APPENDICES TO THE REPORT OF THE SAGE WORKING GROUP ON VACCINE HESITANCY

01 October 2014

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Appendix for Section 3

Appendix A3.1: Review of Models of Determinants of Vaccine Hesitancy

The 2011 Determinants of Vaccine Hesitancy Model from Canada (Figure A3.1) while illustrating the wide array of determinants and factors was felt to be thoughtful and useful for academic work but too complex for practical application in the field.

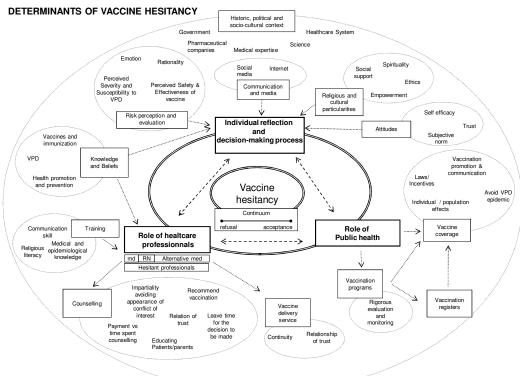


Figure A 3.1 Determinants of Vaccine Hesitancy: Canadian Model

Adapted from results of the "Workshop on the cultural and religious roots of vaccine hesitancy: Explanations and implications for the Canadian healthcare system", Guay and coll., Sherbrooke University, Longueuil, December 5-6 2012

The Working Group also explored arranging factors that impinge on vaccine hesitancy in a systems approach matrix that grouped factors into three main categories of influences: contextual, individual and group and vaccine /vaccination specific influences (Table A3.1, Figure A3.2). Contextual influences were defined as influences that arise due to historic, sociocultural, institutional, economic or political factors; individual and group influences as influences that arise from personal perception or influences of the social /peer environment and vaccine /vaccination specific influences as influences directly related to the vaccine or vaccination. Again the Working Group emphasized that Table A3.1 presented a very complex matrix. Several Working Group members initially commented that while this "influencer" matrix might work well in high income countries, they had concerns that important factors affecting

vaccine hesitancy in low income countries might not fit in well and that the model might hamper thinking in determination of the roots of vaccine hesitancy in these settings. Table A3.1 was modified and simplified into the Working Group Matrix (Table 3.1above) to address these concerns. This Matrix is seen as especially potentially useful in selecting vaccine hesitancy indicators and survey questions (Table 3.2 above). Later review of the Working Group Matrix in terms of the determinants raised in the Working Group systematic review of the literature on determinants (Section 4), review of other published review studies on determinants (Section4) and the findings from the Immunization Managers Survey by the Working Group (Section 4) did not raise any new determinants that could not be fitted into the Working Group Matrix and hence the Working Group Matrix was accepted.

Figure A3.2. Systems Approach to Understanding Reasons for Vaccine Hesitancy

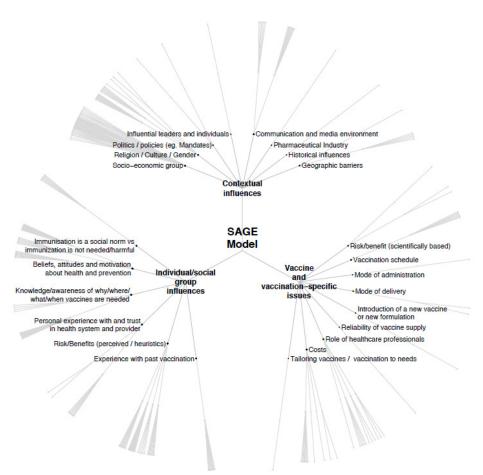


Table A3.1 A model to identify determinants of vaccine hesitancy

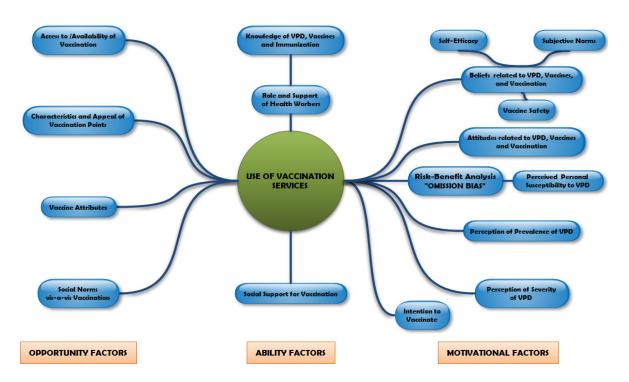
CONTEXTUAL	a.Communication	b. Influential	c.Historical	d.Religion/culture/ge	e. Politics/policies	f.Geographic	g.Pharmaceutic
<u>INFLUENCES</u>	and media	leaders,	influences	nder/socio-economic	(Mandates)	barriers	al industry
	environment	gatekeepers and					
Influences		anti- or pro-	Historic influences	A few examples of the	Vaccine mandates	A population can	Industry may be
arising due	Media and social	vaccination	such as the	interplay of	can provoke vaccine	have general	distrusted and
to historic,	media can create	lobbies	negative experience	religious/cultural	hesitancy not	confidence in a	influence
•	a negative or		of the Trovan trial	influences include:	necessarily because	vaccine and health	vaccine
socio-	positive vaccine	Community	in Nigeria can		of safety or other	service, and be	hesitancy when
cultural,	sentiment and	leaders and	undermine public	Some religious	concerns, but due to	motivated to receive	perceived as
environment	can provide a	influencers,	trust and influence	leaders prohibit	resistance to the	a vaccine but	driven only by
al, health	platform for	including religious	vaccine acceptance,	vaccines	notion of forced	hesitate as the	financial
system/instit	lobbies and key	leaders in some	as it did for polio,		vaccination	health center is too	motives and not
utional,	opinion leaders to	settings,	especially when	Some cultures do not		far away or access is	in public health
economic or	influence others;	celebrities in	combined with	want men vaccinating		difficult.	interest; This
	social media	others, can all	pressures of	children			can extend to
political	allows users to	have a significant	influential leaders				distrust in
factors	freely voice	influence on	and media. A	Some cultures value			government
	opinions and	vaccine	community's	boys over girls and			when perceived
	experiences and it	acceptance or	experience isn't	fathers don't allow			that they are
	can facilitate the	hesitancy.	necessarily limited	children to be			also being
	organization of		to vaccination but	vaccinated),			pushed by
	social networks		may affect it.				industry and not
	for or against						transparent.
	vaccines .						

INDIVIDUAL and GROUP INFLUENCES Influences arising from personal perception of the vaccine or influences of the social/peer environment	a. Experience with past vaccination Past negative or positive experience with a particular vaccination can influence hesitancy or willingness to vaccinate. Knowledge of someone who suffered from a VPD due to non- vaccination may enhance vaccine acceptance. Personal experience or knowledge of someone who experienced an AEFI can also influence hesitancy.	b.Beliefs, attitudes about health and prevention Vaccine hesitancy can result from 1) beliefs that vaccine preventable diseases (VPD) are needed to build immunity (and that vaccines destroy important natural immunity) or 2) beliefs that other behaviors (breastfeeding, traditional/alternativ e medicine or naturopathy) are as or more important than vaccination to maintain health and prevent VPDs.	c.Knowledge/aware ness Decisions to vaccinate or not are influenced by a number of the factors addressed here, including level of knowledge and awareness. Vaccine acceptance or hesitancy can be affected by whether an individual or group has accurate knowledge, a lack of awareness due to no information, or misperceptions due to misinformation. Accurate knowledge alone is not enough to ensure vaccine acceptance, and misperceptions may cause hesitancy, but still result in vaccine acceptance.	d. Health system and providers-trust and personal experience. Trust or distrust in government or authorities in general, can affect trust in vaccines and vaccination programmes delivered or mandated by the government. Past experiences that influence hesitancy can includes system procedures that were too long or complex, or personal interactions were difficult.	e. Risk/benefit (perceived, heuristic) Perceptions of risk as well as perceptions of lack of risk can affect vaccine acceptance. Complacency sets in when the perception of disease risk is low and little felt need for vaccination. E.g. Patient's or caregiver's perceptions of their own or their children's risk of the natural disease or caregivers' perceptions of how serious or life threatening the VPD is.	f. Immunisation as a social norm vs. not needed/harmful Vaccine acceptance or hesitancy is influenced by peer group and social norms
	suffered from a VPD due to non- vaccination may enhance vaccine acceptance. Personal experience or knowledge of someone who experienced an AEFI can also influence	traditional/alternativ e medicine or naturopathy) are as or more important than vaccination to maintain health and	knowledge, a lack of awareness due to no information, or misperceptions due to misinformation. Accurate knowledge alone is not enough to ensure vaccine acceptance, and misperceptions may cause hesitancy, but still result in vaccine	too long or complex, or personal interactions		

VACCINE/	a. Risk/ Benefit	b. Introduction of	c. Mode of	d. Design of	e. Reliability	f. Vaccination	g. Costs	h. Role of
VACCINATION	(scientific	a new vaccine or	administrati	vaccination	and/or source of	schedule		healthcare
-specific	evidence)	new formulation	on	program/Mo	vaccine supply		An individual	professionals
issues				de of		Although there may	may have	
<u>155065</u>	Scientific	Individuals may	Mode of	delivery	Individuals may	be an appreciation	confidence in a	
	evidence of	hesitate to accept	administratio		hesitate if they do	for the importance	vaccine's safety	Health care
Directly	risk/benefit and	a new vaccine	n can		not have	of preventing	and the system	professionals
related to	history of safety	when they feel it	influence	Delivery	confidence in the	individual vaccine	that delivers it,	(HCP)are important
vaccine or	issues can	has not been	vaccine	mode can	system's ability to	preventable	be motivated to	role models for their
vaccination	prompt	used/tested for	hesitancy for	affect vaccine	provide vaccine(s)	diseases, there may	vaccinate, but	patients; if HCPs
10.00	individuals to	long enough or	different	hesitancy in	or might not have	be reluctance to	not be able to	hesitate for any
	hesitate, even	feel that the new	reasons. E.g.	multiple	confidence in the	comply with the	afford the	reason (e.g. due to
	when safety	vaccine is not	oral or nasal	ways. Some	source of the	recommended	vaccine or the	lack of confidence in
	issues have	needed, or do not	administratio	parents may	supply (e.g. if	schedule (e.g.	costs associated	a vaccine's safety or
	been clarified	see the direct	ns are more	not have	produced in a	multiple vaccines or	with getting	need) it can
	and/or	impact of the	convenient	confidence in	country/culture the	age of vaccination).	themselves and	influence their
	addressed	vaccine (e.g. HPV	and may be	a vaccinator	individual is		their child(ren)	clients' willingness
	e.g. suspension	vaccine preventing	accepted by	coming	suspicious of);	Vaccination	to the	to vaccinate
	of rotavirus	cervical cancer).	those who	house-to-	health workers may	schedules have	immunization	
	vaccine due to	Individuals may be	find	house; or a	also be hesitant to	some flexibility that	point.	
	intussusception;	more willing (i.e.	injections	campaign	administer a	may allow for slight	Alternatively,	
	Guillain-Barre	not complacent)	fearful or	approach	vaccine (especially	adjustment to meet	the value of the	
	syndrome	to accept a new	they do not	driven by the	a new one) if they	individual needs	vaccine might	
	following swine	vaccine if	have	government.	do not have	and preferences.	be diminished if	
	flu vaccine	perception of the	confidence in	Alternatively	confidence that the	While this may	provided for	
	(1976) or	VPD risk is high.	the health	if a health	supply will continue	alleviate hesitancy	free.	
	narcolepsy		workers skills	centre is too	as it affects their	issues,		
	(2011) following		or devices	far or the	clients trust in	accommodating		
	(A)H1N1		used.	hours are	them.	individual demands		
	vaccination;			inconvenient	Caregivers may not	are not feasible at		
	milder, local				have confidence	a population level.		
	adverse events				that a needed			
	can also				vaccine and or			
	provoke				health staff will be			
	hesitancy.				at the health			
					facility if they go			
					there.			

Another model reviewed by the Working Group was the complex conceptual model from WHO EURO (Figure A3.3) with factors arranged into *opportunity*, *ability* and *motivational* categories with further breakdown into subcategories for each was also examined.

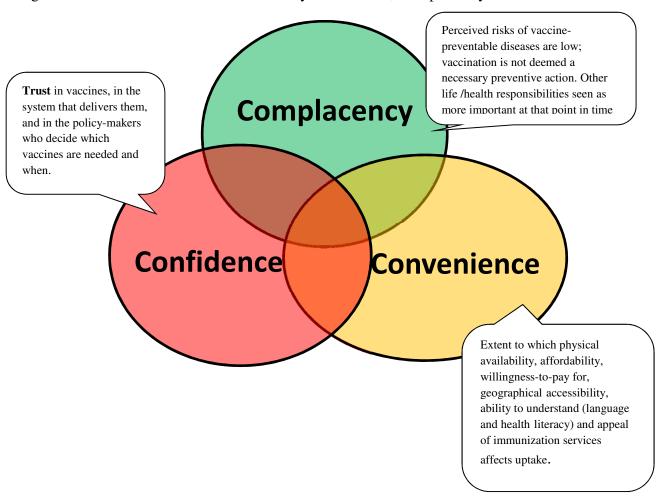
Figure A3.3 A Conceptual Model for Determining Use, Under-Use and Non-Use of Vaccination services. WHO EURO



This model forcefully emphasized the complexity of vaccine hesitancy and the many potentially inter acting factors. While these categories were seen as easier to grasp than the contextural influencer terminology (Figure A3.2 and Table A3.1), this was such a complex model that several Working Group members noted that it would be more useful for research than for application in the field. Thus inclusion of these categories with the complexity they implied in the definition of vaccine hesitancy did not seem useful. Finding a vaccine hesitancy workable model that used easily understood terminology, applicable in both HIC and LIC settings and yet illustrating that factor groupings might overlap and aggravate vaccine hesitancy tendencies was the goal. These more complex matrixes however, were useful in the work on the systematic literature review of vaccine hesitancy including examination of potential strategies and interventions.

The Confidence, Complacency, and Convenience Model: The final model examined was a more simplified conceptual framework also based upon work done in WHO EURO. In this model, the terminology for the factor groups is: *confidence*, *complacency* and *convenience* with overlap not only possible but in some settings probable (Figure A3.4).

Figure A3.4. The 3 C's of Vaccine Hesitancy: Confidence, Complacency and Convenience



In further discussion the Working Group noted that understanding how barriers to vaccine uptake belonging to one or many of the 3 Cs could be important in the design of activities and strategies that could have a positive impact on vaccine hesitancy. These issues require different types of interventions (convenience issues call for activities and strategies such as reducing costs or enhancing geographic access to vaccination services, while confidence issues might need education, counselling support etc.). The Working Group incorporated this very simplified 3 C's determinants concept into the definition of vaccine hesitancy.

In conclusion the Working Group judged that the 3"C" model was the easiest to grasp and a simplified version of the Working Group Matrix was developed. (See main text)

Appendix for Section 4

Appendix A4.1: Systematic review on vaccine hesitancy

Published on WHO SAGE website:

http://www.who.int/immunization/sage/meetings/2013/april/2_Systematic-

lit_Review.pdf?ua=1, accessed 03.10.2014

Appendix A4.2: Mapping vaccine hesitancy- Country specific characteristics of a global phenomenon

Mapping vaccine hesitancy: Country specific characteristics of a global phenomenon **Authors**: Eve Dubé PhD^{a,b,c}, Dominique Gagnon MSc^a, Emily Nickels MSPH^d, Stanley Jeram MD^d, Melanie Schuster MD^d.

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Abstract

Vaccine hesitancy refers to delay in acceptance or refusal of vaccines despite availability and quality of vaccine service. Vaccine hesitancy is complex and context specific varying across time, place and vaccines. It includes factors such as complacency, convenience and confidence. Several hypotheses attempt to explain why acceptance of vaccines is decreasing. The Strategic Advisory Group of Experts (SAGE) on Immunization recognized the global importance of vaccine hesitancy and recommended that an interview study be conducted with immunization managers (IM) to better understand the variety of vaccine hesitancy challenges existing on the ground. Interviews with 13 selected IMS were conducted between September and December 2013. Challenges around vaccine hesitancy were found. The term was not consistently defined and many IMs interpreted it as vaccine refusal. Although vaccine hesitancy existed in all 13 countries surveyed, some IMs considered the impact of vaccine hesitancy on immunization programs as a minor problem. The causes of vaccine hesitancy were variable and context-specific suggesting the need to strengthen the capacity of countries to identify context-specific factors and to develop adapted strategies to address them.

Keywords: Vaccine hesitancy, immunization, determinants, vaccination, interviews. immunization managers

Mapping vaccine hesitancy- Country specific characteristics of a global phenomenon

1. Introduction

Vaccine hesitancy refers to delay in acceptance or refusal of vaccines where uptake of a vaccine or the immunization program in a community is lower than would be expected in the context of information provided and the services available. Vaccine hesitancy is complex and context specific varying across time, place, and vaccines. It recognizes that factors such as complacency, convenience, as well as confidence in vaccines(s) or immunization programs may all contribute to the delay or refusal of one, some or almost all vaccines [1].

Many factors influence the decision to demand, accept, delay or refuse immunization. Several hypotheses have been put forward to try to explain why acceptance of vaccines is decreasing. In high income countries, one factor maybe decreased visibility or absence of vaccine preventable diseases leading to questioning of the necessity of vaccination and a waning of trust in vaccines. Discussions in the general population in HIC about the utility and practicality of vaccines have increased [2-5]. However, in low- and middle-income countries where vaccine-preventable diseases—still pose a more imminent threat to public health, absence or decreased in their visibility does not explain the decrease in vaccine acceptance [6-9]. This suggests different underlying determinants maybe contributing to hesitancy to receive vaccination [3].

The Strategic Advisory Group of Experts (SAGE) on Immunization recognized the global importance of vaccine hesitancy as an emerging issue. At the November 2011 meeting, SAGE welcomed the decision to create a working group to address this issue. The SAGE Working Group on Vaccine Hesitancy was established in March 2012 with the mandate to prepare for a SAGE review and advice on how to address vaccine hesitancy and its determinants [10]. In April 2013, following the presentation of the Working Group's interim findings, SAGE recommended that interviews be conducted with immunization managers in order to better understand the variety of challenges existing on the ground [1, 3].

This paper reports the results of the interviews conducted with selected immunization managers from different regions between September and December 2013. It is a first attempt to broadly assess the status of vaccine hesitancy on a global level from the perspective of different national immunization managers.

2. Methods

The SAGE Working Group developed a telephone-based interview guide designed to qualitatively capture unanticipated responses whilst assessing known determinants of vaccine hesitancy. Data were collected using semi-structured interviews, the standard method to explore complex phenomena [11, 12].

In order to create a representative sample of countries with a broad range of socio-economic contexts and population sizes over all regions, purposive sampling technique was used. Criteria for selection included:

- i. Representation from all six WHO Regions orchestrated by the WHO regional offices, Africa (AFR), Europe (EUR), Eastern Mediterranea (EMR), Americas (AMR), South-East Asia (SEAR), and Western Pacific (WPR);
- ii. Representation from the three economic categories recognized by the World Bank: low, middle and high income countries (respectively, LIC, MIC, and HIC) [13].
- iii. To be eligible for the interview, the national immunization manager had to be experienced and responsive.

In consultation with WHO immunization regional advisors, 15 countries were selected that together met the range of criteria. Key staff from WHO regional offices contacted immunization managers from each of the selected countries. In order to improve response rate, an introductory email was sent from WHO to the immunization managers outlining the request and the importance of the data collection. Countries who had not responded to the initial email within one month were sent a reminder email from WHO.

The semi-structured interview was conducted by two interviewers from WHO. To ensure consistency, the interviewers remained the same throughout the study. Interviews were conducted in English, Spanish, or French.

The interviews were recorded and summarized by the interviewer. Interview transcription was sent back to all immunization managers for approval; if needed, changes were made to more accurately reflect the country's situation. A structured electronic data extraction form was developed with predefined data fields for extracting consistent data. For all interviews, data were extracted and entered by two independent researchers at WHO and *Institut National de Santé Publique du Québec*, Canada. A third independent senior researcher checked for accuracy and completeness of the two datasets. In order to ensure consistency, the two datasets were combined and discrepancies were highlighted. In case of discrepancies, reasons were assessed by the senior researcher. These were then discussed by the research team until a decision about relevance was reached by consensus. If there was no agreement, the senior researcher adjudicated to make a final decision. Data analysis was conducted by the researchers from *Institut National de Santé Publique du Québec* with thorough experience in the field of qualitative research. Data were analyzed by question and mapped against a matrix of determinants developed by the Vaccine Hesitancy Working Group [14].

3. Results

Interviews were conducted with 13 immunization managers from the six different WHO regions: 2 from the AFR (Congo, Zimbabwe), 1 from the SEAR (India), 2 from the EMR (Saudi Arabia, Yemen), 3 from the EUR (Armenia, Belgium, Montenegro), 4 from the WPR (Japan, Lao PDR, Malaysia, The Republic of the Philippines), 1 from the AMR (Panama) and

represented mostly low and middle income countries (n=11). Interviews lasted an average 30 minutes.

3.1. *Definition of vaccine hesitancy*

Four immunization managers explicitly defined their understanding of vaccine hesitancy. One defined hesitancy as "those persons resisting to get vaccinated due to various reasons" and another mentioned "someone who does not believe vaccines are working and are effective and that vaccines are not necessary". A third indicated that hesitancy was twofold and included 1) "parents who would not allow immunization of their child" and 2) "policy makers who hesitate to introduce a vaccine especially in regard to new vaccines vs other existing public health interventions". The fourth defined vaccine hesitancy as "an issue that should be addressed when reaching 90% vaccination coverage". Although other immunization managers' views regarding vaccine hesitancy were less explicit, most (n=9) associated vaccine hesitancy with parental refusal of one or more vaccines. Vaccination delays were not included in vaccine hesitancy by immunization managers, except in one country, where the immunization managers stated: "There is not a problem with undervaccinated or unimmunized. There are issues with timely vaccination — with following the schedule. Parents are delaying the vaccines". Table 1 summarizes immunization managers' opinions regarding vaccine hesitancy in their country.

3.2. Impact of vaccine hesitancy on the country's' immunization program

At the time of the interview, all except one immunization manager had heard reports of people hesitating to accept one or all vaccines in their country. In the country where no reports had been heard, the actual problem reported was vaccine refusal due to religious beliefs, not hesitancy). In another country, the immunization manager had not heard of any reports of vaccine hesitancy, but acknowledged that a small proportion of the whole population had some concerns regarding vaccine safety and could be considered as vaccine-hesitant.

In several countries, immunization managers reported current or past issues of lack of acceptability related to one specific vaccine or to specific combinations of vaccines. These vaccines included: tetanus toxoid vaccine (TT); combined vaccine against diphtheria, tetanus, and pertussis (DTaP); combined vaccine against measles, mumps and rubella (MMR) or measles vaccine; oral polio vaccine (OPV); vaccine against human papilloma virus (HPV); influenza vaccine; vaccine against tuberculosis (BCG) and combined vaccine against diphtheria, tetanus, pertussis, polio and *Haemophilus influenzae* type b (pentavalent vaccine).

Even if with reports of vaccine hesitancy in their country, 11 out of 13 immunization managers did not consider vaccine hesitancy to be common and felt it did not have a significant impact on the uptake in the routine immunization programs. Immunization managers from two countries indicated that mass immunization campaigns, and not routine

immunization programs, were affected by vaccine hesitancy. Two immunization managers indicated that vaccine hesitancy was an important issue in their country.

When immunization managers were asked about the percentage of non- and under-vaccinated individuals in their country due to lack of confidence, eight of 13 provided estimates ranging from less than 1% to 30% (Table 1). Five did not answer. Only one immunization manager cited the two seasonal uptake estimates for OPV to support the estimate while three others either had planned to quantify the extent of the problem in their countries or had recently completed a survey.

Three immunization managers reported issues of complacency in their countries. In contrast, four other immunization managers stated that there were no issues of complacency because immunization was perceived as a priority by most of the population. Another immunization manager stated that there were complacency issues among a particular indigenous group who had refused vaccination because vaccination activities coincided with a cultural event. The other immunization managers did not respond to this question.

