PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Electronic and postal reminders for improving immunisation coverage in children: protocol for a systematic review and meta-analysis
AUTHORS	Chachou, Martel; K Mukinda, Fidele; Motaze, Villyen; Wiysonge, Charles

VERSION 1 - REVIEW

REVIEWER	K. Michael Peddecord, Dr.P.H. Professor Emeritus, Public Health Sr. Researcher, Center for Human Dynamics in the Mobile Age
REVIEW RETURNED	15-May-2015

GENERAL COMMENTS	I would anticipate some difficulty comparing the outcome of different studies both across environments and years. I suspect that some outcomes will be described as “up to date” where the package of vaccines may be very different across locations and time. This may require some weighting or adjustment. It would be far easier to bring a child who needs 3 vaccines with 12 doses to be considered up to date versus 7 vaccines with 24 doses. Care will be needed to deal with the study populations and the ability to generalize (external validity) results. Many studies will be from a single or sample of medical practice or clinic settings. Most often the clinics are voluntary and thus convenience samples. We have a rule “if you have seen one medical group, you have seen one medical group”. The immunization promoters who often establish the randomized trials are highly motivated and their results are naturally infected with the “the enthusiasm bias” . It is good that you are trying to get a measure of cost or cost effectiveness, unfortunately (having tried to do this) I know how problematic it is to measure costs in a single setting, let alone in a multi-center cross-sectional study or trial. To be effective and SUSTAINABLE in a variety of environments methods need to be cost-effective. It would seem prudent to add newer methods of reminders such as text messages, twitter and other forms of social media. Phone call reminders are another very common method of providing reminders (both manual and “robo” calls). Some of the available software provides email as well as telephone reminders. There are a number of studies using newer technologies. Some of

	these are cited in a recently published paper by our group. Morris et. al. Comparison of Reminder Methods in Selected Adolescents. With Records in an Immunization Registry. Journal of Adolescent Health 56 (2015) S27eS32. I realize that by including phone, text and other methods would greatly increase the complexity of your protocol, however from my U.S. perspective, I would only find this systematic review useful if it includes these new approaches. Knowing the rapidly growing use of cellular and smart phones in many developing countries I think the new media review is critical to improve the utility of any review. I think it is reasonable to stick with the 0-5 year old age group. There are probably more studies for that group than for other ages.

REVIEWER	Lawrence Mbuagbaw McMaster University, Canada
REVIEW RETURNED	24-Jun-2015

GENERAL COMMENTS	The authors of this protocol propose to investigate the effects of electronic and postal reminders on childhood immunisation coverage by conducting a systematic review. They have a clear research questions and will search relevant electronic databases to retrieve articles which will be appraised in duplicate. The data retrieved will be synthesized using conventional methods. This is an important topic which warrants a concise summary of the evidence. I have a few comments that should help the authors achieve their goals. The title is a bit hard to follow and can be revised. I would suggest something along the lines of “Electronic and postal reminders for improving immunisation coverage in children”. Abstract: The introduction of the abstract doesn’t really flow with the objectives of the paper. If the reasons for suboptimal coverage are multifactorial, why are you focusing on one? The methods section of the abstract is over-elaborate in the description of what a randomized study is. This sort of detail, if the authors deem necessary is better in the main text and not the abstract. It can be removed to increase flow. The first level of appraisal of heterogeneity should be clinical. If the studies are too different to pool, they should not be. Little is mentioned of your dissemination strategy. It would be nicer to state if this was a master’s thesis and if it would be presented at conferences, department rounds or published in a journal. No limitations are reported. There is always something you might not feel confident about, including your ability to appraise non-English language manuscripts, or to retrieve unpublished papers. Page 2, line 44 should read “PROSPERO” Introduction: Page 3, line 31 should be “children’s health” Please provide a timeline for the immunization rates reported. Readers will be interested in knowing how recent it is. Page 3, line 46 should be “children’s” Objectives: Page 4, line 11 is missing a full stop. Method and analysis: You can delete the purpose of the PROPERO database. If you wish

