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Review

A systematic review of strategies for reducing missed opportunities for vaccination

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ABSTRACT

Background: Missed opportunities for vaccination (MOVs) occur when persons eligible for vaccination visit a health facility and do not get the vaccines they need. We conducted a systematic review to assess effects of interventions for reducing MOVs.

Methods: We searched PubMed, Scopus, and the Cochrane Central Register of Controlled Trials in April 2017. Three authors independently screened search outputs, reviewed potentially eligible papers, assessed risk of bias, and extracted data; resolving disagreements by consensus. We expressed study results as risk ratios (RR) with 95% confidence intervals (CI) and assessed the certainty of the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool.

Results: Six studies (five trials and one cohort study) met our inclusion criteria, all conducted in the United States of America. All six studies had various limitations and were classified as having a high risk of bias. We found moderate certainty evidence that the following interventions probably improve vaccination coverage: patient education (RR 1.92, 95% CI 1.38–2.68), patient tracking using community health workers (RR 1.18, 95% CI 1.11–1.25), and patient tracking and provider prompts (RR 1.24, 95% CI 1.18–1.31). In addition, we found low certainty evidence that concurrent interventions targeting health-facility (education, prompts, and audit and feedback) and family settings (phone calls) may increase vaccination coverage (RR 1.25, 95% CI 1.08–1.46).

Conclusions: The currently available evidence suggests that patient education, patient tracking, outreach sessions, and provider prompts reduce missed opportunities for vaccination and improve vaccination coverage. Rigorous studies are required to confirm these findings and increase the certainty of the current evidence base. WHO is currently coordinating efforts to generate such evidence, especially from low-income and middle-income countries, and it is likely that the data will be available in the next few years.

Contents

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1. Introduction

Immunization is a proven tool for controlling life-threatening infectious diseases, and is estimated to prevent more than three million deaths annually [1,2]. Immunization has the potential to do more, if missed opportunities for vaccination (MOVs) are eliminated and global vaccination coverage improves [3,4]. An MOV occurs when a person who is eligible for vaccination, and has no contraindication to vaccination, visits a healthcare service and does not receive all the needed vaccine doses [5]. MOVs may occur during visits for preventive or curative services [5]. Eliminating MOVs in both settings will increase the overall immunization coverage [6]. Surveys conducted in multiple settings show that, on average, one-third of children who visit health facilities in low and middle-income countries miss opportunities to receive the vaccine doses that they need [3,5,7]. Such missed opportunities make a substantial contribution to the 19.5 million children who fail to receive the basic set of routine vaccines scheduled for their first year of life [2]. Thus, the objective of this systematic review is to assess the effects of interventions for reducing MOVs, on vaccination coverage.

2. Materials and methods

2.1. Registration of the review

This systematic review was registered in the International prospective register of systematic reviews (PROSPERO), with registration number CRD42017068816 [8].

2.2. Criteria for considering studies in this review

2.2.1. Types of studies

We included randomized trials (with randomization at either individual or cluster levels) and cohort studies.

2.2.2. Types of participants

Eligible studies had to include one or more of the following types of participants:

- individuals eligible for vaccinations;
- caregivers of individuals eligible for vaccinations; and
- healthcare workers responsible for rendering immunization services.

2.2.3. Types of interventions and comparisons

Eligible interventions were those that led healthcare providers to check immunization histories of people attending curative or preventive services, in order to identify people eligible for vaccination and give them the required vaccine doses. Such interventions could target recipients of care (e.g. educating patients to prompt providers to check their vaccination cards), providers of care (e.g. training, supervision, reminders, audit and feedback, incentives), or the healthcare system (e.g. changing practices at healthcare clinics, systematic screening of immunization histories of individuals admitted to hospital, bringing vaccination services closer to consultation rooms). These interventions had to be compared to no intervention, standard practices in the study settings, alternative interventions, or the same interventions implemented at a different intensity.

2.2.4. Types of outcome measures

Our outcomes were the rate of MOVs and vaccination coverage, as defined by the authors of included studies. MOVs are a surrogate for vaccination coverage, since a decrease in MOVs translates to an increase in vaccination coverage. This explains why in this review we have mostly reported vaccination coverage and not both outcomes.