Seven of the 13 immunization managers perceived convenience/access issues to be important. Convenience issues were associated with sub-populations not using the health services provided (e.g. illegal settlers) or hard-to-reach population (e.g. conflict areas and refugee camps or remote communities). In one country, more than 25% of the population has no access to health services. In this country, access is challenging for immigrants, refugees, nomad populations, those living in remote areas and women (mainly because of the socionorms that they need somebody to travel with them if they need to get healthcare). In another country, convenience was not major issue, because barriers to access such as language or culture are handled and addressed locally. The only sub-group that was said to potentially experience convenience issues were migrant populations.

3.3. Determinants of vaccine hesitancy using the Working Group matrix

Figure 1 summarizes immunization managers' opinions for their country regarding the determinants of vaccine hesitancy in the matrix developed by the Working Group.

3.3.1. Contextual influence

Religious beliefs were often associated with vaccine hesitancy by nine of 13 immunization managers. Several were able to specifically identify religious groups in their country that were known to be opposed to all vaccines while others discussed "religious reasons" without specifically identifying a religion or a group. Religious beliefs were mostly linked to refusal of all vaccines, except in one country, where there were specific problems of acceptance of the HPV vaccine among those who were Catholic. Other groups associated with vaccine hesitancy were ethnic or indigenous groups, people of higher socioeconomic status and people living in urban areas. One immunization manager indicated that the older generation

was more hesitant than the younger generation and another, that women were more hesitant than men.

Six of 13 immunization managers mentioned the role of influential leaders in increasing vaccine hesitancy among the population. These leaders were associated with anti-vaccination groups, religious groups or health professional groups.

Five of 13 immunization managers identified causes of vaccine hesitancy linked to the "communication and media environment". Two immunization managers spoke broadly about "rumors and misconceptions" regarding vaccination circulating in their country and three directly identified negative information conveyed in the mass media (television and internet) as causes of vaccine hesitancy.

Six immunization managers identified the involvement of geographic barriers in reducing access to vaccination services, but the association with vaccine hesitancy was not clear. In one country, political conflicts and instability leading to poverty, internal population displacements and insecurity, could partially explain vaccine hesitancy. More than one quarter of the population has no access to health services, as noted above. Access to services was stated to be particularly difficult for women.

Finally, in one country, vaccine hesitancy was mostly clustered around illegal settlers or immigrants without an official status. These individuals hesitate to use health services because of fear of being reported to the police, even though the Expanded Programme on Immunization (EPI) offers immunization with permission from the government.

3.3.2. Individual and group influences

Three main determinants of vaccine hesitancy pertaining to individual and group influences were identified. First, seven of 13 immunization managers identified risk perceptions as associated with vaccine hesitancy. This included concerns regarding vaccine safety, lack of perceived benefits of vaccination and lack of understanding the burden of vaccine-preventable diseases.

Second, seven immunization managers identified issues to the population's trust in the health system and health providers. One noted that how people were treated in the health services could have a negative impact on whether they returned while others highlighted the influential role that health care workers have on vaccine acceptance among the population. In one country, women prefer to receive care by female providers, which are scarce in that country and could at least partially explain the lack of vaccination among women.

Finally, four immunization managers identified that lack of knowledge (or misinformation) in the population regarding vaccination was a contributing factor to vaccine hesitancy. One immunization managers specified that lack of knowledge about vaccination among health professionals was linked to vaccine hesitancy.

3.3.3. <u>Vaccine and vaccination specific issues</u>

Risk of adverse events following immunization was identified by three immunization managers as contributing to vaccine hesitancy.

Three immunization managers noted that the design of the vaccination program contributed to vaccine hesitancy. In two countries, vaccine hesitancy was related to mass vaccination programs and not routine immunization programs. In the other country, religious members were refusing to bring their children to the hospital or health centers for immunization but agreed to have them immunized if offered at home.

In one country, reliability of the vaccine supply was also noted as a difficulty; because vaccines were out of stock, vaccination series were not completed. In another one, the provenance of the vaccines, was linked to vaccine hesitancy. There was distrust in vaccines produced in developing countries (India and Indonesia) caused vaccine hesitancy among health care workers who would prefer to use vaccines produced in Europe. In two countries, immunization managers noted that there were concerns among the Muslim population due to suspected use of porcine components in vaccines. Finally, introduction of new vaccines or new indications was perceived (more or less explicitly) as contributing to vaccine hesitancy in four countries. In one country, the introduction of new and costly vaccines was seen as triggering vaccine hesitancy.

4. Discussion

This study revealed a number of challenges concerning vaccine hesitancy including the presence of discrepancies in how vaccine hesitancy was understood by immunization managers. It was not consistently defined and several immunization managers interpreted it, explicitly or implicitly, as including or limited only to vaccine refusal. Several noted stock outs as a cause. Yet the definition developed by the Working Group specifies that vaccine hesitancy refers to delay in acceptance or refusal of vaccines despite availability and quality of vaccine service. This indicates that the proposed definition, while broad and inclusive, will need to be promoted among immunization managers in the field if hesitancy is to be comparably assessed. A common understanding of what falls under the umbrella of vaccine hesitancy is essential in order to measure the scope of vaccine hesitancy, to look at potential causes, to identify differences between countries and sub-populations, and to monitor the changes over time.

Some immunization managers considered the impact of vaccine hesitancy on immunization programs as a minor problem possibly due to the lack of understanding of the term. The findings when lack of vaccine confidence was queried well illustrate the problem. The immunization managers all struggled (and 5 of 13 did not answer) when asked to provide an estimate of the percentage of non- and under-vaccinated individuals in their countries in whom lack of confidence was an issue. This could be related to difficulty in quantifying such

a variable or to a lack of understanding of what is considered in the terms "lack of confidence" and even term vaccine hesitancy. This further highlights the need for common understanding of terminology.

While some immunization managers considered the impact of vaccine hesitancy on immunization programs as a minor problem in their country, others saw it as more serious. Although some immunization managers associated vaccine hesitancy to particular religious or ethnic groups, most agreed that vaccine hesitancy is not exclusively clustered to specific communities, and exists across all socioeconomic strata of the population. Some immunization managers often associated it with highly educated individuals. This is in agreement with previous studies conducted in different settings that have shown that non-compliant individuals appear to be well-informed individuals who have considerable interest in health-related issues and actively seek information [15, 16]. Three IMs emphasized that health professionals could be vaccine-hesitant themselves. This is of particular concern as health professionals' knowledge and attitudes about vaccines have previously been shown to be an important determinant of their own vaccine uptake, their intention to recommend the vaccine to their patients, and the vaccine uptake of their patients [17-20].

The sense that vaccine hesitancy is not uniform in the country is also a challenge. Immunization managers may need to not only carry out a country assessment of hesitancy, but also a sub-national and even a district level assessment, to fully understand the extent of hesitancy within a country. This will be especially key when planning for supplementary immunization activities, surveys or specific campaigns to catch up the non- or undervaccinated, with vaccine-hesitant being one possible choice of target groups.

The immunization managers surveyed noted variable and context-specific causes of vaccine hesitancy. Confidence, complacency and /or confidence issues were all raised. Overall, the findings fit well within the matrix of determinants of vaccine hesitancy developed by the SAGE Working Group. All issues raised by the countries were reflected within the matrix and no additional determinants were identified. Among frequent determinants raised by immunization managers were concerns regarding vaccine safety sometimes due to scientifically proven adverse events after immunization while others were triggered by rumors, misconceptions or negative stories conveyed in the media. A more frequently named determinant of vaccine hesitancy was religious beliefs and the influence of religious leaders. Refusal of some or all vaccines among religious communities has been well-documented [21, 22]. Opposition to vaccination based on religious motives is not a new phenomenon and can be explained, at least partially, by the idea that vaccination is not in line with religious considerations of the "origin of illness, the need for preventive action and the search for a cure" [21]. The influence of communication and media, the lack of knowledge or education, and the mode of vaccine delivery (i.e. mass vaccination campaigns) were other determinants of vaccine hesitancy identified by immunization managers. In LMICs, geographic barriers to vaccination services, political conflicts and instability or illegal immigration were linked with vaccine hesitancy.

The findings from this survey, further emphasize the usefulness of the new concept "vaccine hesitancy" if we are to better understand determinants of vaccine acceptance. It represents a shift from the dichotomous perspective "anti- versus pro-vaccine" to an approach picturing vaccination behaviour on a continuum ranging from active demand for vaccines to complete refusal of all vaccines [23]. This study is the first to report immunization managers understanding of this term and emphasizes the need for further education about this term. The results have provided useful insights on the actual situation in different countries, showing the variability in manifestation of vaccine hesitancy. However, the results should be considered in light of some limitations. The countries were selected by WHO in order to represent a diversity of regions and situations, but it was difficult to obtain participation of some countries. Two IMs could not participate for different reasons. Most interviews were conducted in English and this may have been challenging for non-English speakers, resulting in information bias. Interviews were loosely conducted and some questions were not asked to every IM. As with all qualitative study, desirability bias cannot be excluded and findings are not generalizable to all countries. It is important to note that the country-specific situation in regard to vaccine hesitancy was reported by a single IM, often based on his/her own opinions and estimations, and it is thus very possible that different views could have been expressed if we had interviewed another informant in the same country. That being said, the IM is generally very well-informed on issues surrounding vaccination.

To conclude, because the success of immunization programs relies mainly on population and health professionals confidence, it is particularly vulnerable to controversy [24]. Understanding the specific concerns of the various groups of vaccine-hesitant individuals, including health professionals is important as hesitancy may result in vaccination delays or refusals. Vaccine hesitancy is an individual behavior, but is also the result of broader influences and should always be looked at in the historical, political and socio-cultural context in which vaccination occurs. Many predictors of vaccine acceptance have been identified at the individual level, and include knowledge, attitudes or perceived risks. This study suggests that an individual's choice to use vaccination services is far more complex involving emotional, sociocultural, spiritual, political and structural factors as much as cognitive factors. There is a need to strengthen the capacity of countries to identify context-specific roots of vaccine hesitancy and to develop adapted strategies to address them.

Conflict of interest statement: Nothing to declare.

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Table 1. Summary of IMs' opinions on vaccine hesitancy

Countries

IM perspective on vaccine hesitancy in their country

Vaccine hesitancy is mostly associated with mass vaccination campaigns, especially against polio. It is mostly clustered in large cities and associated with particular religious groups. Routine immunization programs are not affected by vaccine hesitancy and access is the main issue.

Country A

 % of un- or under-vaccinated in whom lack of confidence was a factor: unanswered.

Vaccine hesitancy is not considered a problem in the country. Instead, there is vaccine refusal, which is associated with religious groups and higher socioeconomic status. However, vaccine refusal is also not considered a major problem.

Country B

• % of un- or under-vaccinated in whom lack of confidence was a factor: 10% (estimated)

Vaccine hesitancy is not considered a major issue in the country. However, there is a small proportion of the whole population who has concerns about the safety of vaccines and could be categorized as vaccine-hesitant. This is mostly related to the new and costly vaccines, such as the pentavalent vaccine and is mostly seen in the well-educated population group. There are no issues of complacency or convenience (except for migrant populations). Vaccine hesitancy is not considered to have a significant impact on overall coverage rates.

Country C

 % of un- or under-vaccinated in whom lack of confidence was a factor: < 5% (estimated)

Vaccine hesitancy is not an issue in the country. Vaccine hesitancy is limited to illegal settlers.

Country D

• % of un- or under-vaccinated in whom lack of confidence was a factor: < 1% (estimated)

Country E

Although political conflict and instability negatively affect overall access to health services, vaccine hesitancy is not a major issue in the country. Some negative rumors about vaccination have circulated in selected regions and groups of people. Access to immunization services is challenging for women and nomads.

 % of un- or under-vaccinated in whom lack of confidence was a factor: unanswered Vaccine hesitancy is not a major issue in the country and most children are fully immunized by the age of two. Vaccine hesitancy is mainly associated with medical academics and health care workers who don't believe vaccines are safe and effective (especially combination vaccines and vaccines produced in developing countries). Additionally, there have been issues with religious groups being advised against vaccines because it is forbidden by their religion as well as concerns regarding the safety of combination vaccines.

Country F

• % of un- or under-vaccinated in whom lack of confidence was a factor: unknown

Country G

In the country, vaccine hesitancy leading to vaccine refusal is not very frequent and is rather localized. Vaccine hesitancy issues have come up in particular groups such as anthroposophist schools, the orthodox Jewish community and Roma societies. In Belgium, complacency and access to certain communities are bigger issues than hesitancy.

 % of un- or under-vaccinated in whom lack of confidence was a factor: unanswered

Country H

Vaccine hesitancy exists but is not a major issue in the country. It is not linked to particular groups or geographic areas. Vaccine hesitancy is associated with a lack of perceived benefit of vaccination due to low prevalence of vaccine-preventable disease in the country. There are also concerns regarding vaccine safety and the negative influence of "Internet stories".

 % of un- or under-vaccinated in whom lack of confidence was a factor; unknown

In the country, there are two major groups hesitant to get vaccinated: 1) a small minority of religious groups who do not believe in the benefit of vaccines due to religious or philosophical reasons and 2) the general public concerned by adverse events following immunization (AEFI). Vaccine hesitancy is associated with specific vaccines being in "the focus of attention" (such as HPV or OPV). Media reports of rare adverse events make parents hesitant to vaccinate their children, resulting in decreased uptake. While access and complacency are not important issues, it is speculated that vaccine hesitancy could explain up to 30% of the decrease observed in OPV vaccine coverage (prior to IPV introduction).

Country I

• % of un- or under-vaccinated in whom lack of confidence was a factor: 30% (OPV only, measured)

Country J Vaccine hesitancy is an important issue in the country. Vaccine hesitancy is

associated with particular ethnic minorities (ethnic Hmong) and remote communities, with a particular focus on the education level of the local population in remote communities. Vaccine hesitancy is associated with lack of perceived benefits of immunization and negative beliefs based on myths (such as vaccination of women leading to infertility).

• % of un- or under-vaccinated in whom lack of confidence was a factor: 30% (estimated, % of Hmong tribe population)

Country K

Vaccine hesitancy exists in the country, but is rather small. Vaccine hesitancy is mostly associated with people of high socio-economic status living in urban areas who have concerns regarding vaccine safety (especially thiomersal containing vaccines). Concerns regarding porcine components in vaccines by Muslim populations also contribute to vaccine hesitancy in the country.

• % of un- or under-vaccinated in whom lack of confidence was a factor: <5% (estimated)

Vaccine hesitancy is mostly related to Tetanus Toxoid (TT) mass vaccination campaigns. As a result of vaccine hesitancy due to concerns with vaccine safety, up to 20% of eligible population is un- or under-vaccinated. Serious AEFI-inflammation at the site of injection and Catholic pro-life groups stating that TT vaccination was resulting in abortion or infertility have contributed to vaccine hesitancy regarding TT vaccination. Routine vaccination programs are not affected by vaccine hesitancy.

Country L

• % of un- or under-vaccinated in whom lack of confidence was a factor: 20% (estimated), 8% refused vaccine (measured)

Vaccine hesitancy is not an important issue in the country and the immunization program has a positive image. However, vaccine hesitancy did occur in particular situations and populations. For example, vaccine hesitancy originated from the Catholic Church when HPV vaccine was introduced, and from healthcare professionals when influenza vaccine and TDaP were recommended to be administered to pregnant women. Vaccine hesitancy also occurred among indigenous groups. Additionally, there are vaccine refusals among indigenous groups when vaccination week coincides with cultural events. Geographic barriers may limit the percent vaccinated in some remote areas, but is not linked with vaccine hesitancy. There are no anti-vaccine groups in the country and there is not much vaccine refusal.

Country M

• % of un- or under-vaccinated in whom lack of confidence was a factor: unknown

Figure 1. IMs' opinions regarding determinants of Vaccine Hesitancy*

SAGE WG Vaccine Hesitancy Model **CONTEXTUAL** INDIVIDUAL AND **VACCINE AND INFLUENCES GROUP** VACCINATION **INFLUENCES SPECIFIC ISSUES** Religion/ culture/ Risk/ benefit Risk/ Benefit gender/ socio-(perceived, heuristic) (scientific evidence) economic Design of vaccination Health system and providers - trust and program/ Mode of Influential leaders and personal experience delivery anti- or pro-vaccination lobbies Knowledge/ awareness Reliability and/or source of vaccine supply Communication and Experience with past vaccination media environment Beliefs, attitudes about health and Introduction of a new prevention vaccine or new formulation Geographic barriers Immunisation as a social norm vs. Costs not needed/ harmful Politics/ policies (Mandates) Vaccination schedule Historical influences Mode of administration Pharmaceutical industry Role of healthcare professionals

^{*}Larger font size represents greater number of mentions while determinants under the line were not mentioned by the IMs.

Appendix for Section 5

Appendix A5.1: Pilot Test of Vaccine Confidence Indicators 2012

Pilot Test of Vaccine Confidence Indicators 2012

GAVP Strategic Objective 2

Background

Vaccine hesitancy is not a new phenomenon, although more attention has been paid to it in recent years. Vaccine hesitancy is an emerging term in the discourse on determinants of vaccine acceptance where uptake of a vaccine or immunization program in a community is lower than would be expected in the context of information given and services available. Vaccine hesitancy recognizes that issues of complacency, convenience and/ or confidence in vaccine(s) or immunization programs may all contribute to the delay or refusal of one, some or almost all vaccines. These factors which influence vaccine acceptance vary by setting and responses need to be locally assessed.

In 2012, the WHO Strategic Advisory Group of Experts on Immunization (SAGE) established a Working Group to address the issue of vaccine hesitancy which defined vaccine hesitancy and its scope and identified drivers of vaccine hesitancy.

In light of the Decade of Vaccines Global Vaccine Action Plan, the working group was asked to develop and pilot test one or several indicator(s) of vaccine confidence that could be used to monitor the issue on a global and on a national level. The group was asked to pilot test these two indicators over a broad range of regions in countries with representing all levels of income to assess response, comparability and feasibility.

Methods

Sampling frame

The WHO PAHO and the EUR region volunteered to pilot test the questions related to the indicators in their 2012 UNICEF/WHO Joint Reporting Form (JRF). The JRF was sent to the countries in December 2012 and January 2013. The countries were asked to return the completed forms by 15. April 2013. In addition self-administered questionnaires were personally distributed at the Intercountry Support Team South & East and Central Africa immunization managers' meeting in Q1 2013 to selected EPI managers. The self-administered questionnaire allowed immunization managers to comment on the two indicators.

Indicators and definition

The questions related to the indicators to assess vaccine confidence were translated in 4 WHO languages, French, Russian, Spanish and English. The questions were accompanied by the definition of vaccine confidence.

Definition

Vaccination confidence is one of a number of factors that affect individual and population-level willingness to accept a vaccine. It means having confidence in the safety and efficacy of a vaccine, having confidence in the reliability and competence of the health services and health professionals who deliver and administer the vaccine, and having trust in the motivations of the policy-makers who decide which vaccines are needed and when.

If vaccine coverage is understood as being determined by a combination of supply and demand factors, confidence is primarily a demand factor, although it can be influenced by supply factors such as ease or difficulty in accessing services, competence of the vaccinator and reliability of the vaccine supply. It can also be influenced by factors outside the health system.

Indicator 1: % of countries that have assessed (or measured) the level of confidence in vaccination at subnational level.

Ouestion 1:

Has there been some assessment (or measurement) of the level of confidence in vaccination at subnational level in the past?

Question 2:

If yes, please specify the type and the year the assessment has been done.

Indicator 2: % of un- and under-vaccinated in whom lack of confidence was a factor that influenced their decision.

Question 1:

What is the % of un- and under-vaccinated in whom lack of confidence was a factor that influenced their decision (this applies to all vaccines)?

Question 2:

Was this % measured or estimated?

Ouestion 3:

Any comments or specific issue?

Classification

We classified the countries by level of income using the World Bank's main criterion for classifying economies, the gross national income (GNI) per capita.

Data collection and analysis

Data were collected by the respective regional offices, submitted to WHO HQ and analyzed using Microsoft Excel and Stata 11.0.

Inclusion and Exclusion criteria

Inclusion criteria

- Recognized member state of WHO PAHO, EUR or AFR region Exclusion criteria
 - No indication of country

Results

Response rate:

The pilot test was conducted in three WHO regions: <u>PAHO</u> Member States supports the 35 countries in the Americas. <u>WHO EURO</u> supports the 53 Member States in the European Region. Until 05.07.2013 not all countries had returned the completed JRF. In the EUR region 48/53 countries (91%) provided a JRF for 2012. In the PAHO region, all 35 countries (100%) provided a JRF for 2012.

Countries which did not provide a JRF were: The Former Yugoslav Republic of Macedonia, Turkey, Austria, Finland and Monaco.

In <u>AFRO</u>, 14 national immunization managers were asked to complete the questionnaire. Of these 11 provided the questionnaire which met the criteria to be included in the analysis.

Indicator 1:

Indicator 1 assessed whether a measurement of vaccine confidence had been done in countries at a subnational level in the past. Of the countries which submitted a JRF or a questionnaire, 17% in the European region had done a measurement, 20% in the Americas and 27% of the participating African countries. (Table 1)

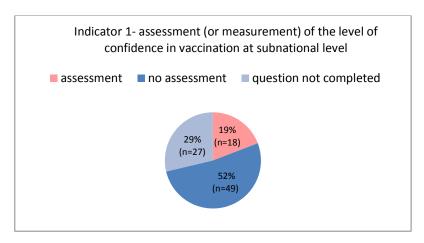
For complete list of countries and countries by indicator see ANNEX.

Table 1. Number of countries reporting an assessment (or measurement) of the level of confidence in vaccination at subnational level

Region	EUR		РАНО		EUR and PAHO		AFR	
	Numbe	Percenta	Numbe	Percenta	Number	Percenta	Numbe	Percentage
	r	ge	r	ge		ge	r	
Assessment	n= 8	17%	n=7	20%	n=15	18%	n=3	27%
No assessment	n=17	35%	n=24	69%	n=41	49%	n=8	73%
Question not completed	n=23	48%	n=4	11%	n=27	33%	n=0	0%
Total	n=48	100%	n=35	100%	n=83	100%	n=11	100%

Of all participating countries, 19% (n=18) had assessed or measured the level of confidence on a subnational level. (Figure 1)

Figure 1. Assessment of vaccine confidence of all participating countries



Countries were asked to provide specific information on the type of assessment and the year this assessment was done (Table 2).

Table 2. Type of assessment by year

Country	Type of assessment	Year of assessment
Brazil	Rapid monitoring of vaccination provided information to explain the reasons for non-vaccination or for abandoning the recommended vaccination schedule.	No year indicated
Chile	Conducted a small study, requested by the Ministry of Finance in 2012, study focused on the perception of the National Immunization Program.	2012
Cuba	Not specified	2012
Dominican Republic	Not specified	2012
Guatemala	Random Survey (1164 mothers / guardians) house to house. May 2011	2011
Jamaica	Evaluation of the Immunization Program in 2003; user survey	2003
Mexico	National Survey of Health and Nutrition 2006	2006
Belgium	Vaccination coverage study of infants (18-24 months of age) and adolescents in Flanders, 2012.	2012
Czech Republic	Administrative control	2011

Germany	Representative survey targeting parents of children aged 0-13 years	2010					
Iceland	Survey among parents	2010					
Italy	1.) Survey on communicative and organizational aspects of vaccination campaign against HPV and acceptance of the vaccination in the Italian						
	Regions and proposal for a technical document for future campaigns (VALORE), report not yet available; 2) Survey on Social Determinants of Vaccine Refusal in the Veneto Region. Report available: http://prevenzione.ulss20.verona.it/indagine_scelta_vaccinale.html						
Lithuania	Prevalence study	2011					
Russian Federation	Questioning during European Immunization Week	2012					
Democratic Republic of Congo	National immunization coverage survey	2012					
Eritrea	EPI program review were carried out at national, subnational &district level &caregivers with technical support from AFRO/IST	2011					
Uganda	Social survey on evidence based communication, During SIAs/NIDs: Independent survey reports, social mobilization survey in 35 districts	2012					

Indicator 2:

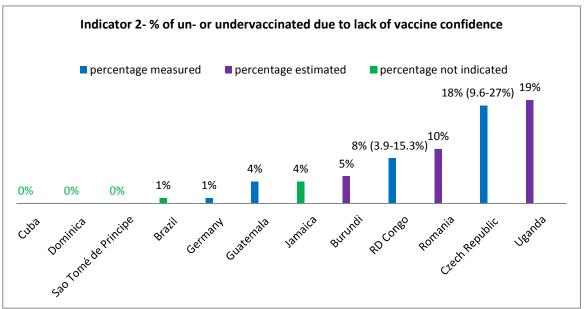
Countries were asked to provide a measured or estimated percentage of un- and undervaccinated in whom lack of confidence was a factor which influenced their decision to get vaccinated. 10% of the countries answering the JRF provided an estimate of un-or undervaccinated, 90% did not provide any answer to this question. Of the African countries, 45% provided a percentage (Table 3)

Table 3: Number and percentage of countries which provided a measured or estimated percentage of un- or undervaccinated.

