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**MOBILE PHONE TEXT MESSAGING FOR IMPROVING
THE UPTAKE OF VACCINATIONS:
A SYSTEMATIC REVIEW**

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Abstract

The research undertaken for this MPH dissertation examines the effectiveness of SMS as an intervention to promote vaccination.

Part A is the research protocol, which outlines the background and the process of this research. This study utilizes systematic review methods based on those of the Cochrane Collaboration to synthesize the best current evidence from articles archived in various bibliographic databases and clinical trial registers.

Part B presents the entire research project in a format suitable for journal submission. The background of this research project is summarised and the results are presented and discussed.

PART A: PROTOCOL

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Abstract

Background: Low vaccine coverage is a major public health concern, the consequences of which contribute to around 1.5 million child deaths from vaccine-preventable diseases. Thus, innovative strategies to rapidly increase coverage and recall rates for vaccinations are urgently required. Mobile phone text messaging (or short messaging service, SMS) has the potential to help increase vaccination coverage and therefore we propose to conduct a review of the current best evidence for the use of SMS as an intervention to promote vaccination coverage.

Methods/Design:

This article describes the protocol for a systematic review of the effectiveness of SMS in improving the uptake of vaccination. Primary and secondary outcomes of interest are pre-specified. We will preferably include randomized controlled trials (RCTs). However, non-randomized studies (NRS) will be considered if there is an inadequate number of RCTs. We will search several bibliographic databases (for example PubMed, EMBASE, CINAHL, CENTRAL, Science Citation Index, Africa-Wide Information, and WHOLIS electronic databases and search sources for grey literature. Following data extraction and assessment of risk of bias, we will meta-analyze studies and conduct sub-group analyses, according to intervention subtypes. We will assess clinical heterogeneity and statistical heterogeneity. For outcomes without quantitative data, a descriptive analysis will be used.

Discussion:

Our results can be used by researchers and policy-makers to help inform them of the efficacy of mobile phone text messaging interventions to promote increased vaccination coverage.

Keywords: Vaccine coverage, vaccination, Mobile text messaging, short messaging service, SMS

Background

Vaccinations, when given at the most sensitive developmental years of childhood, help to promote comprehensive and capable immunity, enabling children to fight off certain diseases (Garde, 2010, Multiple Authors., 2009). In addition, vaccinations are widely regarded as one of the most cost-effective public health interventions that help to reduce global child morbidity and mortality (Machingaidze et al., 2013, Bloom, 2011). Low coverage of vaccinations is a major public health concern. In Africa alone, more than seven million children did not receive the full spectrum of vaccinations recommended before reaching one year of age in 2009 (Stockwell et al., 2012). It is also estimated that 1.5 million children died globally from vaccine-preventable diseases where World Health Organization (WHO) pre-qualified vaccines were available (World Health Organisation and UNICEF: Global Immunization Data.).

The Global Vaccine Action plan (GVAP) is the most recently launched global effort by the WHO to help increase vaccination coverage. The GVAP has set a target that by 2020 vaccination coverage for populations should reach 90% national vaccination coverage and at least 80% at district levels utilizing national vaccination programmes (WHO Global Vaccination Action Plan). It is guided by six principles: country ownership, shared responsibility and partnership, equity, integration, sustainability, and innovation (Decade of Vaccines (DoV) Collaboration: Draft global vaccine action plan.)

A variety of factors impact achieving low coverage rates; challenges such as immunisation awareness, demand for immunisation, level of trust in the health system, adequate human

resources, access, timeliness of vaccinations, service delivery, poor infrastructure and vaccination monitoring (Machingaidze et al., 2013). Vaccination coverage seems to be lower in low-income households, where limited access to health education, contributes to poor health-seeking behaviour along with an inability to improve general wellbeing (Garde, 2010, Multiple Authors., 2009, Kaewkungwal et al., 2010). Uneducated adults as well as parents of children who require vaccinations may be less likely to understand the importance of vaccinating to prevent potentially harmful diseases. In light of these obstacles to vaccination coverage, the strategy to improve vaccination coverage needs to be innovative as alluded to in the GVAP, well thought out and able to penetrate low income households effectively.

Globally, mobile phone use is rapidly increasing, with an estimated six billion mobile phone users worldwide at the end of 2011 (Nglazi et al., 2013). In particular, mobile phone text messaging has gained popularity among people living in low- and middle-income countries and may be the key to penetrating hard to reach areas in the developing world. Text messaging has proven to be a cost effective method of relaying health information and reminders than the more traditional methods such as face to face, phone calls, pamphlets, mail and email (Stockwell et al., 2012). As immunisation usually requires multiple consecutive monthly visits after the first vaccine dose in order to complete the schedule, short messaging service (SMS) can be used as reminder for an upcoming visit and recall when a visit has been missed (Garde, 2010). In addition, an SMS intervention, also known as mobile phone text messaging, can be delivered alone or bundled with other interventions (Mohammed et al., 2012). Diseases that have used mobile technology successfully include HIV where a 90% adherence was observed among text message recipients compared with a

40% adherence in the control group (Pop-Eleches et al., 2011). Similarly, SMS interventions have been shown to improve self-management interventions for chronic conditions including behaviour modification smoking quit rates (Jones et al., 2014)

We therefore propose to conduct a systematic review of the current best evidence for the use of mobile phone text messaging to improve vaccination coverage.

Methods

The review protocol has not been registered in any prospective registers of systematic reviews.

Criteria for considering studies for this review

Type of studies

We will include randomized controlled trials (RCTs), interrupted time series and controlled before and after studies (CBA).

Types of participants

Participants will be adults, children or their caregivers of those receiving vaccinations, in community-based settings.

Types of interventions

We will include interventions in which mobile phone text messages are used to promote uptake of vaccinations. The text messaging needs to be delivered to a person needing a vaccination, or in the case of an infant or child, to a caregiver. Eligible studies will be those that compare SMS to no intervention, or to other interventions for increasing vaccination coverage. If we find less than ten studies that include only SMS as the intervention, we will include studies in which (1) mobile phone voice speaking or voice messaging are interventions including interactive voice response known as IVR; (2) studies in which the use of a beeper or pager is the intervention; (3) studies in which the use of multimedia messaging service is the intervention; (4) studies in which text messages are bundled with other interventions. In such circumstances, we will stratify the analysis by type of intervention.

Types of outcome measures

Results must include quantitative data for outcomes measured.

Primary outcomes:

The primary outcome is vaccination coverage, irrespective of disease.

Secondary outcomes:

Secondary outcomes are the recall rate in persons who had previously missed their vaccinations.

Search methods for identification of studies

A comprehensive and exhaustive search will be performed by RK with the help of the University of Cape Town librarian, to identify all relevant studies available by 30 June 2013, regardless of language or publication status. We will search both peer-reviewed journal articles and grey literature (unpublished, internal or non-reviewed papers and reports).

Database

We will search the following electronic databases: PubMed; EMBASE; Cochrane Central Register of Controlled Trials (CENTRAL); ISI Web of Science (Science Citation Index); Africa-Wide Information, Cumulative Index of Nursing and Allied Health (CINAHL), and WHO library databases (WHOLIS). We will use both text words and medical subject heading (MeSH) terms; for example vaccination*, immunization*, immunisation*, "Immunization"(MeSH), "Vaccination"(MeSH), "Immunization, Secondary"(MeSH) OR "Immunization Programs"(MeSH), "Immunization Schedule"(MeSH), "Mass Vaccination"(MeSH), mobile phone, text messaging, text*, SMS, reminder*, recall, telemedicine, mHealth, and eHealth. These terms will be used in varying combinations. The literature search strategy will be adapted to suit each database. Table 1 shows the main search strategy we will use.

Conference proceedings

We will search the following conference proceedings for relevant abstracts: Vaccine and International Society for Vaccines Congress, International African Vaccinology Conference, Annual Vaccines Congress, Annual Conference on Vaccine Research, World Congress on

Pediatric Infectious Diseases, International Pediatric Association Conference, National Immunization Conference, and the Annual Infectious Diseases in Children Symposium.

Searching other sources

For ongoing studies, we will search the WHO International Clinical trials Registry Platform, Clinicaltrials.gov, Pan African Clinical Trials Registry (PACTR), and contact individual researchers working in the field as well as the following organizations: WHO, Global Alliance for Vaccines and Immunisation, Centers for Disease Control and Prevention, and mHealth Alliance. We will also search the website of mHealth Alliance and mHealth in the Low Resource Settings resources database [20] for eligible studies.

Reference lists

We will obtain reference lists of relevant studies identified and the full-text articles reviewed for inclusion in the review will be checked for additional information.

Data collection and analysis

The methods for data collection and analysis will be based on the Cochrane Handbook of Systematic Reviews for Interventions (Higgins et al., 2009).

Selection of studies

We will construct a screening guide to ensure that the inclusion criteria are adhered to and consistently applied by all review authors. Two review authors (RK and ME), working

independently, will screen the titles and abstracts of all studies identified through the literature searches for eligibility. RK will obtain the full text of studies deemed potentially eligible. The two authors (RK and ME) will independently assess the full text of each article for eligibility, and compare their results and resolve discrepancies by discussion and consensus, consulting a third author (CW) to resolve any persistent disagreements. For all studies excluded by the assessors we will describe the reasons for exclusion.

Data extraction and management

References will be managed using Thomson ISI Research-Soft Endnote 9.0 (Thomson). Two authors will independently extract descriptive and outcome data for each included article using a standardized data collection form, resolving any discrepancies by discussion and consensus; failing which, a third author (CW) will arbitrate. RK will enter the final data into the Cochrane Collaboration Review Manager Version 5.1 statistical software (<http://ims.cochrane.org/RevMan>). CW will crosscheck the data entered to ensure that there are no data entry errors.

