

# Strategies to Overcome Vaccine Hesitancy: A Systematic Review

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## Research

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## Abstract

**Background:** Vaccination, albeit a necessity in the prevention of infectious diseases, requires appropriate strategies for addressing vaccine hesitancy at an individual and community level. However, there remains a glaring scarcity of available literature in that regard. Therefore, this review aims to scrutinize globally tested interventions to increase the vaccination uptake by addressing vaccine hesitancy at various stages of these interventions across the globe and help policy makers in implementing appropriate strategies to address the issue.

**Methods:** A systematic review of descriptive and analytic studies was conducted using specific key word searches to identify literature containing information about interventions directed at vaccine hesitancy. The search was done using PubMed, Global Health, and Science Direct databases. Data extraction was based on study characteristics such as author details; study design; and type, duration, and outcome of an intervention.

**Results:** A total of 105 studies were identified of which 33 studies were included in the final review. Community-based interventions, monetary incentives, and technology-based health literacy demonstrated significant improvement in the utilization of immunization services. On the other hand, media-based intervention studies did not bring about a desired change in overcoming vaccine hesitancy.

**Conclusion:** This study indicates that the strategies should be based on the need and reasons for vaccine hesitancy for the targeted population. A multidimensional approach involving community members, families, and individuals is required to address this challenging issue.

## Background

Vaccines have always been one of the most innocuous and effective approaches for the prevention of many infectious diseases. In spite of this, vaccine-preventable diseases are still widespread. In the preceding years, there have been outbreaks of infectious diseases in many parts of the world regardless of having effective vaccines against such diseases. The plausible reason for it could be “vaccine hesitancy”. [1]

Vaccine hesitancy refers to a delay in acceptance or refusal of vaccination despite availability of vaccination services. [2] Against the backdrop of a large number of unimmunized children globally<sup>2</sup> and frequent outbreaks of vaccine-preventable diseases, [3] WHO has listed vaccine hesitancy as one of the top ten global health threats in 2019, [4] and has drawn major concerns across the world due to increase and resurgence of vaccine-preventable diseases. The reasons of reluctance or refusal are complex varying across time, place, and vaccines, [5, 6] and context-specific such as related to confidence, convenience, and complacency. Similarly, multiple factors such as religious beliefs, geographic barriers, parent-provider relationship, perceived risk of adverse events following immunization (AEFI), lack of knowledge about vaccination, and disease risk perception give rise to vaccine hesitancy. [7] A survey conducted by WHO and UNICEF showed that vaccine hesitancy emerged a decade ago; [8] however, it has gained attention due to the current changing scientific, cultural, medico-legal, and media environments, despite all the efforts made to increase the awareness and increase the vaccines uptake. [9] The trend has been realized in several countries across the world including United Kingdom, United States, and India. [9] This has triggered global researchers to understand the determinants of this emerging issue throughout the world. [10]

Various strategies such as community activity by community health workers and medical interns, monetary incentives, educational videos as well as media-based approach have been piloted and evaluated in diverse settings to understand their impact on reducing the vaccine hesitancy. However, there is a paucity of critical synthesis of all these interventions across the globe and contextual summarization to guide program managers and policy makers in implementing appropriate strategies to address vaccine hesitancy. Therefore, this systematic review aims at improving vaccination coverage by retrieving the lost trust in the vaccination system through globally tested interventions for people with different degrees of vaccine hesitancy.

## Methods

This systematic review was performed in line with the quality requirements of the PRISMA [11] guideline, from June to September and the flow chart has been mentioned as Figure 1 for understanding the method followed. The checklist of PRISMA guideline has also been added as Additional Document.

A search was conducted in the PubMed, Global Health, and Science Direct electronic databases to identify peer-reviewed literature. Search was not restricted to any time period and included literature search for title, abstract, and full-text in English language only.

### **Search strategy**

The search strategy was set up using database-specific vocabularies. The literature search was conducted using the keywords “immunization,” “vaccine,” “vaccination,” “vaccine strategy,” “vaccine intervention,” “vaccine hesitant,” “vaccine hesitancy,” “vaccine refusal,” “trust in vaccination,” “vaccine confidence,” “vaccine resistance,” “vaccine impact,” “vaccine concern,” “vaccine rejection,” and “vaccine side effects” using “AND” and “OR” operators.

### **Inclusion and Exclusion criteria**

While searching for vaccination strategies, we considered universally recommended vaccines for children, adolescents, and adults such as diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, measles, mumps, rubella, Hemophilus influenza b (Hib), varicella, pneumococcal vaccine, meningococcal vaccine, Human papillomavirus (HPV), and seasonal influenza vaccine. Based on the objective, we included interventions that were targeted towards addressing vaccine hesitancy among parents and caregivers. For review, descriptive and analytical studies that described the effect of strategies on addressing vaccine hesitancy were included.

Studies that were opinion-based or did not focus primarily on populations eligible to receive vaccine or their parents, or that did not allow the authors to extract information on vaccination were excluded from our analysis.

### **Study selection process**

Two researchers independently reviewed the identified studies for eligibility using a two-step process. In the first step, title, abstract, and keywords were screened to segregate the eligible studies followed by a full-text retrieval and screening. Similarly, data extraction was performed independently by two researchers and unmatched studies were included or excluded in consensus with a third researcher.

### **Data extraction and synthesis**

Data extraction included study characteristics such as: (1) author, year, journal, study design, study setting, study period, and study population; (2) the vaccines considered; (3) information about the intervention being studied such as type of intervention and duration of the intervention; and (4) information on follow-up time, analysis performed, and outcomes of interest.

We categorized the review under four broad themes, i.e., community health training, incentive-based approach; technology-based health literacy; and media engagement using participants, interventions, comparisons, outcomes, and study design (PICO) strategy (Figure 2).[11]

1. *Community health trainings*: It included community health information dissemination through health workers, mobilizers, medical officers; social mobilization through medical interns, prominent religious leaders; and knowledge- and experience-sharing by influential women from the community to accelerate vaccine uptake.[12]
2. *Incentive-based approach*: It involved incentives to encourage parents to immunize their children, including provision of food, other goods, and certificates of recognition or monetary support to encourage vaccination.[12]
3. *Technology-based health literacy*: It involved use of technology in informing beneficiaries through various modern age-technologies such as mobile phone. Activities in this category included mobile phone recall text messages in local

languages, pictorial messages, and automated phone calls or interactive voice recording for spreading awareness.[12]

4. *Media engagement*: Mobilization through various campaigns and platforms such as radio, TV, and print media should feature concise, easily understood public service announcements by national public figures, well-known and authoritative local representatives, and representative members of the target population.[12]

### **Critical appraisal**

The Effective Public Health Practice Project (EPHPP) quality assessment tool for quantitative studies was applied to determine the risk of bias in all eligible studies.[13] Literature screening and data extraction piloting was done on five documents by all three reviewers to standardize the review and data extraction process. Furthermore, disagreements during review were resolved by consensus.

