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EXPOSING CONCERNS ABOUT VACCINATION IN LOW AND MIDDLE INCOME COUNTRIES: A SYSTEMATIC REVIEW

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Abstract:	<p>OBJECTIVES Concerns about vaccination lead to under- and no-vaccination. Our objective is to expose and synthesise evidence on individuals' and communities' concerns about vaccination to influence current debates on strategies to improve vaccination coverage in low- and middle-income countries.</p> <p>METHODS Systematic literature review till February 2014, following standard methods. Published and grey literature that focused on individuals and community concerns on childhood vaccinations were selected.</p> <p>RESULTS 45 quantitative, qualitative and mixed-methods studies were included. Main reported concerns referred to perceptions of vaccines harms (e.g. attribution of fatal events) . Other concerns included programme distrust (mainly due to rumours and conspiracies) and health systems unfriendliness.</p> <p>CONCLUSIONS Concerns about vaccination are widespread and further worsen the challenges related to programmatic and health systems barriers to vaccination. There is a disconnection between qualitative and quantitative research which misses the opportunity to quantify what is reported in the former. Strikingly, there is a wealth of evidence on concerns but much lesser evidence on interventions to address them. We welcome WHO initiative to tackle vaccine hesitancy and call for the synthesis of evidence and production of guidance on strategies to address concerns on vaccination.</p>	

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ABSTRACT

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45 quantitative, qualitative and mixed-methods studies were included. Main reported concerns referred to perceptions of vaccines harms (e.g. attribution of fatal events) . Other concerns included programme distrust (mainly due to rumours and conspiracies) and health systems unfriendliness.

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EXPOSING CONCERNS ABOUT VACCINATION IN LOW AND MIDDLE INCOME COUNTRIES: A SYSTEMATIC REVIEW

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INTRODUCTION

Vaccination programmes have become more complex over the last years due to the availability and introduction of new vaccines (WHO 2014a), the incorporation of other interventions alongside vaccination programmes (Wallace 2009) (e.g. vitamin A supplementation) and the setting up of ambitious global targets for disease control, such as polio eradication (WHO 2012a) and measles elimination (WHO 2012b). These facts pose new challenges in the delivery of vaccines, especially in resource-constrained settings. The complexity of logistics, costs and strategies for delivering existing, underused and new vaccines has increased exponentially (WHO 2014b) and disease control targets require even higher vaccine coverage rates. Accomplishing these goals requires efforts at community level and in each tier of health systems and globally. Under- and no-vaccination remains a problem in many countries (Bosch-Capblanch 2012), a challenge not only for health systems, but also for communities and families. Vaccination coverage has been increasing in the last decades worldwide; however, Sub-Saharan Africa coverage rates remain constantly below other regions, and countries within it show large disparities in coverage (WHO 2014d)

Perceived concerns about vaccination have been associated with suboptimal compliance with vaccination schedules in children, low vaccination uptake or even vaccine refusal (Brown et al. 2010; Falagas and Zarkadoulia 2008). Lack of confidence in vaccination has become a problem in many different settings (SAGE Working Group on Vaccine Hesitancy 2013a), for a wide array of reasons. Addressing this issue requires engaging consumers, journalists, decision makers, health care professionals and researchers (Larson 2011). Lack of confidence in vaccines and health systems has strongly contributed to decreases in vaccination coverage and increases in morbidity and mortality of vaccine-preventable diseases (Brown 2010). The problem has been recognized by policy makers, international institutions and the scientific community, motivating efforts to understand why the public lacks confidence in vaccination and what factors cause delays or even refusal to vaccinate.

The term “vaccine hesitancy” has become widely used for demand-side barriers to vaccination. According to the World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE), the term refers to “*a behaviour [related to vaccination], influenced by a number of factors including issues of confidence (do not trust vaccine or provider), complacency (do not perceive a need for a vaccine, do not value the vaccine), and convenience (access)*” (SAGE Working Group on Vaccine Hesitancy 2013b). The SAGE is addressing the issue of vaccine hesitancy and guiding efforts to improve vaccination coverage (WHO 2013).

The objective of this review is to expose the perceived concerns on vaccination through a synthesis of qualitative and quantitative evidence on caregivers’ concerns regarding vaccines included in the routine childhood vaccination schedule in low- and middle-income countries (LMIC).

METHODS

We conducted a systematic literature review based on Cochrane methods (Higgins 2011) and following the PRISMA criteria for reporting of systematic reviews (Moher et al. 2009).

SEARCH STRATEGY

The following literature databases were searched (including grey literature databases): MEDLINE, Embase, Global Health, PsycINFO, CINAHL, Social Science Citation Index, Campbell, WHO Global Health Library, Popline and Proquest Social Sciences Premium Collection (includes 14 social science databases). The search strategy is available as an Online Resource. The search was run for all databases until February 2014 for all years available. We structured the search strategy around four main concepts:

- Concerns: we adapted the search strategy developed by SAGE in their vaccine hesitancy systematic review (SAGE Working Group on Vaccine Hesitancy 2013b).
- Participants: individuals and communities receiving vaccinations.
- Immunisation: vaccines included in the children systematic immunisation schedule of LMIC. Searches were not limited by the way vaccines were delivered (e.g. routine immunisation, campaigns).
- LMIC: based on the World Bank List of Economies defined as “low income”, “lower middle income” and “upper middle income” in 2014 (World Bank 2014)

SELECTION OF STUDIES

Any study design (i.e. qualitative, quantitative or mixed-methods) describing concerns about vaccinations in LMIC were included in the review.