Assessment of risk of bias in included studies

Two authors will independently assess the risk of bias in the included studies. Separate criteria will be used to assess RCTs and non-randomized studies. The criteria used to assess the risk of bias of in RCTs will be random sequence generation; allocation concealment; blinding of participants, study personnel; blinding of outcome assessors; incomplete outcome data; selective outcome reporting; other sources of bias, and overall risk of bias, in accordance with the methods used by the Cochrane Collaboration (Higgins et al.) as well as the Cochrane Consumers and Communication Review Group (Ryan R, 2011). The criteria

used for risk of bias assessment for non-randomized studies will include selection bias (with regard to comparability of groups, confounding and adjustment); performance bias (in terms of the fidelity of the interventions, and quality of the information regarding who received which interventions, including blinding of study subjects and healthcare providers); detection bias (regarding unbiased and correct assessment of outcomes, including blinding of assessors); attrition bias (with regard to completeness of sample, follow-up and data); and reporting bias (with regard to publication biases and selective reporting of results) (Higgins et al., 2009). Studies will be scored as having low, high or unclear risk of bias. The two authors will resolve disagreements in the assessment of risk of bias by discussion and consensus, consulting a third author to resolve any persistent disagreements.

Measures of treatment effect

Data analysis will be conducted using the Cochrane Collaboration Review Manager Version 5.1 statistical software (<http://ims.cochrane.org/RevMan>). The outcomes of interest will be either dichotomous or continuous. We will calculate risk ratios and their corresponding 95% confidence intervals or p-values for dichotomous outcomes, and mean differences for continuous outcomes.

Dealing with missing data

In cases of missing or incomplete information presented in the included studies, we shall contact authors for further information.

Data synthesis, assessment/investigation of heterogeneity

We will assess clinical heterogeneity by examining types of participants, interventions, and outcomes in each study. Statistical heterogeneity in each meta-analysis will be assessed using the chi-square test and quantified using the I-squared statistic. If studies are sufficiently homogenous (in terms of study populations, interventions, and outcomes), then we will pool the data across studies and estimate summary effect sizes using a fixed-effects model; otherwise, we will use the random-effects model. We will perform subgroup analyses by intervention subtypes: long versus short messages; daily versus weekly messages; short weekly messages versus long weekly messages; short daily messages versus long daily messages; and two-way interactive communication versus one-way communication (Horvath et al., 2012) (Thirumurthy and Lester, 2012, Pop-Eleches et al., 2011). We will also stratify analysis by study design (randomized controlled separate from non-randomized studies) and intervention type (multiple interventions involving text messaging separate from text messaging alone). Finally, we will use the grading of recommendations assessment, development, and evaluation (GRADE) approach (Balshem et al., 2011) to assess the quality of evidence for the effectiveness of the SMS intervention. This method results in an assessment of the quality of the body of evidence as high, moderate, low, or very low. Evidence is considered of high quality if 'further research is very unlikely to change our confidence in the estimate of effect'; and moderate quality if 'further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate'. Low quality evidence implies that 'further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate', and very low quality that 'we have very little confidence in the effect estimate'.

Subgroup analyses

Several subgroup analyses will be performed: first to determine whether the study design (RCT versus nonrandomized study) could influence the results of the meta-analysis; second, to evaluate whether the model of the statistical method (random-effects vs fixed-effects model) could change the results, and third, to determine the impact of excluding studies with a high risk bias on the results, with emphasis on allocation concealment, blinded outcome assessment, and losses to follow-up (with a cut off of 25% loss to follow-up).

Presenting and reporting of results

Findings in our systematic review will be presented in several ways. Flow diagrams will be used to summarise the study selection process. Funnel plots will be used to assess publication bias if we identify 10 or more eligible studies. The kappa statistic (Landis and Koch, 1977) will be used to assess agreements between the full-text screening, data extraction and risk of bias assessment by the two authors (RK and ME). GRADE summary of tables of findings, risk of bias tables or graphs, and forest plots will also be used where appropriate. The reporting of outcomes without quantitative data will be descriptive. Lastly, we will provide a list of excluded studies with reasons for exclusion.

Ethics

Systematic reviews draw on publicly available data and do not directly involve human subjects, and therefore do not require formal ethical review (Emanuel et al., 2004). The study protocol will be reviewed by supervisors with expertise in methodology (systematic

review) and submitted to the University of Cape Town Departmental Research Committee for approval.

Discussion

Expected significance of the study

The findings of this systematic review will have implications for policy, practice and research. We will discuss the relevance of our findings to childhood immunisation programmes in Africa in the decade of vaccines with emphasis on applicability, effects on equity, cost implications, and monitoring and evaluation.

Our systematic review will provide evidence of whether policy-makers can adopt mobile phone text messaging alone or in combination with other interventions in efforts to improve uptake of vaccines in national immunisation programmes. It will also inform clinic or hospital managers of how best to use the intervention to improve vaccination coverage. The systematic review may also identify specific considerations that would need to be taken into account for future studies, such as study location, content and timing of messages, whether or not parents or caregivers replied to text messages, how text messages were sent (automated versus manual), indicators for immunisation programmes, variety of text messages sent (inclusion of jokes or lifestyle tips), duration of the study, whether or not participants were provided with the mobile handsets, and sample size (Karanja et al., 2011).

Abbreviations

WHO: World Health Organization; GVAP: Global Vaccine Action plan; SMS: Short messaging service; RCT: Randomized Controlled Trials; CBA: Controlled Before and After study; MeSH: medical subject heading;

Competing interests

The authors declare that they have no competing interests.

Author's contributions

CW conceived of the review. All authors developed the design of the protocol and will be involved in data acquisition. RK undertook the drafting of the manuscript. RK and ME will analyze the data and participate in the interpretation of the results. All authors have given their approval for publication.

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Supervisor information

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Accessed 10 June 2013.

Appendix 1: Search strategy

Table 1. PubMed search strategy, modified as needed for use in other databases

Search	PubMed
#1	(immunization[Mesh]) OR ((immunis* OR immuniz* OR vaccin*))
#2	(adolescents OR children OR teenagers OR adults)
#3	"SMS" OR cellphone OR "mobile phone" OR "text messaging" OR "short message service" OR "text reminder"
#4	#1 AND #2
#5	#3 AND #4

MeSH, medical subject heading

Appendix 2: Data Extraction Form

Data Extraction Form

Reviewer ID :

Study ID:

Full Article Title:

Citation:

Language of Publication:

Type of study

	yes	unclear	If no, exclude
RCT			
CCT			
CBA			
Quasi-randomised trials			
Cross-over study			

Trial Intervention:

Was the intervention a short message service [sms] to remind participants of the first dose of vaccination?

yes	
unclear	
If no, exclude	

Was there a control or comparison group that did not receive the same intervention ?

yes	
unclear	
If no, exclude	

Was there a secondary message [sms] sent to remind participants to come back if first visit was missed to assess recall rate?

yes	
unclear	

Tick as appropriate:

include	
---------	--

exclude	
Uncertain-requires full text article	
Pending-study still in progress	

Reasons for exclusion:

TRIAL CHARACTERISTICS

Study design:

Randomization method:

Allocation concealment:

Duration of trial:

Duration of follow up:

Loss to follow up

	Intervention	Control	Total
Total number randomized			
Number available at follow up			
Number Loss to follow up			
Number included in the analysis			

Was analysis done as intention to treat Yes No Unclear

(Were all the randomised participants included in the analysis?)

PARTICIPANT CHARACTERISTICS

Country and setting: _____

Developing country: Yes ___ No ___

Disease:

Vaccination Schedule:

Number of persons in trial

	Intervention	Control	Total
Number			
% of Total			100%

Gender

	Intervention		Control		Total	
	N	%	N	%	N	%
Male						
Female						
Total						

Age

	Intervention		Control		Total	
	N	%	N	%	N	%
Mean Age						
<13 years						
>13 years						

INTERVENTION CHARACTERISTICS**Intervention: sms reminder**

SMS	
Frequency	
Details of the sms	
Recall sms sent for unvaccinated participants	
Other remarks	

Control –usual care

sms	
Frequency	
Recall sms sent for unvaccinated participants	
Other remarks	

OUTCOMES**1. Outcomes measured:****2. Primary outcomes: receipt of one or more vaccination within the specified period**

	M	F	Total
Total Number SMSs			
Undeliverable			
Incorrect number			
Declined			
Other			
Total (per protocol)			

VACCINATION COVERAGE**Authors' definition of coverage:****Primary Outcome**

	Intervention	%	Control	%	Difference	RRR
Total SMSs						
Primary: Number vaccinated						
Age-group Breakdown						
	/					

Secondary Outcome

	Intervention	%	Control	%	Difference	RRR
Total SMSs						
Secondary: Recall Rate						
Age-group Breakdown						
	/					

Part B: Journal Manuscript

Mobile phone text messaging for improving the uptake of vaccinations: a systematic review

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List of Abbreviations

CENTRAL:	Cochrane Central Register of Controlled Trials
CI:	confidence intervals
GRADE:	Grading of recommendations, assessment, development and evaluation
GVAP:	Global Vaccine Action Plan
Hib:	<i>Haemophilus Influenzae B</i>
HPV:	Human Papilloma Virus
ITT:	intention-to treat
MCV4:	meningococcal virus
MesH:	Medical subject headings
RCT:	Randomised Controlled trial
RR:	Risk Ratio
SIM:	subscriber identity module
SOC:	Standard of care
SMS:	short message service
Tdap:	tetanus/diphtheria/acellular pertussis
WHO:	World Health Organisation

Abstract

Background: Low vaccine coverage is a major public health concern, the consequences of which contribute to around 1.5 million child deaths from vaccine-preventable diseases. Thus, innovative strategies to rapidly increase coverage and recall rates for vaccinations are urgently required. Mobile text messaging (or short messaging service, SMS) has the potential to help increase vaccination coverage and therefore, we propose to conduct a review of the current best evidence for the use of SMS as an intervention to promote vaccination coverage.

Methods: This is a systematic review of the effectiveness of SMS in improving the uptake of vaccination. We searched several bibliographic databases (Pubmed, Web of Knowledge and Scopus) and the clinical trials register available by November 2013, regardless of language or publication status. Two authors independently screened eligible studies and assessed risk of bias in included studies, resolving discrepancies by discussion and consensus.