## **Results**

The search identified 2495 peer-reviewed articles. After removing duplicates, 1141 articles were screened using title, abstract, and keywords, which excluded 1036 papers leaving 105 full-text papers for review. Of these, 33 were evaluated and described. Among the evaluated peer-reviewed literature, nine were related to community health trainings theme,[11-20] five were related to incentive-based approach,[21-24] eight were related to technology-based health literacy,[14, 20, 28-38] and eleven were related to media engagement (Tables 1 and 2). [12, 36-39]

### **Figure 1: Literature review data synthesis flowchart**

#### **Community health trainings**

Out of the total 33 studies considered, there were nine studies that were based on community health training strategy. Majority of the studies revealed parents/caregivers of children as the study population except for one study that primarily addressed the issue of vaccine hesitancy in religious leaders of a community. The most targeted vaccines were diphtheria pertussis tetanus (DPT1, DPT2, DPT3) vaccine, Bacilli Calmette-Guerin (BCG) vaccine, poliovirus 3, measles, influenza, and HPV vaccine. Lack of knowledge, negative parental attitude, and misconceptions were the foremost encountered causes for vaccine hesitancy that were addressed predominantly by health workers/medical interns.[11,12,14,15,20] Home visits and information campaigns were the most common types of community training modalities except for the two studies that had personally controlled health management systems (PCHMS) and community-level nutrition information system for action (COLNISA) as community health training strategies that led to an overall 21% to 33% rise in vaccine coverage.[37,38,41,42] Community activity for systematic engagement of parents and home visits by community health workers and medical interns significantly improved program acceptance and utilization of immunization services (Table 2).

#### **Incentive-based approach**

Five studies published between 2008-2013 were identified, that focused on performance-based incentives for vaccination. [18,22-25] Incentive-based approach mostly involved general hospitals in the rural and lower socio-economic strata of the society. Most of these studies suggested monetary incentives only. Influenza, BCG, polio, DPT2, DPT3, measles, HBV, meningococcal 4 (MCV4), and tetanus diphtheria-acellular pertussis (Tdap) were the most sought-after targeted vaccines. A dearth of financial burden and negligence were the suggested reasons for vaccine hesitancy. Findings of these studies suggested that incentives had a high impact on the uptake of immunization services.[23] The effect of non-financial incentives on vaccine uptake for parents and communities located in low-income settings (India) was moderate (RR: 2.16, [CI: 1.54, 2.78]) [25] except for one study that depicted no increase in vaccine acceptance using incentive-based search strategy (Table 2).

#### **Technology-based health literacy**

Lately, leveraging on the health literacy using technology such as informative posters, leaflets and videotapes, social media, organizing lectures, etc., were used to bring behavioral change regarding vaccination. The studies depicted that this intervention strategy was mostly acted upon in urban primary care practices and large multispecialty medical organizations. Inadequate

information /rumors, parental concerns about safety and lack of awareness, clinicians' beliefs and practice concerns attributed to vaccine hesitancy.[15-17,19,21] The eight studies available highlighted and dealt with vaccine hesitancy towards polio vaccine, pertussis, varicella, pneumococcal influenza (DTAP), hepatitis B (HBV), Hemophilus influenza B (HiB), inactive polio vaccine (IPV), and measles mumps rubella (MMR). These studies suggested that educational intervention using videos, posters, and lectures demonstrated an improved vaccine acceptance (Table 2). [32,39,40]

### **Media engagement**

Interventions such as reminder calls, SMS, and emails were adopted as media-based strategy in nine studies to address vaccine hesitancy. Most of the studies targeted general vaccines whereas only three out of nine studies had interventions directed towards meningococcal (MCV4), Tetanus diphtheria-acellular pertussis (Tdap), MMR, and influenza vaccines.[26,27,29] Low income, negative attitude towards immunization, and lack of knowledge were the most recorded reasons for vaccine hesitancy. The overall study outcome with this intervention strategy revealed that simple recall messages through SMS and email were preferred; however, these did not bring the desired change in overcoming vaccine hesitancy (Table 2). [30,31,33,35]

### **Risk of Bias**

Out of the 33 studies reported, 29 studies noted a high risk of bias and one study reported no risk of bias (Table 1).

## **Discussion**

The studies included interventions with diverse approaches that were implemented in different settings and targeted various populations, which helped us to get a holistic view of interventions globally to build confidence on vaccines, increase acceptance, and promote adequate immunization behaviors. In the review, we observed that the strategies suggested or evaluated were similar to traditional strategies such as through education and empowerment, financial and non-financial incentives, and technology assistance to bring about a behavioral change.

Studies done by Fiks et al,[19] Williams et al,[16] Zhang et al,[13] and Rahman et al [14] reported a lower risk of bias when compared to other studies, which could be due to variation in the study design and settings.

Most of the interventions analyzed in the review were primarily either to inform or to educate the target population about the risks and benefits of vaccination using community health training strategy, as lack of knowledge or awareness about vaccines was observed to be the major cause of vaccine hesitancy.[20] These studies reported effective improvement in vaccines uptake after the exercise. Two of these studies focused on the involvement of mothers for knowledge and experience sharing.[11] A study conducted by Brugha et al [12] revealed a significant rise of 60% to 80% in vaccine coverage after 6 months of home-visit community health training program. Involvement of mothers showed a significant improvement in vaccination coverage (33%-85%) in another similar study done by Usman et al.[42] Nine studies were based on parent-centered information or education about vaccination and social mobilization of parents by health workers/medical interns.[14,15,20] All these studies showed a significant impact in changing parents' attitude towards their child's vaccination. Messaging on vaccination from political and religious leaders also imparted a positive impact on vaccination uptake.[13,14] A study conducted in Denver, USA, found significant difference in attitude and practices related to immunization among vaccine-hesitant and non-hesitant religious leaders.[14] Similarly, effective communication regarding polio vaccination with the community had shown positive impact in Nigeria.[15] However, variation in study sample and size with no consideration towards population dynamics was a potential limitation of all the nine studies.[37,38,41,42]