Duplicate references were removed and studies were assessed for relevance using titles and abstracts. Relevant papers were identified and full texts were assessed for inclusion using a pre-specified set of criteria. Articles were included if: 1) the study context was a LMIC; 2) vaccines studied were included in childhood systematic vaccination; 3) the study population were individuals or communities (i.e. studies focusing on health workers concerns about vaccination were excluded); 4) the main focus of the study was on concerns about vaccinations; 5) the language of the full text of the document was in English, French, Spanish or Portuguese; 6) the study reported primary data; and 7) it was produced after the year 2000. All articles that met the inclusion criteria were included for quality assessment and data extraction.

QUALITY ASSESSMENT

Quality of studies was assessed using criteria adapted from several quality assessment tools for qualitative (Bedford et al. 2013; Critical Appraisal Skills Programme (CASP) 2014) and quantitative studies (Effective Public Health Practice Project 2010; Jackson et al. 2005).

Quantitative studies were given an overall rating of ‘strong’, ‘moderate’ or ‘weak’ quality following the methodology described elsewhere (Effective Public Health Practice Project 2010). Qualitative studies were not given an overall rating or score as no consensus exists in this area. We rather present the results for each criteria in the quality assessment.

Methodological quality was not used to exclude studies or for sub-groups analyses.

DATA EXTRACTION AND ANALYSIS

Qualitative and quantitative data were extracted using data extraction templates. Data were categorised according to a pre/defined set of themes and sub/themes using those identified by Mills et al. in their review of parental beliefs and attitudes towards childhood vaccination (Mills et al. 2005b) (see Table 1 in the Online Resource).

Quotes referring to concerns about childhood vaccinations were extracted from qualitative studies. We extracted two main types of statements: quotes from respondent comments in interviews or participant remarks in focus group discussions (FGD), and authors’ relevant statements in the discussion sections of the articles.

Data extracted from quantitative studies included frequency measures of specific concerns and/or their impact on vaccination outcomes. Both point estimates and confidence intervals were extracted if available.

Results from quantitative and quantitative studies are reported in a narrative way following categories and subcategories. Vaccination status in most of the quantitative studies was self-reported.

RESULTS

DESCRIPTION OF THE STUDIES

The screening and selection process is represented in Figure 1. 7,012 hits were obtained, which yielded 44 included studies from 45 published articles. Tables 2, 3 and 4 in the Online Resource report the characteristics of the qualitative (n=19), quantitative (n=20) and mixed-methods (n=5) included studies, respectively.

Included studies were conducted in 19 countries: 23 studies in Asia, 16 studies in Africa, four studies in South America and one in Oceania.

Qualitative data were available and extracted from 23 studies (17 qualitative studies, four mixed-methods studies and two surveys; two articles reported on the same study: Dasgupta 2008 and Chaturvedi 2009). The most frequent qualitative methodologies were FGD (14 studies) and in depth interviews or key informant interviews (13 studies), followed by surveys with open ended questions (four studies), ethnographic (two studies) and documentary approaches (one study).

Quantitative data were extracted from 25 studies (21 surveys, two case control studies and two mixed methods studies). 16 studies used structured interviews, one used self-administered questionnaires and eight used other types of data collection methods. These data represented a total of 14,981 participants (median: 320; range: 117 to 4,442 per study). We found measures of frequency of specific concerns (usually expressed as a percentage of individuals who gave a given answer to a question) and measures of association between concerns and vaccination behaviour or vaccination outcomes (expressed as Odds Ratios). We also found two main types of information. First, questions about knowledge or beliefs of interviewees about vaccination (e.g. percentage of people that believed that vaccination can harm); second, some surveys included questions regarding concerns as a reason for incomplete vaccination or non-vaccination. In cases where an indicator was estimated for a specific subgroup in the sample, we report the subgroup as defined in the original study.

QUALITY ASSESSMENT

Tables 5 and 6 in the Online Resource show the detail of the quality assessment of the qualitative and quantitative studies, respectively.

We could not find any qualitative study that complied with all 10 CASP quality criteria. 10 studies complied with eight or more criteria, 12 complied with five to seven criteria and one study complied with less than five criteria. All papers of qualitative studies properly reported the aims of the study and defined their methodological orientation. Ethical clearance, informed consent of participants and confidentiality were reported in six studies. Nine studies partially reported these criteria and seven studies did not report any information regarding ethics. The majority of authors reported their findings using quotes from the interviews or FGD to support their statements (17 studies). In most cases, non-compliance with quality criteria was due incomplete or unclear reporting to assess the methods used. Finally, almost none of the papers properly explained the relationship between researchers and participants and only two papers fully explained the selection of participants.

The overall rating score for the methodological quality in quantitative studies was moderate for three studies and weak for the rest. None of the studies scored as 'strong' in the overall rating. Most studies (n=22) were cross-sectional and three were case-control studies. In most of the studies, neither participants nor assessors of outcomes were blinded and confounders were properly dealt with. Data collection was rated as 'strong' in eight studies and 'weak' in the rest. Only one case-control study reported loss to follow-up and number of participants who completed the study. Only one of the estimates of frequency extracted for our analysis was reported with confidence intervals.

PERCEIVED CONCERNS ABOUT VACCINATION

A total of 213 quotes reported individuals and communities' vaccination concerns and 56 measures of their frequency were extracted from quantitative studies. The ten most reported concerns in qualitative studies are shown in Table 1. Table 2 presents data extracted from quantitative studies included in this review (odds ratios of concerns and outcomes are shown in Table 7 of the Online Resource). The geographical distribution of concerns based on data extracted from qualitative studies is shown in Figure 2.