Results: Six studies comprising seven populations with a total of 12,484 participants were analysed to investigate the effects of SMS as an intervention to promote vaccination among adults, adolescents and parents or caregivers of children. Compared with participants receiving usual standard of care, participants receiving text messages were 25% more likely to comply with vaccination (risk ratio [RR] 1.25, 95% confidence intervals [CI] 1.07, 1.46). This finding was consistent for vaccinations requiring multiple visits (RR=1.38, [95% CI 1.21, 1.58]) as well as across all age categories (Non-adult vs Adult: RR=1.29, [95% CI 1.04; 1.60] vs RR=1.26, [95% CI 1.08, 1.48]). Furthermore, country setting did not affect the positive findings. Where studies looked at influenza only, we found the effect was significant in

favour of the text message intervention (RR 1.17, [95% CI, 1.03; 1.33]) compared with diseases other than influenza where the evidence indicates 62% increased likelihood of vaccination uptake due to SMS; however, the result was not statistically significant (RR= 1.62, [95% CI, 0.84; 3.10]). The quality of evidence in this systematic review was rated as moderate using the GRADE approach. Sensitivity analyses revealed that heterogeneity generally had a negligible effect on the findings.

Discussion/Conclusion: There is moderate quality evidence a text message intervention is effective in increasing vaccination coverage. However, there is insufficient evidence to support its use for non-influenza vaccines. Furthermore there is a dearth of evidence emanating from low- and middle-income countries.

Keywords: Vaccine coverage, vaccination, Mobile text messaging, SMS, short messaging service

1. Background

Vaccinations, when given at the most sensitive developmental years of childhood, help to promote comprehensive and capable immunity, enabling children to fight off certain diseases [1, 2]. In addition, vaccinations are widely regarded as one of the most cost-effective public health interventions that help to reduce global child morbidity and mortality [3, 4]. Low coverage of vaccinations is a major public health concern. In Africa alone, more than seven million children did not receive the full spectrum of vaccinations recommended before reaching one year of age in 2009 [5]. It is also estimated that 1.5 million children died globally from vaccine-preventable diseases where World Health Organization (WHO) pre-qualified vaccines were available [6].

The Global Vaccine Action plan (GVAP) is the most recently launched global effort by the WHO to help increase vaccination coverage. The GVAP has set a target that by 2020 vaccination coverage for populations should reach 90% national vaccination coverage and at least 80% at district levels utilizing national vaccination programmes [7]. It is guided by six principles: country ownership, shared responsibility and partnership, equity, integration, sustainability, and innovation [8]

A variety of factors impact achieving low coverage rates; challenges such as immunisation awareness, demand for immunisation, level of trust in the health system, adequate human resources, access, timeliness of vaccinations, service delivery, poor infrastructure and vaccination monitoring [3]. Vaccination coverage seems to be lower in low-income households, where limited access to health education, contributes to poor health-seeking

behaviour along with an inability to improve general wellbeing [1, 2, 9]. Uneducated parents therefore are less likely to understand the importance of vaccinating to prevent potentially harmful diseases. In light of these obstacles to vaccination coverage, the strategy to improve vaccination coverage needs to be innovative as alluded to in the GVAP, well thought out and able to penetrate low income households effectively.

Globally, mobile phone use is rapidly increasing, with an estimated 6.6 billion mobile phone subscriptions end of 2012 [10]. In addition, the number of unique mobile phone subscribers at the end of 2012 was estimated to be 3.2 billion, with an average of 1.85 SIM cards per individual and mobile operators are including inactive SIM cards in their reported global mobile phone subscription totals [11]. However, the number of mobile phone users has continued to increase and is spreading to the most remote areas in the world.

In particular, mobile phone text messaging has gained popularity among people living in low- and middle-income countries and may be the key to penetrating hard to reach areas in the developing world. Text messaging has proven to be a cost effective method of relaying health information and reminders than the more traditional methods such as face to face, phone calls, pamphlets, mail and email [5]. As immunisation usually requires multiple consecutive monthly visits after the first vaccine dose in order to complete the schedule, short messaging service (SMS) can be used as a reminder for an upcoming visit and recall when a visit has been missed [1]. In addition, an SMS intervention, also known as mobile phone text messaging, can be delivered alone or bundled with other interventions [12]. Diseases that have used mobile technology successfully include HIV where a 90% adherence

to uptake of anti-retroviral medication was observed among text message recipients compared with a 40% adherence in the control group [13].

An earlier systematic review looked at the role of SMS as an intervention for promoting adherence to anti-tuberculosis treatment and found that in two of the studies, an SMS intervention significantly improved the adherence to tuberculosis treatment. The remaining studies reported no evidence for a significant effect in favour of an SMS intervention. Furthermore, the authors of this review were concerned with the lack of high quality data and rated the current evidence as reported in this review, as being of low quality. [14]

In another review, SMS was reported to significantly improve adherence to appointments and antiretroviral therapy, short-term smoking quit rates, and selected clinical and behavioral outcomes. [15] There is also some indication that SMS interventions could change behavior in weight loss reduction, although results were not significant.[16] SMS interventions have been successful in optimizing clinic time and at improving the relationship between post-operative patients in reducing clinic visits and drainage time of wounds. [17] SMS has also had a beneficial effect in diabetes patients where it was shown to have better health outcomes and significant improvement in the SMS group in relation to blood results analyzing HbA1c and plasma lipids. [18]

In order to understand the evidence available where a text message intervention was used to increase the uptake of vaccinations, we conducted a systematic review of the current best evidence for the use of mobile phone text messaging to improve vaccination coverage.

2. Methods

The methods for this review is largely based on the Cochrane Handbook of Systematic Reviews for Interventions [19].

2.1 Criteria for considering studies for this review

2.1.1 Type of studies

We included all randomized controlled trials and non-randomized controls if a comparison group was included in the study, which assessed using a text message intervention to promote the uptake of a vaccine as a primary or secondary outcome.

2.1.2 Type of participants

Participants were children or caregivers, adolescents, adults including pregnant women that were drawn from a community-based setting.

2.1.3 Types of interventions

Text messages that delivered a reminder to be vaccinated, educational informational or information regarding the vaccine availability and clinic details were considered as a valid text message intervention. We excluded studies where a comparison group did not form part of the analysis. Some studies compared the intervention to usual care and others offered both the control and intervention group a text message; one with only educational

information and the other both educational information and vaccination reminders and clinic availability respectively.

2.1.4 Types of outcome measures

The primary outcome for this review was uptake of vaccination. For the secondary outcome, we considered recall rate in persons who had previously missed their vaccinations.

2.1.5 Search methods for the identification of studies

We developed a highly sensitive search strategy combining key terms that may indicate uptake of vaccination via an text message intervention(eg. text message, sms, cell, mobile, vaccination and phone) with the MeSH headings “vaccinat*” and “text message or sms” and search terms for all existing randomized and non-randomised trials. Two investigators searched independently (RK and DB), in duplicate the following databases (from inception to October 2013.): MEDLINE via PubMed, EMBASE, Scopus, Web of Knowledge, and Cochrane CENTRAL. We also conducted a search within clinical trials.gov to ascertain if any ongoing studies have been completed before conclusion of this systematic review [20]. The search strategy used for searching the PubMed database is detailed in Table 1.

Table 1. PubMed search strategy, modified as needed for use in other databases

Search	PubMed
#1	(immunization[Mesh]) OR ((immunis* OR immuniz* OR vaccin*))
#2	(adolescents OR children OR teenagers OR adults)
#3	"SMS" OR cellphone OR "mobile phone" OR "text messaging" OR "short message service" OR "text reminder"
#4	#1 AND #2
#5	#3 AND #4

MeSH, medical subject heading

2.2 Study Selection

Using a predefined protocol (available from corresponding author on request), two investigators (RK, DB) worked independently for 1 month, in duplicate, screening all abstracts and obtaining the full text articles that indicated that a text message intervention was used to improve the uptake of a vaccination. After obtaining full reports of the candidate studies (either in full peer-reviewed publication, conference abstract or non peer-reviewed article) the same reviewers independently assessed eligibility. Reviewers were not blinded to study authors, study conclusions and outcomes as blinding has been shown to have little effect on systematic review results [21].

To obtain full information regarding conference abstracts and registered trials, we attempted contact with all study authors for full information through email and telephone communication. After all potentially relevant full-text articles and abstracts were identified, we consulted as a team of (RK, DB) to achieve consensus regarding eligibility and consulted an arbitrator (ME) for adjudication.

2.3 Data extraction

During November 2013, RK and DB independently extracted data in duplicate, using a standardized pre-piloted form. Data collected included information about the study setting, study populations, sample size, and methods of vaccination uptake as a result of a text message intervention. We considered different measures of vaccination uptake as the primary outcome. Five studies measured the outcome using online vaccination records and one study used self-reporting as the measure. Our primary endpoint was the number of

individuals in the exposure and control groups achieving vaccination uptake at the study endpoint. We entered the data into an electronic database such that duplicate entries existed for each study; when the two entries did not match, we reached consensus through discussion. We considered study quality according to reporting of randomization method, adjustment of experimental confounders, allocation concealment, blinding of analysts, objectivity of outcome measures, use of intention-to-treat analysis and loss to follow-up larger than 20%.

2.4 Data analysis

RK and ME conducted all statistical analyses. We calculated the Relative Risk (RR) and appropriate 95% Confidence Intervals (CIs) of the primary outcomes according to the number of events reported in the original studies or sub studies as intent-to-treat analyses. Where studies did not report intent-to-treat, we analysed outcomes as all-patients randomized.

We pooled studies as an analysis of vaccination uptake using the random effects method, which recognizes and anchors studies as a sample of all potential studies, and incorporates an additional between-study component to the estimate of variability [22]. We calculated the I^2 statistic for each analysis as a measure of the proportion of the overall variation that is attributable to between-study heterogeneity [23], and calculated the appropriate I^2 confidence intervals. We imputed the experimental and control event rates from our meta-analysis and applied a 95% power at the 5% significance level. All outcomes are reported as intention-to-treat. Forest plots are displayed for each vaccination uptake analysis, showing

individual study proportions with 95% CIs, and the overall. All p-values are exact and 2-sided. We considered a p-value <0.05 to be significant. Analyses were conducted using Revman 5.1 statistical software (<http://ims.cochrane.org/RevMan>). Subgroup analyses were performed to evaluate the effect of study design and conduct, type of intervention and participants as well as method of confirmation of vaccination uptake.

2.5 Role of the Funding Source

We did not receive funding for this study.

2.6 Ethics

Systematic reviews draw on publicly available data and do not directly involve human subjects, and therefore do not require formal ethical review [24]. The study protocol was reviewed by supervisors with expertise in the systematic review method and submitted to the University of Cape Town Departmental Research Committee for approval.