Findings of studies conducted by Mouzoon et al,[18] Banerjee et al,[22] and Stitzer et al [24] suggested that incentives had a high impact on the uptake of immunization services. Conditional cash transfer program led to a huge increase in vaccination coverage resulting in 95% coverage in rural Nicaragua.[22] Incentive-based interventions were also found to be effective in a study by Barham et al[23] who reported an increase of more than 95% for DPT3 in the treatment group compared with 85% in the control group in the vaccine coverage rates for 12-23-month-old children. It was evident from the synthesis that the incentive-based strategies had a positive impact on bringing about vaccination acceptance.[25] The benefit of incentive-based health

promotions had always been significant but sustainability and adherence after intervention was debatable.[22] Furthermore, the implementation of incentives in large populations remained a challenge. At the same time, integration of incentives with other mother and child health services such as the Janani Suraksha Yojana implemented by Govt. of India,[23] can bring a positive change in improving immunization uptake along with education on delivery and nutrition in low-income and low-education settings.

Gaps in awareness such as complete absence of knowledge, less knowledge, and misconceptions, were known to be the principal factors for lack of adequate health-seeking behavior. Strategies focusing on behavior change through knowledge and awareness will be most suitable for complex behavioral dynamics as it targets multiple layers of decision-making – individual, family, and society.[15] Additionally, the benefits of health literacy using technology to bring about public awareness is not only multi-faceted but also has potential to change the whole health-seeking behavior paradigm and not just the behavior towards vaccines.[16]

Recently, educational videos, lectures in hospital settings, mobile vaccination team visits, social marketing, and web-based questionnaires have been used to bring about a behavioral change regarding vaccination. A study conducted in the rural areas of North Carolina using social marketing campaign raised the awareness among parents and reduced barriers in accessing the HPV vaccine successfully.[19] Similarly, HPV vaccination rates were 2% higher among 9-13-year-old girls within six months of campaign launch.[40] Evaluation of social media interventions by Muehleisen et al[21] showed a positive effect on uptake of MMR vaccine[37] in Canada. In Northern Nigeria, a relative increase of ~310% in the polio vaccination uptake was observed through an educational intervention with an 8-min video.[16]

Furthermore, the intervention focusing on the engagement of various kind of media to reach the population has also proved to be efficient in creating awareness and promoting beneficial health-seeking behaviors.[32,39] Therefore, in conjunction with awareness-creating strategies, utilization of mass media in various forms such as print, audio, television, and social media can stimulate a positive perception among the population in different settings. However, improper documentation and socio-economic disparity in demographics was the major downside in the health literacy using technology-based intervention strategy. [39]

Among all the strategies, recall strategies showed least improvement in mobilizing people from negative perception to acceptance. Furthermore, findings from a study in USA showed that parents aged 30 years and above preferred e-mail reminders as compared to other modes such as phone calls and text messages.[13] Few studies from New York city, Kansas in USA, and Nigeria have revealed a wide support and acceptability of text messages or SMS as a mode of immunization reminder or recall. [35,36] A large proportion of parents had also shown willingness to be reminded about vaccinations by their health departments and via novel modalities such as email or text messaging.[26] Urban parents preferred reminders from their child's doctor (46.7%) as compared to rural parents (33.7%).[29,31,33]

Although the recall strategies showed improvement in vaccine uptake, they were inconsistent in all studies. Therefore, it can be perceived that these kinds of passive reminders sent through modern communication channels may be only effective in case of technology-friendly populations. It is unlikely that mere recall messages through SMS or email, which were found to be preferred, will bring a desired change in the confidence on vaccines.[27]

In light of the above knowledge, it is difficult to predict the superiority of any intervention over the other. Therefore, more studies with a better study design and targeting specific populations are required. Another reason for the lack of literature can be our limited access to indexing databases, which severely limits our capability to extract large amount of published literature.

## Conclusions

Vaccine hesitancy not only increases an individual's risk of contracting a disease but also increases the risk for the community. Vaccine hesitancy is a complex issue, and no standalone strategy can address it. Despite the complexity of vaccine hesitancy and the broad range of its determinants, increasing awareness about benefits of vaccination, social media engagement activities, and carefully tailored strategies addressing the determinants of the hesitancy can bring about the desired change.

## Abbreviations

AEFI: Adverse Events Following Immunization

BCG: Bacilli Calmette-Guerin

CI: Confidence Interval

COLNISA: community-level nutrition information system for action

DPT: diphtheria pertussis tetanus

DTaP: Diphtheria, Tetanus and Pertussis vaccines

EPHPP: Effective Public Health Practice Project

HBV: Hepatitis B virus

Hib: Hemophilus influenza b

HPV: Human papillomavirus

IPV: Inactivated polio vaccine

MCV: Meningococcal Vaccine

MMR: Measles Mumps Rubella

PCHMS: Personally controlled health management systems

PICO: Participants, Interventions, Comparisons, Outcomes

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RR: Relative Risk

SMS: Short Message Service

Tdap: tetanus diphtheria-acellular pertussis

TV: Television

UNICEF: United Nations International Children's Emergency Fund

USA: The United States of America

WHO: World Health Organization

## Declarations

### **Ethics approval and consent to participate**

Not applicable

### **Consent for publication**

Not applicable

## Availability of data and materials

Presented in the manuscript; Any additional data can be sent if requested, specifically.

## Contributors

PS originated the idea of the study and helped in conceptualization and review. PD, SG, GKS, PN reviewed and revised the draft. MKM, SK and SG conducted the literature search, data analysis and wrote first draft.

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## Conflict of interest

The authors have declared that no competing interests exist.

