TECHNICAL REPORT

Rapid literature review on motivating hesitant population groups in Europe to vaccinate

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This report was commissioned by the European Centre for Disease Prevention and Control (ECDC), under the Framework Service Contract ECDC/2014/013 with World Health Communication Associates and sub-contracted to London School of Hygiene and Tropical Medicine.

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Abbreviations

EEA	European Econmic Area
HCP	Healthcare provider
MMR	Measles, mumps and rubella
PACV	Parent Attitudes About Childhood Vaccines
SAGE	Strategic Advosory Group of Experts
UNICEF	United Nations Children's Fund

Introduction and aims

This rapid literature review by the London School of Hygiene and Tropical Medicine Vaccine Trust Group is part of a European Centre for Disease Prevention and Control (ECDC) project entitled 'Comprehensive expert opinion on motivating hesitant population groups to vaccinate', managed by World Health Communication Associates.

Vaccine hesitancy is defined as 'a behaviour, influenced by a number of factors including issues of confidence (level of trust in vaccine or provider), complacency (do not perceive a need for a vaccine, do not value the vaccine), and convenience (access). Vaccine-hesitant individuals are a heterogeneous group that are indecisive in varying degrees about specific vaccines or vaccination in general. Vaccine-hesitant individuals may accept all vaccines but remain concerned about vaccines, some may refuse or delay some vaccines, but accept others, and some individuals may refuse all vaccines' [1].

The aim of the rapid literature review is to bring together knowledge and research related to vaccine hesitancy in the EU and in EEA countries into a format that is easy to understand and follow. The review focuses on identifying what is known about:

- who the hesitant populations are
- what are enablers and barriers to vaccination uptake for these hesitant populations
- what is known about successful interventions targeting these populations; especially, interventions provided for and by healthcare providers (HCPs).

The results of this review are summarised in this document which lists all key references (peer reviewed and grey literature) with columns on country, targeted population, specific vaccine(s), identified determinants of hesitancy, intervention (if proposed), as well as an indication of whether the intervention was evaluated.

Gaps in knowledge identified will be used to inform the development of a qualitative study in three countries. Knowledge gained from the rapid literature review and the qualitative study will be used to inform the development of a 'Let's talk about hesitancy' supplement to the ECDC 'Let's talk about protection' guide.

Methods for the rapid literature review

The methodology chosen was a rapid assessment of the literature rather than a systematic literature review. What differentiates this rapid assessment from a systematic review is the method used to screen for articles. The most relevant articles were selected through a rapid screen of titles and abstracts by one reviewer rather than in a systematic manner with multiple reviewers. In order to ensure that the search was as inclusive as possible, a search for articles was performed using a 'systematic review' method: searching through multiple general databases using a detailed search strategy with keywords and MeSH terms. The initial selection of articles was done by removing duplicates and excluding articles published before 2004. Initially selected articles were then screened based on agreed criteria for final inclusion in the study

The search strategy was developed in Medline and then adapted as required by differential indexing across several multidisciplinary mainstream and regional databases including: Embase Classic & Embase, Global Health, Scopus, Web of Science, and OpenGrey. The strategy included an extensive list of keywords (Table 1) and related MeSH/subject headings in an effort to capture the many dimensions and expressions of vaccine confidence, trust and hesitancy. All articles in all languages were included in the search but only articles in English, French, Greek or Croatian were kept after sorting through all selected articles. These were selected to match the countries which responded to ECDC's call for interest in participating in the 'Comprehensive expert opinion on motivating hesitant population groups to vaccinate' project. The reviewer chose to restrict articles to these languages with the aim of informing the development of the qualitative study, to be conducted in France, Greece and Croatia. The search was performed across all databases during the period 3–4 November 2014. In addition, various experts in the field were contacted with a request for relevant literature; and national and international organisations' websites (ECDC, World Health Organization, National Institiute for Public Health and the Environment – Netherlands, and the United Nations Children's Fund) were searched for additional relevant documents in English as well as in languages of countries within which qualitative studies will be conducted, such as French.