Region	EUR		РАНО		EUR and PAHO		AFR	
	Numbe	Percentage	Number	Percentag	Numbe	Percentag	Numbe	Percentag
	r			e	r	e	r	e
% provided	n= 3	6%	n=5	14%	n=8	10%	n=5	45%
No % provided	n= 45	94%	n=30	86%	n=75	90%	n=6	55%
Total	n=48	100%	n=35	100%	n=83	100%	n=11	100%

Countries from all 3 regions provided percentages, which varied between 0%- 19% of un- or undervaccinated due to lack of confidence. Czech Republic specified that the percentages ranged from 9.6-27% according to vaccine. The RD Congo provided a range of percentages, 8% lack of confidence on a national level and percentages ranging from 3.9-15.3% in different provinces of the country. (Figure 2)

Figure 2. Percentage of measured, estimated or unknown (did not specify either from measured or estimated) of un- and under-vaccinated in whom lack of confidence was a factor that influenced their decision



Further the countries were asked to provide comments or specific issues in regard to Indicator 2. (Table 4)

Table 4: Specific comments or issue in regard to indicator 2

Country	Comments or specific issues related to percentage of un- and under- vaccinated in whom lack of confidence was a factor that influenced their decision
Brazil	In the reasons provided, the mothers or caregivers inform that the children are not vaccinated due to non-acceptance of the vaccine. Others indicate that reasons for non-vaccination were due to contraindication or adverse events following immunization.
Cuba	High percentage of acceptance of the population to vaccinate their children, there is great demand for this service locally (health areas) as vaccination running in schools and in the adult population.
Germany	Assessment report: http://www.bzga.de/forschung/studien-

	untersuchungen/studien/?sid=10⊂=64
Grenada	Vaccination confidence is an important factor in understanding reasons why persons object to vaccination of their children.
Guatemala	Percentage of distrust most common side effects in mothers over 40 years with no / primary education level.
Iceland	97-99% of parents were positive towards vaccinations.
Saint Lucia	No survey has been conducted to determine lack of confidence in vaccination of un- and under- vaccinated individuals.
Botswana	EPI manager conducted in 2007 revealed various reasons related to non-compliance to immunization serviced but lack of confidence was not a factor.
Eritrea	We didn't experience or had a reports from regions that households lacking confidence influenced decision for un-& undervaccination of their children.
Guinée equatorial	Serious issues of hesitancy during the last campagne with parents claiming vaccine to have caused death of a child. Most parents claim that vaccines cause illness or death.
Lesotho	Assement of the level of confidence in vaccination has not been done in the country as a result the country does not have any indication of confidence levels.
Sao Tomé de Principe	Lack of confidence is not an issue.
Tanzania	Lost-to-follow up due to nomad population contributes to number of unand undervaccinated.
Democratic Republic of Congo	Primarily religious considerations contribute to vaccine hesitancy.

Income status

Of all 94 participating countries, 40% were high income countries, 54% middle income countries and 6% low income countries. (Table 5)

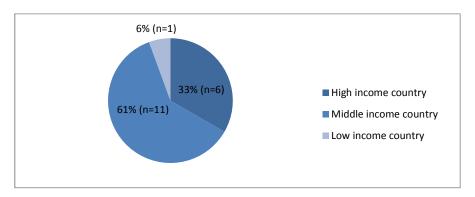
Table 5: Income level of countries by region

Region	EUR		РАНО		AFR		All regions	
	Numbe	Percentag	Number	Percentag	Numbe	Percentag	Numbe	Percentag
	r	e		e	r	e	r	e
High income	n=28	58%	n=7	20%	n=3	27%	n=38	40%
Middle income	n=18	38%	n=27	77%	n=6	55%	n=51	54%
Low income	n=2	4%	n=1	3%	n=2	18%	n=5	6%
Total	n=48	100%	n=35	100%	n=11	100%	n=94	100%

Indicator 1 and level of income:

One assessment of vaccine confidence had been done in one low income country, 11 in middle income countries and 6 in high income countries. (Figure 3)

Figure 3: Assessment of vaccine confidence by level of income



Indicator 2 and level of income:

Populations with lack of confidence in vaccinations were reported from all three levels of income. 13 countries provided a percentage. Of these 3 countries were high income countries, 9 were middle income countries and one country was a low income country.

General comments on the indicators

Two African immunization managers provided specific feedback on the indicators (Table 6); other used the comment section to further specify their issues in regard to vaccine confidence.

Table 6: General comments on the indicators

Might be advisable to conduct a study in each zone

Assessing the level of confidence in vaccine is a good approach in determining the level of willingness and acceptance of the service and this can be put in place. This will also contribute in improving immunization services.

Discussion

Overall 94 countries representing all levels of income were included for pilot testing of the vaccine confidence indicator.

Response differed between the two methods used, with more countries responding an assessment and a percentage when being asked directly to complete a questionnaire (immunization managers' survey in AFR) than when filling in the JRF (PAHO and EUR region).

In regard to Indicator 1, the assessment of vaccine confidence at a subnational level in the past, 71% of all countries provided specific feed-back whether this had or had not been done in their country. 19% of all participating countries had done an assessment of the level of confidence in their country demonstrating that vaccine confidence was an issue in their country. 52% had not done an assessment and 29% had not completed the question. For the 29% not providing feedback it was not possible to differentiate whether no assessment had been done or if the immunization manager filling in the questionnaire/ JRF could not provide any answer to this question.

In regard to type of assessment countries provided examples from national and subnational level, hence the question might need to be reworded to have a uniform approach which captures all types of assessments countries provide feedback on.

Assessments of vaccine confidence had been done in countries of all income levels and not only in high income countries.

For Indicator 2, only 14% provided a measured or estimated percentage of un-or undervaccinated in whom lack of confidence was a factor which influenced their decision to get vaccinated. It needs to be further assessed whether not providing a percentage indicates that there are no persons with lack of confidence or if it was not feasible for the immunization manager to provide an estimate. Lack of vaccine confidence ranged from 0% in Cuba, Dominica, Botswana and Sao Tomé de Prinicpe to 19% in Uganda. These results demonstrate that the lack of confidence can be significant problem even in countries which would not be primarily assumed to have issues of vaccine confidence, such as Uganda.

Comments on Indicator 2 represented the large scope of issues around vaccine confidence, from confidence being an important issue to not being relevant at all. It further unveiled a

variety of determinants of vaccine confidence, from religious dimension to safety issues around the vaccine.

In regard to the format of the JRF, consistency and clarity is needed to receive comparable results. During this pilot test, there were variations of the form even within one region. Countries might have been confused using the drop-down selection of YES/NO in regard to Indicator 2 where in fact they were asked to provide a percentage.

The pilot test demonstrates that vaccine confidence is an issue throughout the three regions and throughout all levels of income. Issues around vaccine confidence are not restricted to high income countries in the European or American region, but were also reported from middle and low income countries and countries in the African region.

The developed indicators need to be further refined by the vaccine hesitancy working group to provide valid and comparable responses from all countries. Feedback from African immunization managers was appreciative of the indicators, yet active follow-up with selected immunization managers from the other regions should be sought to further assess the feasibility and clarity of the two indicators. ANNEX

ANNEX: List of countries by Indicator 1

country	assessment	type	%	measured/
				estimated
Antigua and Barbuda	no			no response
Argentina	no			no response
Bahamas	no			no response
Bolivia	no			no response
Canada	no			no response
Colombia	no			no response
Dominica	no		0%	estimated
Ecuador	no			no response
El Salvador	no			no response
Grenada	no			no response
Guyana	no			no response
Haiti	no			no response
Honduras	no			no response
Nicaragua	no			no response
Panama	no			no response
Paraguay	no			no response
Peru	no			no response
Saint Lucia	no			no response
Saint Kitts and Nevis	no			no response
St Vincent and the Grenadines	no			no response
Suriname	no			no response
Trinidad and Tobago	no			no response

Uruguay	no		no response
Venezuela	no		no response
Belarus	no		no response
Bosnia and Herzegovina	no		no response
Bulgaria	no		no response
Cyprus	no		no response
Estonia	no		no response
Georgia	no		no response
Hungary	no		no response
Ireland	no		no response
Kyrgyzstan	no		no response
Latvia	no		no response
Norway	no		no response
Republic of Moldova	no		no response
Romania	no	10%	estimated
Slovakia	no		no response
Sweden	no		no response
Tajikistan	no		no response
Ukraine	no		no response
Angola	no		no response
Botswana	no	0%	no response
Burundi	no	5%	estimated
Guinée equatorial	no		estimated
Lesotho	no		no response
Namibia	no		no response
Sao Tomé de Principe	no	0%	no response

Tanzania	no			no response
Brazil	yes	Rapid monitoring of vaccination provided information to explain the reasons for non-vaccination or for abandoning the recommended vaccination schedule.	1%	no response
Chile	yes	Conducted a small study, requested by the MINISTRY of Finance in 2012, study focused on the perception of the National Immunization Program.		no response
Cuba	yes		0%	no response
Dominican Republic	yes			no response
Guatemala	yes	Random Survey (1164 mothers / guardians) house to house. May 2011	4%	measured
Jamaica	yes	Evaluation of the Immunization Program in 2003; user survey	4%	no response
Mexico	yes	National Survey of Health and Nutrition 2006		no response
Armenia	yes			no response
Belgium	yes	Vaccination coverage study of infants (18-24 months of age) and adolescents in Flanders, 2012.		no response
Czech Republic	yes	Administrative control	18%	measured
Germany	yes	Representative survey targeting parents of children aged 0-13 years,	1%	measured
Iceland	yes	Survey among parents		no response
Italy	yes	1.) Survey on communicative and organizational aspects of vaccination campaign against HPV and acceptance of the vaccination in the Italian Regions and proposal for a technical document for future campaigns (VALORE): REPORT NOT YET AVAILABLE; 2) Survey on Social Determinants of Vaccine Refusal in the Veneto Region: REPORT AVAILABLE: http://prevenzione.ulss20.verona.it/indagine_scelt a_vaccinale.html		no response
Lithuania	yes	Prevalence study		measured

Russian Federation	yes	Questioning during European Immunization Week		no response
Eritrea	yes	In December 2011 EPI program review were carried out at national , subnational &district level &caregivers. By the technical support from AFRO/IST		no response
RD Congo	yes	Enquete national de coverture vaccinale	8%	measured
Uganda	yes	Social survey on evidence based communication. 2012 SIAs/NIDs: Independent survey reports. 2012: SIA: Social mobilization survey to consultant for 35 districts	19%	measured

Appendix 5.2: Pilot Test of Revised 2013 Vaccine Hesitancy Indicators Pilot Test of revised 2013 Vaccine Hesitancy Indicators

GVAP Strategic Objective 2

Background

Vaccination is considered to be one of public health's most important achievements. However, this success has been challenged by anti-vaccine groups and individuals who question the need, safety and importance of immunizations. Although growing attention on "vaccine hesitancy" has been emerging at greater rate in recent years, it is not a new phenomenon. Vaccine hesitancy is an emerging term in the discourse on determinants of vaccine acceptance where uptake of a vaccine or immunization programme in a community is lower than would be expected in the context of information given and services available. Vaccine hesitancy is influenced by a complex network of factors including issues of complacency, convenience and/or confidence in vaccine(s) or the immunization programme that may result in refusal, delay or uncertainty towards some or all vaccines. The factors which influence vaccine acceptance vary by setting and responses need to be locally assessed.

In 2012, the WHO Strategic Advisory Group of Experts on Immunization (SAGE) established a Working Group to address the issue of vaccine hesitancy which defined vaccine hesitancy and its scope and identified drivers of vaccine hesitancy. In light of the Decade of Vaccines Global Vaccine Action Plan, the working group was asked to develop and pilot test one or several indicator(s) of vaccine confidence that could be used to monitor the issue on a global and on a national level. As a part of WHO/UNICEF Joint Reporting Form (JRF), a questionnaire based monitoring tool usually completed by national immunization managers designed to examine national immunization coverage, reported cases of vaccine-preventable diseases, immunization schedules and indicators of immunization system performances, the group had developed and pilot tested a set of two indicators on vaccine confidence. The indicators consisted of the following questions:

Indicator 1: % of countries that have assessed (or measured) the level of confidence in vaccination at subnational level.

Question 1:

Has there been some assessment (or measurement) of the level of confidence in vaccination at subnational level in the past?

Question 2:

If yes, please specify the type and the year the assessment has been done.

Indicator 2: % of un- and under-vaccinated in whom lack of confidence was a fact or that influenced their decision.

Question 1:

What is the % of un- and under-vaccinated in whom lack of confidence was a factor that influenced their decision (this applies to all vaccines)?

Ouestion 2:

Was this % measured or estimated?

Ouestion 3:

Any comments or specific issue?

The two indicators were pilot tested in the 2012 JRF with the region of the Americas (PAHO) as well as the European region (EURO). In addition, the two indicators were tested within a self-administered questionnaires distributed to the IST South & East and Central African Regional immunization managers' meetings in 2013 in the African region (AFRO). Pilot testing within three regions ensured coverage of a broad range of countries representing all levels of income in order to representatively assess response, comparability and feasibility of the indicators. Analysis of the collected data revealed a suboptimal response rate indicating the need for revision of the scope on vaccine confidence as well as the indicators. As a result, the working group on vaccine hesitancy broadened the scope from vaccine confidence to vaccine hesitancy and revisited indicator 2 during its December 2013 face-to-face meeting.

Methods

Sampling frame

The WHO EUR region volunteered again to pilot test the revised vaccine hesitancy indicators in their 2013 UNICEF/WHO JRF. The pilot test was conducted in the <u>WHO EURO</u> region which supports 53 member states. The JRF for the year of 2013 was sent to the countries in the region in January 2014, which were asked to return the completed form by 15 April 2014.

Indicators and definition

Given its importance, the working group on vaccine hesitancy decided to keep the previous indicator 1 only expand to the assessments done on the national level. Indicator 2 was completely revisited to assess the top 3 reasons for vaccine hesitancy in the country, rather than providing a measured or estimated percentage of un- and undervaccinated in whom confidence was an influencing factor in their decision (Indicator 2 in 2012).

Indicator 1: % of countries that have assessed the level of hesitancy in vaccination at a national or subnational level.

Question 1:

Has there been some assessment of vaccine hesitancy or refusal among the public at national or sub-national level?

Ouestion 2:

If yes, please provide assessment title(s) and reference(s) to any publication/report.

Indicator 2: Reasons for vaccine hesitancy.

Ouestion 1:

What are the top three reasons for not accepting vaccines according to the national schedule?

Question 2:

Is this response based or supported by some type of assessment, or is it an opinion based on your knowledge and expertise?

The questions were accompanied by a narrative on vaccine hesitancy:

Introduction

Vaccine hesitancy is an emerging term in the discourse on determinants of vaccine acceptance where uptake of a vaccine or immunization program in a community is lower than would be expected in the context of information given and services available.

Vaccine hesitancy recognizes that issues of complacency, convenience and/or confidence in vaccine(s) or immunization programs may all contribute to the delay or refusal of one, some or almost all vaccines. These factors which influence vaccine acceptance vary by setting and responses need to be locally assessed.

Vaccine hesitancy refers to delay in acceptance or refusal of vaccines despite availability of vaccine services. Vaccine hesitancy is complex and context specific varying across time, place, and vaccines. It includes factors such as complacency, convenience, and confidence.

Data collection and analysis

A drop down- list (yes/ no; evidence-based/ opinion) were provided for Indicator 1, Question 1 and Indicator 2, Question 2. For the remaining two questions, free-form text could be entered. The questions related to the indicators were translated into 2 of the 6 WHO languages (Russian and English). Completed JRF questionnaires were collected by the regional office of Europe and later submitted to WHO headquarters in Geneva, Switzerland. The data collected from the vaccine hesitancy indicators were analysed, summarized using Microsoft Excel 2010 and compared to the 2012 European JRF data.

Results

Response rate:

The JRF form was sent to all 53 WHO EURO member states. 45/53 countries (85%) provided a JRF for 2013 by June 26, 2014. Countries which did not provide the JRF were: Austria, Bosnia and Herzegovina, Bulgaria, Ireland, Italy, Monaco, Poland, and Ukraine. In 2012 ccountries which did not provide a JRF were: Austria, Finland, Monaco, The Former Yugoslav Republic of Macedonia and Turkey.

Indicator 1:

Indicator 1 assessed whether a measurement of vaccine hesitancy had been done in the member states at a national or subnational level. The only modification of the indicator to the previous version included in the 2012 JRF was the expansion of the assessments to the subnational and the national level.

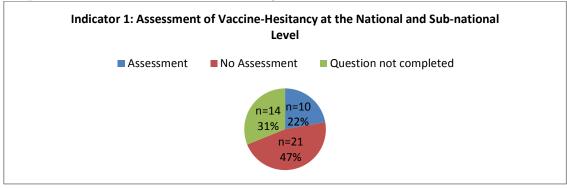
Of those countries which submitted the 2013 JRF, 10/45 (22%) reported an assessment of vaccine hesitancy and 21/45 (47%) reported not having done an assessment. The questions were not completed by 14/45 countries (31%). In comparison to the JRF 2012, the response rate for indicator 1 for the WHO EUR region increased from 52% (25 out of 48) in 2012 to 69% (31 out of 45) in 2013. More countries indicated some form of vaccine hesitancy assessment in 2013 compared to 2012, 22% (10 out of 45) versus 17% (8 out of 48) respectively. This decreased non-response by 17% from 48% within the 2012 EURO JRF to 31% within the 2013 EURO JRF (Table 1).

Table 1. Number of countries reporting an assessment of vaccine hesitancy at a national/ subnational level*.

Region	Е	UR 2013	EUR 2012	
	Number	Percentage	Number	Percentage
Assessment	n=10	22%	n= 8	17%
No assessment	n=21	47%	n=17	35%
Question not completed	n=14	31%	n=23	48%
Total	n=45	100%	n=48	100%

^{*}For a complete list of countries and countries by indicator see Annex 1.

Figure 1. Assessment of Vaccine Hesitancy at the National and Sub-national level in 2013



Of the 10 countries which indicated the presence of an assessment, 7 countries provided assessment title(s) and reference(s) to any publication or report on vaccine hesitancy (Table 2).

Table 2. Title(s) and reference(s) to any publication reported on vaccine hesitancy by country in 2013

Country	Title(s) and reference(s) to publications
Denmark	Wójcik OP, Simonsen J, Mølbak K, Valentiner-Branth P. Validation of the 5-year tetanus, diphtheria, pertussis and polio booster vaccination in the Danish childhood vaccination database. Vaccine. 2013 Jan 30; 31(6):955-9. Doi: 10.1016/j.vaccine.2012.11.100. Epub 2012 Dec 13.
Estonia	Estonia participated in VACSATC project http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19181
Germany	1) "representative survey targeting parents of children aged 0-13 years" (German Federal Institute for Health Education); assessment report: http://www.bzga.de/forschung/studien-untersuchungen/studien/?sid=10⊂=64
	2) "KAP study among the general population towards Protection against Infection" (German Federal Institute for Health Education); assessment report: http://www.bzga.de/forschung/studien-untersuchungen/studien/impfen-und-hygiene/?sub=79
Luxembourg	Krippler S., 2014, « Enquête de couverture vaccinale au Grand Duché de Luxembourg 2012 », Ed. Ministère de la Santé
Kazakhstan	None indicated on questionnaire
Kyrgyzstan	In 2013 in Kyrgyzstan, with technical support from UNICEF, conducted a study on the quality perception of the population immunization
Portugal	http://repositorium.sdum.uminho.pt/bitstream/1822/11888/1/Raz%c3%b5es%20de%20Sa%c3%bade_Cunha%2cDurand.pdf
Republic of Moldova	Report of the independent Center for Sociological and Marketing Research CBS-AXA commissioned by UNICEF and the Ministry of Health of the Republic of Moldova, 2012
Romania	None indicated on questionnaire
Slovakia	None indicated on questionnaire

Indicator 2:

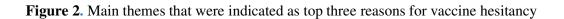
Indicator 2 was modified from the previous version included in the 2012 JRF to assess the top three reasons for not accepting vaccines included in the national schedule. Of the countries who submitted the 2013 JRF form, 16/45 (36%) provided at least one reason for vaccine hesitancy while 29/45 (64%) countries did not answer the question (Table 3).

Table 3. Number and percentage of countries which provided a response to top three reasons for vaccine hesitancy.

Region	EUR	
	Number	Percentage
Reasons provided	n=16	36%
No reasons provided	n=29	64%
Total	n=45	100%

Countries were further asked whether these reasons were evidence-based or opinion-based relying on the expertise of the immunization manager. Of the 16 countries that provided reasons, 7 based their response on evidence and 9 on opinion. The named reasons were mapped against the matrix of determinants¹ developed by the vaccine hesitancy working group. The list of reasons is indicated by country in Table 4 and summarized within the matrix of determinants in Figure 2.

¹



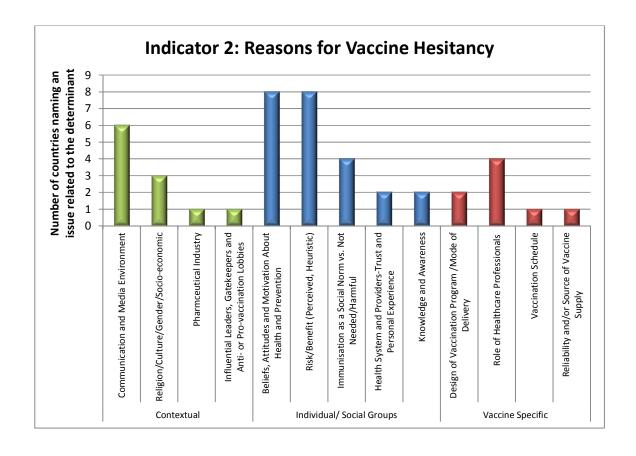


Table 4. Top three reasons for vaccine hesitancy and basis of response

Country	Top three reasons for vaccine hesitancy	Basis of response
Belarus	 The large number of negative information on immunization in the media. Distrust of security used vaccines. Lack of vaccine-preventable diseases. 	Opinion
Czech Republic	 The fear of side effects of vaccination. The lack of knowledge of the course of real diseases. Perception of pharmaceutical companies like those, whose main interest is 	Opinion
Denmark	to earn money. 1. Forgot. 2. Did not want to be vaccinated. 3. Other reasons.	Evidence
Estonia	 Other reasons. Too much different information concerning vaccines and vaccination in the Internet and media. Whom to trust? Doubts in vaccine safety. 	Opinion
Finland	 There are alternative methods of prophylaxis. Fear of adverse events. Anthroposophic philosophy. 	Opinion
Germany	 Religious points of view. Complacency. Convenience. Confidence. 	Opinion
Iceland	1. Fear of adverse effects.	Opinion
Kazakhstan	 Naturalistic views. Religious. On personal beliefs (fear of AEFI). 	Evidence
Kyrgyzstan	 Negative information from the media, internet. Religious beliefs. Doubts about the quality and safety of vaccines. 	Evidence
Luxembourg	 Low public awareness of vaccines. Fear of adverse effects. Vaccination not necessary - unserious illness. 	Evidence
Malta	 Kid was ill the day of the planned immunization. Fear of adverse reactions. Anti-vaccine internet sites. Lack of interest. 	Opinion
Montenegro	 Activities of anti-vaccination individuals and groups. Misinformation through internet. Sensational approach of media who give a lot of space to everyone who 	Opinion
Republic of Moldova	 has something to say against official approach to immunization. Inadequate communication of medical staff with parents. Unjustified Medical Contraindications. Negative publications and TV/radio shows on vaccination and quality of vaccines. 	Evidence
Romania	 No presentation on call. Refusal. Medical contraindication. 	Evidence
Slovakia	 Fear of adverse reactions. Distrust. 	Evidence
Turkey	 Uselessness. The side of the vaccines learnt from some websites by the public. Some religious reasons. The thought of having so many vaccines (antigens) in the vaccination schedule and so many administration would be harmful child health. 	Opinion

Conclusion and Discussion

Modifications to the 2013 JRF were threefold: 1) the scope was widened from the more narrow perspective of vaccine confidence to vaccine hesitancy, which, in addition to vaccine confidence, includes issues related to convenience and complacency 2) the indicators created to measure vaccine confidence of JRF 2012 had been refined following poor response rates in the JRF 2012 questionnaire 3) the narrative included in the JRF was adjusted.