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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## References

1. World Health Organization. Report of the sage working group on vaccine hesitancy. *Geneva, Switz*, [https://www.who.int/immunization/sage/meetings/2014/october/1\\_Report\\_WORKING\\_GROUP\\_vaccine\\_hesitancy\\_final.pdf](https://www.who.int/immunization/sage/meetings/2014/october/1_Report_WORKING_GROUP_vaccine_hesitancy_final.pdf); WHO 2014. Accessed 20 Jan 2020.
2. Global immunization coverage sustained in the past five years. [https://www.who.int/immunization/global\\_vaccine\\_action\\_plan/gvap\\_2017\\_secretariat\\_report\\_coverage.pdf](https://www.who.int/immunization/global_vaccine_action_plan/gvap_2017_secretariat_report_coverage.pdf); WHO (2016). Accessed 13 Dec 2019.
3. Dubé E, Gagnon D, Nickels E, Jeram S, Schuster M. Mapping vaccine hesitancy-Country-specific characteristics of a global phenomenon. *2014*;32(49):6649-54; doi:10.1016/j.vaccine.2014.09.039
4. MacDonald NE, SAGE Working Group on Vaccine Hesitancy. Vaccine hesitancy: Definition, scope and determinants. *2015*;33(34):4161-4.
5. Gowda C, Dempsey AF. The rise (and fall?) of parental vaccine hesitancy. *Hum Vaccin Immunother*. *2013*; 9(8):1755-62;doi:10.1016/j.vaccine.2015.04.036
6. The Strategic Advisory Group of Experts (SAGE). Appendices To the Report of the SAGE Working Group on Vaccine Hesitancy. [https://www.who.int/immunization/sage/meetings/2014/october/2\\_SAGE\\_Appendicies\\_Background\\_final.pdf](https://www.who.int/immunization/sage/meetings/2014/october/2_SAGE_Appendicies_Background_final.pdf); 2014. Accessed 12 Feb 2020.
7. Marti M, De Cola M, MacDonald NE, Dumolard L, Duclos P. Assessments of global drivers of vaccine hesitancy in 2014 - Looking beyond safety concerns. *PLoS One*. *2017*;12(3):e0172310; doi: 10.1371/journal.pone.0172310
8. Larson HJ, Jarrett C, Schulz WS, Chaudhuri M, Zhou Y, Dube E, et al. Measuring vaccine hesitancy: The development of a survey tool. *Vaccine*. *2015*;33(34):4165-75; doi:10.1016/j.vaccine.2015.04.037
9. Streefland P, Chowdhury AM, Ramos-Jimenez P. Patterns of vaccination acceptance. *Soc Sci Med*. *1999*;49(12):1705-16; doi: 10.1016/s0277-9536(99)00239-7

10. Jarrett C, Wilson R, O'Leary M, Eckersberger E, Larson HJ; SAGE Working Group on Vaccine Hesitancy. Strategies for addressing vaccine hesitancy - A systematic review. 2015;33(34):4180-90; doi: 10.1016/j.vaccine.2015.04.040
11. Oche MO, Umar AS, Ibrahim MTO, Sabitu K. An assessment of the impact of health education on maternal knowledge and practice of childhood immunization in Kware, Sokoto State. *J Public Heal Epidemiol.* 2011;3(10):440-7.
12. Brugha RF, Kevany JP. Maximizing immunization coverage through home visits: A controlled trial in an urban area of Ghana. *Bull World Health Organ.* 1996;74(5):517-24.
13. Zhang EJ, Chughtai AA, Heywood A, MacIntyre CR. Influence of political and medical leaders on parental perception of vaccination: A cross-sectional survey in Australia. *BMJ Open.* 2019; 9(3):e025866; doi: 10.1136/bmjopen-2018-025866
14. Abdul Rahman MA, Al-Dabbagh SA, Al-Habeeb QS. Health education and peer leaders'role in improving low vaccination coverage in Akre district, Kurdistan region, East Mediterr Health J. 2013;19(2):125-9.
15. Ansari MA, Khan Z, Khan IM. Reducing resistance against polio drops. *J R Soc Promot Health.* 2007;127(6):276-9; doi: 10.1177/1466424007083705
16. Williams SE, Rothman RL, Offit PA, Schaffner W, Sullivan M, Edwards KM. A Randomized Trial to Increase Acceptance of Childhood Vaccines by Vaccine-Hesitant Parents: A Pilot Study. *Pediatr.* 2013;13(5):475-80; doi: 10.1016/j.acap.2013.03.011
17. Maltezou HC, Maragos A, Raftopoulos V, Karageorgou K, Halharapi T, Remoudaki H, et al. Strategies to increase influenza vaccine uptake among health care workers in Greece. *Scand J Infect Dis.* 2008;40(3):266-8; doi: 10.1080/00365540701642658
18. Mouzoon ME, Munoz FM, Greisinger AJ, Brehm BJ, Wehmanen OA, Smith FA, et al. Improving influenza immunization in pregnant women and healthcare workers. *Am J Manag Care.* 2010;16(3):209-16.
19. Fiks AG, Grundmeier RW, Mayne S, Song L, Feemster K, Karavite D, et al. Effectiveness of decision support for families, clinicians, or both on HPV vaccine receipt. 2013;131(6):1114-24; doi: 10.1542/peds.2012-3122
20. Spleen AM, Kluhsman BC, Clark AD, Dignan MB, Lengerich EJ; ACTION Health Cancer Task Force. J. An increase in HPV-related knowledge and vaccination intent among parental and non-parental caregivers of adolescent girls, age 9-17 years, in Appalachian Pennsylvania. *J Cancer Educ.* 2012;27(2):312-9; doi:10.1007/s13187-011-0294-z
21. Muehleisen B, Baer G, Schaad UB, Heininger U. Assessment of Immunization Status in Hospitalized Children Followed by Counseling of Parents and Primary Care Physicians Improves Vaccination Coverage: An Interventional Study. *J Pediatr.* 2007;151(6):704-6; doi: 10.1016/j.jpeds.2007.07.051
22. Banerjee AV, Duflo E, Glennerster R, Kothari D. Improving immunisation coverage in rural India: Clustered randomised controlled evaluation of immunisation campaigns with and without incentives. 2010;340:1291; doi:10.1136/bmj.c2220
23. Barham T, Maluccio JA. Eradicating diseases: The effect of conditional cash transfers on vaccination coverage in rural Nicaragua. *J Health Econ.* 2009;28(3):611-21; doi: 10.1016/j.jhealeco.2008.12.010
24. Stitzer ML, Polk T, Bowles S, Kosten T. Drug users' adherence to a 6-month vaccination protocol: Effects of motivational incentives. *Drug Alcohol Depend.* 2011;107(1):76-9; doi: 10.1016/j.drugalcdep.2009.09.006
25. Robertson L, Mushati P, Eaton JW, Dumba L, Mavise G, Makoni J, et al. Effects of unconditional and conditional cash transfers on child health and development in Zimbabwe: A cluster-randomised trial. 2013;381(9874):1283-92; doi: 10.1016/S0140-6736(12)62168-0
26. Stockwell MS, Kharbanda EO, Martinez RA, Lara M, Vawdrey D, Natarajan K, et al. Text4health: Impact of text message reminder-recalls for pediatric and adolescent immunizations. *Am J Public Health.* 2012;102(2):15-21; doi: 10.2105/AJPH.2011.300331
27. Milkman KL, Beshears J, Choi JJ, Laibson D, Madrian BC. Using implementation intentions prompts to enhance influenza vaccination rates. *Proc Natl Acad Sci U S A.* 2011;108(26):10415-20; doi: 10.1073/pnas.1103170108
28. Moniz MH, Hasley S, Meyn LA, Beigi RH. Improving influenza vaccination rates in pregnancy through text messaging: A randomized controlled trial. *Obstet Gynecol.* 2013;121(4):734-40; doi: 10.1097/AOG.0b013e31828642b1
29. Lemstra M, Rajakumar D, Thompson A, Moraros J. The effectiveness of telephone reminders and home visits to improve measles, mumps and rubella immunization coverage rates in children. *Paediatr Child Health.* 2011;16(1):1-5; doi:

30. Clark SJ, Butchart A, Kennedy A, Dombkowski KJ. Parents' experiences with and preferences for immunization reminder/recall technologies. 2011;128(5):1100-5; doi: 10.1542/peds.2011-0270
31. Kharbanda EO, Stockwell MS, Fox HW, Rickert VI. Text4health: A qualitative evaluation of parental readiness for text message immunization reminders. *Am J Public Health*. 2009;99(12):2176-8; doi: 10.2105/AJPH.2009.161364
32. Ahlers-Schmidt CR, Chesser A, Hart T, Paschal A, Nguyen T, Wittler RR. Text messaging immunization reminders: Feasibility of implementation with low-income parents. *Prev Med (Baltim)*. 2010;50(5-6):306-7; doi: 10.1016/j.ypmed.2010.02.008
33. Hofstetter AM, Vargas CY, Kennedy A, Kitayama K, Stockwell MS. Parental and provider preferences and concerns regarding text message reminder/recall for early childhood vaccinations. *Prev Med (Baltim)*. 2013;57(2):75-80; doi: 10.1016/j.ypmed.2013.04.007
34. Brown VB, Oluwatosin OA. Feasibility of implementing a cellphone-based reminder/recall strategy to improve childhood routine immunization in a low-resource setting: A descriptive report. *BMC Health Serv Res*. 2017;17(Suppl 2): 703; doi: 10.1186/s12913-017-2639-8
35. Williams JTB, O'Leary ST. Denver Religious Leaders' Vaccine Attitudes, Practices, and Congregational Experiences. *J Relig Health*. 2019;58(4):1356-67; doi: 10.1007/s10943-019-00800-2
36. Saville AW, Beaty B, Dickinson LM, Lockhart S, Kempe A. Novel Immunization Reminder/Recall Approaches: Rural and Urban Differences in Parent Perceptions. *Acad Pediatr*. 2014;14(3):249-55; doi: 10.1016/j.acap.2014.02.003
37. Lau AY, Sintchenko V, Crimmins J, Magrabi F, Gallego B, Coiera E. Impact of a web-based personally controlled health management system on influenza vaccination and health services utilization rates: A randomized controlled trial. *J Am Med Inform Assoc*. 2012;19(5):719-27; doi: 10.1136/amiajnl-2011-000433
38. Nasiru SG, Aliyu GG, Gasasira A, Aliyu MH, Zubair M, Mandawari SU, et al. Breaking community barriers to polio vaccination in Northern Nigeria: The impact of a grass roots mobilization campaign (Majigi). *Pathog Glob Health*. 2012;106(3):166-71; doi: 10.1179/2047773212Y.0000000018
39. Cates JR, Shafer A, Diehl S J, Deal AM. Evaluating a county-sponsored social marketing campaign to increase mothers' initiation of HPV vaccine for their preteen daughters in a primarily rural area. *Soc Mar Q*. 2011;17(1):4-26; doi: 10.1080/15245004.2010.546943
40. Pandey D, Vanya V, Bhagat S, Vs B, Shetty J. Awareness and Attitude towards Human Papillomavirus (HPV) Vaccine among Medical Students in a Premier Medical School in India. *PLoS One*. 2012;7(7):e40619; doi: 10.1371/journal.pone.0040619
41. Ofstead CL, Sherman BW, Wetzler HP, Langlay DAM, Mueller NJ, Ward JM, et al. Effectiveness of worksite interventions to increase influenza vaccination rates among employees and families. *J Occup Environ Med*. 2013;55(2):156-63; doi: 10.1097/JOM.0b013e3182717d13
42. Usman HR, Rahbar MH, Kristensen S, Vermund SH, Kirby RS, Habib F, et al. Randomized controlled trial to improve childhood immunization adherence in rural Pakistan: redesigned immunization card and maternal education. *Trop Med Int Health*. 2011;16(3):334-42; doi: 10.1111/j.1365-3156.2010.02698.x
43. Brown VB, Oluwatosin OA. Feasibility of implementing a cellphone-based reminder/recall strategy to improve childhood routine immunization in a low-resource setting: A descriptive report. *BMC Health Serv Res*. 2017;17(Suppl 2):703; doi: 10.1186/s12913-017-2639-8
44. Moniz MH, Hasley S, Meyn LA, Beigi RH. Improving influenza vaccination rates in pregnancy through text messaging: A randomized controlled trial. *Obstet Gynecol*. 2013;121(4):734-40; doi:10.1097/AOG.0b013e31828642b1

## Tables

**Table 1: A descriptive summary of the characteristics of the included studies.**

Author	Study type	Name of country	Study setting	Participants	Interventions	Risk of bias score
<sup>11</sup> Oche et al, 2011	Controlled community trial	Nigeria	Town with the vast majority of the population largely farmers and illiterates	Mothers of children aged 0 to 23 months	Community health training	6
<sup>12</sup> Brugha et al, 1996	Controlled trial	Ghana	Town where regular immunization services were available.	Mothers of 12-18-month-old children	Community health training	7
<sup>13</sup> Zhang et al, 2019	Cross-sectional	Australia	Nationally representative sample	Parents with at least one child under 5 years	Media engagement	4
<sup>14</sup> Rahman et al, 2013	Pre-post interventions without control	Iraq	District with both rural and urban population	Villages with a DPT 3 coverage rate <20% and 15-24 infants below 1 year	Community health training	5
<sup>35</sup> Williams et al, 2019	Cross-sectional	United States	Urban geographic area	Religious organizations with at least one religious leader or equivalent located in Denver county	Community health training	NA
<sup>38</sup> Nasiru et al, 2012	Pre-post interventions without control	Nigeria	Local council with high reported cases of polio disease and very low vaccination uptake	Children under the age of 5	Community health training	7
<sup>41</sup> Ofstead et al, 2013	Pre-post interventions with control	United States	Manufacturing corporation	Full-time employees and their dependents	Community health training	6
<sup>15</sup> Ansari et al, 2007	Pre-post	India	High risk urban areas	High-risk urban areas	Technology-based health literacy	7
<sup>42</sup> Usman et al, 2011	Randomized controlled trial	Pakistan	Rural EPI centers	All children visiting the selected EPI centers for DTP1	Community health training	9
<sup>16</sup> Williams et	Cluster-	United	Private pediatric	Parent with a full-	Technology-	9