Table 1. Keywords for the search strategy

vaccin*	**AND**	anxiety	fear*	intent*	**AND**	europe	finland	norway
		attitude*	hesitanc*	controvers*,		austria	france	spain
		awareness	concern*	misconception*		belgium	germany	switzerland
		behavi*r	decision making	misinformation		estonia	greece	great britain
		belief*	trust	opposition		latvia	iceland	united kingdom
immunis*		criticis*	mistrust	delay		lithuania	ireland	netherlands
		accept*	Perception*	knowledge		bulgaria	italy	scandinavia
		confidence	refus*	parent* con*		croatia	liechtenstein	european union
		doubt*	rejection	dilemma*		portugal	luxembourg	
		distrust	rumo*r	objector*		hungary	cyprus	
immuniz*		dropout*	compulsory	uptake		poland	malta	
		exemption*	anti-vaccin*	barrier*		romania	czech republic	
		choice*	resist*	sceptic*		slovakia	denmark	
		mandatory				slovenia	sweden	

Once retrieved, articles were screened by title and abstract according to the agreed set of inclusion and exclusion criteria (see Box 1). Articles were included if they were published between 2004 and 2014 in Europe (with exception noted below), and if they focused on the following topics: vaccine hesitancy, public trust/distrust, perceptions, concerns, confidence, attitudes, beliefs about vaccines and vaccination programmes by individuals (such as parents, healthcare workers), groups or communities. Articles were excluded if they were not about human vaccines, were about vaccines that are not yet available (such as the HIV vaccine), or were publications on research and development (unless about public trust, confidence, concern or hesitancy). A decision was made to include a selection of highly relevant articles from other parts of the world so as to reinforce the quality of the review. These articles were identified through communication with experts (see PRISMA flow diagram in Annex 2).

Box 1. Inclusion and exclusion criteria to be applied to peer-reviewed studies

Inclusion criteria

- Articles that:
  - include research on the following: vaccine hesitancy, public trust/distrust, perceptions, concerns, confidence, attitudes, beliefs about vaccines and vaccination programmes by individuals (such as parents, healthcare workers), groups or communities
  - have the following keywords: Strateg*, intervent*, campaign, evaluation, approach, program* in title or abstract
  - suggest, describe or evaluate an intervention addressing hesitancy; or evaluated studies or reports needed to relate to primary and/or secondary outcomes of interest. Primary outcome indicated a change in behaviour (such as vaccination uptake/coverage), and secondary outcome indicated a change in knowledge/awareness or attitude.
- Location: Europe
- Publication years: 10 years
- Vaccine: all vaccines and vaccination programmes.
- Populations: all
- Languages: English, French, Greek or Croatian

Exclusion criteria

- Not about vaccines
- Non-human vaccines
- Vaccines not currently available, such as HIV vaccine
- Research and development; unless about public trust, confidence, concern or hesitancy
  - safety research
  - serologic investigations
  - immunogenicity studies
  - efficacy trials
  - pre-clinical trial research
  - cost-benefit analysis or cost effectiveness trials.

Box 2. Inclusion criteria applied to grey literature studies

Inclusion criteria

- Keywords: immunisation, vaccine, vaccination, strategy, intervention, evaluation, hesitancy, refusal, trust, confidence, acceptance, engagement, anxiety, concern, distrust, barrier, rejection, fear
- Grey literature research publication years: open
- Languages: English
- Non-peer reviewed literature.

Data from the selected articles was extracted, coded and analysed by country, hesitant population, vaccine, determinants of vaccine hesitancy, intervention and target audience, and evaluation of interventions (see Tables A1-A3).

