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The effects on childhood immunisation coverage of mailing reminders and recalls through electronic mails or postal services: a systematic review protocol

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Abstract

Introduction: Every year, suboptimal immunization coverage leads to several deaths from vaccine-preventable diseases. Reasons for suboptimal coverage are multifactorial, therefore a combination of interventions is needed to improve immunisation coverage and prevent vaccine-preventable deaths. We therefore undertake this systematic review to investigate the potential of reminders or recalls using e-mails, letters or postcards to improve immunization coverage.

Methods and analysis: Studies to be included in this review will be both studies that allocated participants to interventions at random, for example, intervention assignment using sequentially numbered, opaque and sealed envelopes (i.e. randomized controlled trials) and those in which intervention assignments were non-random such as allocation based on day of admission (non-randomized controlled trials). We will search for published and unpublished studies in PubMed, Scopus, CINAHL, CENTRAL, Science Citation Index, WHOLIS, relevant conference proceedings, Clinicaltrials.gov, and the WHO International Clinical Trials Platform. We will conduct screening of search results, study selection, and data extraction in duplicate, resolving disagreements by consensus. In addition, we will use the chi-square test of homogeneity to assess statistical heterogeneity, defining the latter at the 10% alpha level; quantify heterogeneity of effects using the I-square index statistic; and pool data using fixed effects method if there is no significant statistical heterogeneity and the random-effects method if there is..

Ethics and dissemination: Systematic reviews draw on publicly available data and do not directly involve human participants, and therefore do not require formal ethical review. The results will provide invaluable evidence on the effects of e-mails, letters and postcards for reminder and recall interventions for promoting and increasing immunization coverage. We will discuss cost implications, impacts on equity, and monitoring and evaluation considerations of our findings. The main consumers of this systematic review will be health professionals, policy makers and researchers.

Review Registration: ROSPERO registration number CRD42014012888

Keywords: Immunisation coverage, reminders, recall, mail, e-mail, letters, postcards, cost implication, effect on equity, monitoring and evaluation

Strengths and limitations of this study

A comprehensive search strategy will be used to identify relevant English and non-English language peer-review Randomized control Trials and Non-Randomized controlled Trials, also grey literature publication. The review will fill the gap of systematic review using combination of communication strategies to communicate immunization dates to parents and caregivers. Two reviewers' authors will independently conduct the screening and data extraction steps of this systematic reviews.

Introduction

The World Health Organization (WHO) defines immunization as healthcare process in which individual gains immunity or resistance to an infectious disease through administration of a vaccine [1]. Immunization is important in all stages of an individual's life as it helps children and adolescents fight infectious diseases and restores waning immunity in adults [2]. Besides benefits received by the individual, immunization helps protect friends, neighbours, family members and the community at large [3].

Vaccination coverage can be defined as the percentage of people who receive one or more vaccines of interest in relation to the overall population [4]. The vaccination coverage for the third dose of the diphtheria-tetanus-pertussis vaccine is regarded as a proxy for childhood immunisation coverage. Low childhood immunization coverage is a significant public health issue, with great implication on children health [7]. Despite global efforts, including the Global Immunization Vision and Strategy [11] and the Global Alliance for Vaccines and Immunisation [6], 22.4 million children are not fully vaccinated at 12 months of age [5]. As a consequence, 1.5 million children continue to die from vaccine-preventable diseases worldwide yearly [5,7-14]. Immunization coverage is affected by a number of individual and community level factors [10]. At the individual level, factors such as mother's age, level of income, mother's education, maternal access to mass media, and maternal health seeking behaviour are reported to have an effect on immunization coverage. At the community-level, poverty, unemployment, place of residence, culture, and availability, accessibility and quality of services are reported to affecting immunization coverage [8,12,13].

Innovative communication strategies are needed to inform caregivers on their children vaccination needs in a timely manner. In line with the optimization of immunization coverage, healthcare professionals, policy makers and researchers need to put in place purposeful, structured, repeatable and adaptable approaches to sustain high immunization coverage irrespective of socio-economic status. Some of the strategies in place are around communicating the vaccination dates and details to those in need as well as reminding those who have missed vaccination appointments to come and receive the vaccines due [14]. The practice of reminding or recalling people of their up-coming or overdue vaccination dates through telephone, and short message services, and personal home visits have been shown to increase vaccination coverage[15,16]. However, it unclear if mailing reminders and recalls through electronic mails (emails) or postal services (letters, postcards)

improve childhood vaccination coverage, especially in low and middle-income countries thus the need for this systematic review[17;18].