2.3. Data sources

In April 2017, we searched PubMed, Scopus, and the Cochrane Central Register of Controlled Trials (CENTRAL) with no language or date restrictions. As shown in Appendix 1, we used combinations of the following terms in the search strategy, adapted to each database: immunization, vaccination, uptake, coverage, adhering, adherence, and missed opportunities. In addition, we searched reference lists of included studies and related systematic reviews. Two authors developed the search strategy, with input from the other authors. One author conducted electronic searches and three authors searched reference lists of relevant publications.

2.4. Study selection

Three review authors independently screened the titles and abstracts of records identified in the search output, for potentially eligible studies. We obtained the full text publication for any study that was considered potentially eligible by one or more of the three authors. The three authors independently assessed the full text of each potentially eligible study and classified it as either included or excluded. We have provided reasons for excluding potentially eligible studies from the review. Disagreements among the three authors, during the screening of search outputs and study selection, were resolved through discussion and consensus. The

consensus decision of the three authors on study selection was final, with no arbitration by another author.

2.5. Data extraction

Three review authors independently extracted data using a specially designed data extraction form. Information was extracted on country of study, study design, participants, intervention and comparison, outcome measures, and results. The three authors compared extracted data and resolved discrepancies through discussion and consensus. A fourth author verified and made final decisions on the extracted data.

2.6. Risk of bias assessment

Three authors assessed risk of bias in randomized trials using the Cochrane Risk of Bias Tool [9]. Assessment was done using seven domains: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, completeness of outcome data, completeness of outcome reporting, and other sources of bias. Each domain was recorded as low, high, or unclear risk of bias. Overall, each randomized trial was considered to have a low risk of bias if it scored "low risk" for allocation concealment, blinding of outcome assessors, and completeness of outcome data. A trial was deemed to have a high risk of bias if it recorded 'high risk" for at least one of the three domains. All other trials would be considered to have a moderate risk of bias.

The risk of bias for the cohort study was evaluated using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool [10]. The ROBINS-I tool assesses whether there exists bias in a study due to confounding, selection of participants into the study, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result. We scored each domain as "no" if there was no risk of bias or "yes" if there was a risk of bias. We would have considered the cohort study to have a low risk of bias if the study scored "no" for risk of bias due to each of the following three domains: confounding, deviations from intended intervention, and measurement of outcomes. We would have considered the study to have a "high risk of bias" if the study scored "yes" for risk of bias due to one or more of the three domains. If the study did not satisfy the conditions for a "low" or "high" risk of bias, we would have considered the study to have a moderate risk of bias.

The three authors compared their risk of bias assessments, and resolved discrepancies through discussion and consensus. A fourth author verified the risk of bias assessments, and made final decisions on the risk of bias in included studies.

2.7. Data synthesis

We conducted analyses using the Cochrane Review Manager [11]. We expressed study results as risk ratios (RR) with their 95% confidence intervals (CI). We did not conduct a meta-analysis, due to the variation in interventions among the included studies. Two authors independently assessed the certainty of the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [12].

The GRADE approach categorizes the certainty of a body of evidence as high, moderate, low, or very low. Randomized trials start with high certainty of evidence; and this can be downgraded for study limitations (i.e. risk of bias in included studies), inconsistency in study results (i.e. presence of significant statistical heterogeneity), indirectness of the evidence, imprecision of intervention effects (i.e. wide confidence intervals for the estimate of effects), or publication bias. The certainty of the evidence for cohort (and other observational) studies, start as low, and can be upgraded if there is a strong association; or a dose–response relationship; or if all plausible confounding or bias would decrease the size of the effect. In this review, we downgraded the certainty of the evidence from randomized trials by one to two levels because of study limitations and imprecision of the findings. We kept the certainty of the evidence for the cohort study as low. Two authors conducted data syntheses, with verification by a third author as required.

2.8. Reporting of the review

We have prepared this systematic review in line with guidance on preferred reporting items for systematic reviews and meta-analyses (PRISMA) [13]. The PRISMA statement contains items deemed essential for non-biased reporting of systematic reviews, including a four-phase flow diagram (Fig. 1).

3. Results

3.1. Study selection

The literature search yielded 343 records; 29 from CENTRAL, 51 from PubMed, 261 from Scopus, and 2 from reference lists of included studies [14,15]. Titles and abstracts of the papers were screened and 321 clearly irrelevant articles were excluded (Fig. 1). Full texts of the 22 remaining articles were assessed for eligibility, and six papers met the inclusion criteria [14–19]. The characteristics of the six included studies are shown in Table 1. Reasons are provided for excluding the 16 publications [20–35] in Table 2.