ISSUES WITH HARMFUL EFFECTS OF VACCINATION

The perception of potential harms of vaccines was the most frequently reported concern in qualitative studies. The belief that vaccines could produce serious negative effects on children's health was reported in all three continents and in nine of the 15 countries which reported this concern. Their frequency measured through surveys in the general population showed that up to 43% of the respondents believed that vaccines were harmful (Qutaiba et al. 2014). A study conducted in Kyrgyzstan estimated that even though 3% of the respondents believed that vaccinations were not harmless, 62.0% believed that the immune system is weakened after vaccination (Akmatov et al. 2009). Results from Nigeria showed similar results with 32.7% of the respondents agreeing that immunization can harm the child (Oladokun et al. 2010) and 7.3% reporting specific concerns about polio vaccine (Obute et al. 2007). Concerns about the potential harm of vaccines were more frequent among parents with unimmunized children or with general negative views about vaccination (Kaur 2010; Naeem et al. 2011). Parents from India, Mozambique, Nigeria and Pakistan were asked about the reasons for non-vaccinating their children. Potential harm of vaccines was the first reason raised by 57.8%, 1.0%, 38.8% and 3.3% of all parents respectively (Joseph et al. 2011; Sheldon et al. 2003; Abdulraheem et al. 2011; Naeem et al. 2012).

Some study authors suggested that fear of serious adverse effects could be a consequence of past experiences with Adverse Events Following Immunisation (AEFI) which may be more or less easily attributed to the vaccination event. As one participant in a FGD explained: "At one time our neighbour in a 'rural geographical area' immunised a child in the morning and by 5.00 p.m. the child was dead. From that time I fear taking children for immunisation and all my children are not immunised" (Babirye et al. 2011). In another case: "Sometimes after immunisation children get fever and spend the whole night crying so the health worker must tell the mother in advance what will happen to the baby, that the baby might become weak, or get a fever or the injection is painful so he will cry a lot" (Babirye 2011).

Nine studies reported concerns related to minor side effects, to which they attributed a significant impact on vaccination behaviour. Perry et al. concluded in their study in Bangladesh: "a number of mothers mentioned that their children had developed fever, swelling at the injection site, or had otherwise become sick after immunisation and they, therefore, did not want to take their children back for any further immunisations" (Perry et al. 2007). Quantitative studies found that this reason was less prominent (between 1.1% and 18.8% among people with negative views about vaccination or with a child partially or totally unimmunized respectively (Babalola 2011; Naeem et al. 2012; Torun et al. 2008)). The fact that vaccines produced side effects, such as fever, after vaccination also strengthened the belief that vaccines could be harmful: "If you vaccinate the child and then on the following day it has a hot body, then his mother no longer wants him to be vaccinated. She tells herself that this is due to the vaccination" (Sia et al. 2011).

Some attributed effects of vaccination were based on rumours with little or no support from evidence. Babalola et al (Nigeria) described that "there (were) widespread rumours about serious health consequences of immunisation that are believed to come from credible sources and have the support of respectable people in the community" (Babalola 2011). Although a wide variety of rumours about vaccination were reported in different settings, vaccination causing sterility was one of the most frequently reported. Khowaja et al. concluded in their study in Pakistan that "most of the parents thought that the polio vaccine caused sterility in adulthood" (Khowaja et al. 2012). 3.3% of the people surveyed in one study in Pakistan reported that fears that vaccines produced sterility as their main

1 reason for not vaccinating their children. This proportion went up to 21.6% and 40.2% among those
2 who did not consider having their children vaccinated as useful and who had negative views about
3 vaccination respectively (Naeem 2012).

4 Other reported concerns were the high number of vaccines administered at once and a widespread
5 rumour that a sick child cannot be vaccinated, the latter shared by parents and health professionals. A
6 survey in Kyrgyzstan estimated that up to 62% of parents were worried about the high number of
7 vaccines that their children were receiving (Akmatov 2009) and 26.9% of the people surveyed in
8 Mozambique believed that receiving more than one vaccine per day could be dangerous (Sheldon
9 2003).

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12 These concerns have the potential to affect parents' behaviour in terms of adherence to vaccination as
13 noted by Braka in Uganda: "Experiences with AEFI and concerns about vaccine safety negatively
14 affected caretakers' decisions to vaccinate their children, notably in rural areas" (Braka et al. 2012).
15 Quantitative studies also reported similar findings. A study in Nigeria found that the odd of incomplete
16 vaccination was 1.86 (CI95% 1.63 to 2.22) times higher among children whose parents had concerns
17 about vaccination safety (Abdulraheem et al. 2011). In contrast, having heard about deaths due to
18 vaccination or believing that vaccines produce diseases were not associated with incomplete
19 vaccination in Colombia (Tirado Otavaro et al. 2006). Having a complication from a previous injection
20 or having fear of injections were associated with missed opportunities and delays in measles
21 vaccination, respectively (Abdulraheem et al. 2011; Logullo 2008).
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24 *ISSUES WITH PROGRAMME DISTRUST*

25
26 We include in this section concerns related to lack of trust in vaccines or immunization programmes
27 based on the belief that vaccines are part of a global conspiracy against some communities or
28 religious beliefs (e.g. Muslims, dark-skinned people or Africans). Despite this issue was the second
29 most frequently reported concern in qualitative studies, we could not find any quantitative estimate of it
30 in quantitative studies.
31