al, 2013	randomized controlled trial	States	practices in urban area	term infant less than 30 days old	based health literacy	
<sup>17</sup> Malteizou et al, 2009	Cross-sectional	Greece	Public hospitals	Greek public hospitals	Technology-based health literacy	6
<sup>18</sup> Mouzoon, M. et al, 2010	Retrospective study	United States	A large multispecialty medical organization	Pregnant women and healthcare workers	Incentive based approach	8
<sup>19</sup> Fiks, A.G et al, 2013	Cluster-randomized controlled trial	United States	Urban primary care practices	Girls 11 through 17 years of age due for at least 1 dose of the HPV vaccine	Technology-based health literacy	5
<sup>20</sup> Spleen, A.M, et al, 2011	Pre-post	United States	Rural population with high poverty rates, high unemployment rates, low access to healthcare, and excess cancer burden, including cervical cancer	Parents of daughters age 9-17 years	Community health training	7
<sup>21</sup> Muehleisen et al, 2007	Pre-post with control	Switzerland	Hospital in urban setting	Children aged 61 days to 17 years	Technology-based health literacy	7
<sup>22</sup> Banerjee et al, 2010	Cluster-randomized controlled trial	India	Rural Rajasthan	Children aged 1-3 years	Incentive-based approach	9
<sup>23</sup> Barham et al, 2008	Cluster-randomized controlled trial	The Republic of Nicaragua	Rural	Children 12-23-month-old and above	Incentive-based approach	7
<sup>24</sup> Stitzer, M.L, et al 2009	Randomized controlled trial	United States	General Hospital	Individual aged 18 – 64 years	Incentive-based approach	7
<sup>25</sup> Robertson et al, 2013	Cluster-randomized trial	Zimbabwe	Four socioeconomic strata were selected: subsistence farming areas, roadside trading settlements, agricultural estates, and small towns.	households with children younger than 18 years	Incentive-based approach	8
<sup>26</sup> Stockwell	Two	United	Urban, low-income	Parents with	Media	8

et al, 2012	randomized controlled trials	States	population	children aged 11 to 18 years and families with a child aged 7 to 22 months lacking 1Hib dose	engagement	
<sup>27</sup> Milkman et al, 2011	Randomized controlled trial	United States	A large firm	Employees	Media engagement	8
<sup>29</sup> Lemstra, M. et al 2011	Cluster-randomised trial	Canada	Low-income setting	Parents of children who were behind in MMR immunizations	Media engagement	8
<sup>30</sup> Clark et al, 2015	Internet-based cross-sectional survey	United States	Nationally representative sample	Parents of children 0 to 17 years of age	Media engagement – (preferred mode of communication)	8
<sup>31</sup> Kharbanda et al, 2009	Qualitative evaluation	United States	Three urban community health centers and two private practices in New York City	Parents with at least 1 child aged 10 to 19 years	Media engagement	8
<sup>32</sup> Ahlers-Schmidt et al, 2010	Formative survey	United States	Low-income setting	Parents with children under 6 years of age at a Midwestern Pediatric Residency clinic	Technology-based health literacy	6
<sup>33</sup> Hofstetter et al, 2013	Cross-sectional study	United States	Urban setting	Parents of 6–59-month-old children and providers	Media engagement – (preferred recalled reminder mode)	7
<sup>37</sup> Lau et al, 2012	Randomized controlled trial, Cross-sectional study	Australia, Nigeria	University urban setting	University students and staff. Mothers and their infants aged 0-3 months	Community health training	9
<sup>35</sup> Brown et al, 2015	Cross-sectional study	Nigeria	Urban and sub-urban community health facility	Mothers of infants	Media engagement (preferred recalled reminder mode)	6
<sup>36</sup> Saville	Cross-	United	Both urban and rural	Parents of	Media	6

et.al, 2014	sectional, randomized, controlled trial	States, Australia	university	children 19-35- month-old  University students and staff.	engagement (preferred recalled reminder mode)	
<sup>39</sup> Cates et al, 2011	Assessment	4 North Carolina Counties	Rural area	Mothers of girls aged 11-12	Media engagement (preferred recalled reminder mode)	6
<sup>40</sup> Pandey et al, 2011	Cross- sectional	India	Medical school	Students of medical school	Technology- based health literacy	6
<sup>43</sup> Brown, V.B, et al 2017	Cross- sectional study	Nigeria	urban setting	Mothers and their infants aged 0-3 months	Media-based approach	6
<sup>44</sup> Moniz et al, 2013	Randomized controlled trial	United States	Outpatient clinic	Obstetric patients at less than 28 weeks of  gestation pending the flu shot	Media-based approach	8

**Table 2: A descriptive summary of the target vaccine, reason for hesitancy, outcomes, and limitations for each strategy**