Objectives

The objective of this systematic review is to assess the effects of reminders or recalls using emails, letters or postcards on childhood immunisation coverage

Methods and analysis

This systematic review protocol has been registered in the PROSPERO International Prospective Register of Systematic Reviews, registration number: CRD42014012888. The PROSPERO database helps prevent unintended duplication and allows for comparison of reported methods and outcomes in published reviews with those in the review registration document. [19]

We will include randomised controlled trials (RCTs, defined as studies in which participants were allocated to interventions at random) and non-randomised controlled trials (Non-RCTs, defined as studies that allocated participants to treatment arms by a non-random method such as alternation between groups and the use of birth dates or weekdays). The participants of interest for this review will be caregivers (that is parents or other persons fulfilling the parental role), residing in children community. Eligible interventions will be mail (e-mails, letters or postcards) compared to no intervention, to other interventions, or to the same interventions at different levels of intensity. The mails (e-mails, letters or postcards) have to be delivered to the caregiver of a child in need of vaccination. The primary outcome is the vaccination status of the child, irrespective of disease targeted. The secondary outcomes will be the cost of the intervention, the incidence of vaccine preventable diseases, the acceptability of the intervention, adverse events following immunisation (AEFI), and undesirable effects from the interventions.

We developed a comprehensive search strategy (Appendix 1) that includes both text words and medical subject heading (MeSH) terms relating to immunisation and mails. Sources of peer-reviewed literature will include PubMed, Scopus, Cochrane Central Register of Controlled Trials (CENTRAL), ISI Web of Science (Science Citation Index), and Cumulative Index of Nursing and Allied Health (CINAHL). We will also check reference lists of full-text articles assessed for eligibility as well as proceedings of relevant conferences, including the Vaccine and International Society for Vaccines Congress, the International Pediatric Association Conference, the World Congress on Pediatric Infectious Diseases, the Annual Vaccines Congress, the Annual conference on Vaccine Research, the Annual Infectious Diseases in Children Symposium, the International African Vaccinology Conference, and the National Immunization Conference. We will search for ongoing studies in the WHO International Clinical Trials Registry Platform and Clinicaltrials.gov. In addition, we will search websites of WHO, the Global Alliance for Vaccines and Immunisation, and the Center for Disease Prevention and Control. We will include articles available in any language, and obtain English translations for eligible articles published in languages other than English and French.

Two review authors will independently screen the abstracts of articles identified by the search for eligibility using the study design, participants, interventions, and outcomes. We will obtain the full text of studies deemed potentially eligible and the two authors will independently assess the full text articles for eligibility and compare their results, resolving discrepancies by discussion. A third author will be consulted to resolve any persistent disagreements between the two authors. Risk of bias in included studies will be assessed independently by the two authors, using the Cochrane Risk of bias tool [20]. The following domains will be assessed: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, completeness of outcome data, completeness of outcome reporting, and other potential sources of bias (baseline imbalance, and conflicts of interest). Judgements will be made as low risk of bias, unclear risk of bias, or high risk of bias according to the criteria in the Cochrane handbook. The two authors will compare their assessments and resolve differences by discussion and consensus. In case of failure to resolve any differences, a third author will be called upon to arbitrate. Two authors will independently extract data from each included study using a pre-designed and piloted form. Extracted data will include study characteristics (settings, design, and period of study), participants' characteristics (age, gender, and other demographic details), intervention characteristics, and outcome data (numbers of participants allocated to each group and numerical results per specified outcomes, number of withdrawals from each group with reasons for withdrawal). In case of missing data in any of the included studies, we will contact the authors in an attempt to obtain the missing information. The two authors will compare extracted data for each study and resolve any differences by discussion and consensus, with a third author arbitrating if necessary. The first author will enter the data into the Cochrane Cochrane Collaboration Review Manager software (RevMan) [21], the second author will cross-check the entered data for any data-entry errors and rectify where needed before statistical analyses.

We will conduct data analysis using RevMan We will express each study result as a risk ratio and its 95% confidence intervals. For cost of interventions we will report the costs in the currencies provided by the trial authors, with the current United States Dollar equivalents. We will assess heterogeneity using the Chi-squared test and the I-squared statistic in each meta-analysis. In the absence of significant statistical heterogeneity (i.e. heterogeneity $p < 0.1$), we will use fixed-effect meta-analysis and should there be significant statistical heterogeneity, we will use the random-effects meta-analysis. We will carry-out subgroup analyses, with subgroups defined by intervention subtype (e-mails, letters, and postcards), study setting (middle-income and low-income countries), and study design (randomized controlled trials and non-randomised controlled trials). Where appropriate, intention-to-treat (ITT) principle and the available case principle will be used to analyse the data. We will conduct sensitivity analysis to assess the effect of missing data. In addition, we will conduct sensitivity analysis to investigate the robustness of the results to risk of bias (low versus high risk of bias). For sensitivity analyses, we will define 'high risk of bias' based on each of three criteria, namely, inadequate concealment of intervention allocation, inadequate blinding of outcome assessment, and differential loss to follow-up (i.e. 20 percentage points or more difference in the proportion of incomplete outcome data between intervention groups).