3 Results

3.1 Study flow and description of studies

A flow diagram of studies included in the analysis is detailed in Figure 1. From the initial search, we identified 348 titles from the various databases. After removing duplicates and examining titles, 76 articles were included. Of these, 10 studies were deemed as being potentially relevant with perfect agreement between reviewers. Following a review of the abstracts, six articles remained eligible for inclusion. All full text papers and abstracts were published in English. Five studies were conducted within the USA while the remaining study was conducted in China. (Table 2 summarizes the characteristics of the six included studies). Detailed information on included studies are provided in Appendix 1.

Four studies were excluded for the following reasons: no comparison group [25], an earlier version of an already included study [26], non-community setting [27] and, conference presentation lacking sufficient detail [28]. (Details are provided in Table 3, “Table of Excluded Studies”).

Of the 15 trials rendered by a search in ClinicalTrials.gov [20], 13 matched our inclusion criteria. From these, two had already been included as published articles [29, 30], (See Table 4: NIH Clinical trials Register).

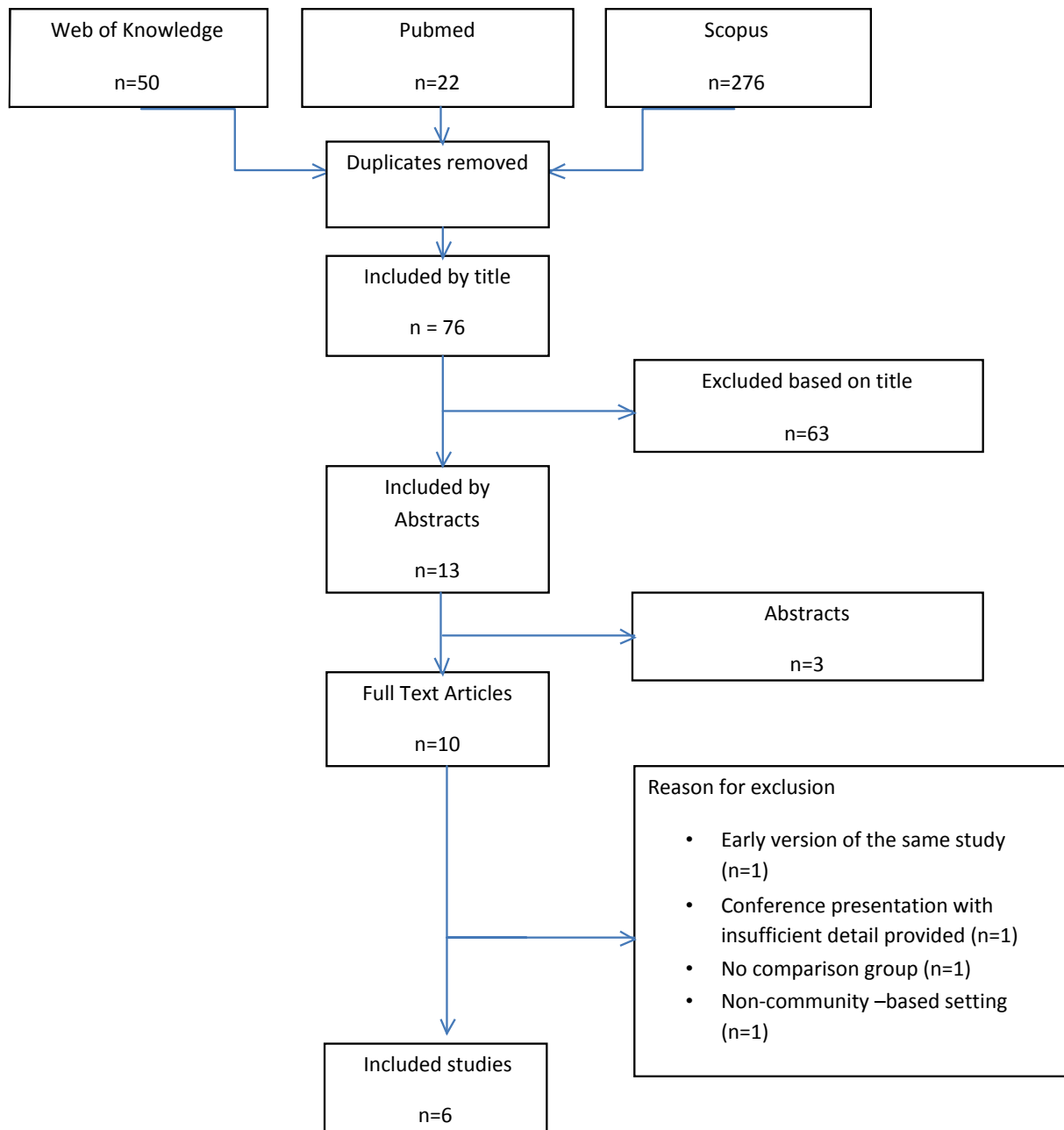


Figure 1. Flowchart for the identification of articles

Table 2: Characteristics of Included Studies

Study	Setting, Country	Age Range of those receiving vaccinations	% male	No of participants	Disease	Intervention / Control	Primary Outcome
Ahlers-Schmidt, 2012	Academic Centres, USA	2-6 months	83.33%	90	2, 4, 6 month infant vaccines	SMS / SOC	Receipt of vaccine
Chai, 2013	Clinic population, China	18->60 yrs	48%	1998	H1N1 influenza	SMS / SOC	Receipt of vaccine
Kharbanda,2011	Clinic population, USA	9-20 yrs	Only female	1512	HPV	SMS / SOC	Receipt of vaccine
Moniz, 2013	Medical centres, USA	14-50 yrs	Only female	216	Influenza	SMS / SOC	Receipt of vaccine
Stockwell b (adolescents),2012	Clinic population, USA	11-18 yrs	42%	361	MCV4/Tdap	SMS / SOC	Receipt of vaccine
Stockwell b (paediatric),2012	Clinic population, USA	7-22 months	50%	174	Hib	SMS / SOC	Receipt of vaccine
Stockwell(a), 2012	hospital population,USA	6 months-18 yrs	49%	9213	influenza	SMS / SOC	Receipt of vaccine

N, number; SMS, short message service; SOC, standard of care; yrs, years; HPV, human papilloma virus; Hib, Heamophilus Influenzae

TABLE 3: Characteristics of Excluded studies

<i>Study</i>	<i>Reason for exclusion</i>
Vilella, 2004	non-community based setting
Wakadha, 2013	no comparison group
Kharbanda, 2011	early version of the same study
Russel 2012	conference presentation with limited data

Participants within studies were exclusively adults [31, 32], adolescents [26] and infants [29] while two studies included both infants and adolescents [30, 33]. One study, however, [33] analysed adolescent and paediatric populations separately. Therefore, from the six studies, 7 populations are analysed. Kharbanda et al had two control groups, an “opt-out” and a historical control group comprising 308 and 1080 participants respectively [26].

Vaccinations included those against human papilloma virus [26], influenza [30-33], meningococcal (MCV4) or tetanus/diphtheria/acellular pertussis (Tdap) [33]. One study comprised routine infant immunisations [29]. Two studies [26, 33] incorporated follow-up doses for completion of the vaccination schedule; the first vaccination uptake data from these studies were pooled with those from the rest of the studies. One study relied on self-reported data, [31] while the rest used online vaccination records to verify vaccination uptake.

Table 4: NIH Clinical Trials Register

Title	Trial number	Status	Include/exclude	If published, citation
Text Message Reminder-Recalls For Early Childhood Vaccination	NCT00076804	Active, not recruiting	Exclude	
Adult Influenza Vaccination Text Message Reminders	NCT01942824	Not yet recruiting	Exclude	
TextFluena: Using Technology To Promote Flu Vaccination In Underserved Maternal And Child Populations	NCT01146912	Completed	Include	Stockwell, JAMA, 2012
Pilot Text Message for Influenza Vaccination	NCT01761734	Active, not recruiting	Exclude	
Effectiveness of SMS (Short Message Service) Text Messaging in Increasing Adherence to Gardasil	NCT01276184	Unknown	Exclude	
Vaccine Health Literacy Related Text Message Reminders to Increase Receipt of Second Dose of Influenza Vaccine for Young, Low Income, Urban Children	NCT01662583	Completed	Exclude: information not yet supplied	
Adolescent Vaccination in the Medical Home: Established and Innovative Strategies	NCT01577979	Enrolling by invitation	Exclude	
Influenza and Text Messaging in Pregnancy	NCT01248520	Active, not recruiting	Exclude	
PregText: Feasibility of Monitoring Influenza Vaccine Safety in Pregnant Women Using Text Messaging	NCT01974050	Not yet recruiting	Exclude	

Text Messaging Reminders for Influenza Vaccine in Primary Care	NCT01892631	Not yet recruiting	Exclude	
Text Reminders for Immunization Compliance in Kids (TRICKS) Pilot Study	NCT00367172	Completed	Include	Ahlers-Schmidt, Vaccine, 2012
Text Reminders to Immunize in a Managed Care Organization	NCT01806714	Recruiting	Exclude	
The Efficacy of Reminders to Complete HPV Series	NCT01731496	Recruiting	Exclude	
Real-time Influenza Vaccine Surveillance	NCT01233388	Completed	Exclude	
Human Papilloma Viruses (HPV) Vaccine Adherence Community Clinic Study	NCT01908517	Not yet recruiting	Exclude	

The SMS interventions comprised reminders of appointment dates [26, 29, 30, 33], (adolescent and paediatrics) or indications of the availability of the vaccine at a local clinic [30-33]. Three studies incorporated an additional educational component within the SMS [30-32]. None of the studies analysed the results for recall rates and thus, we were unable to provide results for our secondary outcome.

3.2 Assessment of Risk of Bias in included studies

Five studies were randomised controlled trials (RCTs) and reported the randomisation method; allocation concealment was unclear across all but one study [32]. The remaining study incorporated non-randomised enrolment of clinic attendees [26]. Three studies reported blinding of study analysts or the researchers [30-32], while the remainder provided insufficient detail as regards blinding. Despite statements to the contrary, only two studies reported intention-to-treat analyses [26, 33]. All the studies provided reasons for loss-to-follow up which included: disconnected/wrong number, relocation, excluded from analysis as participants were vaccinated prior to randomisation, did not receive text messages, terminated pregnancies, did not respond to post-SMS messaging survey. The Cochrane Collaboration tool for assessing study quality is presented in Figure 2.