32
33 As one health provider explained in an interview: "Each time, you will hear newer and more and more
34 weird things about the vaccine They can stretch the limits of imagination... Last time there was a
35 strong rumour that the polio vaccine is prepared by the Jews and America is using them to finish
36 Muslims" (Chaturvedi et al. 2009). Several participants saw vaccines as a tool of "Western powers" to
37 control or harm their communities (Khowaja et al. 2012; Olufowote 2011). Some say that this is a
38 strategy to reduce our capacity to procreate so that there will be birth spacing". For others, vaccines
39 were "poisons created by white people to harm us and to do experiments on us in giving us diseases"
40 (Fourn et al. 2009) or they "are intended to kill off Africans" (Braka et al. 2012). This view could also be
41 supported and promoted by community and religious leaders: a Nigerian pastor admitted in an
42 interview "(...) to have voiced his constituents' beliefs that the polio vaccinations were part of a
43 Western plot to depopulate developing nations, particularly Muslim communities" (Olufowote 2011).
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47 Religious beliefs were another source of lack of trust in vaccines. An example of this belief was that
48 vaccination was against the will of God; vaccinating a child is like making a "deal with the Devil"; the
49 act of vaccination was seen as "the work of the white witch doctor, contrary to biblical scriptures"
50 (Fourn et al. 2009). Religious beliefs also affect the perception of effectiveness among faithful parents:
51 "Polio is due to mammy water (water mermaid). The solution is not immunisation. The solution is to
52 sacrifice to the mermaid by 12 midnight in any river close to where the child was born, on the night of
53 the child's birth. Once this is done, the child can never have polio" (Etokidem and Wondifon 2013).
54 Religious taboos were given as the first reason for non-vaccination in 8.2% and as the second reason
55 in 31.4% of people surveyed in Pakistan (Sheikh et al. 2013).
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58 One concern was actually rooted in a 'public health' rationale, reported by Khowaja as a quote from an
59 interview in Pakistan: "Why do the government and health system give so much emphasis to polio
60 vaccine? There are so many other diseases that should be addressed first. There must be some other
61 reason (negative reason) for their giving so much importance to polio vaccine" (Khowaja et al. 2012).
62
63

HEALTH SYSTEM ISSUES

1 Regarding health system issues, nine studies reported people's anxiety about health care workers
2 being unpleasant. One mother participating in a FGD in Burkina Faso explained: "The health care
3 worker shouts, is arrogant, argues, makes a fuss, is ill-tempered, uses awkward words and scolds
4 you" (Sia et al. 2011). As concluded by Perry et al. in their study in Bangladesh: "The fear of being
5 'scolded' by the vaccinator after losing the immunisation card (a not uncommon event), and the
6 necessity of having to pay to obtain a new one" was one of the major barriers to access vaccination
7 services (Etokidem and Wondifon 2013; Perry et al. 2007). Some mothers feared going to the health
8 facility for vaccination if they did not have a good enough "baby shawl" to carry the baby. They have
9 reported being harassed by nurses as a consequence of that (Babirye et al. 2011). Sheikh et al.
10 reported that 2.4% and 7.9% of people surveyed reported poor previous experience with physicians as
11 the first and second reasons for not vaccinating their children, respectively (Sheikh et al. 2013).
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14
15 Concerns related to costs of accessing immunisation services were also reported. Costs of the
16 immunisation card or transport or "under the table" payments represented some of the sources of
17 anxiety for caregivers. One mother explained during an in-depth interview in Gabon: "Somebody, who
18 has an outstanding debt [hospital bill] for example, if he does not have the financial means to settle the
19 debts, he cannot come back. Some people are actually afraid to come back" (Schwarz et al. 2009).
20 They also worried about spending some money to get to the health facility and then not being able to
21 get the vaccine. Frequent vaccine stock-outs lessen the confidence of parents on the health system
22 (Schwarz et al. 2009).
23
24

25 Participants in qualitative studies also raised concerns related to the quality of vaccines administered
26 at health facilities. Several issues were reported regarding vaccines being expired (Babirye et al. 2011;
27 Braka et al. 2012), weak cold chain (Braka et al. 2012; Fowler et al. 2007; Khowaja et al. 2012) or
28 health workers reusing syringes (Dasgupta et al. 2008). Concerns with vaccines purchased by the
29 government were reported in Kazakhstan and Uganda. Fowler et al. concluded in their study in
30 Kazakhstan: "The most widespread concern among key informants was that the government would
31 purchase low quality vaccines that could put children's health at risk" (Fowler et al. 2007).
32
33

OTHER ISSUES

34
35 Canavati found a specific concern from migrants in Thailand during a series of FGD. They were
36 worried of being arrested if they attended the clinic to vaccinate their children. As a father explained:
37 "We are afraid of the police. There are several checkpoints from our place to the vaccine site and we
38 can get arrested anytime (...) The only reason we would risk accessing a Thai clinic is when our child
39 is very ill because under those circumstances the Tai police would not do anything to us" (Canavati et
40 al. 2011).
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DISCUSSION

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46 We have exposed and synthesised evidence on individual and community concerns about childhood
47 vaccination and have highlighted the most frequently reported concerns in qualitative studies and
48 prevalence rates from quantitative studies. We have described the whole range of caregivers'
49 concerns about vaccination and their variations across geographical areas and cultural settings.
50
51

52 Concerns about harmful effects of vaccination seemed to be the most common factor influencing
53 vaccination behaviour, followed by mistrust of vaccination programmes. Other concerns were less
54 prevalent. Fear of side effects, fear of sterility or disability after vaccination or concerns about receiving
55 too many vaccines at once were some of the most commonly reported. Health system issues were
56 also widely reported as source of concerns. The lack of trust on vaccine effectiveness, concerns about
57 health staff being unpleasant or concerns about not being able to get the vaccine at the health facility
58 were reasons reported to avoid vaccination in some cases. This large array of issue only worsens
59 existing programmatic and health systems challenges (Favin et al. 2012) of childhood vaccination.
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1 Although there were concerns that were spread across most settings (e.g. the belief that vaccines
2 could produce serious negative effects on children’s health), they were highly influenced by cultural,
3 religious or social beliefs. For instance, concerns about vaccines being part of a conspiracy to harm
4 specific groups were common among Muslim communities and worries about the quality or cost of the
5 services provided were more reported in studies from African countries.