Results of the rapid literature review

A total of 7 492 articles were gathered through the initial database search, which was complemented by four articles imported from other sources. After removing duplicates, there were 5 024 articles left, out of which 2 673 were excluded based on publication year (published before 2004). A rapid assessment of the remaining 2 899 articles was performed by screening titles and abstracts. Based on the agreed exclusion and inclusion articles, 226 articles were selected for fuller screening and 29 articles were included in the full data extraction phase. Final selection of the 29 articles were made and agreed by two reviewers based on the relevancy and importance of articles. As this was a rapid assessment of the literature, only the most highly relevant articles, agreed by both reviewers, were kept for data extraction. Articles were excluded which were not on currently available human vaccines, and which did not focus on vaccine hesitancy, trust, confidence or concern (see full list in Box 1 and 2). Out of the 29 articles, five were from the Netherlands, five from the UK, two from Sweden, two from the US, one from Romania, one from Germany, one from France, one from Greece, one from Poland, and one from Hungary. Three articles looked at hesitancy in the world, two in Europe and four studied various countries at once (England, Romania, Russia, Norway, the Netherlands, Poland, Spain, Sweden, Germany and Belgium). There were 10 articles looking specifically into the seasonal influenza vaccine, four into the HPV vaccine, two into the 2009 pandemic influenza A (H1N1) vaccine, one into the herpes zoster vaccine, and one into the pertussis vaccine. In addition, seven articles studied all types of vaccines and six focused on childhood vaccines.

