns in high-income countries, [69]. In each case, the vaccine-preventable disease was well known and feared. Cases were well publicised. Political and religious leaders from all levels were actively involved. Communities were directly involved in helping with the campaigns and access to vaccination was made as easy as possible. Social norms of acceptance were publicised. All of these appeared to increase vaccine acceptance, although hesitancy was not measured and their impact on it is unknown. More evaluation of successful mass campaigns is needed to determine whether there are particular hesitancy determinants that are more common in mass campaigns in particular settings and what strategies are most effective in addressing them.

Finally, key principles for optimising the development of strategies to address vaccine hesitancy can be identified through a review of the literature. To be effective, interventions should be developed using a planning framework, such as the WHO *Guide to Tailoring Immunization Programmes*, [70] and should be based on a theoretical model. The use of a combination of different interventions (multiple-component) appears to be more effective than single-component interventions [26,71]. Interventions are most likely to succeed when they are based on empirical data and situational assessment – both to have a detailed level of understanding of the vaccine hesitancy situation (susceptible populations, key determinants of vaccination, barriers and enabling conditions, etc.) and to properly evaluate the impact of the intervention [70]. The development of culturally adapted and personalised interventions has been shown to be effective in enhancing compliance with preventive behaviours, including vaccination [72–74].

In conclusion, the SAGE Working Group on Vaccine Hesitancy emphasizes the importance of understanding the specific concerns of the various groups of vaccine-hesitant individuals, as an effective "one size fits all" intervention is unlikely ever to exist. Nevertheless promising strategies to increase vaccination coverage have been identified and should be applied [11,75]. Given the paucity of information on effective strategies to address vaccine hesitancy, whenever interventions are implemented, planning a rigorous evaluation of their impact on vaccine hesitancy/vaccine acceptance is essential, as is sharing of lessons learnt.

Conflict of interest

The LSHTM research group "Project to monitor public confidence in Immunization Programs" has received research funding from Novartis as well as funding from GSK to host a meeting on vaccine confidence. Heidi Larson has done consulting on vaccine confidence with GSK.

None of the other authors had any potential conflict of interest.

Some of the authors are World Health Organization staff members. The opinions expressed in this article are those of the authors and do not necessarily represent the decisions, official policy or opinions of the World Health Organization.

Appendix. SAGE Working Group on Vaccine Hesitancy

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U.S.A.; Susan Goldstein, Soul City: Institute for Health and Development Communication, South Africa; Heidi Larson, London School of Hygiene and Tropical Medicine, U.K.; Noni MacDonald, Dalhousie University, Canada; Mahamane Laouali Manzo, Ministry of Health, Niger; Arthur Reingold, University of California at Berkeley, U.S.A.; Kinzang Tshering, Jigme Dorji Wangchuck National Referral Hospital, Bhutan; Yuqing Zhou, Chinese Center for Disease Control, China with the WHO/UNICEF Secretariat; Robb Butler, World Health Organization, Denmark; Philippe Duclos, World Health Organization, Switzerland; Sherine Guirguis, UNICEF, U.S.A.; Ben Hickler, UNICEF, U.S.A.; Melanie Schuster, World Health Organization, Switzerland.

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