In total more countries reported to have undertaken an assessment or to have not undertaken an assessment in 2013, which suggests a higher response rate to the similar indicator implanted in the JRF 2012.

This result may be due to an increased number of assessments amongst the countries in the EUR region, better understanding of the question convened by the revised narrative or a result of the inclusion of both national and sub-national assessment in the indicator question in comparison to only sub-national assessment in 2012. For those countries not responding to indicator 1, it remains unclear if non-response is a proxy for no assessment or lack of understanding or willingness to answer the question.

In regard to Indicator 2, 36% (16 out of 45) of the countries responded to the question and provided reasons for vaccine hesitancy. Response rate to this newly revised indicator was higher compared to the previous indicator: only 6% (3 out of 48) of the European countries in 2012 had provided a measured or estimated percentage of un- or under-vaccinated in whom a lack of confidence in vaccination was a factor.

The top three reasons for vaccine hesitancy, categorized by the determinants within the matrix developed by the vaccine hesitancy working group were 1) Beliefs, attitudes, motivation about health and prevent, 2) Risk/benefit of vaccines (perceived, heuristic), and 3) Communication and media environment. Major issues were fear of side effects of vaccination and distrust in the vaccine, lack of perceived risk by vaccine-preventable diseases and the influence anti-vaccination reports in the media. Interestingly, 3 countries mentioned unjustified medical contraindications, medical contraindications or the child as being ill the day of the vaccination as reason for vaccine hesitancy. This was accounted to the determinant on the role of the health care professional. The issue of false contraindications should be specified within the matrix of determinants.

A plausible reason for the lower response rate on indicator 2 compared to indicator 1 may be linked to the current structural format of the indicators. Upon analysing the data, it was found that 67% (14 out of 21) countries who answered "No" to indicator 1 failed to continue on and answer indicator 2. Meanwhile, only one country of the ten that answered "Yes" to indicator 1 did not complete indicator 2. This suggests that countries may have believed that if they answered "No" to indicator 1, they were not required to continue on and complete the remaining questions of the vaccine hesitancy indicator. The JRF questionnaire may require some modification to clarify that indicator 1 and 2 are unrelated and that indicator 2 should be completed regardless of the response in indicator 1.

The overall response rate to both indicators is still suboptimal but not a surprising finding given that, in general, it takes a time period of approximately 3 years to obtain an adequate response rate within newly-introduced indicators into the JRF. Nevertheless, compared to the European JRF in 2012, analysis of the 2013 JRF questionnaire indicates an overall increase in response to the two indicators.

With further familiarity and adjustment, the vaccine hesitancy indicators of the JRF may prove to be beneficial in identifying key reasons for vaccine hesitancy and examining assessment levels at a national and sub-national level. Data on vaccine hesitancy, collected on an annual basis, will be a potentiating source of information as well as a monitoring tool to assess potential shifts in the drivers and importance of vaccine hesitancy.

ANNEX 1: List of countries by Indicator 1

Member State	<u>Assessment</u>	Туре	<u>To</u>	o 3 Reason	Assessment /Opinion Based
Andorra	No				Evidence
Azerbaijan	No				
Cyprus	No				
Georgia	No				
Hungary	No				
Latvia	No				
Lithuania	No				
Norway	No				
Spain	No				
Sweden	No				
Switzerland	No				
Tajikistan	No				
Uzbekistan	No				
Slovenia	No				
Montenegro	No		 2. 3. 	Activities of antivaccination individuals and groups Misinformation through internet Sensational approach of media who give a lot of space to everyone who has something to say against official approach to immunization	Opinion
Finland	No		1. 2.	Fear of adverse events Anthroposophic philosophy	Opinion
Iceland	No		1. 2.		Opinion
Malta	No		1.	Fear of adverse reactions Anti-vaccine internet	Opinion
			3.	sites Lack of interest	

Czech Republic	No		1. 2.	The fear of side effects of vaccination The lack of knowledge	Opinion
				of the course of real diseases. Perception of pharmaceutical companies like those, whose main interest is to earn money.	
Turkey	No	But, there are lessons learnt from the public and the public health directorates that day by day vaccine refusal and groups against vaccines	1. 2. 3.	The side of the vaccines learnt from some websites by the public.	Opinion
Belarus	No		2.	наличие большого количества негативной информации по иммунизации в СМИ [the large number of negative information on immunization in the media] недоверие к безопасности применяемых вакцин [distrust of security used vaccines] отсутствие вакциноуправляемых инфекций [lack of vaccine-preventable diseases]	Opinion
Portugal	Yes	http://repositorium.sdum.u minho.pt/bitstream/1822/1 1888/1/Raz%c3%b5es%20d e%20Sa%c3%bade Cunha% 2cDurand.pdf		uiscuscsj	
Romania	Yes		1. 2. 3.	No presention on call Refusal Medical contraindication	Evidence
Slovakia	Yes		1. 2. 3.	Fear of adverse reactions	Evidence

Germany	Yes	1) "representative survey targeting parents of children aged 0-13 years" (German Federal Institute for Health Education); assessment report: http://www.bzga.de/forsch ung/studien-untersuchungen/studien/?si d=10⊂=64 2) "KAP study among the general population towards Protection against Infection" (German Federal Institute for Health Education); assessment report: http://www.bzga.de/forsch ung/studien-untersuchungen/studien/im pfen-und-hygiene/?sub=79	1. 2. 3.	Complacency Convenience Confidence	Opinion
Estonia	Yes	Estonia participated in VACSATC project http://www.eurosurveillanc e.org/ViewArticle.aspx?Artic leId=19181	 2. 3. 	Too much different information concerning vaccines and vaccination in the Internet and media. Whom to trust? Doubts in vaccine safety There are an alternative methods of prophylaxis	Opinion
Denmark	Yes	Wójcik OP, Simonsen J, Mølbak K, Valentiner-Branth P. Validation of the 5-year tetanus, diphtheria, pertussis and polio booster vaccination in the Danish childhood vaccination database. Vaccine. 2013 Jan 30; 31(6):955-9. Doi: 10.1016/j.vaccine.2012.11.1 00. Epub 2012 Dec 13.	 1. 2. 3. 	Forgot Did not want to be vaccinated Other reasons	Evidence

Kyrgyzstan	Yes	В 2013 году в Кыргызстане, при технической поддержке ЮНИСЕФ проведено исследование по качественному восприятию населения иммунизации [In 2013 in Kyrgyzstan, with technical support from UNICEF, conducted a study on the quality perception of the population immunization]	 2. 3. 	По религиозным убеждениям [religious beliefs] Сомнения в качестве и безопасности вакцин [Doubts about the quality and safety of vaccines] Низкая информированность населения в вопросах вакцинопрофилактики [Low public awareness of vaccines]	П одкреплен о фактами [supported by facts]
Kazakhstan	Yes	в работе	 2. 3. 	религиозные [religious] по личным убеждениям (боязнь НППИ) [on personal beliefs (fear of AEFI)] негативная инфорамция со стороны СМИ, интернет [negative information from the media, internet]	Подкрепле но фактами [supported by facts]
Luxembourg	Yes	Krippler S., 2014, « Enquête de couverture vaccinale au Grand Duché de Luxembourg 2012 », Ed. Ministère de la Santé	1. 2.	Fear of adverse effects. Vaccination not necessary - unserious illness. Kid was ill the day of the planned immunization.	Evidence
Republic of Moldova	Yes	Отчет независемого Центра Социологических и Маркетенговых исследований CBS-AXA по заказу ЮНИСЕФ и МЗ РМ, 2012 год	2.	Недостаточная коммуникация медперсонала с родителями [Inadequate communication of medical staff with parents] Необоснованные медотводы [Unjustified medical contraindications]	Подкрепле но фактами [supported by facts]

Appendix A5.3 Vaccine Hesitancy Survey Questions Related to SAGE Vaccine Hesitancy Matrix

Examples of survey questions designed to assess determinants of vaccine hesitancy

Vaccine hesitancy is an emerging term in the literature and discourse on vaccine decision-making and determinants of vaccine acceptance. To date various surveys have been developed to assess individual attitudes as well as concerns around the risks and benefits immunization yet few surveys are available to specifically assess or measure the prevalence or degree of vaccine hesitancy in a population in Even less surveys have been validated In addition the majority of available surveys has been conducted in high income countries and predominately focuses on identifying vaccine hesitancy at the individual level only and not its underlying determinants.

A universally validated compendium of survey questions is needed to identify vaccine hesitant populations and the drivers of their reluctance at the global, national or subnational level, in order to tailor targeted interventions aiming at increasing vaccine acceptance and ultimately immunization rates. A standardized compendium of survey questions would further ensure intra- and intercountry comparison of the determinants leading to vaccine hesitancy.

The SAGE Working Group on Vaccine Hesitancy^{xii} defined the term Vaccine Hesitancy: "Vaccine hesitancy refers to delay in acceptance or refusal of vaccines despite availability of vaccine service. Vaccine hesitancy is complex and context specific varying across time, place and vaccines. It is influenced by factors such as complacency, convenience and confidence."

In addition the Working Group developed a model of determinants of vaccine hesitancy, based on a systematic review of literature ⁱ and interviews with immunization managers, which categorized drivers into contextual influences, individual and group influences and vaccine or vaccination specific issues^{xiii}. The model of determinants was seen as a useful tool to guide the selection of survey questions sensitive and specific to vaccine hesitancy in order to provide information not only on the overall prevalence of vaccine hesitancy but also its underlying determinants.

The Working Group developed de-novo survey questions tailored to the specific determinant. In addition, survey questions * from a validated parental assessment instrument of vaccine hesitancy were categorized to fit the specific determinants.

The working group notes that these example survey questions represent a range of questions to draw from which could be considered based on the circumstances and context. The list of example survey questions can be found in the Table A5.3.1, Table A5.3.1 and Table A5.3.2 below. Questions highlighted in *italics bold*, are question within the 18 item-containing validated Parent Attitudes about Childhood Vaccines (PACV) survey to assess vaccine hesitant parents in the US $^{\times}$. Factor analysis was used to confirm survey sub-domains and Cronbach's α to determine the internal consistency reliability of sub-domain scales. Construct validity was assessed by linking parental responses to their child's immunization record $^{\times i}$.

The listed example questions are not intended to all be used within one questionnaire but rather present a set of questions to be considered and chosen from based on the individual needs. The Working Group acknowledges that the survey question selection needs to fit the context they are used in. Construct and content validity to assess the individual determinant of vaccine hesitancy of this survey question compendium needs to be assessed. To further ensure that the objective of the compendium is met, the assessment of vaccine hesitancy and its determinants within various settings covering all levels income, pilot-testing of these survey questions needs to be ensured in low-, middle and high-income countries^{xiv} within all 6 WHO regions^{xv}. Particular attention needs to be given to ensuring validity when translating the compendium to languages other than English. Based on the results of this pilot-testing, questions may need to be added or altered.

Table A5.3 .1: Survey questions to assess contextual influences of vaccine hesitancy

CONTEXTUAL INFLUENCES Influences arising due to historic, socio-cultural, environmental, health system/institutional, economic or political factors						
a. Communication and media environment	b. Influential leaders, gatekeepers and anti- or pro-vaccination lobbies	c. Historical influences	d. Religion/culture/gender/ socio-economic	e. Politics/policies (Mandates)	f. Geographic barriers	g. Pharmaceutical industry
Media and social media can create a negative or positive vaccine sentiment and can provide a platform for lobbies and key opinion leaders to influence others; social media allows users to freely voice opinions and experiences and it can facilitate the organization of social networks for or against vaccines.	Community leaders and influencers, including religious leaders in some settings, celebrities in others, can all have a significant influence on vaccine acceptance or hesitancy.	Negative historic influences such as the Trovan trial/ Wakefield MMR-autism scare can undermine public trust and influence vaccine acceptance, especially when combined with pressures of influential leader/media. Community experience isn't necessarily limited to vaccination but may affect it.	A few examples of the interplay of religious/cultural influences include: Some religious leaders prohibit vaccines Some cultures do not want men vaccinating children Some cultures value boys over girls and fathers don't allow children to be vaccinated).	Vaccine mandates can provoke vaccine hesitancy not necessarily because of safety or other concerns, but due to resistance to the notion of forced vaccination	A population can have general confidence in a vaccine and health service, and be motivated to receive a vaccine but hesitate as the health center is too far away or access is difficult.	Industry may be distrusted and influence vaccine hesitancy when perceived as driven only by financial motives and not in public health interest; This can extend to distrust in government when perceived that they are also being pushed by industry and not transparent.
Who do you trust the most for information? Who do you trust the least?	Some groups or leaders do not agree to vaccination for different reasons. In general, do you agree or disagree with these groups?	Do you remember any events in the past that would discourage you from getting a vaccine(s) for yourself or your children?	Do you know anyone who does not take a vaccine because of religious or cultural reasons? Do you agree or disagree with these persons? Do you think they are risking their health or the health of their child if they do not take a vaccine?	Do you trust (or distrust) that your government is making decisions in your best interest with respect to what vaccines are provided?	Has distance, timing of clinic, time needed to get to clinic or wait at clinic and/or costs in getting to clinic prevented you from getting your child immunized?	Do you believe the vaccine producers are interested in your health?
Have reports you heard/read in the media/ on social media made you re-consider the choice to have your child vaccinated?	Do leaders (religious, political, teachers, health care workers) in your community support vaccines for infants and children?	Can you name an event in the past that diminished your trust in vaccination?	Does your religion/ philosophy/ culture recommend against (a certain) vaccination? If so, which/all vaccines? What is the reason?	Did you ever disagree with the choice of vaccine or vaccination recommendation provided by your government?	The time/cost/effort of traveling to the doctor/health post/ clinic with young children is not worth for receiving vaccination only?	Do you think governments are "pushed" by lobbyists or industry to recommend certain vaccines?

Do you share information related to vaccination within your social media network? What type of information?	Would it trigger doubts to have your child vaccinated, if a celebrity advocates against (a certain) vaccine?	Has your community ever felt the need to urgently introduce a new vaccine?	What do you consider more important- vaccination of boys or vaccination of girls? Why?	I'm convinced that my government purchases the highest quality vaccines available.	What is the maximum amount of time you would be able or willing to spend to get a vaccine for yourself or your children?	Do you trust pharmaceutical companies to provide safe and effective vaccines?
Do you recall a vaccine that was positively debated in the media? If so, which one and would you still want this vaccine for yourself/ your child?	Has your imam/priest/ rabbi ever advocated against vaccination? Did you follow this advice?	Has your community in the past refused to accept certain vaccines? Which vaccine(s) and why?	Have you ever refused a vaccine as you considered it to include porcine or other animal derived ingredients (non-halal, non-kosher)?	Did you ever have the impression your government/health care provider did not provide you with the best vaccine on the market?	If you have to spend more than one hour getting a vaccine, is it important enough to travel for it?	
Do you believe in reports in the media by parents claiming to have lost a child to a vaccine preventable disease? Does this affect your decision to vaccinate your child?			Would you refuse a vaccine for you/your child if the vaccinator was male/female or from a different ethnic background/religion than yourself?	The only reason I have my child get shots is so they can enter daycare or school.	Has your life-style (nomadic/ located in different places throughout the course of the year) ever prevented you to receive a vaccine for yourself/your child?	
				Does your child's daycare/ school require/ advice to have your children vaccinated? Do you agree?		

Table A5.3.1: Survey questions to assess individual and group influences of vaccine hesitancy

INDIVIDUAL and GROUP INFLUENCES Influences arising from personal perception of the vaccine or influences of the social/peer environment							
a. Experience with past vaccination	b.Beliefs, attitudes about health and prevention	c.Knowledge/awareness	d. Health system and providers- trust and personal experience.	e. Risk/benefit (perceived, heuristic)	f. Immunisation as a social norm vs. not needed/harmful		
Past negative or positive experience with a particular vaccination can influence hesitancy or willingness to vaccinate. Knowledge of someone who suffered from a VPD due to nonvaccination may enhance vaccine acceptance. Personal experience or knowledge of someone who experienced an AEFI (adverse event following immunization) can also influence hesitancy.	Vaccine hesitancy can result from 1) beliefs that vaccine preventable diseases (VPD) are needed to build immunity (and that vaccines destroy important natural immunity) or 2) beliefs that other behaviors (breastfeeding, traditional/alternative medicine or naturopathy) are as or more important than vaccination to maintain health and prevent VPDs.	Decisions to vaccinate or not are influenced by a number of the factors addressed here, including level of knowledge and awareness. Vaccine acceptance or hesitancy can be affected by whether an individual or group has accurate knowledge, a lack of awareness due to no information, or misperceptions due to misinformation. Accurate knowledge alone is not enough to ensure vaccine acceptance, and misperceptions may cause hesitancy, but still result in vaccine acceptance.	Trust or distrust in government or authorities in general, can affect trust in vaccines and vaccination programmes delivered or mandated by the government. Past experiences that influence hesitancy can includes system procedures that were too long or complex, or personal interactions were difficult.	Perceptions of risk as well as perceptions of lack of risk can affect vaccine acceptance. Complacency sets in when the perception of disease risk is low and little felt need for vaccination. E.g. Patient's or caregiver's perceptions of their own or their children's risk of the natural disease or caregivers' perceptions of how serious or life threatening the VPD is.	Vaccine acceptance or hesitancy is influenced by peer group and social norms		
Have you ever not accepted a vaccination for your child? What was the reason?	Can you tell me what a vaccine is? What does it do to the body?	Do you feel that you know which vaccines you should get for yourself? Your children?	Information on side-effects following immunization is discussed openly by the authorities.	How concerned are you that any one of the childhood shots might not be safe?	I agree that it is important for everyone to get the recommended vaccines for themselves and their children.		
Most children tolerate vaccination very well.	It is my role as a parent to question shots.	Do the vaccinators in door-to- door or mass immunization campaigns provide you with sufficient information to address your concerns around vaccination?	Have you ever felt healthcare professional, government, local authorities are pushing you into a vaccination decision you did not fully support? Why?	Do you think vaccines are still needed even when the disease is no longer prevalent?	Do you think that most parents like you have their children vaccinated with all the recommended vaccines?		
Have you or someone you know ever had a bad reaction to a vaccine which made you reconsider getting vaccines?	Do you think it is possible to have received too many vaccines at one time?	Did you ever inform yourself on a certain vaccine and then decide against it/delay receiving it? If so, why, which vaccine and what resources did you use?	Does having the same provider give all the infant vaccines make you more likely to accept vaccines than having a different provider each time vaccines are due?	I believe that many of the illnesses shots prevent are severe.	Do you think it's important to get a vaccine to protect those that cannot get vaccinated?		

Do you know of a child with a serious disease/ disability because they were not vaccinated?	Do you think vaccines overload the immune system?	Do you feel you get enough information about vaccines and their safety?	I am able to openly discuss my concerns about shots with my child's doctor.	How concerned are you that your child might have a serious side effect from a shot? x	Do the mothers/fathers in your community/ circle of friends have their child vaccinated? Do you have your child vaccinated? Why?
Do you know of anyone who has had a bad reaction to a shot?	It is better for my child to develop immunity by getting sick than to get a shot.	Would you prefer to receive more information on vaccination at your health center? Do you think this would change your choice in favor of a vaccine?	I trust the information I receive about shots.	How concerned are you that a shot might not prevent the disease?	Do you believe that if you vaccinate your child, others are protected as well?
Have you heard of anyone who was disabled after receiving a vaccine? Did this make you reconsider your choice to get yourself/ your child vaccinated?	Do you believe that there are other (better) ways to prevent diseases which can be prevented by a vaccine?	My health professional/HCW's provides me with all the information I need to my questions on immunization.	Do you feel that your health care provider cares about what is best for your child?	Measles/polio/diphtheria is not common where I live. That's why I decided against the vaccine.	Are you worried that some mothers in your community are delaying or refusing vaccines, putting your infant at risk for these diseases e.g. pertussis?
Do experiences with pain with past immunization prevent you or your child form being immunized?	Do you believe that it is better for the child to start to receive them only when over one year of age? Do you believe that shots are given to babies when they too young?	Do you consider that some vaccines are more important than other? Which vaccine(s) and why?		Do you believe that vaccines are still needed when diseasesare rare?	

Table A5.3.2: Survey questions to assess vaccine/vaccination specific issues of vaccine hesitancy

VACCINE/ VACCINATION -specific issues							
Directly related to vaccine or vaccination							
b. Introduction of a new vaccine or new formulation	c. Mode of administration	d. Design of vaccination program/Mode of delivery	e. Reliability and/or source of vaccine supply	f. Vaccination schedule	g. Costs	h. Role of healthcare professionals	
Individuals may hesitate to accept a new vaccine when they feel it has not been used/tested for long enough or feel that the new vaccine is not needed, or do not see the direct impact of the vaccine (e.g. HPV vaccine preventing cervical cancer). Individuals may be more willing (i.e. not complacent) to accept a new vaccine if perception of the VPD risk is high.	Mode of administration can influence vaccine hesitancy for different reasons. E.g. oral or nasal administrations are more convenient and may be accepted by those who find injections fearful or they do not have confidence in the health workers skills or devices used.	Delivery mode can affect vaccine hesitancy in multiple ways. Some parents may not have confidence in a vaccinator coming house-to-house; or a campaign approach driven by the government. Alternatively if a health center is too far or the hours are inconvenient	Individuals may hesitate if they do not have confidence in the system's ability to provide vaccine(s) or might not have confidence in the source of the supply (e.g. if produced in a country/culture the individual is suspicious of); HCWs may also be hesitant to administer a vaccine (especially a new one) if they do not have confidence that the supply will continue as it affects their clients trust in them. Caregivers may not have confidence that a needed vaccine and/or health staff will be at the health facility if they go there.	Although there may be an appreciation for the importance of preventing individual vaccine preventable diseases, there may be reluctance to comply with the recommended schedule (e.g. multiple vaccines or age of vaccination). Vaccination schedules have some flexibility that may allow for slight adjustment to meet individual needs and preferences. While this may alleviate hesitancy issues, accommodating individual demands are not feasible at a population level.	An individual may have confidence in a vaccine's safety and the system that delivers it, be motivated to vaccinate, but not be able to afford the vaccine or the costs associated with getting themselves and their child(ren) to the immunization point. Alternatively, the value of the vaccine might be diminished if provided for free.	Health care professionals are important role models for their patients; if they hesitate for any reason (e.g. due to lack of confidence in a vaccine's safety or need) it can influence their clients' willingness to vaccinate	
What is the first thing you want to know when a new vaccine is introduced or announced? Would you rather wait	Is there any mode of vaccination you would not want?	Is the vaccination process welcoming? Are there any things that could be done to make it easier for you to get vaccines (on	Do you feel confident that the health center or doctor's office will have the vaccine you need, when you need them?	Are there any vaccines that are difficult for you to get because of the schedule?	Would the cost of a vaccine prevent you from getting it, even if you felt you or your child needed it?	Did healthcare professionals ever treat you without respect (e.g. in regard to your appearance, education or cultural background) s	
you wan a new va introduc annound rather w	at to know when accine is sed or sed? Would you	vaccination you would not want? ed or ced? Would you vait	to know when accine is not want? accine is not want? Are there any things that could be done to make it easier for you to get vaccines (on	needed vaccine and/or health staff will be at the health facility if they go there. Is the first thing at to know when accine is not want? Is the vaccination process welcoming? Are there any things that could be done to make it easier for you reed? Would you vait Is the vaccination process welcoming? Are there any things that could be done to make it easier for you reed, when you need them?	needed vaccine and/or health staff will be at the health facility if they go there. Is there any mode of vaccination you would not want? Is there any things ted or ced? Would you vait Is there any mode of vaccination you would not want? Is the vaccination process welcoming? Are there any things that could be done to make it easier for you to get vaccines (on the said of the said of the schedule? Is the vaccination population level. Do you feel confident that the health center or doctor's office will have the vaccine you need, when you need them? Are there any vaccines that are difficult for you to get because of the schedule?	needed vaccine and/or health staff will be at the health facility if they go there. Is there any mode of vaccination you would not want? Is there any things ted or ced? Would you vait Is there any mode of vaccination you would not want? Is the vaccination process welcoming? Are there any things that could be done to make it easier for you to get vaccines (on Is the vaccination process welcoming? Are there any things that could be done to make it easier for you to get vaccines (on Is the vaccination process welcoming? Are there any things that could be done to make it easier for you to get vaccines (on Is the vaccination process welcoming? Are there any things that could be done to make it easier for you to get vaccines (on Is the vaccination process welcoming? The they go there. Are there any vaccines that are difficult for you to get because of the schedule? Individual demands are not feasible at a population level. Are there any vaccines that are difficult for you to get because of the schedule? Individual demands are not feasible at a population level. Are there any vaccines that are difficult for you to get because of the schedule? Individual demands are not feasible at a population level. Are there any vaccines that are difficult for you to get because of the schedule? Individual demands are not feasible at a population level. Are there any vaccines that are difficult for you to get because of the schedule? Individual demands are not feasible at a population level. Are there any vaccines that are difficult for you to get because of the schedule?	