	to provide readers with more information about PROSPERO, you can add a URL to your registration number. Please break down this section into the relevant components (with subheadings): types of studies, types of participants, types of interventions, types of comparisons, types of outcomes, search strategy, data extraction, assessment of study risk of bias, data analysis, reporting etc. Page 4, lines 30-31. It is not clear what you mean by residing in children community. Will you include cluster randomized trials? Most of immunization interventional research is done on the cluster level because as you rightly stated, the benefit of immunization is when the whole group is immunized. Your primary outcome (child's immunization status) is not the same as immunisation coverage as mentioned in the preceding sections. This has statistical implications because one is individual and the other is collective. No mention is made of the kinds of comparisons that will be considered. No mention is made of the kinds of vaccines you are interested in. Please provide examples of what you mean by undesirable effects from the intervention. Page 4, line37. Would you be interested in reminders to health care workers? Page 5, line 7 is missing a reference to the Cochrane Handbook. How will you report you search strategy and the whole systematic review? If you will use the PRISMA statement, please say so and reference it. Kindly add the initials of the two authors working in duplicate those of the arbiter. In your plan for sensitivity analysis, it would be better to investigate missing data for the whole trial instead of using the difference in missing data between arms. Large amounts of data can be missing from both arms, with no difference between the arms. In the event that you chose to include cluster randomized trials, assessment of risk of bias is somewhat different and includes other items such as loss of clusters etc. which should be considered. General comments: I am aware of similar systematic reviews which I am happy to share with you below: 1. Jacobson Vann JCS, P. Patient reminder and recall systems to improve immunization rates. Cochrane Database of Systematic Reviews 2005; (3). 2. Ward KC, Maria Yui Kwan; King, Catherine; Leask, Julie. Strategies to improve vaccination uptake in Australia, a systematic review of types and effectiveness... [corrected] [published erratum appears in AUST NZ J PUBLIC HEALTH 2012; 36(5):490]. Australian & New Zealand Journal of Public Health 2012; 36(4): 369-77. The search strategy attached as an appendix is neither sensitive nor specific. It should include components of study design, time limits and participants. I can see terms related to the intervention and the outcome only. References 16 and 18 are inaccurate. The name of the journals should be "Cochrane database of systematic reviews". I believe the knowledge gaps identified in references 16, 17, 18 call for more primary studies, not more systematic reviews. It would be relevant to justify how your review fits into all this.

REVIEWER	Pierre Verger Observatoire régional de la santé Paca, Marseille, France INSERM912, SESSTIM, Marseille France
REVIEW RETURNED	06-Jul-2015

GENERAL COMMENTS	"The effects on childhood immunization coverage of mailing reminders and recalls…" It is of utmost importance to assess the effectiveness of various strategies to improve childhood vaccine coverage; implementing systematic reviews and/or meta-analyses of the published studies on these aspects is thus useful for policy makers, and public health professionals. This article proposes the protocol of such an approach to investigate the potential impact of reminders or recalls using e-mails, letters or postcards to improve childhood immunization coverage. The protocol is based on usual standard methods to implement systematic reviews. There are major points that should be clarified however. Major remarks 1) Main general remark: several reviews or systematic reviews have already been published regarding interventions aiming at improving child immunization coverage: Oyo-Ita et al., 2001, Williams et al., 2011, Harvey et al., 2015. These reviews address reminder or recall strategies. The authors do not cite the two latter articles; they should explain why they think their study will add to these preceding reviews. 2) The scope of the review appear relatively large: any country and language, various outcomes, studies not published in peer-reviewed journals… Has a preliminary search shown that the number of good quality studies was low? 3) At the same time, I wonder whether the search strategy presented in appendix is exhaustive; the authors do not use Mesh key words (such as "reminder systems") or synonyms such as letter, post-card, recall… 4) Abstract, introduction: the authors write that "…a combination of interventions is needed to improve immunization coverage…" but then, they focus on reminders or recall strategies and limit these strategies to "e-mails, letters or postcards": how will they address in their systematic review that, sometimes, reminders or recall strategies are part of a multi-faceted intervention program? This is not sufficiently discussed in their protocol. 5) Paragraph "Strengths and limitations": the sentence "The review will fill the gap of systematic review using combination of communication strategies to communicate immunization dates to parents and caregivers" is unclear: which gap? What are the limitations of the authors' protocol? 6) Introduction section, second paragraph, second sentence: "The vaccination coverage for the third dose of the diphtheria-tetanus-pertussis vaccine is regarded as a proxy for childhood immunization coverage". A reference should be added; and while this statement does not apply to all countries, the authors should specify to which context they refer. 7) Introduction section, second paragraph, last 6 lines: it is surprising that caregivers' attitudes, opinions and beliefs toward immunization are not included among individual factors that are associated with childhood immunization coverage. This is a limit of reminder or recall methods: they are not meant to address vaccine hesitancy and their