6 A number of systematic reviews addressed concerns to vaccination or similar issues. Some of them
7 are restricted to only one or a few vaccines (Brown 2010) or to non-childhood vaccines (European
8 Centre for Disease Prevention and Control 2013, Hendry 2013, Trim 2012) or focus on developed
9 geographical areas (European Centre for Disease Prevention and Control 2013, Falagas 2008) or
10 include only qualitative studies (Mills 2005). Rainey 2011 covers a limited and relatively old time period
11 (1999 to 2009), limiting the evidence to only published studies and explores “reasons and factors”
12 (rather than focusing on concerns) related to non-vaccination and under-vaccination in general. A
13 similar approach was used by Favin (Favin et al. 2012). Larson 2014 provided more recent evidence
14 (2007 to 2012) describing the frequencies of studies reporting concerns rather than the actual
15 descriptions of concerns and their reasons among the caregivers (Larson 2014).

16 There are reasonable doubts that all potentially relevant factors influencing vaccine hesitancy have
17 been identified or thoroughly investigated (Mills et al. 2005b, Larson et al. 2014). Indeed, a recent
18 review of studies conducted in high income countries showed that although reasons why parents
19 refuse to vaccinate their children have been widely studied, little is known about the factors that
20 motivate parents to vaccinate (Williams 2014). In their comparative analysis of concerns about
21 vaccination in qualitative and quantitative studies, Mills et al concluded that surveys failed to capture
22 the whole spectrum of concerns identified in previously published qualitative studies. Concerns
23 identified in qualitative studies were not properly represented in quantitative studies as questionnaires
24 did not include relevant items drawn from qualitative research. One explanation may be that, as we
25 realised, none of the quantitative studies estimating the frequency of different concerns in LMIC was
26 actually specifically designed to assess concerns; rather they were surveys examining wider issues
27 related to the uptake of vaccination, which included concerns.

28 Indeed, quantitative studies failed to capture many issues related to concerns about vaccination
29 identified in qualitative studies in our review (Table 8 in the Online Resource). It is clear that surveys
30 focused their questions on concerns related to the potential harms of vaccination. Fewer studies
31 reported quantitative data of issues related with distrust. For example, although concerns about
32 vaccines being part of a Western plot against Muslims or vaccines containing pig’s blood were
33 consistently reported in qualitative studies, only five of the 19 surveys provided some quantitative
34 estimates about it. Even a more extreme situation was found regarding health system issues: only two
35 studies reported quantitative data on this group of concerns. Concerns about the quality of vaccines
36 provided at the health facility or concerns about health workers being unpleasant were neglected in
37 the surveys included.

38 Several reviews of interventions to improve vaccination coverage report on strategies addressing
39 concerns. A review focusing on LMIC (Oyo-Ita 2011) identified three trials directly or indirectly related
40 to concerns. These studies were of moderate quality and showed promising effects on coverage rates;
41 two of them were the only two studies included in the review by Saeterdal et al ([Saeterdal 2014](#)). The
42 systematic review of Kaufman et al. (Kaufman 2013) included studies which assessed face-to-face
43 communication directed to individual parents and concluded that the low quality evidence available did
44 not seem to make any difference on vaccination status, knowledge or understanding of vaccination. In
45 this sense, it is deeply disappointing that Sadaf et al (Sadaf 2013) could only conclude that their
46 systematic review “did not reveal any convincing evidence on effective interventions to address
47 parental vaccine hesitancy and refusal”. Most of the research on interventions dealt with reminders,
48 recalls, and provider-based interventions and alike, but hardly any intervention addressed vaccine
49 refusal or changes in attitudes.

1 Not surprisingly, no strong recommendations could be issued by SAGE in terms of interventions to
2 address vaccine hesitancy. Recognising that no single intervention addresses all instances of vaccine
3 hesitancy, recommending generic marketing and communication concepts (such as “focusing on
4 benefits of immunization, drawing on emotional values, focusing on 1 or 2 key messages, employing
5 proactive messaging” (WHO 2014c)) fall very short of what could be expected. We believe that careful
6 consideration of the concerns that we have exposed in this review could inform some more concrete
7 recommendations till enough evidence on the effects of interventions to address concerns is available.

8
9 The findings in this review are subject to a number of limitations. We searched only for papers and
10 reports written in English, French, Spanish or Portuguese. We cross-checked previously identified
11 relevant studies to minimize the chances that relevant papers would have been excluded. Single study
12 inclusion decisions could have missed studies. However, we believe that double, independent
13 decisions on inclusion would not have substantially changed the conclusions of this review. Selective
14 reporting in both qualitative and quantitative studies could not be ruled out. Because we could not find
15 any study with the primary aim of describing concerns, it is likely that the prevalence of concerns
16 extracted from quantitative studies have limited external validity and that the literature tends to
17 underreport them.

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19
20 **CONCLUSIONS**

21 Highly influenced by social, cultural and religious beliefs, concerns about vaccinations are prevalent,
22 and impact the vaccination status of populations.

23
24 In the research domain, there is a disconnection between quantitative and qualitative research which
25 misses the opportunity to quantify what is reported in qualitative studies across different strata of
26 populations and geographical settings. There is an important imbalance where research describing
27 concerns is far more abundant than research testing interventions to address them. Assessing
28 interventions to address concerns remains a neglected research area.

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31 We encourage the global health community including WHO to continue its work on vaccine hesitancy,
32 prioritising research which explains the mechanisms of vaccine hesitancy and research which tests
33 interventions to address it. Appropriate funding should be made available for this work. In the absence
34 of robust evidence, guidance can still be produced to assist the global community and countries health
35 authorities to address concerns on childhood vaccination.