	people do?		your children?				return to the healthcare facility?
Me or my child never experienced severe adverse reactions following immunization. experience an AEFI and	I consider rotavirus vaccine/ HPV vaccine/ meningococcal vaccine/ pentavalent vaccine to be safe.	Do you fear the pain/ to you/your child or fear the needles when receiving a vaccine make you hesitate be to immunized?	Would you rather receive a vaccine as conveniently as possible or with as much medical consultation as possible? Why?	Did you ever not return to a health center/ your doctor after not receiving the vaccine during an initial visit? What were the reasons why you did not receive the vaccine initially?	How sure are you that following the recommended shot schedule is a good idea for your child?	Which medication do you consider more effective- the free-of-charge drugs provided at your health care center/doctor/ by your government or the ones you need to pay for yourself? Why?	Did you choose your doctors based on their willingness to alter or delay the vaccination schedule according to your requests?
Do you consider some vaccine products preventing a disease (influenza-LAIV or standard/ measles (M only or MMR) safer than others?	Do you feel your child to be at risk of diarrhea/ cervical cancer? Do you think a vaccine is needed to prevent these diseases?	Has pain following immunization ever made you reconsider to have yourself/ your child vaccinated?	What would you prefer for yourself/your child: Receive a vaccine at your health center/ from your doctor or from door-to-door vaccinators/ during mass vaccination campaigns/ school-based programs? Why?	Have you ever been sent home from the health center/ doctor's office due to lack of vaccine? If so, did you go again to try and receive it?	If you had another infant today, would you want him/her to get all the recommended shots?	Do you consider all important vaccines provided/ covered by your health insurance/ health care plan/ health care provider? Would you pay for additional vaccines yourself?	Has your healthcare provider ever advised you that a certain vaccine was not necessary or had too many side effects? Which one?
Before administering the vaccine, my health care worker (HCW) always provided me with enough information on the side-effects that might follow.	New vaccines are not trialed to the same rigorous standard as any normally prescribed drug?	Would you be willing to accept more vaccines for yourself/ your child if there was no pain involved?	Would you let your child get vaccinated within a school-based immunization program? If yes, what are the advantages?	At your health center, did you ever not receive a vaccine as the HCW indicated there were too few people to start vaccinating?	Children get more shots than are good for them.	I wouldn't mind taking time off from work to make sure my child gets vaccinated?	Was your doctor ever reluctant to administer a vaccine you wanted for yourself/ your child? Which vaccine and why?
	Have you ever delayed vaccinating your child with a newly introduced/ recommended vaccine? Why?	Do you trust your HCW to safely administer the vaccine to you/ your child?	Did you ever refrain from having yourself/ your child vaccinated during a mass immunization campaign? Why?	Did you ever decide against a vaccine as it was produced by a manufacturer you did not trust? Do you believe vaccines made in Europe or America are safer than those made in middle income countries?	It is better for children to get fewer vaccines at the same time.	Would you be willing to pay for a vaccine privately? If so, for which ones?	Do you trust the door- to-door vaccinators?

References: Please see p. 105

Appendix A5.4 WHO EUR Tailoring Immunization Program (TIP)

The TIP framework can be accessed:

http://www.euro.who.int/The-Guide-to-Tailoring-Immunization-Programmes-TIP.pdf

Appendix A5.4.1:Principles for TIP

PSI Delta Marketing Planning Process 7 Steps; Principles of TIP

- The Situation Analysis analyzes the context in which the intervention operates in order to
 ensure selection of the most appropriate target group and behavior, and identify strategic
 priorities for the marketing plan.
- Audience Insight means getting to know the target group as a real person one with a face
 and a name and one with aspirations and desires, not just as a bunch of demographics.

 Creating such profiles is a technique that has been used successfully by commercial sector
 giants such as Proctor and Gamble.
- 3. **Brand Positioning** is the identification and promotion of the most important and unique benefit that the product/ service/ behavior stands for in the mind of the target group. This is the emotional "hook" upon which one can hang the marketing strategy.
- 4. **Marketing Objectives** specify what you want to achieve during the marketing plan, ensuring it stays focused and true to the evidence. This also facilitates easier monitoring of intervention progress.
- 5. The **Four Marketing "P's"** Product, Price, Place and Promotion -- specify what strategies one will use to achieve the marketing objectives.
- 6. The **Research Plan** details how the intervention will monitor and evaluate implementation of the plan, as well as identifying and prioritizing any information gaps about the target group and how they will be explored.
- An integrated **Budget** and **Work Plan** specify how financial resources will be allocated among
 the 4Ps and help managers allocate human and other resources as well as monitor
 implementation.

Appendix for Section 6.

Appendix A6A.1 Executive Summary of the Systematic Review on Strategies to address vaccine hesitancy

The full systematic review document is published on the SAGE share point. After the SAGE October 2014 meeting, the systematic review will be published on the WHO SAGE website.



EXECUTIVE SUMMARY

SAGE working group dealing with vaccine hesitancy - Systematic Review of Strategies

Introduction

The purpose of the systematic review of strategies for addressing vaccine hesitancy is to identify strategies that have been implemented and evaluated across diverse global contexts in an effort to respond to, and manage, issues of vaccine hesitancy. This is to fulfil the requirements of the SAGE working group (WG) dealing with vaccine hesitancy in respect to:

- a) identifying existing and new activities and strategies relating to vaccines or from other areas that could successfully address vaccine hesitancy;
- b) identifying strategies that do not work well, and;
- c) prioritising activities and strategies based on an assessment of their potential impact.

These requirements were translated into the following specific objectives:

- 1. Identify published strategies related to vaccine hesitancy and hesitancy of other health technologies (reproductive health technologies (RHT) were chosen as the additional focus) and provide a descriptive analysis of the findings;
- 2. Map all evaluated strategies to the SAGE WG "Model of determinants of Vaccine Hesitancy" (Appendix 1) and identify key characteristics;
- 3. Evaluate relevant evaluated strategies relating to vaccine hesitancy using GRADE (Grades of Recommendation, Assessment, Development and Evaluation); relevance was informed by the PICO questions defined *a priori* by the WG, and;
- 4. Synthesise findings in a manner which aids the design of future interventions and further research.

Methods

<u>Objective 1</u> - A systematic literature review methodology was applied to access and assess both peer-reviewed and grey literature. Interventions relating to hesitancy towards RHT were analysed to obtain greater insights surrounding lack of uptake of available health technologies and to ascertain whether strategies aimed at addressing hesitancy towards RHTs could be adopted to address vaccine hesitancy.

<u>Objective 2</u> – Characteristics of evaluated interventions were mapped against the SAGE WG Model of determinants of vaccine hesitancy and also grouped according to one of four identified themes which characterise the type of intervention:

- i) Multi-component
- ii) Dialogue-based
- iii) Incentive-based
- iv) Reminder/recall-based

Objective 3 - The GRADE approach was applied for grading the quality of evidence of a selection of peer-reviewed primary studies that evaluated interventions; selection was based on the relevance of studies to the fifteen PICO questions set out *a priori* by the SAGE WG (Table 2). These questions were developed under one of three intervention themes (further defined below): 1) Dialogue-based, 2) Incentive-based (non-financial), and 3) Reminder-recall. The multi-component theme was excluded in this section because of a preference expressed by the WG to focus on identifying and assessing the impact of single component approaches. However, data were included where a multi-component intervention provided suitable data to assess the effect of its individual component parts. Risk of bias was assessed for each study and the evidence was set out against each individual PICO question.

Theme categories for PICO questions:

- Dialogue-based, which included the involvement of religious or traditional leaders, social mobilisation, social media, mass media, and communication or information-based tools for health care workers;
- ii) **Incentive-based (non-financial)**, which included the provision of food or other goods to encourage vaccination, and;
- iii) Reminder/recall-based, including telephone call/letter to remind the target population about vaccination.

There were two outcomes of interest:

- 1. Outcome 1: Impact on vaccination uptake (behavioural shift);
- 2. Outcome 2: Impact on vaccine/vaccination knowledge/awareness and/or attitude (psychological shift).

Results

Objective 1. Identification of published interventions and descriptive analysis of the findings

Table 1 sets out the number of studies identified across the literature that acknowledged interventions relating to hesitancy (vaccines and RHTs), and whether these were evaluated or not. All evaluated interventions were coded by country, WHO region[†], target vaccine, target population and publication year.

[†] The World Health Organization (WHO) divides the world into six WHO regions, for the purposes of reporting, analysis and administration: WHO African (AFR), WHO region of the

Table 1. Number of studies identified across peer-reviewed and grey literature by hesitancy (vaccine/reproductive health technologies) and intervention type (evaluated/suggested)

			Total count	Outcome 1	Outcome 2	Outcomes 1 & 2
Vaccine	Peer- reviewed literature	Primary studies identified	1149	-	-	-
		Evaluated intervention	166 (14%)	115 (69%)	37 (22%)	14 (9%)
		Suggested intervention	983 (86%)	-	-	-
Hesitancy	Grey literature	Studies/articles identified	59	-	-	-
		Evaluated intervention	15 (25%)	9 (60%)	3 (20%)	3 (20%)
		Suggested intervention	44 (75%)	-	-	-
Hesitancy around Reproductive Health Technologies	Grey literature	Studies/articles identified	51	-	-	-
		Evaluated intervention	13 (25%)	4 (31%)	2 (15%)	7 (54%)
		Suggested intervention	38 (75%)	-	-	-

Overall, for the period January 2007-October 2013, the number of peer-reviewed studies evaluating interventions peaked in 2011 and has remained relatively stable since. However, only five studies actually used the terms 'vaccine hesitant/hesitancy', which indicates the relative newness of the concept and use in research vernacular. Studies that did not explicitly mention vaccine hesitancy were however retained because they indicated research on conceptually similar issues that matched one or more of the determinants of vaccine hesitancy as set out in the SAGE WG model of determinants of vaccine hesitancy. Very few evaluated interventions were identified in the grey literature with one or two articles annually at most from 1996-2012. However, in 2013, eight relevant articles were found.

Objective 2. Mapping of evaluated strategies and identification of key characteristics.

Vaccine hesitancy

The majority of evaluated studies were based in the AMR region and primarily focused on influenza, HPV and childhood vaccines. In low- and middle-income regions, particularly SEAR and AFR, the focus was on DTP and polio. All regions had studies anticipating or researching acceptance of the newly introduced HPV vaccine.

Americas (AMR), WHO South East Asia (SEAR) WHO European (EUR), WHO Eastern Mediterranean (EMR) and WHO West Pacific (WPR).

Most interventions targeted parents, healthcare workers and the local community/parents (found mostly in the AMR and EUR regions). Interventions from the AFR region dominated the grey literature and tended to focus on the local community and religious leaders.

When the interventions were assessed against the SAGE WG model of determinants of vaccine hesitancy, the most common type of intervention sought to address individual and social group influences such as using knowledge and awareness raising strategies. For vaccine and vaccination-specific interventions, approaches focused mainly on mode of delivery and the role of healthcare professionals. The engagement of religious and other community leaders was most commonly applied to address contextual influences of vaccine hesitancy such as religious, cultural and gender issues.

Across all the literature and WHO regions, most of the interventions were multi-component. Dialogue-based interventions were common in all regions except EMR; reminder –recall approaches featured predominantly in higher-income regions; and, incentive-based interventions were only found in AMR and AFR (single-component), and SEAR (part of a multi-component approach).

Which interventions have been most successful?

Overall for Outcome 1 (vaccination uptake), the interventions with the largest positive effect estimates are those that (not in order of importance): 1) directly target unvaccinated or undervaccinated populations; 2) aim to increase knowledge and awareness surrounding vaccination; 3) improve convenience and access to vaccination; 4) target specific populations such as the local community and HCW; 5) mandate vaccinations or impose some type of sanction for non-vaccination; 5) employ reminder and follow-up; and 6) engage religious or other influential leaders to promote vaccination in the community. For Outcome 2 (psychological shift), the introduction of education initiatives, particularly those that embed new knowledge into a more tangible process (e.g., hospital procedures, individual action plans), were most successful at increasing knowledge and awareness and changing attitudes. For both outcomes, some education/awareness strategies are, of course, better than others. In particular, those that tailor the intervention to the relevant populations and their specific concerns or information gaps are most effective. Altogether, the most effective interventions employed a number of these strategies (multi-component interventions) to increase vaccine uptake, knowledge and awareness and shift attitudes towards pro-vaccination.

Which interventions have been least successful?

In general, interventions that focused on quality improvement strategies (e.g., standing orders, improved data collection and monitoring, extended clinic hours) at clinics did not reap great changes in vaccine uptake. Similarly, interventions that adopted interventions that were only applicable to the individual from a distance (e.g., posters, websites, media releases, radio announcements) brought little benefit. Incentive-based interventions using either conditional or non-conditional cash transfers were not successful, although these interventions were usually targeting general preventive health engagement and not just vaccination. Lastly, while reminder-recall interventions have been shown to be effective, they can also be ineffective. These findings highlight the importance of not generalising interventions before understanding the different target audiences, vaccine of interest and setting.

RHTs

Interventions relating to hesitancy around RHT were found across all WHO regions but the majority were from in AFR and SEAR. Many interventions did not focus on a specific RHT but male and female

condoms featured prominently. Many interventions sought to address contextual issues such as gender norms (often aimed at men) and the influence of individual/social group determinants, especially beliefs and attitudes about reproductive health. Most interventions, particularly in low income regions, adopted a dialogue-based (57%) approach; the primary target populations were healthcare workers, and religious and influential leaders, who as part of the strategy, were encouraged to involve local community members to bring about change.

Which interventions have been most successful?

The interventions with the largest effect estimates on uptake of RHT focused on leaders having dialogue with their communities. Leaders included those from government, religious institutions, and the local community (both male and female). These interventions centred on the interpretation of local religious and cultural norms, particularly around the understanding and perceptions of men, and sought to create an environment to support pro-RHT decision-making. At a broader contextual level, group sessions with journalists and mass media campaigns were also used to positive effect to support message consistency. As found for vaccine hesitancy, multicomponent interventions proved most effective.

Which interventions have been least successful?

There are not as many examples to draw more general statements from for RHT however, the interventions that were less successful were those that did not engage closely with the individual. Specifically, the use of field workers instead of local opinion leaders was not as effective as employing both in community group discussions. Familiarity and trust with the messenger seems to be a key feature in these instances.

Objective 3. Evaluation of relevant evaluated strategies relating to vaccine hesitancy.

Of 129 studies available to potentially address the questions set out by SAGE, only 13 studies were relevant (reporting on Outcome 1) and eligible (usable data) for inclusion in this section. Overall, of the fifteen original PICO questions, only ten were able to be addressed, and often each had only one study from which to draw evidence.

Thirteen studies met the inclusion criteria for evaluation using GRADE; three were cluster randomised; three were individually randomised; four were single group cohorts and three were two group cohorts. The process of delivering the interventions varied as did the outcomes reported. Consequently only one outcome (two studies) for a single vaccine was pooled; meta-analysis was not feasible for any of the other outcomes. Summary of relative risk ratios (RR) and evidence quality (GRADE) for each question are presented in Table 2.

Table 2. PICO questions proposed by SAGE working group, RR (95% CI), and evidence quality (GRADE)

Theme	PICO#	Question	Evidence available	RR & 95% CI	Evidence Quality (GRADE)
Dialogue- based	1	Does the involvement of a religious leader increase uptake of all vaccines included in primary routine immunisation in populations with low baseline vaccination coverage (≤50%) compared to a control group/no intervention?	Yes	RR 4.12 (3.99, 4.26)	Very low
	2	Does the involvement of a religious leader increase uptake of all vaccines included in primary routine immunisation in populations with high baseline vaccination coverage (≥80%) compared to a control group/no intervention?	No	-	-
	3	Does the involvement of a traditional leader increase uptake of all vaccines included in primary routine immunisation in populations with low baseline vaccination coverage (≤50%) compared to a control group/no intervention?	Yes	RR 4.12 (3.99, 4.26)	Very low
	4	Does the involvement of a traditional leader increase uptake of all vaccines included in primary routine immunisation in populations with high baseline vaccination coverage (≥80%) compared to a control group/no intervention?	No	-	-
	5	Does social mobilisation increase uptake of all vaccines included in primary routine immunisation by parents in low income settings compared to a control group/no intervention?	Yes	Range of findings; RR 1.54 (1.1, 2.15) to RR 1050.00 (147.96, 7451.4)	Range: Very low to Moderate
	6	Do social media interventions increase uptake of all vaccines included in primary routine immunisations by parents in high income settings compared to a control group/no intervention?	Yes	Range of findings; RR 2.01 (1.39, 2.93) to RR 2.38 (1.23, 4.6)	Range: Very low to Low
	7	Do awareness raising/information provision using mass media interventions increase uptake of all vaccines included in primary routine immunisation by parents in high income settings compared to a control group/no intervention?	Yes	RR 1.57 (1.4, 1.75)	Moderate
	8	Does communication tool-based health care worker (HCW) training increase uptake of all vaccines included in primary routine immunisation by (rostered) patients compared to a control group/no intervention?	Yes	Range of findings; RR 1.54 (1.33, 1.79) to RR 3.09 (2.19, 4.36)	Range: Low to Moderate

	9	Does information-based health care worker (HCW) training increase uptake of all vaccines included in primary routine immunisation by (rostered) patients compared to a control group/no intervention?	Yes	Range of findings; RR 0.99 (0.93, 1.06) to RR 2.83 (2.6, 3.08)	Very Low
Non- financial incentive- based	1	Do non-financial incentives increase uptake of all vaccines included in primary routine immunisation in parents compared to a control group/no intervention?	No	-	-
	2	Do non-financial incentives increase uptake of all vaccines included in primary routine immunisation in parents/communities located in low-income settings compared to a control group/no intervention?	Yes	RR 2.16 (1.68, 2.77)	Moderate
	3	Do non-financial incentives increase uptake of all vaccines included in primary routine immunisation in populations targeted by vaccination campaigns compared to a control group/no intervention?	No	-	-
	4	Do non-financial incentives increase uptake of all vaccines included in primary routine immunisation in populations with low baseline vaccination coverage (≤50%) compared to a control group/no intervention?	No	-	-
Reminder /recall- based	1	Do reminder or recall-based interventions increase uptake of all vaccines included in primary routine immunisation in parents or communities located in low-income settings compared to a control group/no intervention?	Yes	RR 1.26 (1.13, 1.42)	Moderate
	2	Do reminder or recall-based interventions increase uptake of all vaccines included in primary routine immunisation in populations with low baseline vaccination coverage (≤50%) compared to a control group/no intervention?	Yes	RR 3.22 (1.59 to 6.53)	Very Low

Dialogue-based interventions

Eleven studies evaluated by PICO and GRADE deployed dialogue based interventions to address vaccine hesitancy (see definition page 7). There was appreciable variability in the quality of evidence supporting the use of these interventions and their impact varied considerably, by type of intervention, by vaccine and by setting.

For polio, the involvement of religious or traditional leaders in populations with low baseline uptake indicated a large, positive effect on vaccine uptake but the evidence quality was assessed as very low.

Five studies using social mobilisation among parents in low-income settings had a positive effect on uptake of measles (RR 1.63 [1.39, 1.91]), DTP3 (RR 2.17 [1.8, 2.61]), DTP1 (RR 1.54 [1.1, 2.15]), and polio (RR 1050.00 [147.96, 7451.4]) vaccines. The quality of evidence for each outcome ranged from moderate (measles, DTP3), to low (polio) and very low (DTP1). Two studies targeting those declining polio vaccination were associated with large increases in uptake in this population.

Two studies evaluated interventions utilising social media; these had a positive effect on uptake for MCV4/Tdap (RR 2.01 [1.39, 2.93]) and seasonal influenza (RR 2.38 [1.23, 4.6] although respectively, the evidence was assessed as of very low and low quality respectively.

A study utilising mass media to target parents with low levels of awareness of health services was associated with increased uptake of all routinely recommended vaccines (RR 1.57 [1.4, 1.75]). The quality of evidence was moderate but the effect size was not large.

The provision of communication tool-based training for health care workers had a positive impact on uptake of EPI (RR 3.09 [2.19, 4.36]) and DTP3 (RR 1.54 [1.33, 1.79]) among rostered patients; evidence quality was assessed as moderate and low respectively.

One study assessed the impact of information-based training for health care workers on uptake for rostered patients, with varying results. There was little or no increase in uptake of DTP/OPV-1 (RR 0.99 [0.93, 1.06]), DTP/OPV-2 (RR 1.04 [0.97, 1.12]), BCG (RR 1.01 [0.95, 1.08]) and measles (RR 1.02 [0.96, 1.09]), a moderate increase in uptake of HepB-2 (RR 1.63 [1.49, 1.79]), HepB-3 (RR 1.89 [1.74, 2.04]) and DTP/OPV-3 (RR 1.42 [1.33, 1.51]), and a substantial increase in uptake of HepB-1 (RR 2.83 [2.6, 3.08]); but the evidence quality was very low for all.

Non-financial incentives

The evidence for non-financial incentives for parents/communities located in low-income settings was moderate for a large, positive effect on uptake of EPI vaccines (RR 2.16 [1.68, 2.77]).

Reminder-recall interventions

Two studies assessed the impact of reminder-recall interventions on vaccine uptake in a) low income and b) under-vaccinated populations. The impact of reminder-recall interventions in low-income settings was positive for DTP3 (RR 1.26 [1.13, 1.42]) with moderate quality evidence. For settings with low baseline uptake, the effects were large and positive for scheduled childhood vaccines (RR 3.22 [1.59, 6.53]) but the quality of evidence was very low.

Discussion

PICO & GRADE studies

All interventions were associated with increases in vaccine uptake but there are several issues that hinder interpretation of the evidence. Interventions varied considerably in outcome impact, type of strategy, setting and target vaccine, which makes generalisability difficult; variations in study design further increased issues of heterogeneity. The majority of studies were observational and so we cannot assume a causal relationship between the intervention and vaccine uptake. Two studies were at major risk of bias and the quality of the evidence varied considerably.

Dialogue-based interventions

Despite the low quality of the evidence for the **involvement of religious or traditional leaders** in populations with low baseline uptake, the strength of the intervention's impact deserves exploration. This intervention is important as it addresses one of the more difficult determinants of vaccine hesitancy, namely misconceptions and community distrust. It attempts to address these using a variety of communication and engagement channels and gives attention to all aspects of community life that might influence vaccination decisions irrespective of age. This intervention also appears to align itself with natural community processes – seeking out community leaders; and encouraging dialogue across multiple levels in order to both inform and influence. In essence, the success of the intervention could be attributed to the efforts made to seek understanding of the target audience, facilitate open dialogue and integrate activities with familiar processes and systems.

The broad success of the **social mobilisation** intervention for populations refusing polio vaccination could be attributed to the design and application of specific strategies that directly targeted this clearly defined population. By comparison, the other two social mobilisation interventions for measles and DTP were much less targeted. Positive outcomes associated with these interventions appear to be due to meaningful dialogue at both the group and individual level.

The use of **social media** interventions showed positive effects but the quality of evidence was low to very low. The examples suggest that this approach might work well for those who have already started their vaccination schedule, or are familiar using such systems to organise difference aspects of their lives. However, there is important evidence that social media is also very open to exploitation if not managed well.