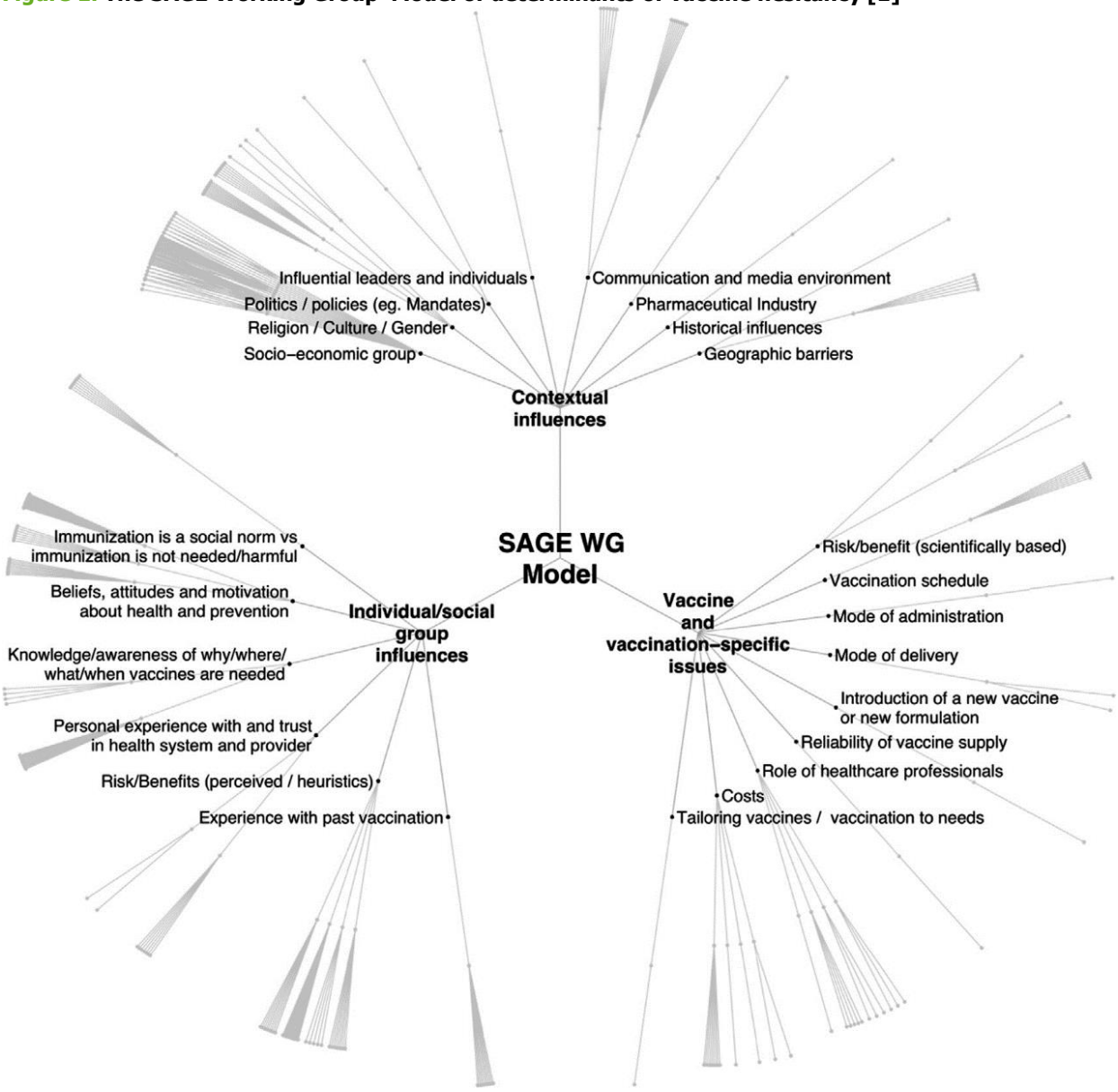
Study populations

The literature review identified several study populations, in which determinants of vaccine refusals or hesitancy were ascertained: parents [2,3,1,4,5,6–9], mothers [10], religious communities [11,12,13], healthcare workers [14,15,1,16–18], immigrants [19], social media users [20], pregnant women [21], patients with chronic diseases [22,23], and the elderly [24]. Although no article focused entirely on 'hesitant populations', researchers detected vaccine hesitant populations within each of their study populations. While no study group was found to be entirely hesitant, researchers raised concerns about the possible formation of clusters of vaccine hesitant populations which might expand and affect the general public [25]. For instance, Lehman raised the concern that when a high proportion of vaccine providers and doctors are hesitant, this might impact vaccine uptake, and other studies have shown that this is especially the case if doctors in these communities are perceived as the most trusted source of information [14,15,16,17,18].

Determinants of vaccination (enablers and barriers)

The term 'determinants of vaccination' incorporates all the concepts of vaccine hesitancy; including, barriers and enablers for uptake, reasons for vaccine refusal, beliefs and attitudes towards vaccination, and vaccine acceptance procedures. In order to capture all these concepts, it was decided to substitute the broader term determinants for enablers and barriers of vaccination. This review has adopted the conceptual framework developed by the World Health Organization Strategic Advisory Group of Experts (SAGE) working group as a way of grouping and classifying 'determinants' identified in the literature review (see Figure 1). This framework identifies three categories of determinants; contextual, individual and group influences and vaccine and vaccination specific issues. The reviewer attempted to provide some quantitative notion of how frequently each determinant appeared in the literature. The following section summarises all the determinants of vaccination retrieved by the rapid literature review, and provides the number of times each one appears in the articles reviewed (see Table 2 and Figure 2). This quantification method was found to be a convenient, although a statistically limited, way of obtaining a broader picture of the range and importance of determinants of vaccine hesitancy in the European literature.

Figure 1. The SAGE Working Group 'Model of determinants of vaccine hesitancy'[1]



Reprinted from Vaccine, 32/19, Larson HJ, Jarrett C, Eckersberger E, Smith D, Paterson P, Understanding vaccine hesitancy around vaccines and vaccination from a global perspective: A systematic review of published literature, 2150–2159., Copyright (2014), with permission from Elsevier.