Ethics and dissemination

Systematic reviews draw on publicly available data and do not directly involve human participants, and therefore do not require formal ethical review. Healthcare professionals, policy-makers and researchers will be the main target consumers of the end product of this systematic review. We will discuss the relevance of our findings to national immunisation programmes in low and middle-income countries especially sub-Saharan Africa; focusing on applicability, effects on equity, cost implications, and monitoring and evaluation. The findings will provide prevailing evidence of whether health policy-makers should adopt mail (e-mails, letters or postcards) alone or in combination with other interventions in efforts to improve uptake of immunisation services. It will also inform healthcare workers and programme managers on how best to use the interventions to improve immunization coverage. The review will also identify gaps in the current research on mail interventions in immunisation programmes and thus suggest areas for further research [22].

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

CW conceived the review, MC wrote the first draft of the protocol, and all authors made substantive input into the manuscript and have given their approval for publication.

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References

1. World Health Organization: WHO Immunisation; 2014, http://www.who.int/topics/immunization/en/.

2. Deeks SL, Lim GH, Simpson MA, Gagne L, Gubbay J, Kristjanson E, et al. An assessment of mumps vaccine effectiveness by dose during an outbreak in Canada. *Cmaj* 2011; Jun 14; 183(9):1014-20.

3. Albrich WC, Madhi SA, Lafond KE, Klugman KP. Herd immunity after pneumococcal conjugate vaccination. *The Lancet* 2007;370(9583):218-9.

4. Scott S, Odutola A, Mackenzie G, Fulford T, Afolabi MO, Jallow YL, et al. Coverage and Timing of Children's Vaccination: An Evaluation of the Expanded Programme on Immunisation in The Gambia. *PloS One* 2014;9(9):e107280.

5. World Health Organization: Global Immunization Data. 2014. http://www.who.int/immunization/monitoring_surveillance/Global_Immunization_Data.pdf?ua=1.

6. Wittet S. Introducing GAVI and the Global Fund for children's vaccines. *Vaccine* 2000;19(4):385-6.

7. Wiysonge CS, Uthman OA, Ndumbe PM, Hussey GD: Individual and contextual factors associated with low childhood immunisation coverage in sub-Saharan Africa: a multilevel analysis. *PLoS* One 2012, 7(5):e37905.

8. Chandran SA, Ramachandra SS, Sekhar PS. National Family Health Survey-3 reported low full-immunization coverage rates in Andhra Pradesh, India: who is to be blamed?. *J Public Health (Oxf)* 2011; Dec;33(4):489-95.

9. Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE, et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. *The Lancet* 2014.

10.Bosch-Capblanch X, Banerjee K, Burton A. Unvaccinated children in years of increasing coverage: how many and who are they? Evidence from 96 low-and middle-income countries. *Tropical Medicine & International Health* 2012;17(6):697-710.

11. World Health Organization: GIVS Global Immunization Vision and Strategy 2006-2015. 2005; http://whqlibdoc.who.int/hq/2005/WHO_IVB_05.05.pdf.

12. Roland D, Ellis C, Blair ME. Assisting healthcare professionals in understanding drivers and barriers to improving pre-school immunisation uptake. *Community Practitioner* 2013;86(9):28-31.

13. Michaela Janks, Sara Cooke, Aimee Odedra, Harkeet Kang, Michelle Bellman, and Rachel E. Jordan: Factors Affecting Acceptance and Intention to Receive Pandemic Influenza A H1N1 Vaccine among Primary School Children: A Cross-Sectional Study in Birmingham, UK.. Influenza Res Treat. 2012; 2012: 182565.

14.Willis N, Hill S, Kaufman J, Lewin S, Kis-Rigo J, Bensaude De Castro Freire S, Bosch-Capblanch X, Glenton C, Lin V, Robinson P, Wiysonge CS. 'Communicate to vaccinate': The development of a taxonomy of communication interventions to improve routine childhood vaccination. *BMC International Health and Human Rights* 2013;13(1):23.

15. Stockwell MS, Fiks AG. Utilizing health information technology to improve vaccine communication and coverage. *Human Vaccines & Immunotherapeutics* 2013;9(8):1802-11.

16. Jacobson Vann JC, Szilagyi P. Patient reminder and recall systems to improve immunization rates. *The Cochrane Library* 2005.

17. Ryman TK, Dietz V, Cairns KL. Too little but not too late: results of a literature review to improve routine immunization programs in developing countries. *BMC Health Serv Res* 2008; Jun 21; 8:134, 6963-8-134.

18. Oyo-Ita A, Nwachukwu CE, Oringanje C, Meremikwu MM. Interventions for improving coverage of child immunization in low-and middle-income countries. *The Cochrane Library* 2011.

19. Chachou MJ, Mukinda KF, Motaze V, Wiysonge CS: The effects on childhood immunisation coverage of mailing reminders and recalls through emails, letters or postcards: a systematic review protocol: PROSPERO 2014; CRD42014012888. http://www.crd.york.ac.uk/PROSPERO/isplay_record.asp?ID=CRD42014012888.