3.2. Characteristics of included studies

The six included studies were conducted in the United States of America (USA). These included three individually randomized trials [14,16,17], two cluster randomized trials [18,19], and one cohort study [15]. The studies enrolled a total number of 92,525 children, adolescents, and adults.

The included studies evaluated the impact of several interventions versus a standard of care or no intervention on the rates of MOVs and uptake of vaccines.

One individually randomized trial assessed the effects of provider prompts with or without tracking by community health workers [14]. A nurse screened the immunization histories of children visiting primary care facilities, irrespective of the purpose of the visit, and placed an MOV sticker on the charts of children in need of vaccination; specifying the required vaccine doses. Another study arm combined the provider prompts with tracking by community health workers. The latter identified under-vaccinated children through medical charts and used postcards, telephone calls, or home visits to recall them to their primary care providers to receive the needed vaccines [14].

The second individually randomized trial assessed the effects of a policy enforcing the screening and vaccination of all eligible children during all visits to primary care providers; with removal of legal guardian signature requirements [16]. Staff nurses screened medical charts for vaccination status at all primary care visits and, if a vaccination was due, attached a brightly colored vaccination reminder card to the front of the medical chart. Regarding the elimination of legal guardian's signature requirement, the legal guardian signed one consent form before the receipt of any vaccinations; and succeeding vaccinations were given without the need for additional consent [16].

The third second individually randomized trial used case management and parent education [17]. The case managers doing

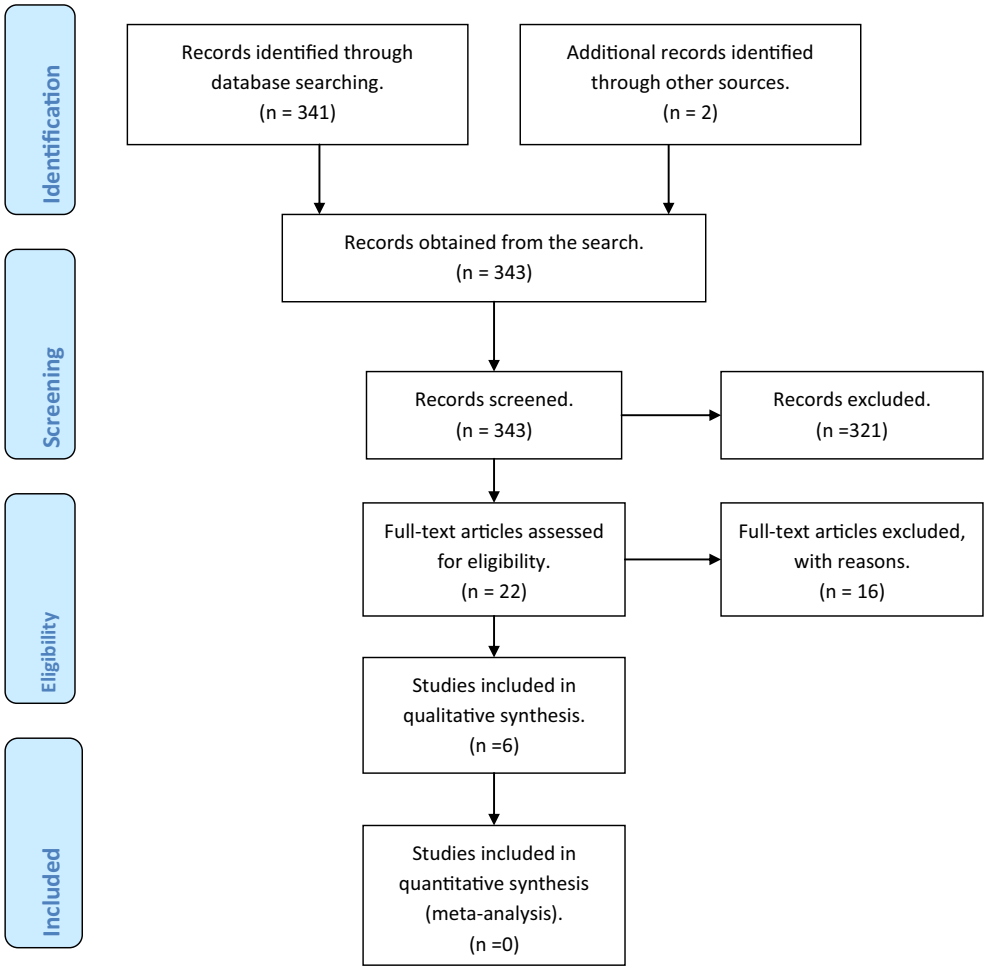

Fig. 1. Study selection process for this review.