Contextual influences include historic, social, cultural, environmental, economic, political and institutional factors which might influence vaccine hesitant populations. The most common 'contextual influence' reported in the reviewed studies (seven mentions) were conspiracy theories, which include a fear that vaccines are introduced to serve the economic and/or political interests of pharmaceutical companies [10,20], Western countries [10,20], governments [20], and a belief that vaccines are implemented as a strategy to reduce world population [10]. Religious fatalism [2,19,20,13,8] was reported five times and included beliefs that 'God's decisions are to be trusted' [2,13] or that humans are created as they should be [19] and that vaccines are not needed. Three articles mentioned negative exposure to the media as a determinant of hesitancy [2,1,4]. This includes hearing, reading or seeing negative rumours and myths about vaccines in the general media. The perception that vaccines are being forced upon the population and violated human rights, was listed three times as a determinant [10,20].

Individual and group influences include personal perceptions or beliefs of the vaccines and influences from the social environment. The most common determinant of non-vaccination was the belief that vaccines are unsafe, and more specifically that they can cause severe diseases and side effects [2,3,11,10,14,26,15,20,21,22,,27,13,4,16,5,17,18 ,22,24,8,9], that their long-term effects are unknown [3,26,20,5], that risks outweigh benefits [2,10], and that they contain dangerous adjuvants [2,12,20,27].

These beliefs were encountered 31 times in 22 articles and were the most common determinants found amongst all categories. There were twelve reports of a lack of information and knowledge about either the vaccine or the disease, which sometimes lead to misperceptions about vaccination or targeted diseases, as a common determinant of vaccine hesitancy [3,11,26,1,27,4, 29, 16,18,28]. The belief that there is a very low risk of getting the disease or suffering severely from its symptoms was found 10 times in the literature [2,11,12,27,29,17,24]. Perceptions that the vaccine is not effective and does not prevent the disease was also found 10 times [2,15,12,16,29,16,5,17,18,23,28,8]. There were nine reports of a general mistrust in institutions, and more specifically in the provision of health services and health systems [3,10,26,12,5,24].

Only one article, reviewing HPV vaccination acceptance amongst mothers in Romania, reported a mistrust in doctors due to their lack of objectivity and commercial interestsm [10]. The review recorded nine mentions of the belief that individuals are healthy enough and that their immune system is strong enough not to require vaccination [2,12,16,23]. Social norms and pressure from friends and family [14,15,4,29,16,8] were reported six times as a determinant of hesitancy, and not prioritising vaccination [14,15,4,29,16,8] was also reported six times. Social norm influences include discussions and informal talks with friends, family members, peers, co-workers or community members. Six articles found that hesitant populations can be against vaccination in general [27,4,29,5,18,24]. The belief that vaccination is not natural and an expressed preference for alternative prevention methods such as homeopathy was recorded five times [20,22,16,5,8]. Four articles reported that individuals sometimes believe that diseases can be beneficial for building resistance and should therefore not be prevented [3,1,4,14]. Fear of injection was found four times [11,26,5,28] and so was having previously had a negative experience with vaccines (personal or from friends and families) [2,29,16,8]. The fear and belief that children's bodies are not strong enough to fight the effects of vaccines was mentioned in three articles [2,10,5], and a feeling of responsibility if something were to happen to children after vaccination was mentioned in one study [10].