20. Higgins J. Green S. Cochrane handbook for systematic reviews of interventions Version 5.1. 0 [updated March 2011]. *The Cochrane Collaboration*, 2011. *Www.Cochrane-Handbook.Org* 2014.

21. RevMan 2008 The Cochrane Collaboration. Review Manager (RevMan). 5.0. *Copenhagen, the Nordic Cochrane Centre: The Cochrane Collaboration* 2008.

22. Wiysonge CS, Volmink J: Strengthening research capacity. *Lancet* 2002, 359(9307):713.

Appendix: 1 Databases searched strategy

Searches	Queries
#1	"postal service"
#2	"mailing"
#3	"electronic mail"
#4	(postal service OR mailing OR electronic mail)
#5	"Immunization"
#6	"Immunisation"
#7	"vaccination"
#8	(immunisation OR immunization OR vaccination)
#9	[(postal service OR mailing OR electronic mail) AND (immunisation OR immunization OR vaccination)]

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Electronic and postal reminders for improving immunisation coverage in children: protocol for a systematic review and meta-analysis

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Electronic and postal reminders for improving immunisation coverage in children: protocol for a systematic review and meta-analysis

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Abstract

Introduction: Worldwide, suboptimal immunisation coverage causes the deaths of more than one million children under five from vaccine-preventable diseases every year. Reasons for suboptimal coverage are multifactorial, and a combination of interventions is needed to improve compliance with immunisation schedules. One intervention relies on reminders, where the health system prompts caregivers to attend immunisation appointments on time or re-engages caregivers who have defaulted on scheduled appointments. We undertake this systematic review to investigate the potential of reminders using e-mails, phone calls, social media, letters, or postcards to improve immunisation coverage in children under five.

Methods and analysis: We will search for published and unpublished randomised controlled trials and non-randomised controlled trials in PubMed, Scopus, CINAHL, CENTRAL, Science Citation Index, WHOLIS, Clinicaltrials.gov, and WHO International Clinical Trials Platform. We will conduct screening of search results, study selection, data extraction and risk-of-bias assessment in duplicate, resolving disagreements by consensus. In addition, we will pool data from clinically homogenous studies using random-effects meta-analysis; assess heterogeneity of effects using the chi-square test of homogeneity; and quantify any observed heterogeneity using the I-square statistic.

Ethics and dissemination: This protocol does not need approval by an ethics committee because we will use publicly available data, without directly involving human participants. The results will provide updated evidence on the effects of electronic and postal reminders on immunisation coverage, and we will discuss the applicability of the findings to low and middle-income countries. We plan to disseminate review findings through publication in a peer-reviewed journal and presentation at relevant conferences. In addition, we will prepare a policymaker-friendly summary using a validated format (e.g. SUPPORT Summary) and disseminate this through social media and email discussion groups

Review Registration: PROSPERO registration number CRD42014012888

Keywords: Childhood immunisation, reminders, recall, mail, e-mail, twitter, letters, postcards

Strengths and limitations of this study

- This protocol complies with the PRISMA-P guidelines.
- We will employ the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to establish the certainty of the evidence on the effectiveness of reminders in improving childhood immunisation coverage.
- Non-randomised controlled trials are eligible for inclusion in this review. This study design tends to have a high risk of selection bias, but we plan to alleviate this risk by conducting sensitivity analyses to evaluate the robustness of the evidence to risk of bias by excluding studies with a high risk of selection bias.
- We anticipate a wide clinical variation across studies relating to participants, study settings, and country income levels. We will mitigate the impact of such heterogeneity on the validity of our findings by pooling data only from clinically homogeneous studies.

Introduction

Immunisation is a healthcare process in which an individual gains immunity or resistance to a disease through administration of a vaccine.[1] Immunisation is important in all stages of an individual's life as it helps children and adolescents fight infectious diseases and restores waning immunity in adults[2] Besides benefits to the individual who receives the vaccine, immunisation helps protect her family members, friends, and the community at large.[3] The World Health Organisation (WHO) estimates that immunisation currently averts 2-3 million deaths every year in all age groups. These are deaths that would have been caused by diphtheria, tetanus, whooping cough (pertussis), measles, and other vaccine-preventable diseases.[4]

The percentage of people who receive one or more vaccines of interest in relation to the target population is referred to as vaccination coverage. The vaccination coverage by one year of age for the third dose of a vaccine containing diphtheria, tetanus, and pertussis (DTP3) is regarded as a proxy for childhood immunisation coverage worldwide.[5] Low childhood immunisation coverage is a significant public health issue, with great implication on children's health.[6] The WHO estimates that DTP3 coverage increased from 76% in 1990 to 86% in 2014 worldwide.[4] However, the increase in immunisation coverage is uneven; in 2014 DTP3 coverage was 96% in Europe and the Western Pacific and only 77% in Africa. The estimated number of children under one year of age who did not receive DTP3 was 18.7 million worldwide in 2014, more than three-fifths of them residing in 10 low and middle-income countries: Democratic Republic of Congo, Ethiopia, India, Indonesia, Iraq, Nigeria, Pakistan, Philippines, Uganda, and South Africa.[4] As a consequence of low immunisation coverage, 1.5 million children continue to die from vaccine-preventable diseases worldwide yearly.[7]