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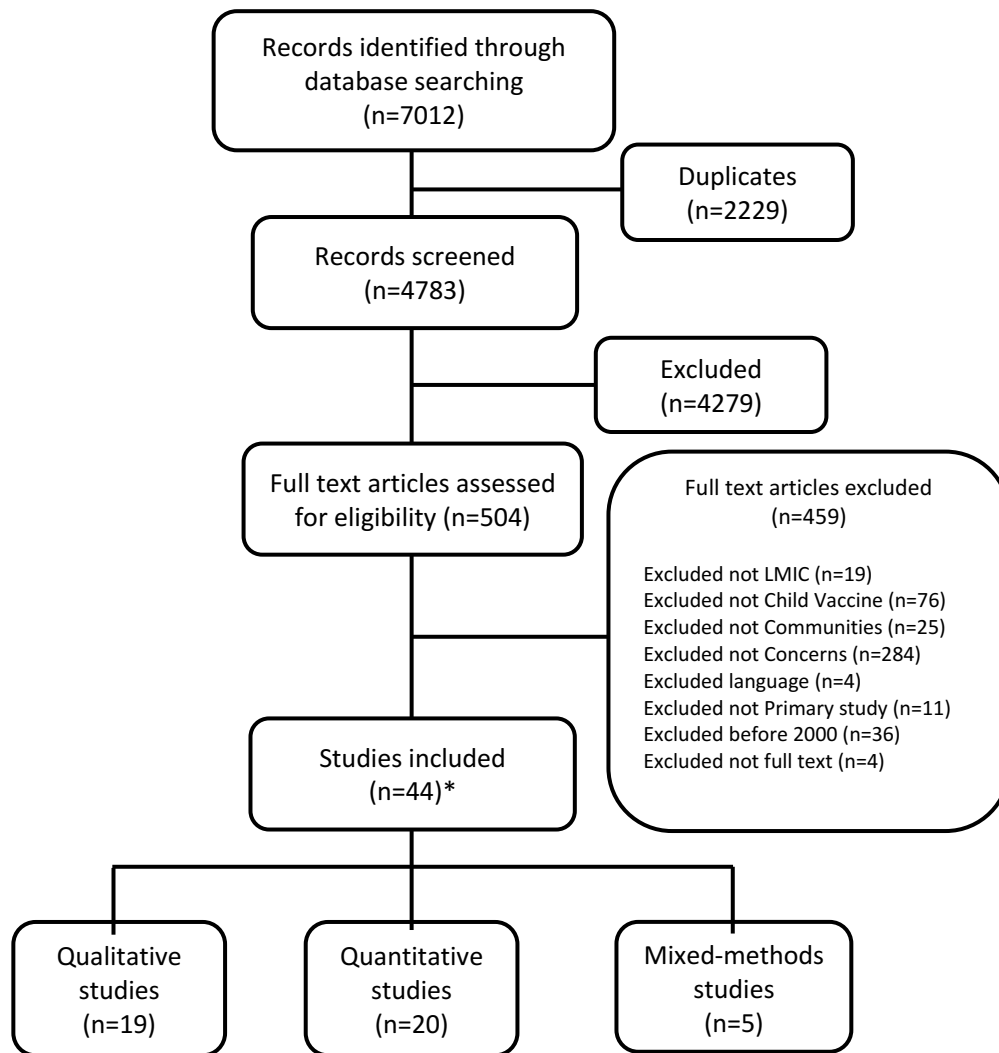
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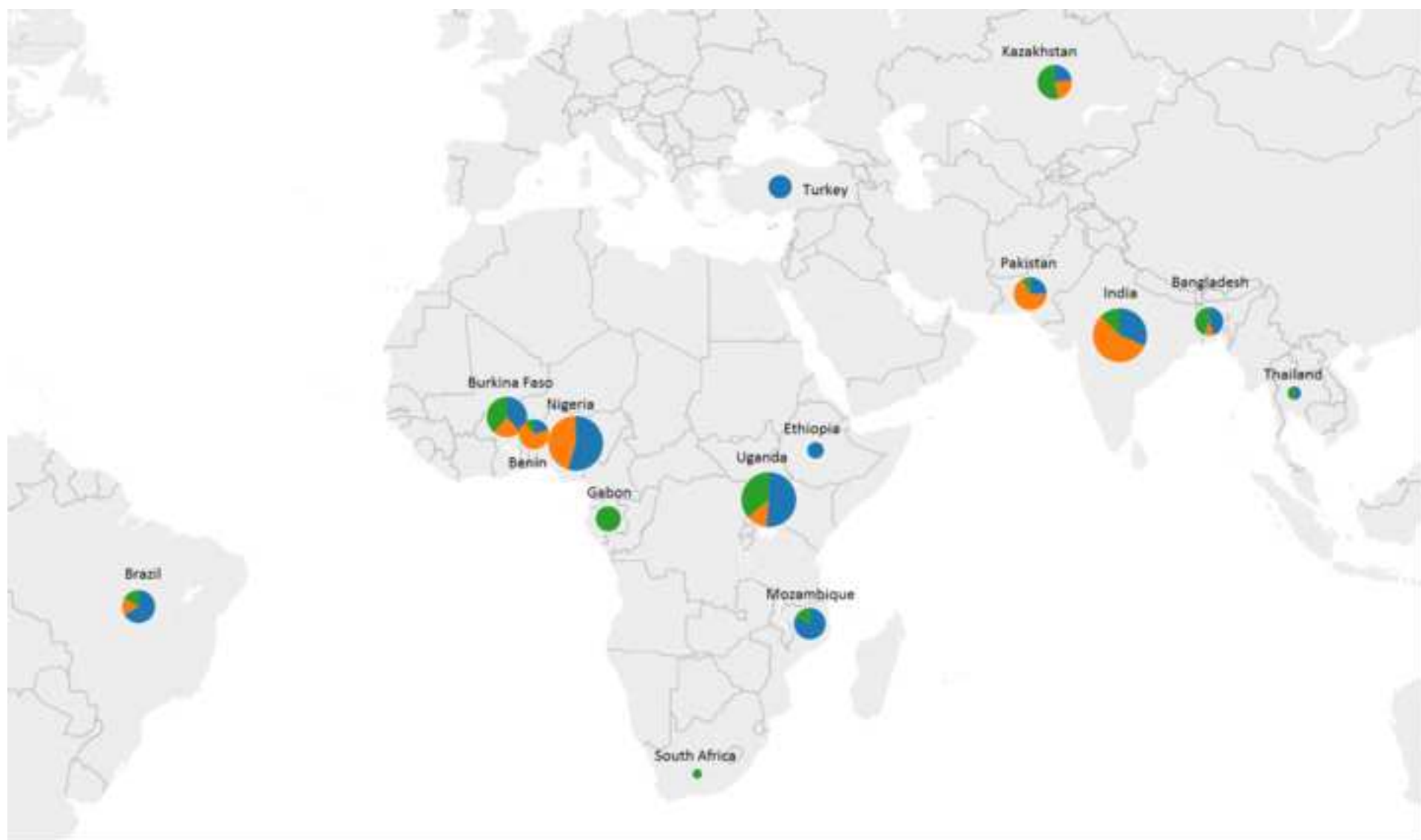
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EXPOSING CONCERNS ABOUT VACCINATION IN LOW AND MIDDLE INCOME COUNTRIES: A SYSTEMATIC REVIEW