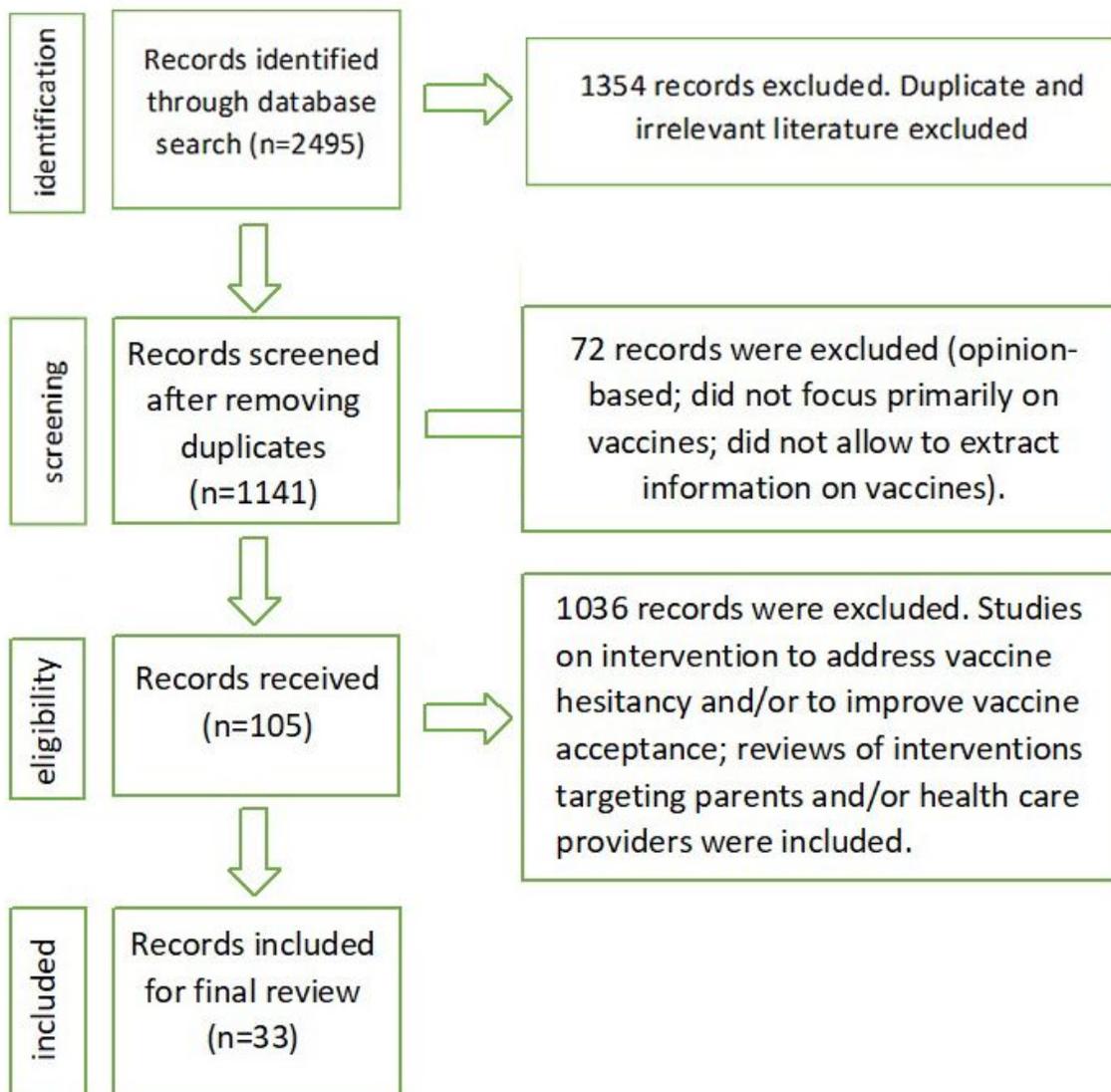
Author	Duration of study	Target vaccine	Reason for vaccine hesitancy	Outcome of interventions	Limitations of the study
<b>Community health training</b>					
<sup>11</sup> Oche et al, 2011	9 months	DPT3	Low level of knowledge amongst mothers and poor attitude of health workers	Improved program acceptance and immunization services	Cost of services; availability of vaccines not considered
<sup>12</sup> Brugha et al, 1996	8 months	BCG; poliovirus, DPT3, measles	Lack of awareness	Improvement of immunization coverage through community health training.	Contamination of control group
<sup>14</sup> Rahman et al, 2013	6 months	DPT1, DPT2, DPT3, Measles	Lack of information/motivation	Vaccination coverage rates improved in intervention villages	Study restricted to a tribe influenced by peer-leader.
<sup>15</sup> Williams et al, 2019	5 months	Influenza	Religious beliefs/attitude	No significant outcome	Small study size
<sup>38</sup> Nasiru et al, 2012	6 months	Polio vaccine	Attitude/misinformation	Effective communication and polio outreach campaigns-increased vaccine uptake	Population dynamics not considered.
<sup>41</sup> Ofstead et al, 2013	3 months	Influenza	Misconceptions	Substantial increase in vaccination rate	No psychometric evaluation
<sup>42</sup> Usman et al, 2011	90 days	DTP	Lack of knowledge	Infant vaccination increased	Lack of complete follow-up
<sup>20</sup> Spleen et al, 2011	1 year	HPV vaccine	Lack of parental attitude/knowledge	Increased vaccine acceptability	Study limited to small parent sub-group
<sup>37</sup> Lau et al, 2012	6 months	Influenza	Lack of knowledge	Improved uptake of influenza vaccination and utilization of health services	Seasonal variations of influenza not considered.
<b>Incentive-based approach</b>					

18Mouzoon et al, 2010	6 years	Influenza	Lack of familiarity or comfort with vaccination in pregnancy	Vaccination acceptability increased in pregnant females.	Lack of baseline data
22Banerjee et al, 2010	18 months	BCG, DPT, oral polio vaccines, Measles	Lack of awareness	Increased uptake of immunization services.	Not a blinded study
24Stitzer et al, 2009	6 months	HBV	negligence	Motivation leading to attending vaccination sessions	Small sample size, homogeneity of sample
23Barham et al, 2008	2 years	BCG, MCV, OPV3, DPT3	Lack of finance and motivation	Vaccination coverage increased dramatically	Proximity to availability of vaccine to study group not considered.
25Robertson et al, 2013	1 year	Childhood vaccination	Lack of motivation	No increase in vaccination uptake.	Short intervention period
<b>Technology-based health literacy</b>					
15Ansari et al, 2007	1-day study	Polio vaccine	Misguided information/rumors	Correct health education leading to vaccine acceptance.	Other parameters and lack of existing immunization not considered.
16Williams et al, 2013	2 months	Pertussis, Varicella, Ppneumococcal	Negative parent attitude regarding safety/necessity of vaccine	Educational intervention with 8-min video improved vaccine acceptance	Social desirability bias
17Maltezou et al, 2009	1 year	Influenza	Lack of time and inconvenience	Lectures in hospital/mobile vaccination team visit-significant impact	No baseline data; no feedback
19Fiks et al, 2013	1 year	HPV	Parental concerns, clinicians' beliefs and practice concerns.	Combined interventions increased vaccination rates	Lack of large-scale study
21Muehleisen et al, 2007	9 months	DTAP, HBV, HiB, IPV, MMR, Td	Lack of parental awareness	Increased reporting of immunization	Improper documentation/lack of prior immunization records, Single-centric study.
32Ahlers-	Not	General vaccine	Parental concerns	Increased vaccine	Demographically not