Immunisation coverage is affected by factors related to the health system, healthcare workers, and caregivers (that is, parents or other persons assuming the parental role).[8-10] Caregiver factors that influence childhood immunisation coverage include (but are not limited to) low socioeconomic status, low parental education, younger maternal age, lack of knowledge about the importance of immunisation, negative attitudes towards immunisation, fear of side-effects, and forgetting vaccination schedules and appointments.[9,10]

In line with the optimisation of childhood immunisation coverage, policymakers and healthcare workers need to put in place purposeful, structured, repeatable and adaptable approaches to sustain high immunisation coverage during childhood, irrespective of who the children are or where the live.[11] A potentially important strategy for achieving and sustaining high childhood immunisation coverage involves communicating the dates of scheduled vaccination visits and details of the vaccines on schedule to caregivers as well as re-engaging those caregivers who have missed vaccination appointments to bring their children to receive the vaccines due.[12-15]

Various systematic reviews have assessed the effectiveness of such reminder methods in improving childhood immunisation coverage, and we summarise the most relevant ones below.[13-16] Williams and colleagues conducted a systematic search and found 46 eligible studies published between 1980 and 2009 on strategies to optimise immunisation coverage among children under five in developed countries.[13] Twenty-two studies focused on reminders to advise parents of upcoming vaccinations that are due and remind parents of those children that are overdue. The reminders ranged from automated telephone calls and generic postcards to personalised letters and home visits. There was heterogeneity of effects between types of reminders, with an overall effect being a median point change in coverage of +11% (range -11% to +24%). However, these data were collected six or more years ago and may not be applicable to low and middle-income countries where most unimmunised children live.

In another review, Oyo-Ita and co-authors assessed the effectiveness of intervention strategies to boost and sustain high childhood immunisation coverage in low and middle-income countries.[14] The authors included six studies published between 1996 and 2009; but excluded studies focusing on reminder and recall methods because they were included in an existing review.[15] The latter assessed the effectiveness of patient reminder and recall systems in improving immunisation coverage, and compared the effects of various types of reminders in different patient populations. The authors included 47 studies available by May 2007 involving participants of all ages, and found that caregiver reminders improved childhood immunisation coverage: odds ratio 1.47, 95% confidence intervals (CI) 1.28 to 1.68). The review focused on high-income countries where (potential) recipients of care have primary healthcare providers whom they visit regularly.[15] Thus, the findings of the review would not be directly applicable to low and middle-income countries.

More recently, Harvey and colleagues conducted a systematic review and meta-analysis of parental interventions to improve early childhood (0–5 years) vaccine

uptake.[16] The authors conducted six pooled analyses involving twenty-eight studies, and report that all interventions were somehow effective, although the effects were inconsistent, with a combination of postal and telephone reminders being the most effective reminder method: risk difference 0.1132, 95% CI 0.033 to 0.193. However, the authors excluded studies that did not provide outcome data in terms of the number of children completely immunised or up-to-date for their age from meta-analyses. In addition, interventions for which only one study was found were excluded from pooled analyses. Overall, included studies of reminder interventions in the analyses were published in 2011 or earlier.[16] The review therefore provides very low-certainty evidence on the effects of newer methods of reminders on childhood immunisation coverage. Recognising this limitation, the authors indicate that strategies used in most included studies may not be relevant to caregivers of today.

It would therefore be prudent to conduct a new systematic review that includes the newer methods of reminders such as text messages, twitter, and other forms of social media. In addition, Harvey and colleagues did not use GRADE (Grading of Recommendations Assessment, Development and Evaluation)[17] or a similar approach to assess the certainty of the evidence on the effectiveness of reminder methods in improving childhood immunisation coverage. We propose to fill this evidence gaps by conducting a systematic review that will include all methods of sending reminders, and use the GRADE system to establish the certainty of the evidence and present the data in "Summary of Findings" tables.[18] In addition, we will use a validated format to summarise the review findings for non-research end users; including, but not limited to healthcare workers, programme managers, and policymakers

Objectives

Our objective is to assess the effects of caregiver reminders on uptake of WHO-recommended vaccines in children less than five years of age.

Methods and analysis

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs, defined as studies in which participants were allocated to interventions at random) and non-randomised controlled trials (Non-RCTs, defined as trials that allocated participants to treatment arms by a non-random method such as alternation between groups and the use of birth dates or weekdays). We will include RCTs and non-RCTs trials with allocation at both individual and cluster levels. For trials with allocation at cluster level, we will only include those with at least two intervention and two control clusters.