Figure 1. Study flow diagram Search and screening results diagram of the systematic review on concerns about vaccination in low- and middle-income countries.



* One study was reported in two published articles (Logullo 2008)



Concerns

- 1. Issues with harmful effects of vaccines
- 2. Issues with mistrust
- 3. Issues with access/health system

Table 21. Ten most frequently reported concerns (as number of quotes) about vaccination from studies with qualitative data in the systematic review on concerns about vaccination in low- and middle-income countries.

Issue	Concern*	Number of quotes
Harm	1.2 Believes cause diseases / general harm / adverse effects	43
Trust	2.1 Conspiracy theory / distrust in medical community	26
Harm	1.4 Concern with side effects after vaccination	25
Trust	2.3 Religious reasons	17
Trust	2.2 Lack of trust in vaccines effectiveness	16
Health system	3.3 Health staff are unpleasant / untrained	15
Harm	1.8 Vaccines are provided at too young age / too many	13
Health system	3.5 Concern with quality of vaccines	12
Health system	3.1 Concern with cost / access	8
Other	4.2 Social stigma for mothers that vaccinate	7

*Concerns are classified according to the items in table 1.

Table 32. Frequency of concerns from studies reporting survey data, by type of concern and country in the systematic review on concerns about vaccination in low- and middle-income countries.

Reference	Country	Vaccines	Type study	Concern	Participants subgroup	Frequency	Methodological quality
1. Issues with harm							
1.1. Believes that vaccination is immune compromising							
Akmatov 2009	Kyrgyzstan	General	KAP	Believe immune system is weakened	All	62.0%	Moderate
1.2 Believes cause diseases / general harm / adverse effects							
Joseph 2011	India	Polio	RNV	Believe that repeated OPV administration causes harm to children	All	57.8%	Weak
Kaur 2010	India	General	KAP	Believe vaccination is not good for health	Totally immunized children	5.7%	Weak
Kaur 2010	India	General	KAP	Believe vaccination is not good for health	Partially immunized children	10.3%	Weak
Kaur 2010	India	General	KAP	Believe vaccination is not good for health	Unimmunized children	48.0%	Weak
Qutaiba 2014	Iraq	General	KAP	Believe that vaccination is harmful	All	43.0%	Weak
Akmatov 2009	Kyrgyzstan	General	KAP	Believe vaccination are not harmless	All	3.0%	Moderate
Sheldon 2003	Mozambique	General	RNV	Believe that vaccine cause diseases	All	1.0%	Weak
Abdulraheem 2011	Nigeria	General	RNV	Parents objection, disagreement or concern about immunisation safety	All	38.8%	Weak
Babalola 2011	Nigeria	General	RNV	Because Myths and rumours related to negative health consequences	Not immunized	11.1%	Weak
Babalola 2011	Nigeria	General	RNV	Because Myths and rumours related to negative health consequences	Partial immunisation	10.0%	Weak
Obute 2007	Nigeria	Polio	KAP	Believed that oral polio vaccine (OPV) contained harmful pathogens	All	7.3%	Weak
Oladokun 2010	Nigeria	General	KAP	Agree that immunisation can harm the child	All	32.7%	Weak
Oladokun 2010	Nigeria	General	KAP	That not sure that immunisation can harm the child	All	27.8%	Weak
Oladokun 2010	Nigeria	General	RNV	Fear of adverse side effects	All	6.5%	Weak
Naeem 2011	Pakistan	Pentavalent	KAP	With misconceptions about vaccine like sterility/being harmful	Negative views	40.2%	Weak