	effectiveness they depend on attitudes of caregivers toward vaccination. 8) Objectives: they should be written more precisely: which age, vaccine, context (all countries? This is not clear); to whom (caregivers)… Moreover, the study does not only consist in a systematic review but also in a meta-analysis. 9) Methods: the authors should briefly justify why they will include non-randomized controlled trials and also unpublished studies. 10) Eligibility criteria of the studies should be precisely specified. In particular, in the selection process of the studies, the authors mention that risk of bias will be assessed: will this be used to select studies, or not, and why? 11) Subgroup analysis: on which criteria will the authors identify countries with different income levels? Minor remarks = Title: the authors should mention that they present a protocol not only for a systematic review but also a meta-analysis. Abstract = First line: “suboptimal immunization coverage leads to several deaths”: several millions deaths? In the world? Or only in low and middle income countries? = Line 4: “therefore” should be omitted. Introduction section = Second paragraph, next-to-last line: “are reported to affecting”: affect? = End of second paragraph: the authors cite three studies regarding the determinants of vaccination compliance but no systematic review. I suggest citing at least one review (e.g. 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(6):1719-1741. doi:10.1185/03007990802085692). = Third paragraph, next-to-last line: “it unclear if”: it is unclear if. Methods = Globally, its presentation should be improved for example by inserting subtitles (data sources, study selection, data extraction, quality assessment…) = Page 5: “Two authors will compare their assessments and resolve differences by discussion and consensus. In case of failure to resolve any difference, a third author will be called upon to arbitrate.” This sentence is repeated three times (at different steps of the analysis). Authors could find a way to avoid this repetition. = Page 5, line 26: Cochrane is repeated. = Methods, page 5, last sentence: (i.e. percentage points or more difference…): a reference should be added.

VERSION 1 – AUTHOR RESPONSE

A. Reviewer: K. Michael Peddecord

Comment:
I would anticipate some difficulty comparing the outcome of different studies both across environments and years. I suspect that some outcomes will be described as “up to date” where the package of vaccines may be very different across locations and time. This may require some weighting or adjustment. It would be far easier to bring a child who needs 3 vaccines with 12 doses to be considered up to date versus 7 vaccines with 24 doses.

Response:
We acknowledge that there will be heterogeneity of environments in which studies were conducted and that vaccination coverage will be defined differently in different studies. To mitigate these differences, we have now described our approach as follows: “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. We will include studies with all these outcomes.” In addition, we will only combine data from clinically homogenous studies: “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…”

Comment:
Care will be needed to deal with the study populations and the ability to generalize (external validity) results. Many studies will be from a single or sample of medical practice or clinic settings. Most often the clinics are voluntary and thus convenience samples. We have a rule “if you have seen one medical group, you have seen one medical group”.
Response:
We acknowledge that there will be heterogeneity in study settings and have specified under “data synthesis” that we will only pool data from clinically homogenous studies. Further, under assessment of heterogeneity, we have indicated that “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…”

Comment:
The immunization promoters who often establish the randomized trials are highly motivated and their results are naturally infected with the “the enthusiasm bias”.
Response:
This is a reality, which is difficult to control for.

