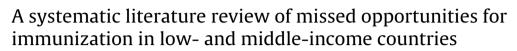
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Vaccine

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### ARTICLE INFO

## ABSTRACT

Article history: Received 24 August 2014 Received in revised form 18 October 2014 Accepted 21 October 2014 Available online 4 November 2014

Keywords: Immunization Missed opportunity Vaccine Vaccine hesitancy Systematic review Meta-analysis *Background:* Missed opportunities for immunization (MOIs) may contribute to low coverage in diverse settings, including developing countries. *Methods:* We conducted a systematic literature review on MOIs among children and women of childbear-

ing age from 1991 to the present in low- and middle-income countries. We searched multiple databases and the references of retrieved articles. Meta-analysis provided a pooled prevalence estimate and both univariate and multivariate meta-regression analysis was done to explore heterogeneity of results across studies.

*Results:* We found 61 data points from 45 studies involving 41,310 participants. Of the 45 studies, 41 involved children and 10 involved women. The pooled MOI prevalence was 32.2% (95% CI: 26.8–37.7) among children – with no change during the study period – and 46.9% (95% CI: 29.7–64.0%) among women of child-bearing age. The prevalence varied by region and study methodology but these two variables together accounted for only 12% of study heterogeneity. Among 352 identified reasons for MOIs, the most common categories were health care practices, false contraindications, logistic issues related to vaccines, and organizational limitations, which did not vary by time or geographic region.

*Conclusions*: MOI prevalence was high in low- and middle-income settings but the large number of identified reasons precludes standardized solutions.

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## 1. Introduction

After the Global Advisory Group of the World Health Organization (WHO) recommended the strategy of immunizing at every opportunity in 1983, protocols were developed for evaluating the magnitude and risk factors for missed opportunities for immunization (MOI) by WHO [1]. It defined a missed opportunity as an occasion when a person eligible for immunization and with no valid contraindication visits a health service facility and does not receive

http://dx.doi.org/10.1016/j.vaccine.2014.10.063 0264-410X/© 2014 Elsevier Ltd. All rights reserved. all recommended vaccines. Following the publication of a systematic review on missed opportunities during 1993 [2], the goal was set to achieve full immunization of 90% of the world's children by 2000. This goal has not been achieved as of 2013, and one of the major contributors is MOIs [3].

The objective of our study was to perform a systematic literature review to assess the prevalence of missed immunization opportunities in low- and middle-income countries since publication of the last summary review during 1993. We focused on children and women of child-bearing age – as these are the target groups for publicly funded immunization programs in the evaluated countries – and assessed the importance of temporal and geographic variations.

## 2. Materials and methods

#### 2.1. Database search

Two authors (SS and NM), conducted the database search and data extraction. We included searches of the following: PubMed, Cochrane, Popline, WHO regional databases (LILACS: Latin American and Caribbean; IMSEAR: Index Medicus of South East Asian



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Abbreviations: AJOL, The African Journal Online; IMEMR, Index Medicus Eastern Mediterranean region; IMSEAR, Index Medicus of South East Asian Region; LILACS, Latin American and Caribbean; MOI, missed opportunity for immunization; PAHO, Pan American Health Organization; UNICEF, United Nations International Children's Emergency Fund; WHO, World Health Organization; WPRIM, Western Pacific Region Index Medicus.

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Region; PAHO: Pan American Health Organization; WPRIM; Western Pacific Region Index Medicus; IMEMR: Index Medicus Eastern Mediterranean region), the African Journal Online (AJOL), and Google Scholar. Databases requiring paid access (EMBASE, CINAHL etc.) were not included because of budget constraints; despite this, after consultation with the WHO librarian, the authors considered that the included databases were likely to have identified all or the great majority of relevant manuscripts.

Our goal was to include immunization terms combined with practices, services and type of study. Our search terms included "immunization" OR "vaccination" (or any of numerous synonyms) in combination with "Health Knowledge, Attitudes, Practice" OR "Attitude of Health Personnel" OR "Immunization/trends" OR "Immunization/utilization" OR "Immunization/physiology" OR "Vaccination/psychology" OR "Vaccination/trends" OR "Vaccination/utilization" OR "Preventive Health Services/trends" OR "Health Services/trends" OR ("Health Services/utilization" AND "Epidemiologic Studies") OR "Follow-Up Studies" OR "Health Surveys" OR "Data Collection". For PubMed, MeSH (Medical Sub-headings) was used to help expand the search. These terms were then combined with the names of individual low- and middle-income countries. Additional manuscripts in French papers were searched on Google using the terms ([Opportunité] AND [manquée/perdue] AND [vaccination/immunization]) OR (Perte AND opportunité AND vaccination).