Schmidt et al, 2010	mentioned		about safety and lack of knowledge	acceptability	generalizable
<sup>39</sup> Cates et al, 2011	6 months	HBV	Lack of awareness	Increase in vaccination acceptance and uptake	Socio-economic disparity in demographics
<sup>40</sup> Pandey et al, 2011	Not mentioned	HPV	Inadequate information	Female students had better awareness; medical teaching had better impact	Single-centric study
<b>Media-based approach</b>					
<sup>35</sup> Brown et al 2015	Not mentioned	Routine vaccine	Not mentioned	60% mothers preferred immunization reminders by cellphones and SMS	Study not including rural population
<sup>36</sup> Saville et al, 2014	4 months	General vaccine	Not mentioned	Preferred modality email or telephone	Socio-economic demography not generalizable
<sup>33</sup> Hofstetter et al, 2013	3 months	General vaccine	Not mentioned	Text messages recall widely accepted	Socio-demographic data not generalizable
<sup>31</sup> Kharbanda et al, 2009	Not mentioned	General vaccine	Not mentioned	Preferred method was text messages	Demographically not generalizable
<sup>30</sup> Clark et al, 2015	Not mentioned	General vaccination	Not mentioned	Parents more willing to communicate by phone call	Lack of specificities.
<sup>29</sup> Lemstra et al, 2011	1 year	MMR	Low income	Limited additional benefits	Substantial study population not able to be contacted; incorrect telephone data
<sup>27</sup> Milkman et al, 2011	1 month	Influenza	Lack of knowledge	Increased vaccination rate	Small sample size; single-centric study
<sup>26</sup> Stockwell et al, 2012	6 months	Meningococcal (MCV4); Tetanus diptheria-acellular pertussis (Tdap)	Low income	Immunization reminders beneficial; Increased vaccine uptake	Lack of sample size of parents recorded in cell phone registry.

13Zhang et al, 2019	Not mentioned	Acceptance of new target vaccination policy	Negative attitude towards immunization	Public figures/media messages can influence attitudes	Small study size. Did not identify demographic predictors.
43Brown et al, 2017	Not mentioned	Routine vaccine	Lack of awareness	Preference of immunization reminders through cell phones	Study conducted in urban setting. No rural involvement
44Moniz et al, 2013	2 years	Influenza	Lack of awareness	Text messages not effective	Single socio-demographic group.

## Figures



**Figure 1**

Literature review data synthesis flowchart

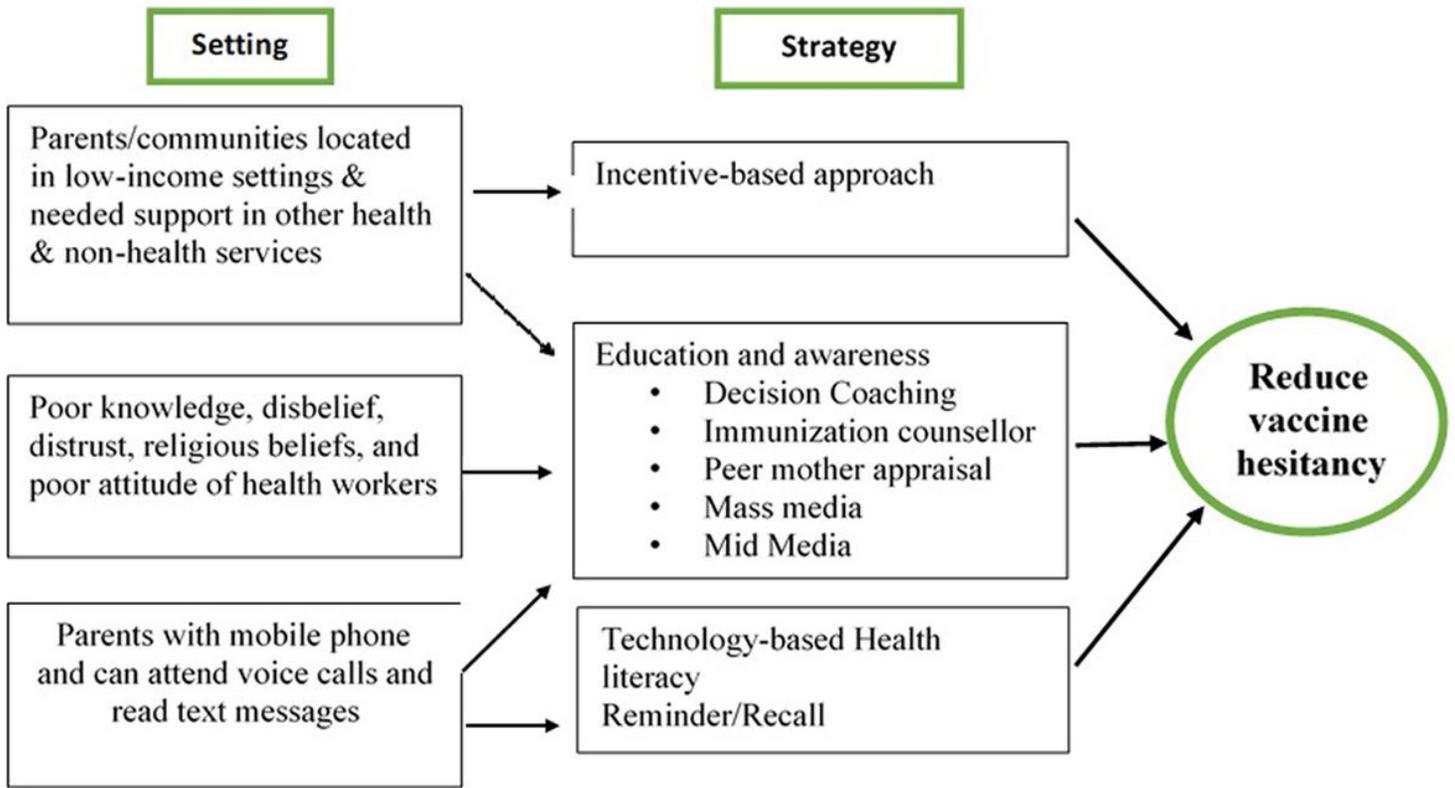


Figure 2

Strategies to remove a vaccine hesitancy