	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 bias
Ahlers-Schmidt 2012	+	?	+	+	-	+	+
Chai 2013	+	?	+	+	+	-	+
Kharbanda 2011	-	?	+	+	+	+	+
Moniz 2013	+	+	+	+	-	+	+
Stockwell 2012a	+	?	+	+	+	+	+
Stockwell 2012b (Adolesc)	+	?	+	+	+	+	+
Stockwell 2012b (Paed)	+	?	+	+	+	+	+

Figure 2: Risk of bias summary

3.3 Quantitative Data Synthesis

3.3.1 Uptake of vaccination in all included studies(Figure 3)

When we pooled all the studies that reported our primary outcome of vaccination uptake (n=12484) as an analysis of text message intervention compared with usual care, we found a significant effect for vaccination uptake (risk ratio (RR)=1.25 [95% confidence interval (CI), 1.07; 1.46]). Substantial heterogeneity was also detected (p = 0.03, I² = 75%). Because of this, the result of this analysis should be interpreted with caution and not be considered a definitive statement..

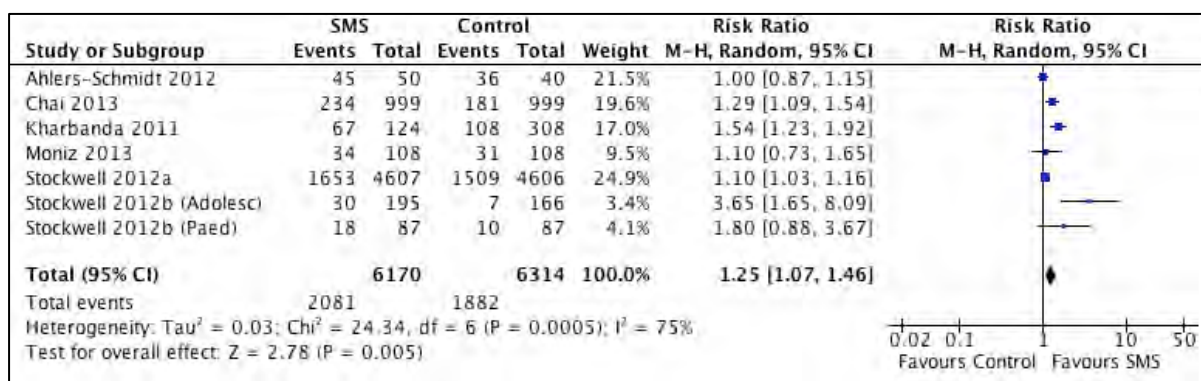


Figure 3: Uptake of vaccination

One study presented an additional analysis using a historical control cohort [26]. We excluded this scenario from the analysis above, given the likelihood of selection bias; nevertheless, including the historical cohort provided similar results with a pooled significant effect favouring SMS (RR=1.28 [95% CI, 1.10; 1.48]). Heterogeneity remained significantly high [I² = 77%].

3.3.2 Type of vaccination (Figure 4)

The overall significant effect of SMS messages favouring the uptake of vaccination was consistent when conducting a subgroup analysis of the four studies of influenza vaccines comprising adults and paediatric communities: participants receiving SMS messages were more likely to take up the vaccination; this was a significant effect (RR=1.17 p=0.02 [95% CI, 1.03; 1.33]); mild heterogeneity [$I^2 = 39\%$ p=0.01]. In studies reporting vaccination for other diseases the results were heterogenous and insignificant (RR=1.62 [95% CI, 0.84; 3.10]).

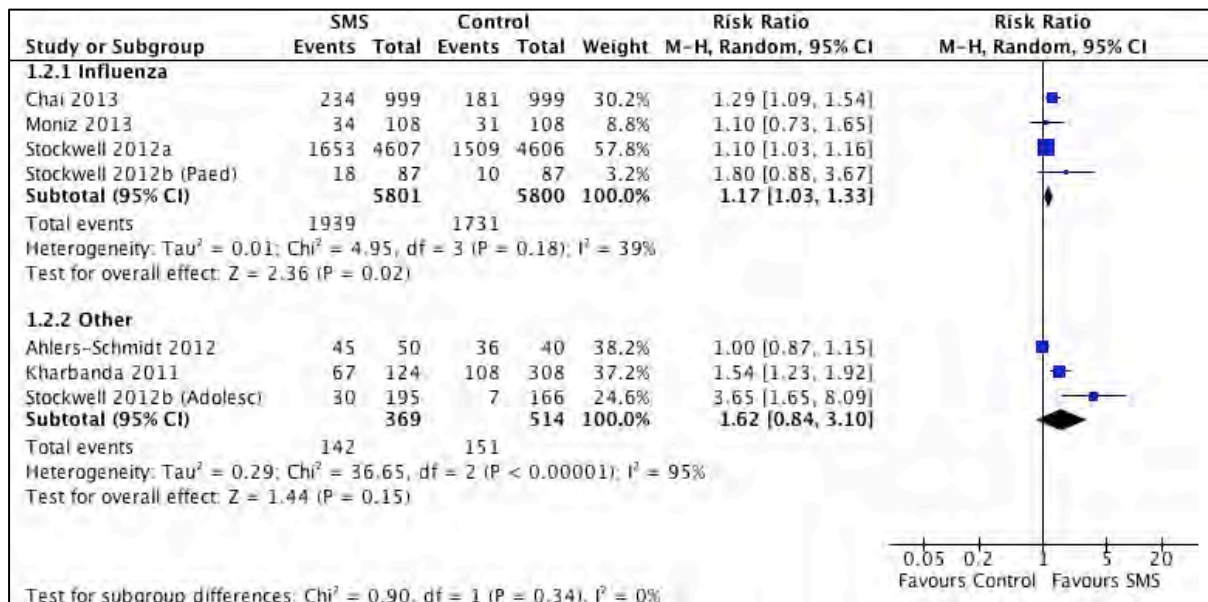


Figure 4: Type of vaccination

3.3.3 Multiple visit vaccinations (Figure 5)

“Two studies required patients to have triple doses within the vaccine schedule. Overall, significant heterogeneity was evident [$I^2=92\%$]”

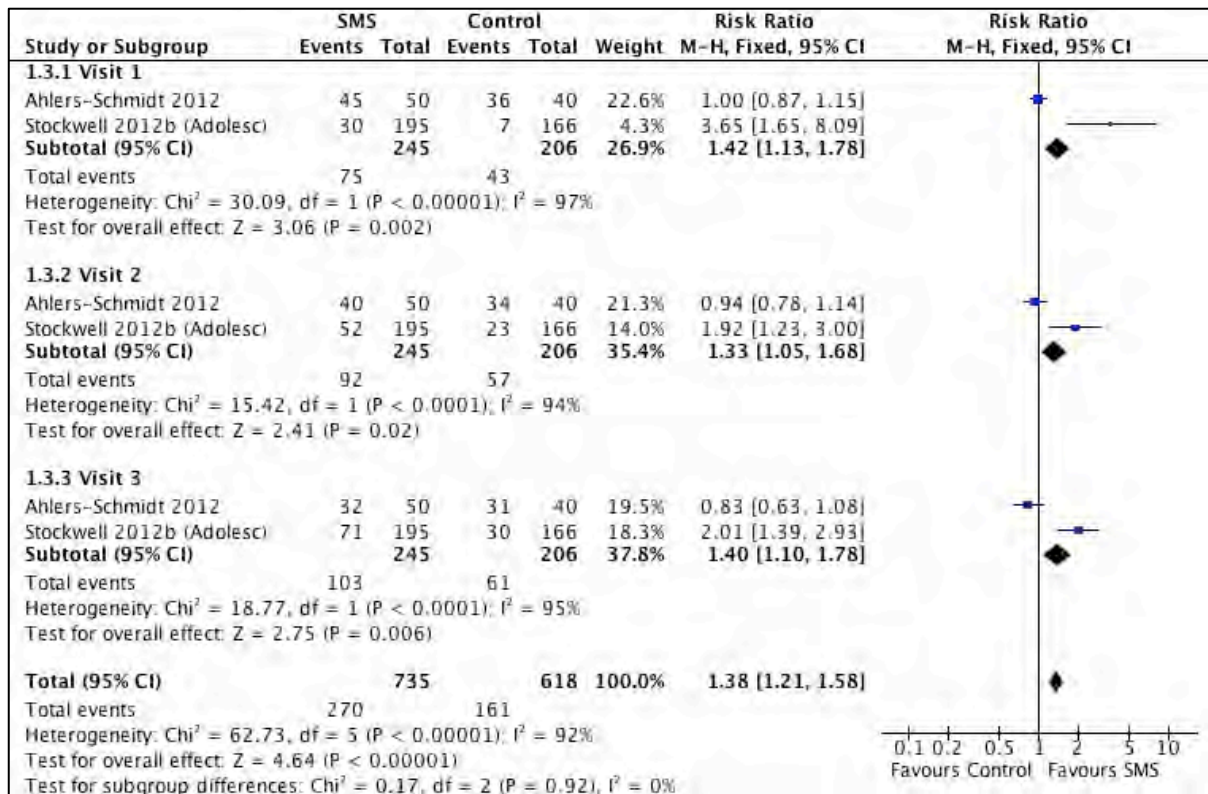


Figure 5: Multiple visit vaccinations

3.3.4 Type of study design (Figure 6)

Five of the studies included were RCTs, and showed significant heterogeneity across the studies [$I^2 = 69\%$]. Only one study was a non RCT and showed a significant effect (RR=1.54, [95% CI, 1.23; 1.92]).