Comment:
It is good that you are trying to get a measure of cost or cost effectiveness, unfortunately (having tried to do this) I know how problematic it is to measure costs in a single setting, let alone in a multi-center cross-sectional study or trial. To be effective and SUSTAINABLE in a variety of environments methods need to be cost-effective.
Response:
We completely agree with the assertion and will report whatever data we get from the trial reports or from the investigators on request.

Comment:
It would seem prudent to add newer methods of reminders such as text messages, twitter and other forms of social media. Phone call reminders are another very common method of providing reminders (both manual and “robo” calls). Some of the available software provides email as well as telephone reminders.
There are a number of studies using newer technologies. Some of these are cited in a recently published paper by our group. Morris et. al. Comparison of Reminder Methods in Selected Adolescents. With Records in an Immunization Registry. Journal of Adolescent Health 56 (2015) S27eS32.
I realize that by including phone, text and other methods would greatly increase the complexity of your

protocol, however from my U.S. perspective, I would only find this systematic review useful if it includes these new approaches. Knowing the rapidly growing use of cellular and smart phones in many developing countries I think the new media review is critical to improve the utility of any review.
Response:
We have now included phone calls and social media as eligible 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).”

Comment:
I think it is reasonable to stick with the 0-5 year old age group. There are probably more studies for that group than for other ages.
Response:
We have now stuck to the 0-5 year age group and revised the objective to “assess the effects of caregiver reminders on uptake of WHO-recommended vaccines in children less than five years of age.”

B. Reviewer: Lawrence Mbuagbaw

Comment:
The authors of this protocol propose to investigate the effects of electronic and postal reminders on childhood immunisation coverage by conducting a systematic review. They have a clear research question and will search relevant electronic databases to retrieve articles which will be appraised in duplicate. The data retrieved will be synthesized using conventional methods. This is an important topic which warrants a concise summary of the evidence. I have a few comments that should help the authors achieve their goals.
Response:
We appreciate this compliment.

Comment:
The title is a bit hard to follow and can be revised. I would suggest something along the lines of “Electronic and postal reminders for improving immunisation coverage in children”.
Response:
We have now rephrased the title to “Electronic and postal reminders for improving immunisation coverage in children…”

Comment:
Abstract:
The introduction of the abstract doesn’t really flow with the objectives of the paper. If the reasons for suboptimal coverage are multifactorial, why are you focusing on one?
Response:
We have now revised the introduction as follows: “…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…”

Comment:
The methods section of the abstract is over-elaborate in the description of what a randomized study is. This sort of detail, if the authors deem necessary is better in the main text and not the abstract. It can be removed to increase flow.
Response:
We have now deleted the description of study designs from the abstract.

Comment:
The first level of appraisal of heterogeneity should be clinical. If the studies are too different to pool, they should not be.
Response:
We have now indicated that “We will pool data from clinically homogenous studies…”

Comment:
Little is mentioned of your dissemination strategy. It would be nicer to state if this was a master’s thesis and if it would be presented at conferences, department rounds or published in a journal.
Response:
We have now described our dissemination strategy: “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”

Comment:
No limitations are reported. There is always something you might not feel confident about, including your ability to appraise non-English language manuscripts, or to retrieve unpublished papers.
Response:
We have now provided some limitations, including the expected clinical heterogeneity of studies as well as inclusion of non-randomised trials, which are prone to a high risk of bias.