Types of participants

The participants of interest for this review will be caregivers (that is, parents or other persons fulfilling the parental role) of children in need of WHO-recommended vaccines.

Types of interventions

Eligible interventions will be electronic mail (e-mails, text messages, twitter, other forms of social media, telephone calls) or postal mail (letters or postcards) delivered to caregivers to remind them of scheduled vaccination visits for their children or recall those who have missed vaccination visits. We will include multi-faceted interventions involving any of the eligible interventions and conduct a subgroup analysis by nature of interventions (single or multi-faceted). Eligible comparisons include no intervention, standard immunisation practices the given setting, other interventions, or same interventions delivered at a different level of intensity. Interventions meant only to inform or educate caregivers about the importance of vaccination are outside the scope of this review, and will be excluded. In addition, we will exclude studies focusing on reminders for providers (rather than recipients) of care. .

Types of outcome measures

The primary outcome for this review is vaccination coverage in children under five (as defined by the authors). Childhood vaccination coverage can be reported in a variety of ways, including coverage with individual vaccines, uptake of a combination of vaccines, DTP3 coverage, the proportion of fully immunised children, and the percentage of children up-to-date with recommended vaccines.[6,14-16] We will include studies with all these outcomes. The secondary outcomes will be the cost of the intervention, the incidence of vaccine-preventable diseases, the acceptability of the intervention, adverse events following immunisation (AEFI), and undesirable effects of the interventions.

Search methods for identification of studies

We have developed a comprehensive search strategy for peer-reviewed literature (See Appendix). Searches will be conducted in PubMed, Scopus, Cochrane Central Register of Controlled Trials (CENTRAL), ISI Web of Science (Science Citation Index), Cumulative Index of Nursing and Allied Health (CINAHL), and PDQ Evidence. We will also check reference lists of relevant reviews and full-text articles assessed for eligibility in this review. In addition, we will search the WHO International Clinical Trials Registry Platform and Clinicaltrials.gov for ongoing trials.

Data collection and analysis

Selection of studies

Two review authors (Martel Chachou [MC] and Villyen Motaze [VM]) will independently screen the search outputs for potentially eligible studies. We will obtain the full text of studies deemed potentially eligible by at least one of the two authors, and the two authors will independently assess them for eligibility against

study inclusion criteria (that is, types of studies, participants, interventions, and outcomes). We will endeavour to obtain English translations for eligible articles published in languages other than English.

Data extraction and management

We will use the Cochrane Collaboration's Review Manager (RevMan: http://ims.cochrane.org/RevMan) for data management and statistical analyses. The two authors will use a pre-designed pilot-tested data collection form to independently extract data on study design and methods, country setting (including income level as defined by the World Bank),[19] participant characteristics, intervention characteristics, study outcomes, and study funding sources.

Assessment of risk of bias in included studies

Risk of bias in included studies will be assessed independently by MC and VM, using the Cochrane Risk of Bias tool.[20] The following domains will be assessed: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, completeness of outcome data, completeness of outcome reporting, and other potential sources of bias (for example, baseline imbalance and conflicts of interest). Judgements will be made for each domain as low risk of bias, unclear risk of bias, or high risk of bias according to the criteria in the Cochrane handbook. For cluster-randomised controlled trials, we will include additional domains for assessment such as "loss of clusters". We will categorise each included study into one of three levels of bias: low, moderate, and high risk of bias. Studies classified as low risk of bias for all domains will be considered to be at low risk of bias. Studies with a high risk of selection, detection, or attrition bias will be categorised as having high risk of bias. All other studies will be considered to have moderate risk of bias.

Resolving discrepancies following duplicate assessments

The two authors (MC and VM) conducting independent screening of search outputs, assessment of study eligibility, extraction of data from included studies, and assessment of risk of bias in eligible studies will compare their results after each stage and resolve any differences by discussion and consensus. Should there be no consensus between the two, a third author (Fidele Mukinda or Charles Wiysonge) with arbitrate

Measures of effect

We will express study results for binary data as risk ratios and 95% confidence intervals (CIs). For cost of interventions we will report the costs in the currencies provided by the trial authors, with the current United States Dollar equivalents. Where the data are reported as a small number of ordinal categories, these data will be converted to binary data. For example, in the event that the acceptability of interventions is categorised as acceptable, moderately acceptable and not acceptable, the groups will be converted into two groups: acceptable (acceptable or moderately acceptable) versus not acceptable. For continuous data, such as incidence of vaccine-preventable diseases, we will calculate unadjusted mean differences (MD) with their standard deviations.