The application of **mass media** to target parents with low levels of awareness of health services appears to have a valid place as an effective intervention, and whilst in the identified example, impact is limited, there is good potential for a true positive effect across a larger population. However, the limited impact in this case also suggests that there may be other underlying issues affecting low impact that need investigation and subsequent tailoring of more-specific strategies in response.

The provision of **communication tool-based training for health care workers** generally had a positive effect (for EPI, DTP3) but the size of the effect and evidence quality varied. The observations about this example and mass media suggests that interventions that adopt a unidirectional (top down) approach to communication, may be successful among some individuals and groups, but not all; success is dependent on the nature and degree of hesitancy.

The impact of **information-based training for health care workers** on uptake of several vaccines for rostered patients was generally poor. A possible explanation for these results is that there was no clear understanding of the underlying reasons for the low vaccination uptake and as such, the intervention was not appropriately targeted. Nonetheless, the intervention did achieve good success with Hepatitis (all doses) and DTP/OPV (dose 3); one possible reason for this is that the health workers exhibited greater confidence but it is not clear whether this was an issue prior to the intervention.

Non-financial incentives

The moderate to large impact of non-financial incentives for parents/communities located in low-income settings on vaccination uptake is promising. However, in this study the target group was very disadvantaged and as such, the food-based incentive, so closely linked with basic survival, was unsurprisingly readily received. Furthermore, the baseline vaccination rates were very low (2%), which suggests that this target group were underserved and more likely to show greater outcome changes with an intervention. In this instance, it is possible that by addressing basic needs, this intervention simultaneously built confidence and reduced vaccine hesitancy because the target population felt that their other critical needs were being recognised, and not superseded by vaccines alone. This symbiotic approach could be particularly important for more marginalised groups.

Reminder-recall interventions

Although positive, the relatively low observed impact of reminder-recall interventions in low-income settings seems to reflect the limitations of using this kind of intervention in isolation. In this example, a complex set of issues was identified in the target population but the intervention only addressed one of them. Reminder-recall on its own is clearly not enough to tackle contexts where there are multiple determinants at play.

Overall completeness and applicability of evidence

Despite the low number of studies, there is some opportunity to be moderately confident in several of the interventions including: social mobilisation, mass media, communication tool-based training for HCW, non-financial incentives, and reminder-recall activities. However, none of these interventions were without shortcomings, and given the additional caveats around indirectness and the variability in content, setting, delivery method, target population composition and effect estimates across outcomes, the success, and potential application, of these interventions must be cautiously considered when looking to deliver them in different circumstances.

Objective 4. Synthesis of findings

Overall this review has found that there are 1) few existing strategies that have been explicitly designed to address vaccine hesitancy; and 2) even fewer strategies that have been evaluated for impact. The first of these issues is most likely because 'vaccine hesitancy' is an emerging issue, which to date, has not had a clear definition from which to explore and interrelate identified concerns. As such, interventions are often only half-conceived; target audiences are not always appropriately identified, and there is a lack of rigorous understanding of the actual problem. Interventions around polio vaccination are the exception to this – and the findings of this review indicate their greater success as a result.

At present, the efforts that have been made to address issues of hesitancy are disparate. This is not surprising given the complexity of the problem but it does make interpretation of the evidence more difficult. Specifically, while a number of interventions did have a positive impact, it was variable. Wide variation was observed in the effect size between studies, settings and target populations. Even within studies there was wide variation on the impact on uptake of specific vaccines. In addition, the high level of heterogeneity across study design and outcomes coupled with few available studies further limited our ability to draw many general conclusions about the effectiveness of different strategies.

Nonetheless, across the literature, interventions that are multicomponent and/or have a focus on dialogue-based approaches tend to perform better. This message is corroborated by the more formal GRADE assessment of the evidence which indicated greater quality of evidence for social mobilisation, mass media and communication tool-based training for HCW. Together, these interventions suggest that taking a comprehensive approach that targets multiple audiences and layers of social interaction are more likely to bring positive results. The evidence for the other interventions, non-financial incentives and reminder-recall activities, was also of good quality, and carries the potential to bring positive change by addressing the more practical aspects of vaccination. It is important to reiterate however, that the key to success seems to lie in designing more complex, but integrated, multi-component interventions.

This review shows that vaccine hesitancy is a complex issue and no single strategy will be able to address it single-handedly. There are some promising examples, but many are incomplete and most are not directly comparable. Perhaps one of the greatest drawbacks of the interventions identified is that so many operate from an assumption-based rather than an evidence-based approach; appropriate evaluation is also lacking. On a more positive note, there is a growing body of research on the determinants of vaccine hesitancy which can help inform and refine currently used approaches that look promising but have not yet been fully implemented nor evaluated, as well as supporting the formative research, design and evaluation of new interventions. This is an opportunity to develop early learnings and set the precedent to advance the understanding and management of issues of vaccine hesitancy.

Limitations

This review may be subject to publication bias, in that unsuccessful interventions may be less likely to be documented in either the peer-reviewed or grey literature. Consequently, although the review gives some indication of interventions that successfully reduced vaccine hesitancy in specific populations and settings, interventions that were found to have no effect or a negative effect may be under-represented.

Conclusions and implications

Literature identified

- Despite extensive literature searches, only 14% (166/1149) of the peer-reviewed studies and 25% (15/59) of the grey literature, discussed evaluated interventions relating to vaccine hesitancy; the bulk of the literature originated from AMR and EUR.
- Across all regions and literature, the majority of interventions were multi-component in nature, followed by dialogue-based approaches (except EMR which only featured multicomponent). Reminder-recall interventions featured only in higher-income regions (AMR, EUR, WPR), and incentives appeared only in AMR and AFR.

Interventions – which were successful and which were not?

- Whilst several approaches taken independently can be successful, the most effective interventions employed a number of strategies (multi-component interventions) to increase vaccine uptake, knowledge and awareness, and shift attitudes towards pro-vaccination. The most promising strategies for Outcome 1 (vaccination uptake) included (in no particular order): 1) directly target unvaccinated or under-vaccinated populations; 2) aim to increase knowledge and awareness surrounding vaccination; 3) improve convenience and access to vaccination; 4) target specific populations such as the local community and HCW; 5) mandate vaccinations or impose some type of sanction for non-vaccination; 5) employ reminder and follow-up; and 6) engage religious or other influential leaders to promote vaccination in the community. For Outcome 2 (psychological shift), the introduction of education initiatives, particularly those that embed new knowledge into a more tangible process (e.g., hospital procedures, individual action plans), were most successful at increasing knowledge and awareness and changing attitudes.
- Consistent with the above and notwithstanding the small number of studies, the GRADE
 approach yielded evidence in which there is moderate confidence for several types of
 interventions including: social mobilisation, mass media, communication tool-based training
 for HCW, non-financial incentives, and reminder-recall activities. However, all studies had
 weaknesses and strategies should be carefully considered before adopting them in different
 settings.
- Review of the interventions adopted to address hesitancy around RHT showed an important
 parallel with those for vaccine hesitancy. Specifically, dialogue-based interventions,
 particularly those incorporating a focus on community engagement/social mobilisation and
 the improvement of HCW communication, were most effective for improved uptake.
- Interventions that were single-component did not work as well as those that were multi-component. Also, interventions that were the most passive (e.g., posters, radio announcements, websites and media releases) that did not have an additional engagement component were less effective. It is possible that there are more examples of interventions that have failed in the field but these receive little attention in the literature; identification of and lessons from these experiences will need to be explored through different means.

Opportunities

- Despite the large body of literature on the many determinants of vaccine hesitancy, most interventions have focused on individual level issues (e.g., knowledge, awareness) and vaccine/vaccination specific concerns (e.g., mode of delivery, role of healthcare professionals). There needs to be more attention given to understanding and addressing hesitancy at the community level (e.g. social norms).
- There is an opportunity to broaden the outcomes of interest when assessing the effects of interventions, in particular, more intermediary outcomes such as changes in knowledge, norms, attitude and awareness. These outcomes might indicate important shifts along the vaccine continuum, either away from or towards acceptance, even if they do not necessarily lead to a change in vaccination uptake. Appreciating where individuals and communities lie on the continuum and what defines this offers another insight to inform intervention design.

Limitations

- The term/concept of 'vaccine hesitancy' has only recently been coined and has not yet found general currency among researchers or immunisation professionals. To overcome this issue, the SAGE WG Model of determinants of Vaccine Hesitancy was used as a default coding tool whereby only those studies that reported on interventions to address one or more of the determinants were included. Studies that reported on strategies that impacted on vaccination uptake in general were excluded (such as system or supply issues).
- Another reason for the paucity of relevant studies is that the questions emphasise specific, single component strategies, but many evaluated strategies are neither designed nor presented in this way. Evaluated, multi-component interventions were identified but only overall impact data were presented and VH data was not separately available.

Key lessons

- Vaccine hesitancy is complex and dynamic; future strategies need to reflect and address
 these complexities in both design and evaluation. In the first instance, implementers must
 adequately identify the target population and understand the true nature of their particular
 vaccine and/or vaccination concerns; this will help ensure a well-informed intervention.
- Well integrated, multi-component strategies should be promoted and must be accompanied
 by an appropriate evaluation process. Specifically, implementers must be able to appreciate
 the influence of individual components which will benefit the immediate operations and the
 design of future interventions.
- Overall, the design and delivery of interventions should try to reflect the following points: 1)
 Target audiences should be clearly identified and specific issues well researched and
 understood; 2) Interventions should focus on meaningful engagement (i.e., dialogue-based,
 social mobilisation) that supports realistic action; 3) Contextual influences, from the
 individual through to the health system, should be acknowledged and accounted for when
 choosing strategies; 4) Interventions should be multi-component and seek to address
 primary determinants of uptake across the different domains of influence; 5) Interventions
 must be evaluated.

Appendix A6A.2 Strategies to address vaccine hesitancy: summary of published literature reviews*:

* Table A6.1 presents Main conclusions of published literature reviews and meta-analysis on strategies to address vaccine hesitancy (2006 to 2014)

Table A6.1 Main conclusions of published literature reviews and meta-analysis on strategies to address vaccine hesitancy (2006 to 2014)

Increasing Appropriate Vaccination, The Community Guide [14]

<u>Recommended</u> interventions to increase Community Demand for Vaccinations:

- Client or family incentive rewards.
- Reminder and recall interventions.
- Community-based interventions implemented in combination.
- Vaccination requirements for child care, school, and college attendance.

Recommended Provider- or System-based Interventions

- Health Care system-Based Interventions Implemented in Combination.
- Immunization Information Systems.
- Assessment and feedback for vaccination providers.
- Provider Reminders
- Standing Orders.

There is **insufficient evidence** to determine the effectiveness of:

- Client-held Paper Immunization Records.
- Clinic-Based Education when Used Alone.
- Community-Wide Education when Used Alone.
- Monetary Sanction Policies.

There is **insufficient evidence** to determine the effectiveness of:

- Provider Education when Used Alone.

What are the factors that contribute to parental vaccine-hesitancy and what can we do about it?, Williams S.E., 2014 [1]

Current data does not support one method for intervention as superiorly effective over others.

- Vaccine decision-making for vaccine-hesitant families is complex and this contributes to the lack of evidence for effective interventions.
- Most reported interventions are primarily educational and few interventions have evaluated the ultimate outcome: on-time vaccination.

Cultural tailoring and message framing of interventions have been used successfully in conjunction with educational material for vaccine-hesitant parents.

A systematic review of interventions for reducing parental vaccine refusal and vaccine hesitancy, Sadaf, A., 2013 [4]

The review did not reveal any convincing evidence on effective interventions to address parental vaccine hesitancy and refusal.

- Main evaluated interventions were: reminder/recall systems; educational interventions; incentives and government and school immunization policies.
- Few intervention studies measured outcomes linked to vaccine refusal (vaccination rates in refusing parents, intent to vaccinate, or

- change in attitudes).
- Most studies evaluating the impact of parent-centered information or education reported a statistically significant improvement on parents' intentions to vaccinate their children. However, parents' attitude changes were inconsistent.

Can lay health workers increase the uptake of childhood immunisation? Systematic review and typology, Glenton, C., 2011 [5]

- Evidence was of low quality for LHWs promoting immunization uptake among families in LMICs.
- However, the LHW programme increased the number of children whose DPT and measles immunizations were up to date

Interventions for improving coverage of child immunization in low- and middle-income countries, Oyo-Ita, A., 2011 [9]

Home visits and health education may improve immunization coverage but the quality of evidence is low.

- There was **low quality evidence** that: facility based health education may improve the uptake of DPT3 coverage; and also that a combination of facility based health education and redesigned immunization cards may improve DPT3 coverage.
- There was also **moderate quality evidence** that: evidence-based discussions, and that information campaigns increase uptake of at least a dose of a vaccine.

Too little but not too late: Results of a literature review to improve routine immunization programs in developing countries, Ryman, T.K. 2008 [10]

Few papers were identified and fewer were of strong scientific quality.

- The strategies to "bring immunizations closer to the community" (including non-health workers to encourage people to seek immunization services, bringing immunization services to communities, and increasing demand through educating communities) could improve childhood vaccine uptake.
- Use of home visits for education and/or immunization service delivery may increase childhood vaccine uptake.

Increasing the demand for childhood vaccination in developing countries: a systematic review, Shea, B., 2009 [11]

Most studies reviewed represented a low level of evidence.

- Interventions with an impact on vaccination uptake included knowledge translation (KT) (mass media, village resource rooms and community discussions) and non-KT initiatives (incentives, economic empowerment, household visits by extension workers). Most claimed to increase vaccine coverage by 20 to 30%.
- Mass media campaigns may be effective, but the impact depends on access to media and may be costly if run at a local level. The
 persistence of positive effects has not been evaluated.

Educational interventions to increase HPV vaccination acceptance: A systematic review, Fu, L.Y., 2014 [6]

No strong evidence to recommend any specific educational intervention for wide-spread implementation.

 Well-designed studies adequately powered to detect change in vaccine uptake were rare and generally did not demonstrate effectiveness of the tested interventions. Few studies used the outcome of HPV uptake. Systematic literature review of the evidence for effective NIS promotional communications, Cairns, G., 2012 [7]

There is good evidence that a range of promotional communications can positively change knowledge, attitudes and behaviours.

- Interventions aiming to promote more favorable attitudes to immunization did **not** report success. Interventions aiming to improve knowledge levels did report success, but did **not** demonstrate any positive effects on vaccine uptake / intention.
- Many interventions combined communication channels and methods, so it is not possible to identify which types of communication initiatives are most effective. Many interventions included structural change to make immunizations more accessible, so it is not possible to determine the net contribution of communications.

Face to face interventions for informing or educating parents about early childhood vaccination, Kaufman, J., 2012 [8]

The limited evidence available is low quality and suggests that face to face interventions to inform or educate parents about childhood vaccination have little to no impact on immunization status, or knowledge or understanding of vaccination.

- Communication about vaccination should be incorporated into a healthcare encounter, rather as separate activities

Strategies to improve vaccination uptake in Australia, a systematic review of types and effectiveness, Ward, K., 2012 [3]

The most effective and common strategies for increasing community demand and provider based interventions were <u>patient</u> <u>reminder/recalls</u> and <u>provider reminders</u>.

- Education for the public and providers (alone or as part of multicomponent strategy) had variable impact on uptake.
- Other effective strategies in target groups / for specific vaccines: integration of vaccination status checks into routine health assessments, individual provider support, and targeted promotion campaigns in the mass media.

Primary care strategies to improve childhood immunization uptake in developed countries: systematic review, Williams, N., 2011 [2]

- Strategies with positive effect on immunization uptake: parental reminders, provider reminder/recall strategies, provider education
 and provider feedback, multicomponent interventions (insufficient evidence to distinguish which component of the intervention has
 had the greatest effect on immunization rates)
- **Insufficient evidence** on the effect of parental education interventions on parental behavior.

Strategies to address vaccine hesitancy: summary of published literature reviews:

Review by Eve Dube, Institut national de santé publique du Québec (INSPQ), Québec (Québec), G1E 7G9, Canada

Since 2006, 11 literature reviews or meta-analysis on strategies to increase vaccine uptake or vaccine acceptance in the public or among health care providers have been published. [1-11] Only 2 of these reviews were directly targeting strategies to address vaccine hesitancy (defined as voluntary refusal or delay of recommended childhood vaccines while vaccination services are available). [1, 4] In addition, in collaboration with the US Centers for Disease Control and Prevention the Community Guide³ also regularly publishes evidence-based recommendations on interventions intended to improve routine delivery of universally recommended vaccinations in the United States, based on a logic framework that has been described by Briss and collaborators in 2000. [12] Table 1 presents a summary of the published literature reviews and a meta-analysis on strategies to increase vaccine uptake or vaccine acceptance.

Additionally, on behalf of the Working Group, the London School of Hygiene and Tropical Medicine (LSHTM) conducted a literature review to identify individual studies that have been implemented across diverse global contexts in an effort to respond to, and manage, issues of vaccine hesitancy.[See Appendix]^[add ref] Of the 1149 primary studies that were identified, only 166 provided information on evaluated interventions and even fewer were directly targeting vaccine hesitant individuals.

Looking at the literature, there is no strong evidence to recommend any specific intervention to address vaccine hesitancy or refusal. The reviewed studies included interventions of diverse content and approaches implemented in different settings and targeting various populations. The number of interventions similar enough to be grouped was often low and insufficient to demonstrate effectiveness using recognized validation criteria [www.cochrane-handbook.orgeditors]. In addition, many of the reviewed studies were conducted in the United States and few were from LMIC, which further limits global generalizability of the findings. The high quality studies that were reviewed were mostly single-component interventions (often educational interventions) that are less challenging to evaluate than multi-component interventions or interventions aiming to change determinants that are difficult to measure (such as social norms). Finally, few studies included in the reviews used vaccine uptake or on-time vaccination as an outcome and even fewer studies directly targeted vaccine hesitant patients.

While acknowledging these caveats, findings indicate that reminders and recall for patients and health care providers are effective means of improving vaccine uptake among various groups and in different settings.^[2, 3, 14] However, there is limited evidence on the effectiveness of reminders and recalls for vaccine-hesitant patients.^[15, 16] There is mixed evidence on the effectiveness of face-to-face communication interventions, health care providers training interventions, community-based interventions and communication interventions using mass media. For instance, many communication tools aimed at helping health care

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³The Community Guide is a website that houses the official collection of all Community Preventive Services Task Force findings and the systematic reviews on which they are based. Available online: Guide to Community Preventive Services. Increasing appropriate vaccination: www.thecommunityguide.org/vaccines/index.html. Last updated: 06/12/2014. Page Accessed: 06/25/2014.

provider discussions with vaccine-hesitant parents have been published, [17-21] but few have been evaluated. Whereas communication frameworks often suggest discussing vaccines in a participatory and open manner, a 2013 study by Opel, et al. found that more directive, presumptive discussion styles might be more effective to improve vaccine acceptance in the middle to upper class vaccine hesitant Seattle population studied. [22] In addition, interventions using mass media, including the internet, are challenging to evaluate and are not well-suited to experimental design; other type of evaluations are subject to various bias due to the many potential confounding factors which limits the quality of the evidence available.

Nevertheless, key principles to optimize the development of strategies to address vaccine hesitancy can be identified when looking at the literature. To be effective, interventions should be developed using a planning framework, such as the TIP toolkit (See Section 5), and should be based on a theoretical model. ^[7] The use of a combination of different interventions (multiple-components) appears to be more effective than single-component intervention. ^[2, 14, 23] Interventions are most likely to succeed when they are based on empirical data and situational assessment – both to have a detailed level of understanding of the vaccine hesitancy situation (susceptible populations, key determinants of vaccination, barriers and enabling conditions, etc.) than to properly evaluate the impact of the intervention. ^[7, 24] Finally, the development of culturally-tailored and personalized interventions have shown to be effective to enhance compliance to preventive behaviors, including vaccination. ^[4, 25-27]

Table 1.Summary of published literature reviews and meta-analysis on strategies to address vaccine hesitancy (2006 to 2014)

Title/ First author/	Description of the reviews			Nb of	Quality	
year of publication	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure	studies included	assessment of studies	Main conclusions
Increasing Appropriate Vaccination, The Community Guide ^[14]	To presents the results of systematic reviews of the effectiveness, applicability, other effects, economic impact, and barriers to use of selected population- based interventions intended to improve vaccination coverage in HIC	Inclusion: Interventions addressing universally recommended adult, adolescent, or childhood vaccinations Primary study Take place in HIC Be written in English Meet the evidence review and Guide chapter development team's definition of the interventions Provide information on one or more outcomes related to the analytic frameworks Compare a group of persons who had been exposed to the intervention with a group who had not been	Vaccine uptake	From 2 to 240 depending on the type of interventions	Reported	Interventions to increase Community Demand for Vaccinations The Community Preventive Services Task Force recommends: Client or family incentive rewards based on sufficient evidence of effectiveness in increasing vaccination rates in children and adults (based on results from six studies that evaluated incentive awards alone or in combination with additional interventions). Reminder and recall interventions based on strong evidence of effectiveness in improving vaccination coverage in children and adults, in a range of settings and populations, when applied at different levels of scale from individual practice settings to entire communities, across a range of intervention characteristics, when used alone or with additional components (62 studies). Community-based interventions implemented in combination (to enhance access to vaccination services, increase community demand, and reduce missed opportunities by vaccination providers) to increase vaccinations in targeted populations, on the basis of strong evidence of effectiveness in increasing vaccination rates (17 studies). Vaccination requirements for child care, school, and college attendance based on strong evidence of effectiveness in increasing vaccination rates and in decreasing rates of vaccine-preventable disease and associated morbidity and mortality, based on findings from 27 studies demonstrating effectiveness of vaccination requirements: for attendance in a variety of settings; for an array of recommended vaccine; in populations ranging in age from early childhood to late adolescence. There is insufficient evidence to determine the effectiveness of: Client-held Paper Immunization Records (7 studies)

Title/ First author/	Description of the	ne reviews		Nb of	Quality	
year of publication	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure	studies included	assessment of studies	Main conclusions
		exposed or who had been less exposed.				Clinic-Based Education when Used Alone (4 studies) Community-Wide Education when Used Alone (6 studies) Monetary Sanction Policies (2 studies) Provider- or System-based Interventions The Community Preventive Services Task Force recommends: Health Care system-Based Interventions Implemented in Combination on the basis of strong evidence of effectiveness in increasing vaccination rates in targeted client populations (62 studies). Immunization Information Systems on the basis of strong evidence of effectiveness in increasing vaccination rates (240 studies) Assessment and feedback for vaccination providers based on strong evidence of their effectiveness in improving vaccination coverage in children and adults, alone or in combination with additional interventions, in a variety of settings and populations (33 studies). Provider Reminders based on strong evidence of effectiveness in improving vaccination coverage in adults, adolescents, and children; when used alone or with additional components; across a range of intervention characteristics; and in a range of settings and populations (48 studies) Standing Orders based on strong evidence of effectiveness in improving vaccination rates in children and adults, alone or in combination with additional interventions, in a variety of settings and populations (40 studies). There is insufficient evidence to determine the effectiveness of: Provider Education when Used Alone (5 studies).
What are the factors that contribute to parental vaccinehesitancy and what	To review the known barriers to vaccination reported by vaccine-	Inclusion: Intervention specifically targeting vaccine- hesitant (VH)	Attitudes, vaccination intent or vaccine uptake of	15 (7 on childhood vaccines	Not reported	Current data does not support one method for intervention as superiorly effective over others. Few interventions have evaluated the ultimate outcome: ontime vaccination of infants or children. Most reported interventions are primarily educational in

Title/ First author/	Description of the	ne reviews		Nb of	Quality	
year of publication	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure	studies included	assessment of studies	Main conclusions
can we do about it?, Williams S.E., 2014 [1]	hesitant parents and the current evidence on strategies to address parental vaccine hesitancy / HIC	parents or healthcare providers working with VH parents Quantitative evaluation of improvement Published between 2003-2013 English language Exclusion: Qualitative studies Interventions not focusing on vaccines recommended by ACIP	children	and 8 on HPV vaccine)		nature, yet the decision-making process for vaccine-hesitant families is likely very complex and influenced by factors which are difficult to measure, such as influences by social networks. This complexity likely contributes to the lack of evidence for effective interventions. Cultural tailoring and message framing of interventions have been used successfully in conjunction with educational material for VHPs. Use of a theoretical model to provide a framework for development of intervention is often recommended; however, few of the studies identified in this review did use a theoretical model.
A systematic review of interventions for reducing parental vaccine refusal and vaccine hesitancy, Sadaf, A., 2013 [4]	To evaluate the literature on interventions to decrease parental vaccine refusal and hesitancy toward recommended childhood and adolescent vaccines	Inclusion: Primary reports of intervention studies Quantitative outcome measures (vaccine refusal, behavior, attitudes and/or intent to vaccinate) Published between 1990-July 2012 English language Exclusion: Non-intervention studies, reviews,	Parental vaccine refusal behavior, attitudes toward immunizati on, and/or intent to vaccinate	30 (25 from USA)	Reported (most studies scored low on GRADE criteria)	Most studies (13) used a before-after intervention design and the remaining were RCTs (3), NRCTs(7) and evaluation studies (6). The review did not reveal any convincing evidence on effective interventions to address parental vaccine hesitancy and refusal. Large number of studies evaluated interventions for increasing immunization coverage rates such as the use of reminder/recall systems, parent, community-wide, and provider-based education and incentives as well as the effect of government and school immunization policies. Few intervention studies measured outcomes linked to vaccine refusal such as vaccination rates in refusing parents, intent to vaccinate, or change in attitudes toward vaccines. Most studies evaluating the impact of parent-centered information or education reported a statistically significant

Title/ First author/	Description of the reviews			Nb of	Quality	
year of publication	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure	studies included	assessment of studies	Main conclusions
		historical articles, case reports, commentaries, clinical guidelines and recommendations				improvement on parents' intentions to vaccinate their children. However, data for parents' attitude changes were very inconsistent and so offered limited insight.
Can lay health workers increase the uptake of childhood immunisation? Systematic review and typology, Glenton, C., 2011	To assess the effects of lay health workers (LHWs) interventions on childhood immunization uptake	Inclusion: Randomized controlled trials (RCTs), non- randomized controlled trials (NRCTs), interrupted-time- series (ITS) studies, controlled before—after studies and studies where the intervention's aim was to increase immunization coverage among children <5 years of age Any intervention delivered by LHWs which aimed to increase childhood immunization coverage Studies where	Immunizati on coverage	12 (7 in HIC)	Reported	In six studies, LHWs promoted immunization uptake among economically disadvantaged families in high-income countries. The LHW programmes increased the number of children whose immunizations were up to date. This evidence was of moderate quality. Evidence was of low quality for LHWs promoting immunization uptake among families in LMICs (However, the LHW programme increased the number of children whose DPT and measles immunizations were up to date) The quality of the evidence was very low for the impact of vaccines given by the LHWs. In two studies, LHWs increased the number of children whose immunizations were up to date compared with standard care. However, it is unclear whether these differences were statistically significant.