Table 1
Study characteristics.

Study and year	Site	Study Design	Participants	Intervention	Control	Target vaccine
Rodewald 1999 [14]	Rochester and New York, USA	Randomized trial	Infants from 0 to 12 months	Provider prompts and tracking using lay health workers.	Standard of care	DTP, influenza, Hib
Minkovitz 2001 [15]	Baltimore, USA	Prospective cohort	Children 3 years or younger	Systematic verification of immunization histories, and provision of chocolate bars labeled, "Immunize On Time"	Standard of care	DTP, hepatitis, and influenza
Szilagyi 1996 [16]	Monroe, USA	Randomized trial	Children aged 0 to 2 years	Screen and vaccinate at all visits; and removing legal guardian signatures.	Standard of care	DTP, OPV, MMR, and Hib
Wood 1998 [17]	Los Angeles and California, USA	Randomized trial	Infants	Parent education and case management.	No intervention	Childhood vaccines
Lin 2016 [18]	Pittsburgh and Houston, United States of America (USA)	Cluster randomized trial	Adults	Provider education and one on-one coaching.	No intervention	Influenza
Mayne 2014 [19]	Philadelphia, USA	Cluster randomized trial	Adolescent girls aged 11–17 years	Education, electronic prompts, & feedback.	No intervention	HPV

home visits or following up with participants by telephone and mail when immunization was due. The case managers also had to educate or inform parents that it was safe to vaccinate the child whether they had a cold, mild ear infection or any other mild diseases [17].

In the cohort study, a screening nurse produced computer printouts of vaccination records of each child at each acute care visit, and attached the records to child's encounter form. In addition, during study visits, providers were given chocolate bars labeled, "Immunize On Time" [15].

Table 2
Characteristics of excluded studies.

Study	Reason for exclusion
Holt (1995) [20]	This is a cross-sectional study
Daley (2005) [21]	This cohort study did not assess any intervention
Kuo (2004) [22]	This is a cross-sectional study
McConnochie (1992) [23]	This study did not assess any intervention
Stille (2004) [24]	This is not a randomized trial or cohort study
Turner (2009) [25]	This study did not assess any intervention
Skull (2007) [26]	This study did not assess any intervention.
Verani (2007) [27]	This cohort study did not assess any intervention
Sabnis (2003) [28]	This is not a randomized trial or cohort study.
Allred (2011) [29]	This study did not assess any intervention
Rao (2016) [30]	This study did not assess any intervention
Dombkowski (2006) [31]	This study did not assess any intervention
Kempe (2001) [32]	This study did not assess any intervention
O'Leary (2014) [33]	This study did not have missed opportunities as an outcome
Shim (2005) [34]	This study did not have missed opportunities as an outcome
de Mattos (2003) [35]	This is a cross-sectional study

One of the cluster-randomized trials assessed the effects of a multi-faceted intervention consisting of: convenient vaccination services; communication with parents about the importance of immunization and availability of vaccines; enhanced office systems to facilitate vaccination; and motivation through an office vaccination champion [18].

Another study assessed the effects of combining clinician-oriented and family-oriented interventions [19]. The clinician-focused intervention consisted of three components, i.e., electronic health record (EHR)-based vaccine awareness for any due vaccines, a one hour educational presentation about the vaccine and three quarterly performance feedback reports of captured immunization opportunities at primary care visits. With regards to the family setting, the interventions involved an outside vendor generated automated phone calls based on an EHR-generated roster. Participants received reminder phone calls to notify them of any due vaccines, they were also referred to an educational website and reminded about upcoming preventive visits [19].

The studies reported outcome data on MOVs and vaccination coverage for diphtheria-tetanus-pertussis (DTP) [14–16], hepatitis B [15], influenza [14,15,18], *Haemophilus influenzae* type b (Hib) [14,16], oral poliovirus (OPV) [16], measles-mumps-rubella (MMR) [16], and human papillomavirus (HPV) [19] vaccines or completion of childhood immunization schedule [17].

3.3. Risk of bias in included studies

All trials had a high risk of bias due to lack of allocation concealment, lack of blinding of outcome assessors, and incomplete outcome data (Table 3).