Data synthesis

We will use both fixed-effect and random-effects methods to pool data from clinically homogenous studies, and compare the results to assess the impact of statistical heterogeneity. We will then present the results from the random-effects method, unless it is contra-indicated (for example, if there is funnel plot asymmetry). In the presence of funnel plot asymmetry, we will present the estimates of effects from both methods of meta-analyses, with the assumption that funnel plot asymmetry indicates that neither method is more appropriate. If both show a presence (or absence) of effect we will be reassured; if they do not agree we will report this. We will include data from eligible cluster RCTs in relevant meta-analyses after controlling for the design effect, using the intra-cluster correlation coefficient (ICC).

We will calculate overall intervention effects using generic inverse variance[20] and use the GRADE approach to categorise the certainty of the evidence for the effect of each intervention on each outcome as high, moderate, low or very low.[17]

Unit of analysis issues

We expect that controlled trials which allocated participants at cluster levels will appropriately control for clustering. However, if such data are instead reported as if allocation to interventions was done at the level of the individual we will request individual participant data to use in estimating the ICC. If individual participant data are not available, we will obtain external ICC estimates from external sources and use it to re-analyse the data. [20]

Dealing with missing data

We will contact the authors of included studies to supply relevant unreported data on our primary outcomes. For studies reporting outcomes only for participants who completed the trial or followed the protocol, we will request the additional information that would permit us to conduct intention-to-treat analyses. Should we not receive any requested missing data, we will describe the missing data and discuss the extent to which the missing data could alter our results. We will conduct sensitivity analyses to assess the impacts of missing data on estimates of effect.

Assessment of heterogeneity

We will assess clinical variation across studies by comparing the distribution of important characteristics relating to participants (for example, age), study settings (e.g. single or sample of medical practice or clinic settings), and country income level according to the World (high, middle, or low). We will pool data from clinically homogeneous studies, examine statistical heterogeneity between study results using the Chi-square test of homogeneity (with significance defined at the alpha level of 10%), and describe any observed statistical heterogeneity between study results using the I-square statistic.[20]

Assessment of reporting biases

Should we include 10 or more studies in a meta-analysis we will use funnel plots to assessment the possibility of publication bias, because when there are fewer studies funnel plot asymmetry tests are not a reliable means of differentiating true

asymmetry from the play of chance.[21] Funnel plot asymmetry can emanate from real inconsistency of effects of interventions; publication and other biases (for example, selective outcome reporting), poor methodological quality (poor methodological design, inadequate analysis, fraud), or chance.[22]

Subgroup analysis

We will carry-out subgroup analyses for the primary outcome (vaccination coverage), with subgroups defined by intervention subtype (e-mails, telephone calls, text messaging, twitter, letters, and postcards), nature of intervention (single or multi-faceted intervention), country income level as defined by the World Bank (high-income, middle-income, and low-income countries),[19] and study design (randomised controlled trials and non-randomised controlled trials). Where appropriate, intention-to-treat (ITT) principle and the available case principle will be used to analyse the data.

Sensitivity analysis

We will conduct sensitivity analyses to investigate the robustness of the results to risk of bias (low versus high risk of bias). For sensitivity analyses, we will define 'high risk of bias' based on each of three criteria, namely, inadequate concealment of intervention allocation, inadequate blinding of outcome assessment, and substantial loss to follow-up and/or withdrawals from allocated interventions. If we include cluster-randomised trials and insufficient information is available to adjust for clustering, we will use individuals as the unit of analysis and perform sensitivity analyses to assess the potential bias that may have occurred as a result of inadequately controlling for the effects of clustering. We will also perform sensitivity analyses if ICCs were obtained from external sources.

Reporting of the review findings

We have written this protocol and will report the review findings as recommended by relevant PRISMA guidelines.[23-24] In addition, we will present the outputs of our data analysis in forest plots and GRADE summary of findings tables.[18]

Ethics and dissemination

The review protocol does not need approval by an ethics committee because we will use publicly available data, without directly involving human participants. We published an outline of the protocol[26] in the PROSPERO International Prospective Register of Systematic Reviews in 2014, registration number: CRD42014012888. The results will provide updated evidence on the effects of electronic and postal reminders on immunisation coverage, and we will discuss the applicability of the findings to low and middle-income countries. We plan to disseminate review findings through publication in a peer-reviewed journal and presentation at relevant scientific conferences. In addition, we will prepare a policymaker-friendly summary using a validated format (e.g. SUPPORT Summary)[27] and disseminate this through social media and email discussion groups.

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Contributors

Martel Chachou led the development of the protocol, wrote the first draft, coordinated and integrated comments from co-authors, and approved the final version for publication. Fidele Mukinda critically revised successive drafts of the manuscript and approved the final version for publication. Villyen Motaze critically revised successive drafts of the manuscript and approved the final version for publication. CS Wiysonge conceived the study, provided supervision and mentorship to Martel Chachou, critically revised successive drafts of the manuscript, approved the final version for publication, and is the guarantor of the manuscript.

Competing interests

None declared

Provenance and peer review

Not commissioned; externally peer reviewed.