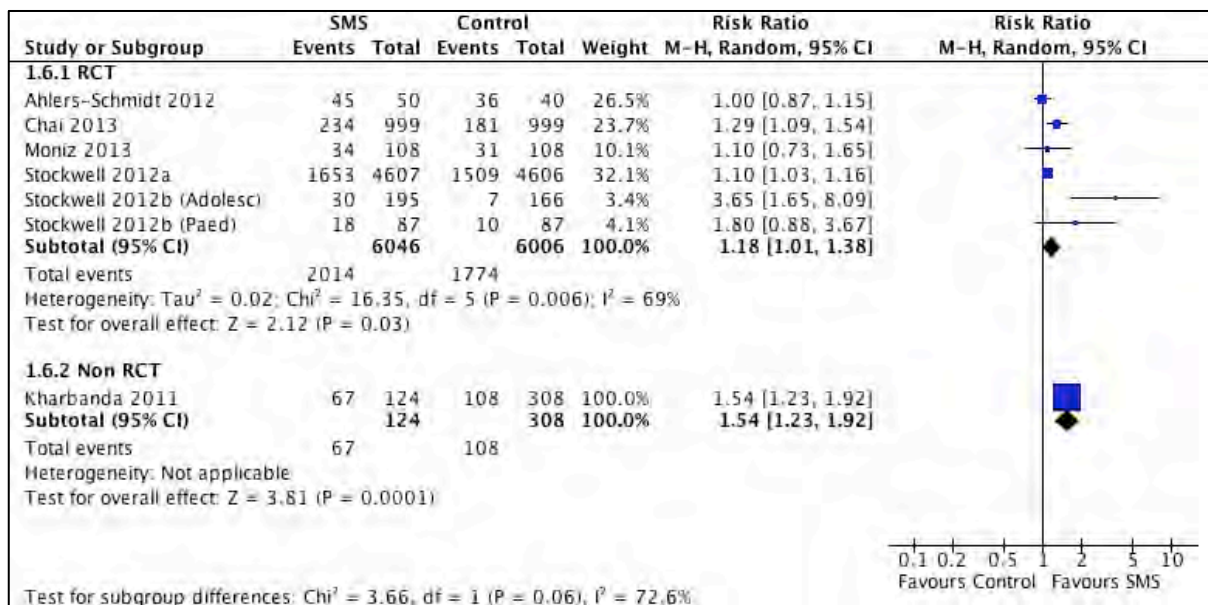


Figure 6: Type of study design

3.3.5. Age categories (Figure 7)

Two studies consisted only of adults receiving vaccines which, when pooled, showed a significant effect for the intervention (RR= 1.26 [95% CI, 1.08; 1.48]) with no heterogeneity [$I^2 = 0\%$]. The remaining five populations comprised parents and caregivers of infants and adolescents showed significant heterogeneity was present [$I^2 = 81\%$], therefore the results could not be pooled.

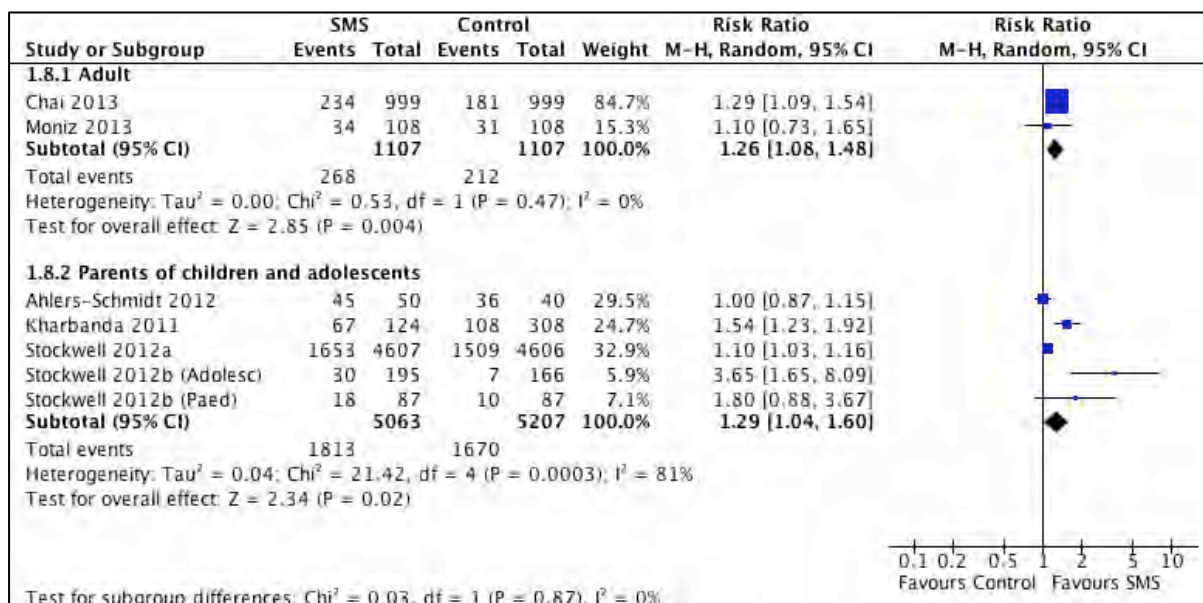


Figure 7: Age categories

3.3.6 Blinding (Figure 8)

For interest, we considered the effect of blinding on outcome. Three studies reported on their blinding method: where blinding was reported, we found a significant pooled effect (RR=1.15 [95% CI, 1.02; 1.29], $I^2 = 38\%$). In contrast, In the four populations where blinding was not reported, no significant effect for SMS was apparent (RR=1.65[0.93; 2.92]) with significant heterogeneity being present ($I^2=92\%$).

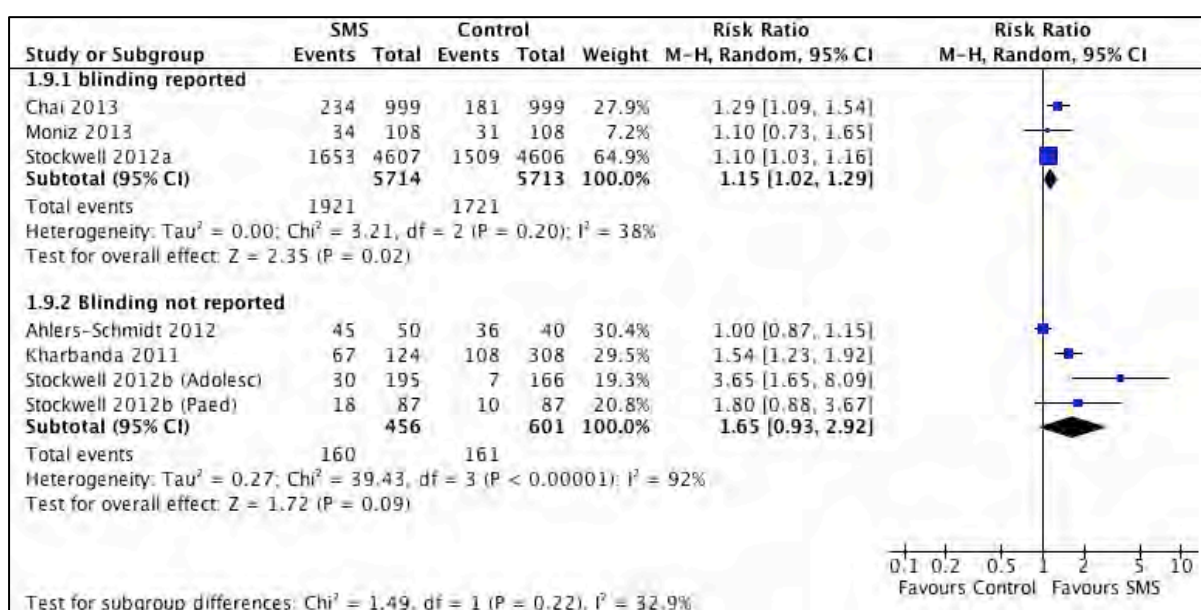


Figure 8: Blinding

3.3.7 Method for assessing Outcomes (Figure 9)

In the five studies where objective assessment (e.g. online verification) of vaccination uptake was used, the pooled estimate showed significant heterogeneity between studies [$I^2 = 77\%$]. One study employing self-reporting to obtain participants' data, showed a significant effect (RR=1.29, [95% CI, 1.09; 1.54]). There was no significant difference between the subgroups ($I^2=0\%$).

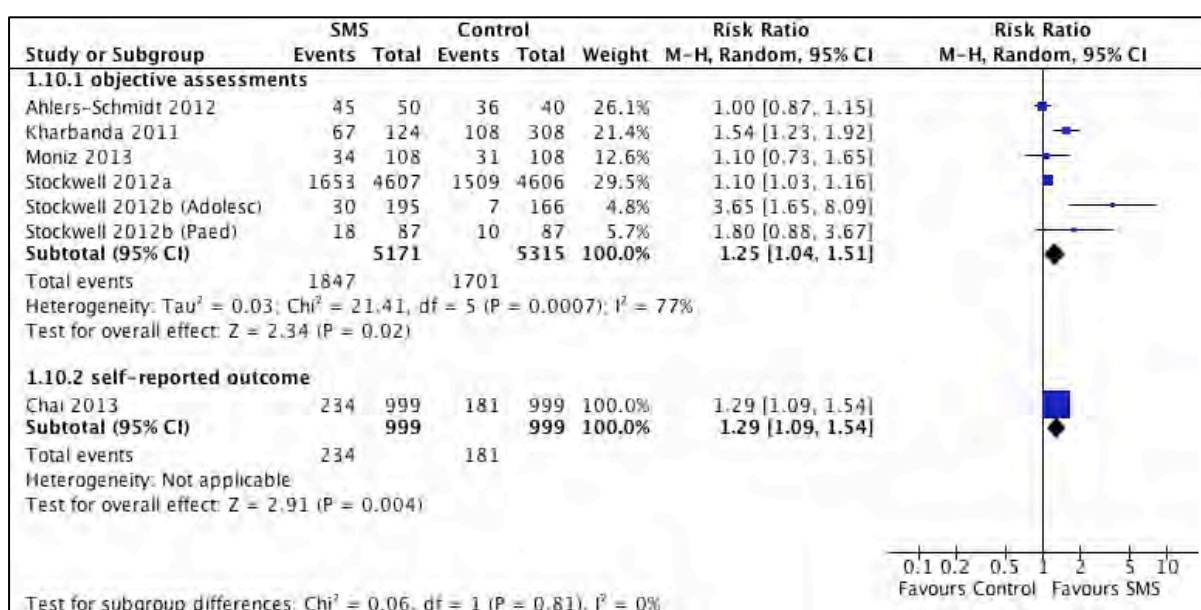


Figure 9: Method for Assessing Outcomes

3.3.8 Country setting (Figure 10)

Five studies were conducted in the USA which, when pooled, showed significant heterogeneity between the studies [$I^2 = 77\%$]. Similarly, the single study conducted in a developing country setting, viz. China, also found a significant effect for SMSs promoting vaccine uptake (RR=1.29, [95% CI, 1.09; 1.54]).