Furthermore, risk of bias was high in all the included studies due to either inadequate, not reported or unclear methods of sequence generation, allocation concealment and blinding for some of the studies. The study by Lin et al. [18] did not report how the allocation was generated while Wood et al. [17] did not mention allocation generation at all. Mayne et al. [19], Rodewald et et al. [14] and Szilagyi et al. [16] respectively used randomly permuted unequal blocks and two-by-two factorial design for allocating participants to the intervention or control groups. However, none of the randomized trials reported any method of allocation concealment. Concerning blinding, Lin et al. [18] and Wood et al. [17] did not report it, whereas the study by Mayne et al. [19] did not clearly state the exact method used. Rodewald et al. [14] and Szilagyi et al. [16] stated that they blinded outcome assessors and abstractors to study hypothesis and study group assignment while they did not specify the method. The cohort study [15] had high risk of bias because it scored yes for bias in measurement of outcomes.

There was incomplete outcome data due to a loss of 654 out of total number of 92,525 paticipants. This is due to some of the participants dropping out of the study, incomplete medical information, and provider records. Additionally, five of the included studies mentioned several biases e.g. that some information was not captured and inadequate provider record keeping.

None of the studies reported a protocol being available; hence it was unclear whether selective reporting was a problem or not.

3.4. Effects of interventions on the rates of missed opportunities for vaccination and vaccination coverage

All studies reported effects of interventions on MOVs and vaccination coverage. Given that MOVs are proxies for vaccination coverage, we have emphasized the effects of on vaccination coverage; rather both MOVs and vaccination coverage.

A study by Lin et al. [18] provided moderate certainty evidence that communicating with patients about vaccines probably leads to a reduction of missed opportunities for vaccination (RR 0.97, 95% CI 0.95–0.98) and an increase in vaccination coverage (RR 1.03, 95% CI 1.02–1.04). In addition, a study by Wood et al. [17] showed low certainty of evidence that educating parents about vaccines may lead to increased vaccination coverage (RR 1.92, 95% CI 1.38–2.68). Another study, by Mayne et al. [19], provided low certainty evidence that education sessions concurrently targeting clinicians and families may lead to increased vaccination coverage (RR 1.25, 95% CI 1.08–1.46). A study by Szilagyi et al. [16] provided low certainty evidence that lifting the requirement to have a legal guardian's signature before vaccination may have little or no effect on vaccination coverage (RR 1.02, 95% CI 0.96–1.09). Finally, a study by Rodewald et al. provided evidence of low certainty that combining patient tracking and provider prompts can substantially reduce missed opportunities and increase vaccination coverage (RR 1.18, 95% CI 1.11–1.25) [14].

Table 3
Risk of bias in included randomized trials.

Domain	Lin 2016	Mayne 2014	Rodewald 1996	Szilagyi 1996	Wood 1998
Random sequence generation (selection bias)	?	+	+	?	?
Allocation concealment (selection bias)	−	?	?	?	?
Blinding of participants and personnel (Performance bias)	−	?	+	+	?
Blinding of outcome assessment (detection bias)	?	?	+	+	?
Incomplete outcome data (Attrition bias)	−	−	−	−	−
Selective reporting (Reporting bias)	−	?	−	−	?
Other biases	+	−	−	?	?

+ Low risk; − High risk; ? Unclear risk.

4. Discussion

4.1. Summary of findings

This review included six studies and investigated the effectiveness of different interventions aimed at decreasing missed opportunities for vaccination and increasing vaccination coverage. The studies (five trials and one cohort study) were carried out in different cities of the United States of America. The interventions assessed included educational sessions, performance feedback, outreach through postcards, phone calls and home visits, generation of printouts of each child's vaccination record, changing practice guideline (i.e., vaccination without legal guardian's signature), communication with patients about the importance and availability of vaccines, parent education and case management.

Regarding data reported on missed opportunities, it is evident from the data provided by Lin et al. [18] that individuals who did not receive the intervention, i.e., communication about the importance and availability of vaccines, had increased chances of missing opportunities for vaccination. Furthermore, the data reported by Rodewald et al. [14] show that individuals who received an intervention were less likely to have missed opportunities for vaccination compared to people in the control group. The results from this study also suggest that the interventions (such as patient tracking, outreach, and provider prompting) are more effective in reducing missed opportunities when they are used concurrently as opposed to when they are used individually.

Although an ealier study by Sabnis et al. [28] did not compare the rate of missed opportunities for vaccination between the intervention and control groups, a decreased rate, following education and feedback interventions was reported.