References

1. World Health Organization. Immunisation. Available from http://www.who.int/topics/immunization/en/ (accessed 12 August 2015).
2. Deeks SL, Lim GH, Simpson MA, et al. An assessment of mumps vaccine effectiveness by dose during an outbreak in Canada. *CMAJ* 2011;183:1014-20.
3. Albrich WC, Madhi SA, Lafond KE, Klugman KP. Herd immunity after pneumococcal conjugate vaccination. *Lancet* 2007;370:218-19.

4. World Health Organization. Global immunization coverage in 2014. Available from http://www.who.int/immunization/monitoring_surveillance/Global_Immunization_Data.pdf?ua=1 (accessed 12 August 2015).
5. World Health Organization. Global Vaccine Action Plan 2011 – 2020. Available from http://www.who.int/immunization/global_vaccine_action_plan/en/ (accessed 12 August 2015).
6. Machingaidze S, Wiysonge CS, Hussey GD. Strengthening the Expanded Programme on Immunization in Africa – looking beyond 2015. *PLoS Med* 2013;10(3):e1001405.
7. Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. *Lancet* 2015;385:430-40.
8. Wiysonge CS, Ngcobo NJ, Jeena PM, et al. Advances in childhood immunisation in South Africa where to now? Programme managers' views and evidence from systematic reviews. BMC Public Health 2012;12:578.
9. Falagas ME, Zarkadoulia E. Factors associated with suboptimal compliance to vaccinations in children in developed countries: a systematic review. Curr Med Res Opin 2008; 24: 1719-41.
10. Wiysonge CS, Uthman OA, Ndumbe PM, Hussey GD. Individual and contextual factors associated with low childhood immunisation coverage in sub-Saharan Africa: a multilevel analysis. *PLoS* One 2012;7:e37905.
11. Lewin S, Hill S, Abdullahi LH, et al. Communicate to vaccinate (COMMVAC). Building evidence for improving communication about childhood vaccinations in low- and middle-income countries: protocol for a programme of research. *Implement Sci* 2011;6:125.
12. Morris J, Wang W, Wang L, et al. Comparison of reminder methods in selected adolescents with records in an immunization registry. J Adolesc Health 2015;56:S27-32.
13. Williams N, Woodward H, Majeed A, Saxena S. Primary care strategies to improve childhood immunisation uptake in developed countries: systematic review. JRSM Short Rep 2011;2(10):81.
14. Jacobson Vann JC, Szilagyi P. Patient reminder and patient recall systems for improving immunization rates. Cochrane Database of Systematic Reviews 2005, Issue 3, Art. No.: CD003941. doi:10.1002/14651858.CD003941.pub2.
15. Oyo-Ita A, Nwachukwu CE, Oringanje C, Meremikwu MM. Interventions for improving coverage of child immunization in low- and middle-income countries. Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD008145. DOI: 10.1002/14651858.CD008145.pub2.
16. Harvey H, Reissland N, Mason J. Parental reminder, recall and educational interventions to improve early childhood immunisation uptake: A systematic review and meta-analysis. Vaccine 2015;33:2862-80.
17. Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011;64:401-6.
18. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011;64:383-94.
19. The World Bank Group. Data. Countries and Economies. Available from http://data.worldbank.org/country (accessed 12 August 2015).

20. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Cochrane Collaboration, 2011.
21. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629-34.
22. Bezuidenhout H, Wiysonge CS, Bentley JM. Risperidone for disruptive behaviour disorders in children with intellectual disabilities [Protocol]. Cochrane Database of Systematic Reviews 2012; Issue 7. Art. No.: CD009988.
23. Shamseer L, Moher D, Clarke M, et al; PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015;349:g7647.
24. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 2009;339:b2700.
25. Welch V, Petticrew M, Tugwell P, et al; PRISMA-Equity Bellagio group. PRISMA-Equity 2012 extension: reporting guidelines for systematic reviews with a focus on health equity. PLoS Med 2012;9:e1001333.
26. Chachou MJ, Mukinda F, Wiysonge CS. The effects on childhood immunisation coverage of mailing reminders and recalls through emails, letters or postcards. PROSPERO 2014:CRD42014012888. Available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014012888.
27. Rosenbaum SE, Glenton C, Wiysonge CS, et al. Evidence summaries tailored for health policymakers in low and middle-income countries. Bull World Health Organ 2011;89;54-61.

PRISMA-P (preferred reporting items for systematic review and meta-analysis protocols) 2015 checklist: recommended items to address in a systematic review protocol

Section and topic	Item No	Checklist item	Page No
Administrative information			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2 & 9
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	10
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	10
Sponsor	5b	Provide name for the review funder and/or sponsor	10
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	10
Introduction			
Rationale	6	Describe the rationale for the review in the context of what is already known	3-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
Methods			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Appendix
Study records			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6-9
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6-7
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate),	7

		any processes for obtaining and confirming data from investigators	
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	7
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	8
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	8
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	9
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	N/A
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	8-9
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	8