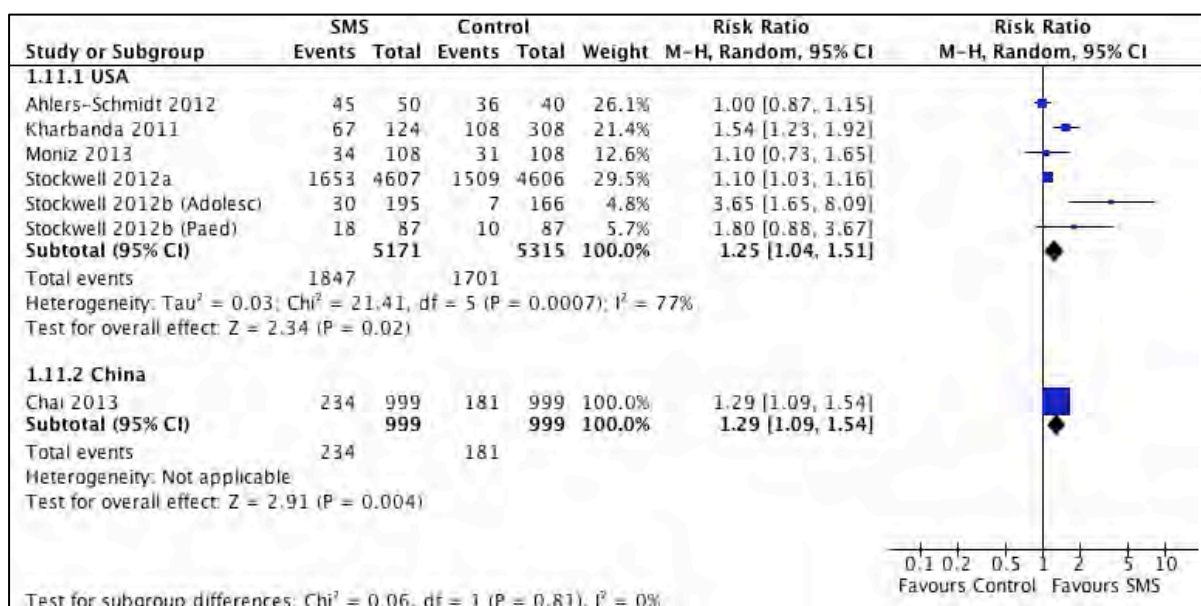


Figure 10: Country setting

3.3.9 Summary of Subgroup analysis

We did not find any important changes in our estimates when we investigated the effect of study design and method of assessment of outcomes. However, the quantitative effect amongst studies not reporting blinding yielded a non-significant estimate (RR=1.65 [95% CI, 0.93; 2.92]) with significant heterogeneity ($I^2 = 92\%$). In addition, we did not find any changes in our overall estimate when using the fixed-effects method (data not shown).

4. Discussion

4.1 Summary of findings

In this review, six studies comprising seven populations with a total of 12,484 participants were analysed to investigate the effects of SMS as an intervention to promote vaccination among adults, adolescents and parents or caregivers of children. Overall, studies showed heterogeneity, thus not making it possible to compare usual standard of care with text messaging for compliance with vaccination schedules. However, when considering adults only (n=2 studies), SMS significantly improved vaccination uptake by 26% (RR=1.26, [95%CI, 1.08;1.48], p=0.004). Among the studies on influenza (n=4), there was a significant effect (RR=1.17, [95%CI, 1.03;1.33], p=0.02). Concerning type of disease, however, the evidence for SMS interventions resulting in a 62% increased likelihood of vaccination for diseases other than influenza, was not statistically significant.

4.2 Quality of the evidence

We used the GRADE approach to assess the level of confidence to be placed on the evidence for the effects of SMS on vaccination coverage [34]. This method results in an assessment of the quality of a body of evidence as high, moderate, low, or very low. In five of the six included studies the method of allocation concealment was unclear. This led us to downgrade the quality of the evidence from high to moderate. Moderate quality evidence implies the pooled effect estimate found in this review provides a good indication of the likely effect of SMS on vaccination coverage. Although moderate quality evidence provides a good basis for making a decision about whether to implement an intervention, monitoring of the impact is likely to be needed and impact evaluation may be warranted if it is implemented.

4.3 Strengths and Limitations

The main strength of this review lies in our adherence to international standardised guidelines on the conduct and reporting of systematic reviews [19]. Five of the included studies were RCTs and the remainder, a site-based intervention study [26]. The data were all published data in peer-reviewed journals and did not appear to have selective reporting biases. The majority of the studies also obtained their data from online vaccination records providing us with very high quality objective data. Although conducted predominantly in the USA, most of the settings were community-based clinics serving the lower socio-economic areas; thus it is reasonable to generalize the findings from this review to communities within countries.

Our review should be evaluated with the following limitations in mind. First, although our review drew from an extensive search and was not limited by language, conference proceedings were not searched. Therefore, it is possible that additional information from conference proceedings not leading to publication was missed. Second, we were only able to find a single study emanating from a resource-limited country. Thus, more studies are required from such areas in order to increase the evidence. It is unclear how representative the participants recruited in the studies were compared with those worldwide receiving vaccinations. A third limitation relates to the moderate quality of the data. We were unable to identify adequate allocation concealment in five of the studies, while one study was unclear regarding random sequence generation. Furthermore, two studies did not provide complete outcome data, thus increasing attrition bias and one study employed selective reporting, and therefore increasing the risk of reporting bias. More high quality data would

aid in strengthening recommendations for successful use of an SMS intervention to improve vaccination coverage.

4.4 Comparison with existing literature

To our knowledge this is the first systematic review of SMS interventions for improving immunisation coverage. The evidence provided for the success of text messaging in achieving desired outcomes is in keeping with those present in another review comprising two studies that assessed the effects of text messaging in promoting adherence to anti-retroviral therapy (ARV) in HIV patients [36]. Text messaging was also shown to be effective in 71% of studies involving non-vaccination related conditions.[37] Similarly, SMS interventions have been shown to promote medication adherence in HIV, contraception and smoking cessation. [38] A review looking at interventions to increase influenza vaccination among healthcare workers in hospitals found that a reminder via SMS as part of an intervention programme increased vaccination uptake. [39] However, a single RCT published more recently, provided contrasting results, concluding that an SMS intervention did not significantly improve ARV adherence with participants withdrawing from the study for privacy reasons; thus, the authors speculate that the reason for this ineffectiveness may include the stigmatization associated with HIV [40].

Stockwell MS, 2013, presented a literature review of a broad range of health information technologies to improve vaccine communication and coverage and suggested that SMS is effective in improving vaccination uptake for a number of reasons: (1) SMS is able to penetrate large populations, (2) cost-effectiveness given the relatively low cost, (3) less

human resource intensive as it can be set up electronically, (4) reaches the specific patient for which it is intended. [41]

4.5 Implications for Practice

The evidence presented in this review shows promise for the employment of SMS interventions to promote the uptake of vaccination. However, the moderate quality of the evidence implies that monitoring of the impact is likely to be needed and impact evaluation may be warranted if SMS interventions are implemented to improve uptake of vaccination services. Also, the specific contribution of educational messages combined with SMS reminders needs further evaluation. Furthermore, when text messaging interventions are to be introduced in resource-limited settings, it is imperative to consider the potential barriers of low-literacy levels, language barriers, lack of access to the owner of a mobile phone given that sharing of mobile phones is common in many places, restrictions on the content of text messages, issues such as habituation and the ignoring of messages when text messages are delivered too frequently, privacy and disclosure issues, poor mobile phone service provision, the inability of mobile phone users to charge their phones due to lack of electricity, the inability to buy pre-paid phone cards and, the high incidence of mobile phone theft and phone number changes in some parts of the world [14].

4.6 Implications for Research

Current evidence is of moderate quality. This implies that the likelihood that further research will find the effect to be substantially different is moderate. Therefore more research is needed from low and middle-income countries, especially for non-influenza vaccines.

5. Conclusion

The findings of this systematic review indicate that SMS interventions present a promising method of promoting the uptake of vaccination. The results of this systematic review highlight the need for further research within developing countries, especially given the rise of mobile phone usage in Africa and other developing nations[10].

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Appendix 1: Detailed Characteristics of Included studies

1. Stockwell 2012 B

Adolescents

Methods: Randomised controlled trial

Participants: Parents or guardians from a low-income minority population from community-based clinics affiliated to the academic centre in New York City were eligible to participate in the study if:

(1) They had an 11- to 18-year-old child with any visit (including sick visits) at a study site within the previous 12 months.

(2) The patient was in need of either or both MCV4 and Tdap, or

(3) A cell phone number was recorded in the registration system. Parents of patients who had not received the Tdap vaccine but had received another tetanus-containing vaccine within the previous 2 years were excluded from study

Intervention: The purpose was to assess the effect of text messaging on receipt of 1 or both of 2 routinely recommended adolescent vaccines:

1. MCV4 (meningococcal) and
2. Tdap (tetanus--- diphtheria---acellular pertussis).

Outcomes: Primary outcome was the uptake of the Meningococcal (MCV4) and Tetanus, diphtheria and acellular pertussis (Tdap).