With regards to vaccination coverage, one study [19] using education sessions as an intervention was more effective if it was targeted at the family and clinician settings concurrently. It was also apparent that there was a positive effect when tracking was combined with prompting and outreach (postcards, phone calls and home visits) [14]. Furthermore, results showed that educating parents about the importance of vaccines was more effective in increasing vaccination coverage than when they were not educated [18]. Moreover, it was interesting to note that vaccinating children without legal guardian's signature was not effective in increasing vaccination coverage [16].

Previous investigations also showed similar results, where individuals who received interventions such as provider education, text messaging, mailed letters and telelphone reminders had increased vaccination rates than those who did not [36–39]. In concordance with Mayne et al. [19], Walling et al. [37] and Niccolai et al. [39] also reported that interventions targeting recipients and providers concurrently were effective in increasing vaccination coverage than when they were used seperately.

4.2. Certainty of the evidence

The certainty of evidence was low to moderate. We downgraded the certainty of the evidence to moderate or low due to imprecision (wide confidence intervals) and high risk of bias.

4.3. Conclusions and implications for future research

The currently available evidence suggests the use of provider education; patient education; and patient tracking, outreach, and provider prompting as interventions to reduce missed opportunities for vaccination and improve vaccination coverage. Rigorous studies are required to confirm these findings and increase the certainty of the current evidence base. WHO is in the process of generating evidence on interventions for reducing MOVs; therefore, there is a possibility of more data being published in the coming years [40].

Role of the funding source

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Conflict of interest

None declared.

Appendix A

Appendix 1: PubMed, Scopus, and Cochrane Library search strategie.

Search	Query
PubMed	
#1	(“Immunization”[Mesh] OR“Vaccination”[Mesh] OR “Immunization Programs”[Mesh] OR Immunization OR immunization) AND (adhering OR adheren* OR uptake OR rate* OR coverage)
#2	“MISSED OPPORTUNITY” OR “MISSED OPPORTUNITIES”
#3	#1 AND #2
#4	(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR “clinical trials as topic”[mesh: noexp] OR randomly [tiab] OR trial [tiab]) NOT (animals [mh] NOT humans [mh])
#5	“COHORT STUDY” OR “COHORT STUDIES”
#6	#3 AND (#4 OR #5
Scopus	
#1	ALL (((“Immunization” OR “Vaccination” OR “Immunization Programs” OR Immunization OR immunization) AND (adhering OR adheren* OR uptake OR rate* OR coverage)) AND (“MISSED OPPORTUNITY” OR “MISSED OPPORTUNITIES”))
#2	(ALL (((“Immunization” OR “Vaccination” OR “Immunization Programs” OR Immunization OR immunization) AND (adhering OR adheren* OR uptake OR rate* OR coverage)) AND (“MISSED OPPORTUNITY” OR “MISSED OPPORTUNITIES”))) AND (“COHORT STUDY” OR “COHORT STUDIES”)
#3	(ALL (((“Immunization” OR “Vaccination” OR “Immunization Programs” OR Immunization OR immunization) AND (adhering OR adheren* OR uptake OR rate* OR coverage)) AND (“MISSED OPPORTUNITY” OR “MISSED OPPORTUNITIES”))) AND (“randomized controlled trial” OR “controlled clinical trial” OR randomized OR placebo)
#4	((ALL (((“Immunization” OR “Vaccination” OR “Immunization Programs” OR Immunization OR immunization) AND (adhering OR adheren* OR uptake OR rate* OR coverage)) AND (“MISSED OPPORTUNITY” OR “MISSED OPPORTUNITIES”))) AND (“COHORT STUDY” OR “COHORT STUDIES”))

Appendix A (*continued*)

Search	Query
	AND ((ALL (((“Immunization” OR “Vaccination” OR “Immunization Programs” OR Immunization OR immunization) AND (adhering OR adheren* OR uptake OR rate* OR coverage)) AND (“MISSED OPPORTUNITY” OR “MISSED OPPORTUNITIES”))) AND (“randomized controlled trial” OR “controlled clinical trial” OR randomized OR placebo))
Cochrane Library	
#1	((“Immunization” OR “Vaccination” OR “Immunization Programs” OR Immunization OR immunization) AND (adhering OR adheren* OR uptake OR rate* OR coverage)) AND (“MISSED OPPORTUNITY” OR “MISSED OPPORTUNITIES”)

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