Title/ First author/	Description of the reviews			Nb of	Quality	
year of publication	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure	studies included	assessment of studies	Main conclusions
		LHWs were used as a substitute for trained health professionals or in addition to health professionals Published until February 2009 Exclusion: Studies based outside of primary health care, such as in hospitals or schools				
Interventions for improving coverage of child immunization in low- and middle-income countries, Oyo-Ita, A., 2011	To evaluate the effectiveness of intervention strategies to boost and sustain high childhood immunization coverage in LMIC	Inclusion: RCTs, NRCTs, and ITS studies Interventions targeting children aged 0 to 4 years, caregivers, and health providers Comparisons with routine immunization practices in the study setting or with different interventions or similar interventions implemented with different degrees	Proportion of target population fully immunized with recommend ed vaccines, by age Number of children aged two years fully immunized per vaccine	6 (5 cluster RCTs)	Reported (4 studies at high risk of bias)	Moderate quality evidence: Evidence-based discussions probably improve DPT3 and measles coverage Information campaigns probably increase uptake of at least a dose of a vaccine. Low quality evidence: Facility based health education alone or in combination with redesigned immunization cards may improve the uptake of combined vaccine against diphtheria, pertussis, and tetanus (DPT3) coverage. One study suggests that this monetary incentive may lead to little or no difference in the uptake of MMR or DPT1. Training of immunization managers to provide supportive supervision for health providers was assessed by one study and may improve the uptake for DPT3, OPV3, and hepatitisB3. Home visits may improve OPV3 and measles coverage. A combination of monetary incentives (patient oriented); quality assurance (provider oriented); and provision of equipment, drugs and materials (health system oriented)

Title/ First author/	Description of the reviews			Nb of	Quality	
year of publication	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure	studies included	assessment of studies	Main conclusions
		of intensity Published until 2010 except 2011 in the case of the MEDLINE search Exclusion: Patient reminder and recall as this is covered in an existing review [28] Controlled before- and-after studies that had only two study locations				interventions was evaluated in another arm of a study. The study suggests that this intervention may lead to little or no difference in MMR.
Too little but not too late: Results of a literature review to improve routine immunization programs in developing countries, Ryman, T.K. 2008 [10]	To identify strategies used to increase routine immunization programs	Inclusion: Studies published in English, French, or Spanish from 1975 through 2004 Primary data on effectiveness of the strategy was not required for inclusion, as the goal was to identify all possible strategies Exclusion: Studies with low quality scores	Percentage change in fully vaccinated children (FVC), percentage change in vaccination coverage for specific antigens, dropout from routine immunizati ons, or timeliness	25	Reported (studies with a score <60 were excluded)	Few papers were identified and in particular, few papers were of strong scientific quality. The strategies to "bring immunizations closer to the community" (including non-health workers to encourage people to seek immunization services, bringing immunization services to communities, and increasing demand through educating communities) could improve the percentage of FVC. Use of home visits for education and/or immunization service delivery may increase in the percentage of FVC. Conflict areas are generally difficult to reach because of security concerns. Three papers evaluated strategies that provided immunizations in conflict areas. Strategies involved using bush planes to gain access to people, providing incentives to attract people to immunization sites, going house-to-house to motivate parents to bring their children for immunization, and working with communities to coordinate provision of services.

Title/ First author/	Description of the reviews			Nb of	Quality	
year of publication	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure	studies included	assessment of studies	Main conclusions
			of vaccination			
Increasing the demand for childhood vaccination in developing countries: a systematic review, Shea, B., 2009 [11]	To review literature on efforts to stimulate demand for routine childhood vaccination.	Inclusion: Studies providing a description of activities that seemed designed to increase demand for childhood vaccination Studies that provided quantitative estimates of the impact of interventions. Published up to September 2008 and searched for primary studies published since 2004 Exclusion: Studies of exclusively supply side initiatives Studies from developed countries	Uptake of routine childhood vaccines	8	Reported	Most studies reviewed represented a low level of evidence. Interventions with an impact on vaccination uptake included knowledge translation (KT) (mass media, village resource rooms and community discussions) and non-KT initiatives (incentives, economic empowerment, household visits by extension workers). Most claimed to increase vaccine coverage by 20 to 30%. Estimates of the cost per vaccinated child varied considerably with several in the range of \$10-20 per vaccinated child. Mass media campaigns may be effective, but the impact depends on access to media and may be costly if run at a local level. The persistence of positive effects has not been evaluated.
Educational interventions to	To summarize and evaluate	Inclusion: RCTs, NRCTs as	Receipt of HPV	33	Reported	Most studies involved populations with higher educational attainment and most interventions required participants to be literate.

Title/ First author/	Description of the		Nb of	Quality		
year of publication	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure	studies included	assessment of studies	Main conclusions
increase HPV vaccination acceptance: A systematic review, Fu, L.Y., 2014 [6]	the evidence for educational interventions to increase HPV vaccination acceptance	well as quasi- experimental designs HPV vaccine acceptance in patients eligible to receive the vaccine, or their parents Presented educational interventions and measured the following outcomes were included: (1) receipt of HPV vaccine (any dose or completion of the3-dose series), (2) intention to receive HPV vaccine, or (3) attitude toward HPV vaccine Published between1946 to August 20, 2013 English language Exclusion: Pilot or descriptive projects which reported only	vaccine, intention to receive HPV vaccine, attitude toward HPV vaccine			The minority of studies used the outcome of HPV uptake. Well-designed studies adequately powered to detect change in vaccine uptake were rare and generally did not demonstrate effectiveness of the tested interventions. There is no strong evidence to recommend any specific educational intervention for wide-spread implementation.

Title/ First author/	Description of the reviews			Nb of	Quality	
year of publication	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure	studies included	assessment of studies	Main conclusions
		qualitative or anecdotal results Studies that did not focus primarily on populations eligible to receive HPV vaccine or their parents or that did not subset results in a way that the authors were able to extract information on these target groups				
Systematic literature review of the evidence for effective NIS promotional communications, Cairns, G., 2012 [7]	To examine the effectiveness of national immunization schedule promotional communications in European context	Inclusion: All included studies reported evaluation, experimental, quasi- experimental, or interrupted time series data on vaccine-uptake or likely behavioral precursors Experimental and pilot studies of communications promoting nationally scheduled	Change in measured immunisati on uptake rates Secondary outcomes included measured changes in the target audience's knowledge, attitudes and other behavioural determinant	33 (22 on interventi ons promoting influenza vaccinatio n, 11 on childhood vaccines)	Reported	Fifteen of the 33 evaluation studies captured in the review were rated as high validity studies on the basis of the quality, validity and applicability appraisal process. Seven high scoring studies reported convincing evidence of positive effect and eight reported no evidence of effectiveness. Interventions that included an aim to promote more favorable attitudes to immunization did not report any evidence of more pro-immunization attitudes. The review found that interventions aiming to improve knowledge levels were usually successful, but did not demonstrate any positive effects on vaccine uptake or intention to be vaccinated. Some interventions that aimed to improve knowledge levels of healthcare workers through education and training did report evidence of improved rates of vaccine uptake. There is good evidence that a range of promotional communications can positively change knowledge, attitudes and behaviors. The evidence for increased immunization uptake is particularly promising for health care workers, patient risk groups (including the elderly), and seasonal flu vaccine promotions. However many of the

Title/ First author/	Description of the reviews			Nb of	Quality	
year of publication	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure	studies included	assessment of studies	Main conclusions
		vaccination were also eligible for inclusion European countries and their territories English and non-English language Academic and grey literature Published from 2000 to 2011 Exclusion: Off topic Not a primary study	S			interventions captured by the review combined communication channels and methods, so it is not possible to identify which types of communication initiatives are most effective, or to estimate their contribution to overall intervention effect. In addition, many interventions included structural change to make immunizations more accessible (e.g. reduced cost, more accessible clinics), further complicating attempts to determine the net contribution of communications.
Face to face interventions for informing or educating parents about early childhood vaccination, Kaufman, J., 2012	To assess the effects of face to face interventions for informing or educating parents about early childhood vaccination on immunization uptake and parental knowledge	Inclusion: RCTs and cluster RCTs .This review focuses on face to face single or combined interventions to inform or educate (oral presentations, one on one or group classes or seminars, information sessions, or home outreach visits) Published until 2012	Primary outcomes are immunisati on status of child and parents' knowledge or understanding of vaccination	7 (6 RCTS and 1 cluster RCT – 3 LMIC, 4 HIC)	Reported	The overall result is uncertain because the individual studyresults ranged from no evidence of effect to a significant increase in immunization. Three studies reported immunization status measured 3 months after a single-session intervention. Effect of the intervention remains uncertain. Four comparisons from these studies showed inconsistent results (studies with higher risk of bias were associated with greater increase in immunization, compared with control, while study with lower risk of bias showed no or little evidence of effect. The quality of evidence was low. Results for interventions where immunization status was measured at the conclusion of a multi-session intervention indicated a very uncertain effect with statistically insignificant effect ranging from reduced to no evidence effect, and had wide confidence intervals. The quality of evidence was very low. Effect was also very uncertain for studies measuring knowledge or understanding of vaccination. The two multi-session interventions

Title/ First author/	Description of the reviews			Nb of	Quality	
year of publication		assessment	Main conclusions			
Chartering	T	Exclusion: Interventions directed to communities				showed non-significant increases in knowledge scores compared with control. The quality of evidence was very low.
Strategies to improve vaccination uptake in Australia, a systematic review of types and effectiveness, Ward, K., 2012 [3]	To profile and critique available evidence of strategies to improve vaccination uptake in Australia and evaluate their effectiveness	Inclusion: Published from 1997 through to May 2011 English language Studies must have reported original research about, or evaluation of, one or more interventions to improve uptake of one or more vaccines available in Australia. Studies must have included a quantitative measure of uptake as a primary outcome Exclusion: Studies describing uptake in the absence of an intervention or reporting only other outcomes (i.e. descriptive or	Vaccine uptake	49	Reported	The most effective and common strategies for increasing community demand and provider based interventions were patient reminder/recalls and provider reminders. Education for the public and providers (either alone or as part of a multicomponent strategy) had variable impact on uptake, with increases less substantial or direct when compared with reminder/recalls. Also effective were integration of vaccination status checks into routine health assessments, individual provider support, and targeted promotion campaigns in the mass media, although studies of these interventions were minimal and confined to particular target groups and vaccines. For enhancing access, catch-up plans for those overdue for vaccination were particularly effective, often reducing the percentage of those overdue by more than 50%. The two studies involving an accelerated vaccination schedule for hepatitis B showed an increase in the overall completion rate compared with the standard schedule. Results from the few studies of home visits for routine childhood vaccination highlighted their effectiveness, particularly when targeting Aboriginal and Torres Strait Islander children. The same effectiveness was observed for expanding access in hospitals and vaccination clinics in public settings. There were several effective regulatory interventions that were beyond 'baseline practice' of funding vaccines on the NIP and school-based vaccination programs. These included national parental incentives; the maternity immunization allowance (MIA) and linking vaccination to the child care benefit as well as a jurisdictional hepatitis B vaccination policy for high-risk infants then subsequently for all newborns. All other regulatory interventions primarily focused on provision of funded vaccine coupled with mandatory vaccination

Title/ First author/	Description of the reviews			Nb of	Quality	
year of publication	General Purpose and setting	Inclusion / Exclusion criteria	Main outcome measure	studies included	assessment of studies	Main conclusions
		qualitative)				policies for health care workers (HCWs) and were implemented at a jurisdictional and/or organizational level. The small number of studies showed limited effectiveness of this strategy.
Primary care strategies to improve childhood immunization uptake in developed countries: systematic review, Williams, N., 2011 [2]	To conduct a systematic review of strategies to optimize immunization uptake within preschool children in developed countries	Inclusion: Experimental studies reporting original research including RCTs, NRCTs, before and after studies and ITS studies Targeting population of children under the age of 5 years living in developed countries Published from inception to 1 June 2010 English language Exclusion: Studies for which the full article was not available, and studies that did not contain any original data	Increase in the proportion of the target population up to date with standard recommend ed universal vaccination s	46	Reported	Parental reminders have been shown to have an overall positive effect on immunization uptake. These effects have been reported with both generic and specific reminders and with all methods of reminders and recall. The limited number of studies precludes from reaching an evidenced-based conclusion on the effect of parental education interventions on parental behavior. Only one study concerned patient-held records and did not demonstrate a significant difference between usual care and a home-based record booklet Provider reminder/recall strategies, provider education and provider feedback shown to have a positive effect on immunization rates. Multicomponent interventions shown a positive effect on immunization rates. It is not possible to distinguish which component of the intervention has had the greatest effect on immunization rates.

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Vaccine Hesitancy Landscape Analysis

List of key players working on the issue of Vaccine Hesitancy[§] SAGE Working Group on Vaccine Hesitancy

July 2014

Background:

Vaccine hesitancy is one of several concepts and ideas that relate to the demand side of vaccine usage. Vaccine hesitancy is an emerging term in the discourse on determinants of vaccine acceptance where uptake of a vaccine or immunization programme in a community is lower than would be expected in the context of information given and services available. Vaccine hesitancy is influenced by a complex network of factors including issues of complacency, convenience and/or confidence in vaccine(s) or immunization programme that may result in refusal, delay or uncertainty towards some or all vaccines. These factors which influence vaccine acceptance vary by setting and responses need to be locally assessed.

This landscape analysis attempts to take a relatively broad view of vaccine hesitancy by including actors working on the issue. The purpose of this document is to stimulate a continuous compilation of organizations involved in vaccine hesitancy work. The intention is that the list becomes more populated and evergreen as stakeholders, organizations, institutes and communities respond with suggested additions. This regularly updated resource could be presented in form of a wiki approach in order to foster collaboration between the different players in the field of vaccine hesitancy.

Objectives:

- Allow to identify what organisations are working on the issue of vaccine hesitancy in various settings/countries.
- Allow those working on the issue of vaccine hesitancy to identify potential partners, donors and collaborators in the field.
- Allow people to identify the regions where work is being done on vaccine hesitancy and what kind of work is being done in each area.
- Be a regularly updated resource on work currently being done in the field of vaccine hesitancy
- Help identify research and funding gaps—particularly in countries where there are more significant vaccine hesitancy issues.

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 $[\]S$ $\,$ No claims can be made about the completeness or adequacy of the contents of this document .

Five categories and **four** sub-categories of actors were determined to represent the groups working on the issue of vaccine hesitancy, including *Government* (national and regional), *Not-for-profit*, *Donors*, *Research Organisations* and *Multinationals*. An *Other* category was included to represent any actor that did not fit in the above categories but was still producing important work related to vaccine hesitancy. Industry was not included as its own category in this framework. Although industry has a major stake in vaccine hesitancy, industry vaccine groups share similar interests in combating vaccine hesitancy and therefore conduct comparable work on the issue. Consequently, limited benefit is seen in analysing each member of vaccine industry individually. Instead, the vaccine industry was included as one entity in the 'other' category, so their work and interests as a group may be presented in the Landscape Analysis.

Excluded were overarching concepts, frameworks or strategies addressing vaccine hesitancy as a sub-component only and which are not a solitary entity but composed of different organizations, stakeholders or collaborators. In this context especially the "'Decade of Vaccines' Collaboration/ Global Vaccine Action Plan" needs to be mentioned¹⁶.

Areas of work:

7 areas of work and/or interest were identified being carried out by actors working on the issue of vaccine hesitancy, these included:

- research
- policy recommendation
- intervention
- education & promotion
- collaboration
- goal setting
- social mobilisation

Search strategies:

Two main strategies were used:

- 1. Literature Search
 - a. Databases/Search engines used:
 - i. Google: Canadian (google.ca), United States (google.com), United Kingdom (google.co.uk) and Hong Kong (google.com.uk)
 - First 5 pages of google were searched for relevant actors
 - ii. Pubmed
 - iii. Refworks database for the systematic review on the rubric of trust and confidence in vaccines currently being produced by the London School of Hygiene and Tropical Medicine (LSHTM).
 - iv. WHO database: Global Information Full Text project (GIFT), more than 10,000 priced and open access journals
 - b. Search terms
 - i. Google (Canadian, US, German and UK), GIFT and Pubmed
 - Used the following search terms: vaccin*, immunization, shot AND hesitan*, resistan* refusal, confidence, acceptance, promotion AND initiative* OR organization* OR strateg*
 - Used the following search terms: impf*, immunisier*, AND gegner, skepsis, verweiger*

- ii. Google (Hong Kong)
 - Used the same search terms as above, translated into Chinese:
 - 疫苗=vaccine
 - 犹豫=hesitant/hesitancy
 - 抗拒=refuse/resist
 - 信心=confident/confidence
 - 接受=accept/acceptance
 - 研究=research
 - 组织=organization/institution

iii. Refworks

 Searched full database, using term: vaccin*, immunization, shot AND hesitan*

2. Snowballing technique

Furthermore, we obtained unpublished information through personal communication with colleagues and experts, i.e. at conferences addressing vaccine hesitancy.

- a. Asked main players working on the issue of vaccine hesitancy (i.e. people in SAGE WG on vaccine hesitancy, and players identified through initial literature search) and colleagues familiar with regional/local circumstances
 - i. Feedback from:
 - Julie Leask, University of Sydney
 - Eve Dubé, member SAGE working group (WG) on vaccine hesitancy
 - Heidi Larson, member SAGE working group (WG) on vaccine hesitancy
 - Noni MacDonald, member SAGE WG on vaccine hesitancy
 - Susan (Yuquing) Zhou, member SAGE WG on vaccine hesitancy
 - Mahamane Laouali Manzo, member SAGE WG on vaccine hesitancy
 - Dr. Bettinger, vaccine researcher at the Child & Family Research Institute at the BC Children's Hospital and UBC, Canada
- b. Based on these responses collaborators and affiliates of players of vaccine hesitancy that were mentioned were looked up and it was determined if/how they were involved in vaccine hesitancy.
- c. The main players working on the issue of vaccine hesitancy also provided additional contact information for other actors working on this issue.

Inclusion/exclusion criteria:

Inclusion:

- i. Actors doing work in at least two of the seven areas of work/interest specified in the introduction.
- ii. Actors give *specific* examples of activities they are engaged relating to the issue of vaccine hesitancy (i.e. not simply stating general mandates).

Fyclusion.

- iii. Actors promoting vaccine hesitancy or who are part of the anti-vaccination lobby.
- iv. Actors that have not worked on the issue of vaccine hesitancy in the last 5 years

Results:

Table 1. Key actors working on vaccine hesitancy

Catego	ries	Key Actors	Areas of Work/Interest**	Actions ^{††}	Region ^{‡‡}	Collaborators and Affiliates ^{§§}
Gov.	National	China CDC (CCDC)	Research Policy Recommendations Interventions	 Research: Survey of KAP (knowledge, attitudes and practices) of measles¹⁷ (MOH, WHO, UNICEF) Person to person communication intervention strategies¹⁶ (MOH, WHO, UNICEF) Evaluation of parents KAP on immunization¹⁶ (MOH, WHO and US CDC) Social marketing campaign 25 April- Children's Immunization Day¹⁸ (MOH, CCDC and provincial health bureau and provincial CDC) Mass Communication Intervention: Information sheets/brochures for parents and caregivers, to address any vaccine concerns.¹⁹ (MOH, CCDC) Religious leader to address vaccine benefits in the sermon. Guide providing info about general knowledge, the benefits of vaccination, situations when not to receive vaccination, preparation work for parents, adverse events, etc. (MOH, CCDC) 	China	Provincial health bureau and CDC WHO US CDC UNICEF China Ministry of Health (MOH)
		China MOH	Research Interventions Education & Promotion	 Social Marketing: Immunization Day (MOH, national wide health bureau and CDC and government) Theme: Vaccination is the responsibility of each household in 2012, each year has different theme based on the priority of work (MOH) Promotion methods (CCDC and Local CDC) Central governor and Local governor attend initiating ceremony Improve awareness and promotion through competitions about vaccine knowledge, expert visits, as well as art and cultural performances (CCDC) Involvement of organisational leaders, including attending vaccine promotion activities, improve cooperation between education and social media departments, motivate village leaders and committee members to promote to the community about the efficacy and safety of the vaccine(MOH, PROVINCIAL HEALTH BUREAU and CDC) Arrange visits to rural areas and visits of minorities which health information may not reach conveniently (CDC) Enforce education to village committees, village doctors, school teachers, and parents CDC 	China	China CDC Provincial health bureau and CDC Central and local governments

Areas of work/interest within vaccine hesitancy including: research, policy recommendation, intervention, education/promotion, collaboration, goal setting, social mobilisation.

Actions: examples of current vaccine hesitancy activities the actors are engaged in

Where (country/setting) where the organization is based and/or where their work on vaccine hesitancy is focused.

Solvy organization that consistently collaborated on vaccine hesitancy or worked on key project related to vaccine are shown in the 'Collaborators and Affiliates' section.