Comment:
Page 2, line 44 should read “PROSPERO”
Response:
Correction done

Comment:
Introduction:
Page 3, line 31 should be “children’s health”
Response:
Correction done

Comment:
Please provide a timeline for the immunization rates reported. Readers will be interested in knowing how recent it is.
Response:
We have now provided the most recent data available i.e. 2014

Comment:
Page 3, line 46 should be “children’s”
Objectives:
Page 4, line 11 is missing a full stop.
Response:
Corrections done

Comment:
Method and analysis:
You can delete the purpose of the PROPERO database. If you wish to provide readers with more information about PROSPERO, you can add a URL to your registration number.
Response:
We have now deleted the purpose of the PROPERO database.

Comment:
Please break down this section into the relevant components (with subheadings): types of studies, types of participants, types of interventions, types of comparisons, types of outcomes, search strategy, data extraction, assessment of study risk of bias, data analysis, reporting etc.
Response:
This section is now subdivided into the relevant components.

Comment:
Page 4, lines 30-31. It is not clear what you mean by residing in children community.
Response:
We have now deleted the phrase “residing in children community” from the types of participants.

Comment:
Will you include cluster randomized trials? Most of immunization interventional research is done on the cluster level because as you rightly stated, the benefit of immunization is when the whole group is immunized.
Response:
Yes, we will include cluster trials in the review.

Comment:
Your primary outcome (child’s immunization status) is not the same as immunisation coverage as mentioned in the preceding sections. This has statistical implications because one is individual and the other is collective.
Response:
We have now rephrased our primary outcome as “vaccination coverage (as defined by the authors).”

Comment:
No mention is made of the kinds of comparisons that will be considered.
Response:
We have now indicated that “Eligible comparisons include no intervention, standard immunisation practices the given setting, other interventions, or same interventions delivered at a different level of intensity”

Comment:
No mention is made of the kinds of vaccines you are interested in.
Response:
We are interested in coverage with any WHO-recommended vaccine (s).

Comment:
Please provide examples of what you mean by undesirable effects from the intervention. Page 4, line37.
Response:
We have now indicated that we will report undesirable effects of the interventions “as defined by the authors.”

Comment:
Would you be interested in reminders to health care workers?
Response:
We have now specified that “we will exclude studies focusing on reminders for providers (rather than recipients) of care.”

Comment:
Page 5, line 7 is missing a reference to the Cochrane Handbook.
Response:
Reference is now provided.

Comment:
How will you report your search strategy and the whole systematic review? If you will use the PRISMA statement, please say so and reference it.
Response:
We have now indicated that “We have written this protocol and will report the review findings as recommended by the relevant PRISMA guidelines.”

Comment:
Kindly add the initials of the two authors working in duplicate those of the arbiter.
Response:
This is now done.

Comment:
In your plan for sensitivity analysis, it would be better to investigate missing data for the whole trial instead of using the difference in missing data between arms. Large amounts of data can be missing from both arms, with no difference between the arms.
Response:
We have now revised as suggested.

Comment:
In the event that you chose to include cluster randomized trials, assessment of risk of bias is somewhat different and includes other items such as loss of clusters etc. which should be considered.
Response:
We have now indicated that “For cluster-randomised controlled trials, we will include additional domains for assessment such as “loss of clusters”.”

Comment:
General comments:
I am aware of similar systematic reviews which I am happy to share with you below:
1. Jacobson Vann JCS, P. Patient reminder and recall systems to improve immunization rates. Cochrane Database of Systematic Reviews 2005; (3).
2. Ward KC, Maria Yui Kwan; King, Catherine; Leask, Julie. Strategies to improve vaccination uptake in Australia, a systematic review of types and effectiveness... [corrected] [published erratum appears in AUST NZ J PUBLIC HEALTH 2012; 36(5):490]. Australian & New Zealand Journal of Public Health 2012; 36(4): 369-77.
Response
We have now taken note of these and other relevant reviews in the rationale.

Comment:
The search strategy attached as an appendix is neither sensitive nor specific. It should include

components of study design, time limits and participants. I can see terms related to the intervention and the outcome only.
Response:
We have now revised the search.

Comment:
References 16 and 18 are inaccurate. The name of the journals should be “Cochrane database of systematic reviews”.
Response:
The journal is now corrected.