Reference	Country	Vaccines	Type study	Concern	Participants subgroup	Frequency	Methodological quality
Naeem 2011	Pakistan	Pentavalent	KAP	With fear to reactions after administration	Negative views	34.3%	Weak
Naeem 2012	Pakistan	Polio	RNV	Wrong ideas / sterility	All	3.3%	Weak
Naeem 2012	Pakistan	Polio	RNV	Wrong ideas / sterility	Not useful to vaccinate	21.6%	Weak
1.3 Believes will be harmful if the child is sick							
Sheldon 2003	Mozambique	General	KAP	Believe that vaccination can be dangerous if the child is sick	All	22.8%	Weak
Torun 2008	Turkey	General	RNV	Because illness of child and misinformation about side effects of vaccination during illness and contra-indications	Non/uncompleted vaccination	11.4%	Weak
1.4 Concern with side effects after vaccination (including pain)							
Uddin 2008	Bangladesh	General	RNV	Afraid of side effects	All	11.0%	Weak
Angadi 2013	India	General	RNV	Fear to side effects	All	13.0%	Weak
Abdulraheem 2011	Nigeria	General	RNV	Complications from previous injections	All	19.0%	Weak
Babalola 2011	Nigeria	General	RNV	Because Fear of side effects	Not immunised	1.1%	Weak
Babalola 2011	Nigeria	General	RNV	Because Fear of side effects	Partial immunisation	2.7%	Weak
Asfandyar 2013	Pakistan	Polio	RNV	do not vaccinate due to fear to side effects*	All	5.1%	Weak
Asfandyar 2013	Pakistan	Polio	RNV	do not vaccinate due to fear to side effects Ψ	All	16.3%	Weak
Naeem 2012	Pakistan	General	RNV	That have fear of reactions	Not useful to vaccinate	1.3%	Weak
Naeem 2012	Pakistan	Polio	RNV	Fear of reactions	All	2.4%	Weak
Naeem 2012	Pakistan	Polio	RNV	Fear to reactions	Not useful to vaccinate	35.3%	Weak
Namuigi 2005	PNG	Measles	RNV	Believed that side effects are too bad	All	38.0%	Weak
Koruk 2013	Turkey	General	RNV	That had fear to side effects	All	11.9%	Weak
Torun 2006	Turkey	General	RNV	Because illness of child and misinformation about the side effects of vaccines	Non or uncompleted vaccination	18.8% [0.7-19%]	Weak
1.5 Parents remembered their own or other adverse experiences							
Naeem 2011	Pakistan	Pentavalent	KAP	With previous bad experience	Negative views	3.0%	Weak

Reference	Country	Vaccines	Type study	Concern	Participants subgroup	Frequency	Methodological quality
Naeem 2012	Pakistan	Polio	RNV	Previous bad experience	Not useful to vaccinate	7.8%	Weak
1.7 Fear to needles							
Asfandyar 2013	Pakistan	Polio	RNV	Do not vaccinate due fear of exposing child to needles	All	6.3%	Moderate
1.8 Vaccines are provided at too young age / too many							
Joseph 2011	India	Polio	KAP	Believe that repeated vaccination leads to over dosage and this is harmful	All	2.2%	Weak
Akmatov 2009	Kyrgyzstan	General	KAP	Believe too many vaccines	All	62.0%	Moderate
Sheldon 2003	Mozambique	General	KAP	Believe that vaccination can be dangerous to receive more than one vaccine/day	All	26.9%	Weak
Obute 2007	Nigeria	Polio	KAP	Believed that there could be polio vaccine overdose due to repeated vacc.	All	39.6%	Weak
Namuigi 2005	PNG	Measles	RNV	Believed that there were too many injections	All	17.0%	Weak
2.2 Lack of trust in vaccines effectiveness							
Ambe 2001	Nigeria	Measles	RNV	That do not believe it works	All	27.2%	Weak
Asfandyar 2013	Pakistan	Polio	RNV	Do not vaccinate due to vaccination not considered effective*	All	3.3%	Weak
Asfandyar 2013	Pakistan	Polio	RNV	Do not vaccinate due to vaccination not considered effective Ψ	All	12.1%	Weak
Naeem 2011	Pakistan	Pentavalent	KAP	Considering vaccine ineffective	Negative views	19.4%	Weak
Naeem 2012	Pakistan	Polio	RNV	Believe vaccination is not effective	Not useful to vaccinate	35.3%	Weak
2.3 Religious reasons							
Asfandyar 2013	Pakistan	Polio	RNV	Do not vaccinate due to religious taboos*	All	8.2%	
Asfandyar 2013	Pakistan	Polio	RNV	Do not vaccinate due to religious taboos Ψ	All	31.4%	Weak
2.4 Not enough information							
Manjunath 2003	India	General	KAP	Lacked information about the programme	All	9.7%	Weak
3.3 Health staff are unpleasant / untrained							
Asfandyar 2013	Pakistan	Polio	RNV	Do not vaccinate due to poor previous experience with physicians*	All	2.4%	Weak
Asfandyar 2013	Pakistan	Polio	RNV	Do not vaccinate due to poor previous experience with physicians Ψ	All	7.9%	Weak
3.4 Concern with not being able to get the vaccine							

Reference	Country	Vaccines	Type study	Concern	Participants subgroup	Frequency	Methodological quality
Logullo 2008	Brazil	General	KAP	Number with concern about not getting the vaccine at the care centre	All	98 of 122	Moderate
4.1 Miscellaneous concerns							
Abhijeet 2013	India	General	RNV	That had false beliefs	Incomplete immunisation	17.8%	Weak
Manjunath 2003	India	General	RNV	Had misconceptions/beliefs about immunisation such as fever after immunisation for a healthy child might be harmful, too any doses, elders believed that vaccines are not needed	All	25.2%	Weak
Naeem 2011	Pakistan	Pentavalent	KAP	That had negative views	All	11.2%	Weak

RNV: Reason for non-vaccination

KAP: Knowledge, attitudes and practices survey

PNG: Papua New Guinea

* % of participants that gave this reason for non-vaccination in the FIRST place

ψ % of participants that gave this reason for non- vaccination in the SECOND place

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