Categories	Key Actors	Areas of Work/Interest**	Actions ^{††}	Region ^{‡‡}	Collaborators and Affiliates ^{§§}
	Department of Health,	• Policy • Intervention	 Systematically collect and manage information of promotion activities CDC Please note that many of these projects were undertaken in concert by both the China Department of Health and the China CDC. Belize deployed a country-wide fully integrated patient centred health information system with eight embedded disease management algorithms and simple analytics. ²⁰ This 	Belize	Canadian Centre for
	Belize Federal	Research Education &	public health strategy is set in place to then meet with all parents at their homes whose children were not immunized in timely fashion. • Health education and health promotion	Germany	Vaccinology • German
	Centre for Health Education (Bundeszent rale für Gesundheitli che Aufklärung, BZgA)	Promotion • Research	Research on parental knowledge, behaviour and attitude concerning vaccinations and the need for information material ²¹	dermany	Ministry of Health • National Public Health Institute
	National Centre for Immunisatio n Research and Surveillance * (NCIRS)	Research Policy Recommendations Interventions Education & Promotion	 Workshops and conferences 2012- Ethical Issues in Immunisation Seminar²² Presentation on 'How far can government go in promoting vaccination?' and 'A little bit more ethics on power an persuasion in immunisation' Social Research Descriptive, identifying immunisation-related beliefs, attitudes and practices of consumers and health professionals, as well as mass communication research. ²³ Survey tracking parental attitudes to vaccination²⁴ MMR Decision Aid²⁵ Used to help parents to decide whether to immunise their child with MMR the vaccine. *Please note that the NCIRS is directly linked with the University of Sydney, however because of its varied work on the issue of vaccine hesitancy it was included as its own actor. 	Australia	Australian Technical Advisory Group on Immunisation (ATAGI) Australian Government Department of Health and Ageing University of Leeds
	African region: Ministries of Health and Communicati on (Niger,Benin, Nigeria,Mali, Burkina Faso,Kenya, Guinée Conakry)	Policy Recommendatio ns Intervention Education& promotion Collaboration Goal setting.	 Solemn declaration by President (swearing on the Koran at Niger) on the safety of the vaccine to overcome reluctance Launching ceremonies of immunization campaigns by heads of state: (Niger, Nigeria, Benin, Burkina Faso, Mali). A meeting is organized with all stakeholders are taking part. Media coverage of this meeting is broadcasted. Media coverage of immunization sessions where families of authorities(health and government) are vaccinated: Niger, Nigeria Integration of home visits in the "minimum package" of health center service delivery: Niger, Benin, Burkina Faso, Mali Broadcast television radio messages explaining the different vaccinations during the EPI immunization schedule and the importance of respecting it (reports by religious association, chief associations and MOH): Niger, Benin, Burkina Faso, Mali, Nigeria Capacity building of EPI managers: WHO and UNICEF support it in most of African region. 	Africa	• UNICEF

Categories	Key Actors	Areas of Work/Interest**	Actions ^{††}	Region ^{‡‡}	Collaborators and Affiliates ^{§§}
			Production of information material (National EPI, National Directorate of Health Education with lean of UNICEF) and distribution of educational media information to raise awareness (illustrated flip charts, booklets, posters) among health workers, religious and chief association		
	Robert Koch- Institute- central federal German institution responsible for disease control and prevention	Research Education& promotion	 Information on the 20 most common prejudices against vaccines²⁶ Publication on the acceptance of vaccination in parents.²⁷ Bi-weekly service hotline for physicians answering specific questions related to vaccination²⁸ 	Germany	• Federal States of Germany • ECDC
	Romania National Institute of Public Health	• Policy/Recomme ndation • Research	Project: Strategic Directions for the Development of the vaccination program and Promotion of vaccination Identifying issues related to vaccine hesitancy and developing a national strategy with best practices and recommended methodologies to tackle caregiver hesitancy.	Romania	
	UK Department of Health	Research Interventions Policy Recommendations	 Joint Committee on Vaccination and Immunisation (JCVI) Research on attitudes on influenza vaccination in children²⁹ Immunisation Market Research Section State: "feedback on attitudes and awareness of immunisation is vital to help inform and shape the work" on successfully promoting and administrating vaccines. Parent tracking research and health professionals surveys³¹	UK	• Health Protection Agency
	US Centers for Disease Control and Prevention (CDC)	Research Interventions Policy Recommendations	 National Center for Immunization and Respiratory Diseases (NCIRD) Online tool for Catch-up Scheduling for Childhood Immunization (www.vacscheduler.org) Funds collaborations and initiatives focusing on vaccine hesitancy: Immunization Action Coalition³⁵ Vaccine Confidence Project (LSHTM)³⁶ Clinical Immunization Safety Assessment (CISA) To enhance public confidence in sustaining immunization benefits for all populations 	USA	• US Department of Health and Human Services State public health departments
	US Department of Health and	• Research • Policy Recommendations	 National Vaccine Advisory Committee (NVAC) Recommendations on Strategies to Achieve the Healthy People 2020 Annual Influenza Vaccine Coverage Goal for Health Care Personnel³⁷ 	USA	CDC

Categor	ries	Key Actors	Areas of Work/Interest**	Actions ^{††}	Region ^{‡‡}	Collaborators and Affiliates ^{§§}
		Human Services	• Goal Setting • Education & Promotion	 Vaccine Hesitancy working group established³⁸ In report, individuals raised concerns over adverse events, vaccine effectiveness, vaccine safety, etc. A Pathway to Leadership for Adult Immunization: Recommendations of NVAC³⁹		
	Regional	Department of Health and Wellness, Nova Scotia, Canada	• Research • Interventions	 Projects to decrease vaccine hesitancy: 41,42 Campaign to mitigate pain with immunization based upon evidence– aimed at parents, adults, HCP anxious about immunization Campaign to increase uptake flu vaccine by pregnant women 	Nova Scotia, Canada	Can Centre for Vaccinology HELPinKIDS Canada
		Institut National de Santé Publique de Québec	Policy/Recomme ndation Research Intervention Goal setting	 Plan Québécois de Promotion de la Vaccination (February 2010) Action Plan for Vaccination Promotion- Phase II (April 2012)⁴³ Phase II addresses goals 3 and 4 of the action plan which related directly to vaccine hesitancy Goal 3: Encourage positive attitudes toward vaccination among health professionals and encourage such professionals to be vaccinated themselves Goal 4: Encourage positive attitudes toward vaccination in the general population	Québec, Canada	• L'Université Laval
		Regional governors, prefects and mayors Regional and department al public health direction Traditional	• Education & Promotion • Interventions • Policy	 Organization of meetings with communities around the reasons of vaccine hesitancy: MOH and, religious and chief association. Discussions with community, religious and traditional leaders, various associations, Organization of home visits by health centers through Community women: (Volunteer Community mobilizes) Niger, Nigeria, Mali, Benin,Burkina Faso Organization of meetings in neighborhoods, villages and health centers: health workers, religious association, traditional chiefs and the community health committee Debates and broadcast messages on local radio stations. Use of media for promotion and surveillance of campaigns: local radio, text messaging and daily evening meetings during campaigns to spot and correct refusals and other problems encountered (e.g. Guinée Conakry) 	Africa	• MOH • UNICEF

Categories	Key Actors	Areas of Work/Interest**	Actions ^{††}	Region ^{‡‡}	Collaborators and Affiliates ^{§§}
	and religious leaders (Imams, Pastors) •Health committees		 Providing rewards e.g. "hygiene kit during immunization session" in Kenya to women whose children are fully immunized financed by MOH,UNICEF. Reward health centers with the best performance vaccination financed by MOH,UNICEF 		
Non-for-profit	California Immunizatio n Coalition	• Education &Promotion • Interventions	 Improving immunization rates (coverage) for Californians of all ages and achieving Healthy People goals relating to immunization rates across the lifespan. Offering leadership in policy development and advocacy with an emphasis on promoting community based advocacy through support of local coalitions. Providing educational activities/opportunities for health care professionals, community stakeholders and the public: e.g. shotbyshot.org Promoting use of immunization registries. Reducing health disparities and improving access to vaccines by addressing barriers that prevent or limit access to immunizations. Virtual Immunization Communication Network (VIC Network) partnership between the National Public Health Information Coalition (NPHIC) and the California Immunization Coalition (CIC)⁴⁴ 	California, USA	National Public Health Information Coalition (NPHIC) CDC
	Canadian Centre for Vaccinology	• Research • Education & Promotion	Vaccine hesitancy, with specific focus on 45 pain mitigation, school based vaccine programs hard to reach populations and their hesitancy, health care professional undergrad curriculum HCP hesitancy for flu vaccine policy and hesitancy	Canada	Variety of local, regional and national partners- both NGOs and govt's
	Canadian Immunizatio n Research Network (CIRN)	• Education &Promotion • Research	• The CIRN includes the Social Sciences and Humanities sub-network (SSH) which will focus on the topic of vaccine hesitancy 46		
	Canadian Association for Immunizatio n Research and Evaluation	• Research • Intervention	 CAIRE actively participates and promotes vaccine related investigations⁴⁷ Organisation of vaccine-related conferences Immunization Competencies Education Program (ICEP), training for Health Professionals CAIRE offers a "second scientific home" to researchers who work in the field of applied vaccinology. 	Canada	• Public Health Agency of Canada (Centre for Immunization and Respiratory Infectious Diseases)
	Canadian Pediatric Society	• Education& Promotion Collaboration	Education materials for parents and health care professionals: Caring for kids Collaboration: provincial governments, PHAC at the Federal Government **A0** **A0	Canada	
	Canadian Nurses	• Education& Promotion	 Position statement of vaccination of nurses against influenza⁴⁹ Immunization myths and facts⁵⁰ 		

Categories	Key Actors	Areas of Work/Interest**	Actions ^{††}	Region ^{‡‡}	Collaborators and Affiliates ^{§§}
	Association	 Interventions 			
	COMMVAC project	• Education& Promotion • Research	The COMMVAC project ⁵¹ aims to: • build research knowledge and capacity to use evidence-based strategies for improving communication about childhood vaccinations with parents and communities in low- and middle-income countries (LMICs) • build the evidence needed to support the implementation of effective communication interventions • translate this evidence into guidance for policymakers in LMICs on communication strategies to improve childhood vaccination uptake		Various affiliates ⁵²
	Global Polio Eradication Initiative	Research Interventions Education & Promotion Research	 Data and monitoring Household survey asking about reasons why child was not immunized (e.g. refusal- religious belief, vaccine safety, no felt need) Polio Pipeline: KAP studies- understanding barriers to immunization	Polio infected countries	UNICEF WHO US CDC Rotary International National governments LSHTM
	Internationa l Vaccine Access Center (IVAC)*	Research Education &Promotion	 Assessing how to increase demand-side strategies which could contribute to achieving high and timely vaccine coverage: Mobile Solutions for IMmUnization (m-SIMU)⁵⁶ Landscape Analysis of Routine Immunization (LARI)in Nigeria: The project aims to identify the key supply- and demand-side bottlenecks to routine immunization coverage in Nigeria, and determine drivers of low coverage and inequalities⁵⁷ *Please note that the IVAC is directly linked with the Johns Hopkins Bloomberg School of Public Health, however because of its varied work on the issue of vaccine hesitancy it was included as its own actor. 		• Johns Hopkins Bloomberg School of Public Health • PATH • WHO • CDC • The Global Coalition Against Child Pneumonia,
	Immunize Canada	Education &Promotion Interventions Research	 A national non-governmental, professional, health, consumer, government and private sector organization with a specific interest in promoting the understanding and use of vaccines recommended by the National Advisory Committee on Immunization. The goal of Immunize Canada is to contribute to the control/elimination/eradication of vaccine-preventable diseases in Canada by increasing awareness of the benefits and risks of immunization for all ages via education, promotion, advocacy and media relations. Development of the ImmunizeCA App, for individuals to easily record and store vaccine information and access vaccination schedules⁵⁸ Immunization fact sheets⁵⁹ Advocacy 		Wide variety of national partners
	National Association offices of	• Policy/Recomme ndation • Intervention	Traditional chief and religious (Muslim and Christian) have an Association in most African countries. Taking the example of Niger: National association of traditional chiefs named Association des Chefs Traditionnels du Niger(ACTN) or Association Islamic du Niger	Africa	MOH, WHO UNICEF

Categories	Key Actors	Areas of Work/Interest**	Actions ^{††}	Region ^{‡‡}	Collaborators and Affiliates ^{§§}
	traditional chief and religious leaders.		(AIN). • Advocacy on media • Preaching in villages • Face-to-face contact with reluctant individuals		
	National Foundation for Infectious Diseases (NFID)	• Education & Promotion • Collaboration	Professional educational program on immunization twice per year – 3 hours devoted to hesitancy each course for now > 5 years ⁶⁰	USA	CDC and others
	Trust for Vaccines and Immunizatio n (TVI)	• Interventions • Education & Promotion	 Mission of TVI is to increase vaccine uptake and to reduce vaccine preventable disease incidence in Pakistan by creating public demand for vaccination and immunization: Several mass vaccination campaign against typhoid fever of children and adults in towns in the province of Karachi⁶¹ Seminars e.g. With School heads on typhoid fever awareness, with paediatricians on pneumococcal disease or administrations of day-care centers.⁶² 	Pakistan	International Vaccine Institute Ministry of Health – Govt of Sindh Expanded Programme on Immunization Ministry of Education – Govt of Sindh City District Government Karachi
	VAX Northwest	Research Intervention Promotion & Education	 Social marketing campaign Increase timely immunizations from birth to age 24 months in Washington State^{63,64} Focus: vaccine hesitant parents Provider toolkit Outreach to parents/social norms⁶⁵ The organisation is using social marketing strategies to develop a provider and a community based intervention. Data on the success of both interventions will be available in 2015 although there is already some early indication of success for the community intervention: One state wide childcare co-op is changing policy – immunization records will be collected and reported. To quantify intervention success specifically with regard to hesitancy, parents are surveyed before and after interventions using Doug Opel's hesitancy index 	Washingt on State, USA	Within Reach Immunization Action Coalition of WA Washington State Department of Health Seattle children's hospital Community pediatric foundation of Washington.
Donors	Bill and Melinda	• Research • Intervention	• Funding o Initiatives related to vaccine hesitancy, as well as vaccine acceptance and promotion ⁶⁶	Global	•Wide variety of global partners

Categories	Key Actors	Areas of Work/Interest**	Actions ^{††}	Region ^{‡‡}	Collaborators and Affiliates ^{§§}
	Gates Foundation	• Education & Promotion	 E.g. Vaccine Confidence Index from LSHTM (global surveillance system to identify and track rumours/misinformation related to immunization. Supporting organisations that are working in the area of vaccine hesitancy. E.g. WHO, UNICEF, LSHTM 		
	Robert Wood Johnson Foundation	• Research • Intervention	 Grants Funding publications and research⁶⁷ ■ E.g. 'Protecting public trust in immunization' 	USA	
Research Organisations	Harvard University	• Research • Collaboration	Working with the American Academy of Arts and Science on a vaccine hesitancy project. The American Academy of Arts and Sciences is planning a meeting for the fall 2014 to explore and hopefully usefully define research questions relating to trust in vaccines and vaccine hesitancy, which, if they received support from other sources, might enable some rational decision policy making to enable useful information to be presented to multiple groups key to immunizing children. Thus far the planning has been done with input from Ed Marcuse and Seth Mnookin, along with people at the Academy.	USA	American Academy of Arts and Science
	John Hopkins School of Public Health (JHSPH)	Research Collaboration	Research parental attitudes, studied the effectiveness of providing vaccination education materials to pregnant women and women who have just delivered to see if that would make them less hesitant. He has also collaborated with the CDC and Kaiser on several studies.	USA	• CDC • Kaiser Permanente
	London School of Hygiene and Tropical Medicine	• Research • Intervention • Promotion & Education	 Vaccine Confidence Project⁶⁸ Symposium on Public Confidence in Vaccines in April 2014: Building Trust, Managing Risk⁶⁹ MOTIV Think Tank: Motors of Trust in Vaccination Developing systematic review on vaccine confidence, acceptance, hesitance, etc. 	ИК	Wide variety of global partners
	Ottawa Hospital Research Institute	• Research • Education & Promotion	• Research on evolution of controversies concerning pediatric vaccination 70	Canada	
	Sherbrooke University (Quebec)	Research Education & Promotion	 Book title on Vaccine Hesitancy (working title): Cultural and Religious Roots of Vaccine Hesitancy: Explanations and Implications for Canadian Health Care. Objectives and target readership: 1) Report on various aspects of phenomenon of vaccine hesitancy (VH) and its features; 2) Propose theories for understanding VH; 3) Support public health (PH) practices and decisions for health professionals facing VH. PH authorities, health professionals and graduate students are targeted. 	Canada	• University of Victoria (British Columbia) • Researchers across Canada
	University of British Columbia (Vaccine Evaluation Center)	Research Education & Promotion	The main research themes involve disease burden studies, vaccine clinical trials, and studies to fine tune public immunization programs, including ongoing assessment of vaccine safety	Canada	
	University of Erfurt	• Research • Education &	 Workshop on culture-sensitive health communication in May 2014⁷¹ Call for papers on improving medical decision making through cultural-sensitive health 	Germany	

Categories	Key Actors	Areas of Work/Interest**	Actions ^{††}	Region ^{‡‡}	Collaborators and Affiliates ^{§§}
		Promotion	communication ⁷²		
	University of Leeds (UK)	ResearchIntervention	 MMR Decision Aid (with NCIRS) Detailed Evaluation of a Childhood Immunisation Decision Aid (D.E.C.I.D.A study)⁷³ 	UK	• University of Sydney
	University of Sydney	• Research • Interventions • Education & Promotion	 Working with the NCIRS and other partners on a variety of projects related to vaccine hesitancy, acceptance and promotion.⁷⁴ E.g. MMR Decision Aid Tool⁷⁵ Provide classes related to vaccine hesitancy and acceptance E.g. Publication Vaccines in Public Health⁷⁶ Content- "risk communication and immunisation myths and realities" 	Australia	• University of Leeds NCIRS
	University of Washington School of Medicine Seattle, Washington	• Research • Promotion& Education	 Research in the field of vaccine refusal/ attitude towards vaccination Parental delay or refusal of vaccine doses, childhood vaccination coverage at 24 months of age, and the Health Belief Model. Washington State Pediatricians Attitudes Towards Alternative Childhood Immunization Schedules 	USA	
Multinationals	European Center for Disease Control and Prevention (ECDC)	• Research • Education & Promotion	 Multi-stakeholder meeting on Individual decision-making and childhood vaccination held in May 2013, Stockholm, Sweden⁷⁹ The meeting resulted in a "Call for papers: Multidisciplinary perspectives on vaccine hesitancy and contemporary vaccination coverage⁸⁰ Various publications, among other: Systematic literature review of the evidence for effective national immunisation schedule promotional communications⁸¹ 	Global	Wide variety of partners: Member states WHO Academia
	UNICEF	• Research • Policy Recommendations • Education & Promotion • Intervention	 Works with GAVI on the Advocacy & Communication Task Force (ACTF) UNICEF works with governments, partners and communities to increase demand for immunization Vaccine strategies include engaging communities: Communication strategies that include advocacy, communication, and social mobilisation Rapid inquiry into attitudes about PCV and introduction in Rwanda Financial and technical support for evidence-based social mobilization and communication for immunization e.g. in countries like Niger, Nigeria, Benin, Tchad, Guinée, Gabon) 	Global	Wide variety of global partners GAVI WHO
	WHO	Research Policy Recommendations Collaboration Education & Promotion	 Strategic Advisory Group of Experts (SAGE) on immunization SAGE Vaccine Hesitancy Working Group (establ. March 2012) Publications and information: E.g. Behavioural Factors in Immunization (Department of Mental Health and Substance Dependence Vaccine Safety Net "websites providing information on vaccines which adhere to good information practices" Surveys: EPI Coverage Survey Reasons for immunization failure cluster form, includes reasons such as 'fear of side reactions', 'no faith in immunisations', 'rumours', etc. Vaccine Safety Net Image: Survey of the support of the suppo	Global	Wide variety of global partners

Categories	Key Actors	Areas of Work/Interest**	Actions ^{††}	Region ^{‡‡}	Collaborators and Affiliates ^{§§}
			Capacity building e.g. of mid-level managers (MLM)in most of African country		
	WHO EURO	• Intervention • Collaboration • Policy/ Recommendations • Goal setting	 Developing TIP (Tailoring Immunization Programme) Toolkit to identify behavioural determinants of vaccination (and barriers) and recommend promising practices to address or respond to such barriers. Includes caregiver hesitancy and presents diagnostic framework for pin-pointing reasons for acceptance, hesitancy and refusal. Vaccine Hesitancy as subcomponent of <i>Communication Strategy</i> Factsheets Talking with parents about vaccines for children' Understanding the risk and responsibilities of not vaccinating your child. European Immunization Week media and caregiver publications: ie. 7 Key Reasons to Vaccinate and documents dispelling the myths that generate hesitancy. Launching a mobile phone app in 2013 to allow parents to track their child immunization status, remind them to vaccinate on time, and serve as a recall system in countries where physicians do not carry out this service. Addresses a consistently reported reason for hesitancy: lack of reminder or recall system (forgetfulness/apathy) 	Europe	Variety of partners
Other	Vaccine Industry	• Research • Intervention	 European Federation of Pharmaceutical Industries and Associations (EFPIA): Sponsoring of educational website on vaccination⁸² GlaxoSmithKline (GSK) supports researchers working on vaccine hesitancy and the development of an education tool on how physicians' should address vaccine hesitancy and resistance. Sanofi Pasteur is supporting researchers working on vaccine hesitancy Development of a standardized tool to measure vaccine hesitancy together with Imperial College. Goal of Vaxi Trends Attitudinal Barometer is to generate a validated tool that can: measure attitudes and perceptions, and how they turn into behaviours; understand drivers and barriers to adult vaccination⁸³. 	Global	Variety of partners
	Public- Private Partnership	• Research • Education & Promotion	 Innovative Medicines Initiative (IMI) supports collaborative research projects and builds networks of industrial and academic experts in Europe that will boost innovation in healthcare: ADVANCE project: Accelerated development of vaccine benefit-risk collaboration in Europe. The goal of ADVANCE is to review, develop and test methods, data sources and procedures which should feed into a blueprint of an efficient and sustainable pan-European framework that can rapidly deliver robust quantitative data for the assessment of the benefits and risks of vaccines that are on the market. 		Variety of partners

Discussion:

It is important to note some specific attributes and limitations of this framework. Vaccine hesitancy is an English term, with possibly no direct translation into certain other languages. Hence, given the search strategy, this review has a strong focus on English-speaking countries or those publishing/making available the information in English language though Working Group members were asked to contribute in order to extend research to languages other than English. Through request by stakeholders, the envisaged wiki-approach would allow active inclusions of these into the list. This approach would ensure that additional stakeholders are reflected in the landscape.

A broad variety of groups focusing on the promotion of vaccines and therefore addressing vaccine hesitancy in the population were found, yet according to our inclusion/exclusion criteria we only listed groups focusing on generating research/studies or implementation/evaluation of interventions where specific examples on the scope of their work could be identified.

There were several cases where actors and their interests could potential fit in more than one category. For instance, as CDC is both a subsidiary of the US national government and it donates money it could have fit in either the *Governmental*- National Category or the *Donors* category. In these cases the actors were organised based on how they identify themselves, and in which of the categories they produce most of their work on the issue of vaccine hesitancy. Therefore, in the case of the CDC, they were placed within the Government- National category, as they identify themselves as a major operating component of the Department of Health and Human Services in the US government and produce most of their work on vaccine hesitancy as a part of the US government.

Furthermore, many of the projects on the issue of vaccine hesitancy were conducted with the help of collaboration between multiple partners. This collaboration can make it difficult to demarcate which organisations are working on which vaccine hesitancy projects. In these cases organisation taking the lead on the project were tried to be identified and classified the action under them. If two groups were highly connected it was noted that many of their projects would be interlinked in the action section.

Retrieving information on low- and middle income countries conducting work on the issue of vaccine hesitancy was difficult to find, possibly due to language or publication issues. Therefore Working Group members were asked to share their knowledge on country activities.

The above framework illustrates that many advisory committees and organizations have started to deal with the issue of vaccine hesitancy, including encountering and defining the problem of lack of confidence in vaccines, gathering information on the problem and suggesting potential strategies to deal with this issue. However, although organisations are starting to view vaccine hesitancy as an important topic many organizations discuss and highlight the issue without making meaningful contributions (e.g. research, interventions, recommendation). In fact, many organizations working on vaccines state in their mandates that they will work to promote the use and acceptance of vaccines among both the public and health professionals. However it is rarely specified how they will achieve this vaccine demand section of their mandate. Few examples of current projects relating to vaccine promotion/acceptance are given.

This landscape analysis, along with the development of indicators of vaccine hesitancy, demonstrates that there are not many global vaccine reporting or surveillance systems currently measuring demand-side indicators, such as vaccine hesitancy. In addition, most of the vaccine-related work is on supply side criteria, rather than demand-side criteria. Most projects focus on vaccine development, production and safety, as well as health systems strengthening, whereas only a few projects focus on the demand-side factors (e.g. vaccine acceptance, confidence and hesitancy).

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