Comment:
I believe the knowledge gaps identified in references 16, 17, 18 call for more primary studies, not more systematic reviews. It would be relevant to justify how your review fits into all this.
Response:
We agree, and have now revised this section to rephrase the knowledge gaps differently: “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.”

C. Reviewer : Pierre Verger

Comment:
It is of utmost importance to assess the effectiveness of various strategies to improve childhood vaccine coverage; implementing systematic reviews and/or meta-analyses of the published studies on these aspects is thus useful for policy makers, and public health professionals. This article proposes the protocol of such an approach to investigate the potential impact of reminders or recalls using e-mails, letters or postcards to improve childhood immunization coverage. The protocol is based on usual standard methods to implement systematic reviews.
Response:
This is a compliment.

Comment:
Main general remark: several reviews or systematic reviews have already been published regarding interventions aiming at improving child immunization coverage: Oyo-Ita et al., 2001, Williams et al., 2011, Harvey et al., 2015. These reviews address reminder or recall strategies. The authors do not cite the two latter articles; they should explain why they think their study will add to these preceding reviews.
Response:
We have now addressed the added value of our review in relation to the mentioned reviews.

Comment:
The scope of the review appears relatively large: any country and language, various outcomes, studies not published in peer-reviewed journals… Has a preliminary search shown that the number of good quality studies was low?
Response:
We agree that the scope is quite large, and a preliminary research reveals many potentially eligible studies. We have now left out the search of conference proceedings.

Comment:

At the same time, I wonder whether the search strategy presented in appendix is exhaustive; the authors do not use Mesh key words (such as “reminder systems”) or synonyms such as letter, post-card, recall…
Response:
We have now revised the search.

Comment:
Abstract, introduction: the authors write that “…a combination of interventions is needed to improve immunization coverage…” but then, they focus on reminders or recall strategies and limit these strategies to “e-mails, letters or postcards”: how will they address in their systematic review that, sometimes, reminders or recall strategies are part of a multi-faceted intervention program? This is not sufficiently discussed in their protocol.
Response:
We have now indicated under types of interventions that “We will include multi-faceted interventions involving any of the eligible interventions, and include nature of interventions (single or multi-faceted) in the subgroup analysis”. In addition, under subgroup analysis, we indicate that “We will carry-out subgroup analyses for the primary outcome (that is, vaccination coverage), with subgroups defined by … nature of intervention (single or multi-faceted intervention)…”

Comment:
Paragraph “Strengths and limitations”: the sentence “The review will fill the gap of systematic review using combination of communication strategies to communicate immunization dates to parents and caregivers” is unclear: which gap? What are the limitations of the authors’ protocol?
Response:
We have now deleted the sentence referred to above and provided some limitations; including the expected clinical heterogeneity of studies as well as inclusion of non-randomised trials, which are prone to a high risk of bias.

Comment:
Introduction section, second paragraph, second sentence: “The vaccination coverage for the third dose of the diphtheria-tetanus-pertussis vaccine is regarded as a proxy for childhood immunization coverage”. A reference should be added; and while this statement does not apply to all countries, the authors should specify to which context they refer.
Response:
We have now indicated that “the third dose of a vaccine containing the diphtheria, tetanus, and pertussis (DTP3) vaccine is regarded as a proxy for childhood immunisation coverage worldwide” and cited the Global Vaccine Action Plan.

Comment:
Introduction section, second paragraph, last 6 lines: it is surprising that caregivers’ attitudes, opinions and beliefs toward immunization are not included among individual factors that are associated with childhood immunization coverage. This is a limit of reminder or recall methods: they are not meant to address vaccine hesitancy and their effectiveness they depend on attitudes of caregivers toward vaccination.
Response:
We have now revised this section with a focus on behaviours that would be affected by reminders. The section now reads “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). 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”

Comment:
Objectives: they should be written more precisely: which age, vaccine, context (all countries? This is not clear); to whom (caregivers)… Moreover, the study does not only consist in a systematic review but also in a meta-analysis.
Response:
We have now put meta-analysis in the title and rephrased the objective: “Our objective is to assess the effects of caregiver reminders on uptake of WHO-recommended vaccines in children less than five years of age.”