#### 2.2. Inclusion criteria and selection process

We included studies that measured the magnitude or described the reasons for missed opportunities in children (0–18 years) or woman of childbearing age in low- or middle-income countries (as defined by the World Bank during 2013) after 1991. Only studies in English, Spanish, French and Portuguese were included based on staff translation capacity.

Following pilot testing of the selection form, two independent reviewers reviewed in a stepwise fashion the title, abstract, and full text using Distiller Software (Fig. 1). Discrepancies were resolved through consensus. The references of all included manuscripts were searched for additional manuscripts. As indicated in Fig. 1, we had three ancillary searches. The African Journal Online database was searched for the terms "missed" AND "immunization" AND "opportunities"; this led to 53 results, of which three manuscripts were included after title abstract and full text screening. The Google search for French references yielded 30 results, of which four manuscripts eventually were included. Lastly, a secondary PubMed search using the term "missed immunization opportunities" led to 307 results and seven included manuscripts.

#### 2.3. Quantitative data extraction

Of 59 [4–62] identified manuscripts, 45 [4–48] were included in quantitative analysis. These 45 studies included data on the number of persons with MOI as well as the total population under study eligible for vaccination (*N*), regardless of study methodology. Study participants were considered to have a MOI if they visited a health-care facility, were not up-to-date on recommended immunizations, and did not receive recommended immunizations irrespective of the number of visits. The total population (*N*) eligible for vaccination equaled the sum of persons who were fully or partially vaccinated, those who had false contraindications for vaccination, and those with missed opportunities. Some manuscripts provided more than one data point, for example data for multiple countries (one report from South America had information on 10 countries) or for both women and children. For these cases, we included each data point separately in analysis (Table 1).

#### 2.4. Qualitative data extraction

Qualitative data included reporting source, definition of missed opportunities, reasons for MOIs, and limits and quality of data.

#### 2.5. Statistical analysis

All analyses were carried out in Stata version 12. Prevalence was calculated directly from manuscripts as a ratio of the number of children or women with MOIs divided by the total eligible population and the standard error calculated. Pooled estimates were calculated during meta-analysis using the *metan* command [63] in Stata on the prevalence and standard error. Heterogeneity was explored statistically using *Cochrane* Q and *I2* values, a statistic that quantifies the degree of inconsistency across studies in a meta-analysis on a scale ranging from 0 to 100%. A random effects model was used for weighting because of a high level of heterogeneity between studies. Results were stratified by WHO region, year of the study (time trend), methodology, and age group of children.

Eight variables in the dataset were reported commonly enough to be evaluated as potential covariates. Bivariate regression analysis was performed to establish the association between each of these variables and the prevalence estimate. Variables associated with missed opportunity prevalence with a *p*-value <0.05 on bivariate analysis were included in a meta-regression analysis [64]. Metaregression was performed with the "metareg" command using prevalence as the outcome variable. All analyses were done separately for women and children.

#### 2.6. Quality assessment

No standard method exists for assessing data quality in descriptive reports. Consequently, we developed the following methodological quality scoring system based on four variables:

- Location: health center based but no details given as to the nature of the site = 0; retrospective community-based = 1; health center based and details provided = 2.
- Methodology: recall/no immunization cards = 0; immunization cards = 1; exit interviews/health center records = 2.
- Definition of missed opportunity used in the study: non-WHO definition = 1; WHO definition = 2.
- Sample size:  $\leq 500 = 0$ , 501 1000 = 1, >1000 = 2.

The study authors developed the scoring system and information for all variables was extracted from the manuscripts themselves. The scoring system was developed as a means of standardizing bias assessment and to account for the lack of explicit bias assessment in most of the included studies. We considered that community-based household surveys due to their retrospective nature were more susceptible to recall bias than studies conducted in health centers. With respect to study methodology, we considered that exit interviews combined with health center records had the least bias in assessing immunization status. With respect to MOI definition, we considered that use of the WHO definition was less biased than an ad hoc definition, although we recognize no empiric data support this decision. These first three variables were used as measures of study validity, while the final variable was used as a measure of study precision. To calculate the total score, we summed values for these four variables.

## 3. Results

We identified 59 studies from 31 countries and 6 WHO regions (Supplemental Table 1). Of these, 45 studies (containing 61 data Download English Version:

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