Results:

At 4 weeks

Relative risk 3.6484

95 % CI 1.6455 to 8.0891

z statistic 3.186

P = 0.0014

At 12 weeks

Relative risk 1.9246

95 % CI 1.2333 to 3.0035

z statistic 2.884

P = 0.0039

At 24 weeks

Relative risk 2.0147

95 % CI 1.3871 to 2.9263

z statistic 3.678

P = 0.0002

P = 0.10

<i>Notes</i>		
<i>Risk of bias</i>		
Bias	Author's Judgement	Support for judgement
Random sequence generation(selection bias)	Low risk	A computer algorithm was used to automatically select a random sample of patients
Allocation concealment(selection bias)	Unclear risk	The intervention patients were matched by gender and age to randomly selected eligible patients from the control sites. Further detail not provided
Blinding of participants and personnel(performance bias)	<i>Low risk</i>	No blinding, but outcome and outcome measurement unlikely to be influenced by lack of blinding
Blinding of outcome assessment(detection bias)	<i>Low risk</i>	No blinding, but outcome and outcome measurement unlikely to be influenced by lack of blinding
Incomplete data(attrition bias)	Low risk	All patients and outcomes are accounted for
Selective reporting	Low risk	Appears to be no evidence of selective reporting. Article has been peer reviewed and published in the Am J Pub Health
Other bias	Low risk	

2. Stockwell 2012 B

Paediatrics

Methods: Randomised controlled trial

Participants: Eligible families from a low-income minority population from community-based clinics affiliated to the academic centre in New York City had:

- (1) A child aged 7 to 22 months lacking 1Hib dose needed to complete his or her primary series,
- (2) A visit for that child in the past 12 months at 1 of 4 paediatric clinical sites, and
- (3) A cell phone number recorded in the clinic registration system.

Intervention: Conducted from May to June 2009, Text4Health---Peds was a quality initiative to mobilize parents to attend special Hib immunization recall sessions for children overdue for primary vaccination because of the national shortage that occurred in response to a voluntary recall.

Outcomes: Uptake of a Hib vaccine.

Results

Relative risk 1.8000

95 % CI 0.8818 to 3.6745

z statistic 1.614

P = 0.1064

<i>Notes</i>		
<i>Risk of bias</i>		
Bias	Author's Judgement	Support for judgement
Random sequence generation(selection bias)	Low risk	A computer algorithm was used to automatically select a random sample of patients
Allocation concealment(selection bias)	Unclear risk	unclear
Blinding of participants and personnel(performance bias)	<i>Low risk</i>	No blinding, but outcome and outcome measurement unlikely to be influenced by lack of blinding
Blinding of outcome assessment(detection bias)	<i>Low risk</i>	No blinding, but outcome and outcome measurement unlikely to be influenced by lack of blinding
Incomplete data(attrition bias)	Low risk	All patients and outcomes are accounted for
Selective reporting	Low risk	Appears to be no evidence of selective reporting. Article has been peer reviewed and published in the Am J Pub Health
Other bias	Low risk	

3. Kharbanda 2011

Methods: Site Based Intervention study (non-randomised study)

Participants: Adolescent girls (9-20 years) from 9 paediatric clinical sites located in New York City (5 were hospital-affiliated academic practices primarily serving publicly insured youth and the other 4 were private practices)

Interventions: 3 weekly text message reminders of next vaccine dose for either HPV1 or HPV2

Controls: 2 control groups:

1. Opt-out- adolescent girls who had received an enrolment card during the intervention period but did not sign up

2. Historical control – adolescent girls who had received the HPV1 or HPV2 vaccine during the control period, prior to the start of the intervention.

Outcomes: Primary outcome: proportion of adolescent girls who received their next vaccination on time (<92 days between HPV1 and HPV2 & 154 days between HPV2 and HPV 3).

Results:

Intervention versus opt-out control

Relative risk 1.5409

95 % CI 1.2337 to 1.9247

z statistic 3.811

P = 0.0001

Intervention versus historical control

Relative risk 1.4198

95 % C I 1.1868 to 1.6986

z statistic 3.832

P = 0.0001

<i>Notes</i>		
<i>Risk of bias</i>		
Bias	Author's Judgement	Support for judgement
Random sequence generation(selection bias)	Moderate risk	Adolescents without a parent could self-select to participate in the study and those who could sign up via mobile phone were eligible
Allocation concealment(selection bias)	Unclear risk	unclear
Blinding of participants and personnel(performance bias)	Low risk	No blinding
Blinding of outcome assessment(detection bias)	Low risk	No blinding
<i>Incomplete data(attrition bias)</i>	Low risk	All participants who enrolled were included in the analysis
<i>Selective reporting</i>	Low risk	No evidence to support this
<i>Other bias</i>	Low risk	

4. Ahlers-Schmidt 2012

Methods: Randomized Controlled Trial

Participants: Parents of newborns being discharged from a local hospital who intended to seek child health care at the University-sponsored paediatric resident and faculty clinic in a Midwestern metropolitan area in Kansas.

Interventions: 3 text messages, 7 days prior to 2, 4, 6 month vaccinations to remind parents that the vaccination was due

Outcomes: Receipt of immunizations due at 2, 4, 6 months of age.

2 month immunization received

Relative risk 1.0000

95 % CI 0.8706 to 1.1487

z statistic 0.000

P = 1.0000

4 month immunization received

Relative risk 0.9412

95 % CI 0.7782 to 1.1383

z statistic 0.625

P = 0.5320

6 month immunization received

Relative risk 0.8258

95 % CI 0.6325 to 1.0782

z statistic 1.407

P = 0.1595

<i>Notes</i>		
<i>Risk of bias</i>		
Bias	Author's Judgement	Support for judgement
Random sequence generation(selection bias)	Low risk	A computer generated randomisation scheme was used
Allocation concealment(selection bias)	Unclear risk	Not detailed
Blinding of participants and personnel(performance bias)	Low risk	No blinding
Blinding of outcome assessment(detection bias)	Low risk	No blinding
Incomplete data(attrition bias)	Moderate risk	Per protocol analysis and intention to treat analysis completed(2 participants were excluded from the intervention randomisation group)
Selective reporting	Low risk	No evidence of self-reporting. Outcome was measured from a clinical database
Other bias	Low risk	

5.Moniz 2013

Methods: Randomised controlled trial

Participants: Women aged 14–50 years who were pregnant at less than 28 weeks of gestation recruited from the Pittsburgh Medical Centre, Pittsburgh, USA. There 108 participants in the intervention group and 108 in the control group.

Intervention: 12 Weekly text messages encouraging general pregnancy health (n = 108) or general pregnancy health + influenza vaccination (n=108). Duration: 2 consecutive influenza seasons from 2010 – 2012.

Outcomes: Primary outcome was the uptake of the influenza vaccination.

Results

Relative risk 1.0968

95 % CI 0.7300 to 1.6479

z statistic 0.445

P = 0.6565

<i>Notes</i>		
<i>Risk of bias</i>		
<i>Bias</i>	<i>Author's Judgement</i>	<i>Support for judgement</i>
<i>Random sequence generation(selection bias)</i>	<i>Low risk</i>	<i>Utilised equal frequency using a permuted block design</i>
<i>Allocation concealment(selection bias)</i>	<i>Low risk</i>	<i>Participant's names were placed in opaque envelopes</i>
<i>Blinding of participants and personnel(performance bias)</i>	<i>Low risk</i>	<i>Health care providers were blinded</i>
<i>Blinding of outcome assessment(detection bias)</i>	<i>Low risk</i>	<i>Record review researchers were blinded</i>
<i>Incomplete data(attrition bias)</i>	<i>Moderate risk</i>	<i>Per protocol analysis done not intention-to-treat</i>
<i>Selective reporting</i>	<i>Low risk</i>	<i>Outcome based on clinical records</i>
<i>Other bias</i>	<i>Low risk</i>	

6.Chai 2013

Methods: Single blinded Randomised controlled trial

Participants: Jan 2010 – 2011, 1998 participants, permanent residents in Shanghai, China aged between 18–65 years. Sms n = 999. Control n = 999.

Intervention: During February 1–10, 2010, one SMS message was sent to each participant each morning for a total of ten different messages on 10 days. During the subsequent 10 days, the same ten messages were sent again to each participant, one daily, to reinforce the messages.

Outcomes: Self-reported H1N1 vaccination uptake.

Results

Relative risk 1.2928

95 % CI 1.0874 to 1.5371

z statistic 2.909

P = 0.0036

<i>Notes</i>		
<i>Risk of bias</i>		
Bias	Author's Judgement	Support for judgement
Random sequence generation(selection bias)	Low risk	Randomised cluster method utilised
Allocation concealment(selection bias)	Low risk	unclear
Blinding of participants and personnel(performance bias)	Low risk	Single blinding reported
Blinding of outcome assessment(detection bias)	Low risk	Single blinding reported
Incomplete data(attrition bias)	Low risk	All patients were accounted for but analysis was per protocol not intention-to-treat.
Selective reporting	Moderate risk	Patients were required to self-report receipt of the vaccine
Other bias		

7. Stockwell 2012 A

Methods: Randomised controlled trial

Participants: 9213 participants in an urban low-income paediatric and adolescent population recruited from community-based clinics in New York City.

Interventions: During the influenza season (2010-2011), 9213 were randomised to SMS (n=4607) or usual care (n=4606). Messages were sent 5 weekly, 3 were about educational information and 2 about dates for the immunization clinics

Controls: n=4606

Outcomes: Primary outcome was receipt of an influenza vaccine dose recorded in the immunization registry via an electronic health record by March 31, 2011.

Results

Relative risk	1.0952
95 % CI	1.0349 to 1.1589
z statistic	3.150
P =	0.0016

<i>Notes</i>		
<i>Risk of bias</i>		
Bias	Author's Judgement	Support for judgement
Random sequence generation(selection bias)	Low risk	Permuted block design was utilised, stratified by age and clinic site
Allocation concealment(selection bias)	Unclear risk	Unclear
Blinding of participants and personnel(performance bias)	Unclear risk	Unclear
Blinding of outcome assessment(detection bias)	Low risk	Reported that study analysts were blinded to individual group assignment
Incomplete data(attrition bias)	Low risk	All participants were accounted for but per protocol analysis was done and not intention to treat
Selective reporting	Low risk	Outcomes were not assessed using self-reporting but online vaccination records
Other bias	Low risk	

Appendix 2: BMC Medicine: Authors' Instructions

Instructions for authors

BMC Medicine

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The Background section should be written in a way that is accessible to researchers without specialist knowledge in that area and must clearly state - and, if helpful, illustrate - the background to the research and its aims. Reports of clinical research should, where appropriate, include a summary of a search of the literature to indicate why this study was necessary and what it aimed to contribute to the field. The section should end with a brief statement of what is being reported in the article.

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Complete book

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Book with institutional author

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PhD thesis

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