Comment:
Methods: the authors should briefly justify why they will include non-randomized controlled trials and also unpublished studies.
Response:
We have now removed reference to inclusion of unpublished studies and will subgroup analysis by study type (randomised versus non-randomised controlled trials).

Comment:
Eligibility criteria of the studies should be precisely specified. In particular, in the selection process of the studies, the authors mention that risk of bias will be assessed: will this be used to select studies, or not, and why?
Response:
We have specified how we will summarise risk of bias and use it in sensitivity analyses: “We will conduct sensitivity analyses to investigate the robustness of the results to risk of bias (low versus high risk of bias).”

Comment:
Subgroup analysis: on which criteria will the authors identify countries with different income levels?
Response:
We have now indicated that we will categorise countries using “country income level as defined by the World Bank (high-income, middle-income, and low-income countries)”

Comments
Minor remarks
= Title: the authors should mention that they present a protocol not only for a systematic review but also a meta-analysis.
Abstract
= First line: “suboptimal immunization coverage leads to several deaths”: several millions deaths? In the world? Or only in low and middle income countries?
= Line 4: “therefore” should be omitted.
Introduction section
= Second paragraph, next-to-last line: “are reported to affecting”: affect?
= End of second paragraph: the authors cite three studies regarding the determinants of vaccination compliance but no systematic review. I suggest citing at least one review (e.g. 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(6):1719-1741. doi:10.1185/03007990802085692).
= Third paragraph, next-to-last line: “it unclear if”: it is unclear if.
Methods
= Globally, its presentation should be improved for example by inserting subtitles (data sources, study selection, data extraction, quality assessment…) = Page 5: “Two authors will compare their

assessments and resolve differences by discussion and consensus. In case of failure to resolve any difference, a third author will be called upon to arbitrate." This sentence is repeated three times (at different steps of the analysis). Authors could find a way to avoid this repetition.
= Page 5, line 26: Cochrane is repeated.
= Methods, page 5, last sentence: (i.e. percentage points or more difference…): a reference should be added. Reviewer(s)' Comments to Author:

Response:
All the minor remarks have been addressed exactly as suggested by the referee.

VERSION 2 – REVIEW

REVIEWER	K. M. Peddecord K. Michael Peddecord, Dr.P.H. Professor Emeritus, Public Health Sr. Researcher, Center for Human Dynamics in the Mobile Age
REVIEW RETURNED	28-Aug-2015

GENERAL COMMENTS	I am very pleased to that there have been many substantive changes that improve the rigor and utility of the proposal. Thank you for including a copy of the copy of the PRISMA-P 2015 checklist. I think it is a good starting framework for reporting a review. As noted below I think some other aspects of these studies need to be shared with your report. The PRISMA protocol does not appear to have any explicit boxes for systematically recording and reporting on cost and cost-effectiveness issues. I am pleased that the protocol includes attention to the cost of the tested interventions. I suspect that many if not most of the studies that will be reviewed do not explicitly take into account cost. I believe that it will therefore be incumbent upon your team, give your expertise after having reviewed all of these studies provide some type of review or rating regarding the cost of the intervention (at least the successful ones that are most likely to be used or reproduced in the future. Sustainability of the recall method is a key to long term effectiveness. As I mentioned in my review of the earlier protocol it's one thing to produce results in a controlled well-funded situation versus in the field in every day practice. Using your judgment and including a report on cost/sustainability in your report will be a valuable contribution to the public health practice community. Thank you for taking on this important review and best of luck. I will look forward to its future publication.

REVIEWER	Lawrence Mbuagbaw McMaster University
REVIEW RETURNED	24-Aug-2015

GENERAL COMMENTS	The reviewer completed the checklist but made no further comments.