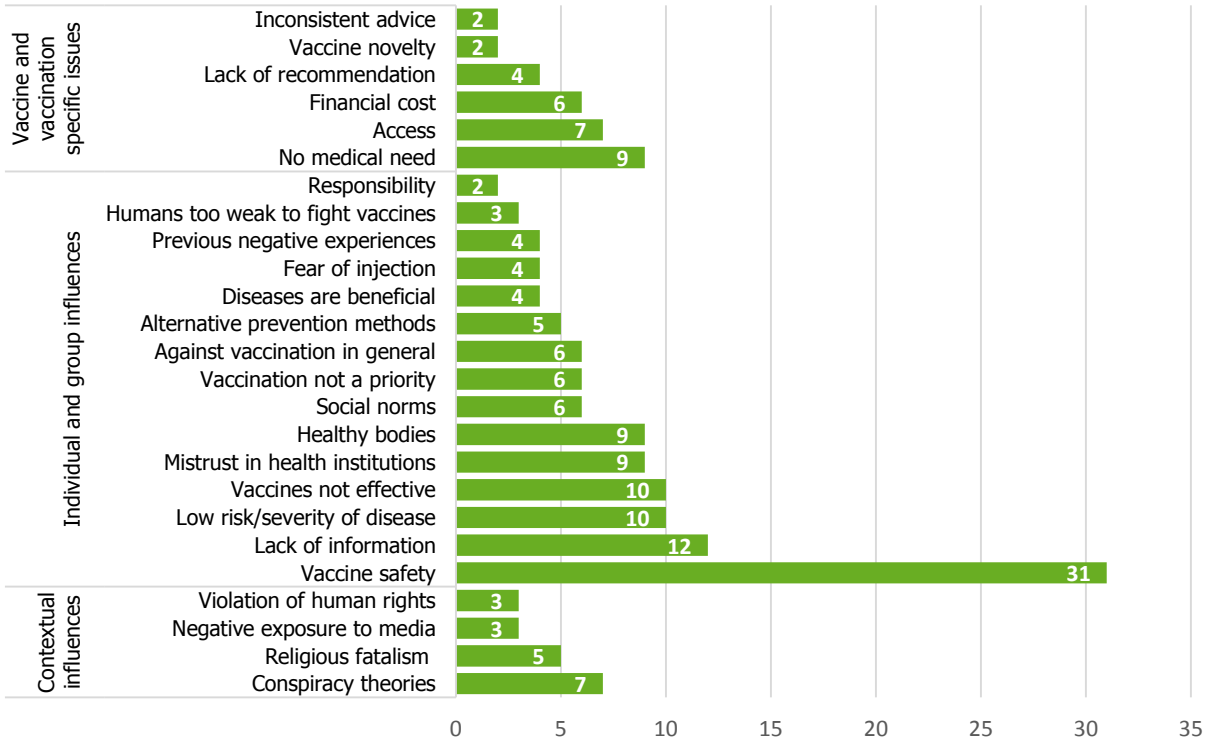
Vaccine and vaccination specific issues include nine results which showed that some individuals did not perceive a medical need for the vaccine [11,14,21,27,13,29,5,18,8]. The problem of access (timing or availability of vaccines) was encountered seven times [14,19,1,22,4,24,8]. Two of these articles were looking at healthcare workers [14] and patients with chronic diseases [4] in the UK, two were looking into immigrants [19] and the elderly [24] in the Netherlands, and one was looking at chronic disease patients [22] in France. Access issues were encountered regarding the influenza vaccine (seasonal or pandemic) and childhood vaccines. The issue of financial cost was found to be a determinant six times [26,1,22,29,23,28]. A lack of recommendations from providers was encountered four times in the literature [4,18,24]. Two studies focused on refusals in response to the novelty of the vaccine [22,5], and a consequent fear of insufficient testing and knowledge. Two other studies pointed to the impact of inconsistent advice from healthcare providers [3,22].

Table 2. Determinants of vaccine hesitancy by category and number of times recorded

	Determinant	Number of times recorded*	References
Contextual influences	Conspiracy theories	7	10,20
	Religious fatalism	5	11,19,20,13,8
	Negative exposure to media	3	2,1,4
	Violation of human rights	3	10,20
Individual and group influences	Vaccine safety	31	2,3,11,10,14,26,15,12,20,21,22,27,13,4, 16,5,17,28,24,8,9
	Lack of information	12	3,10,26,1,27,4,29,16,18,28
	Low risk/severity of disease	10	2,11,12,27,29,17,24
	Vaccines not effective	10	2,15,12,16,5,18,23,28,8
	Mistrust in health institutions	9	3,10,26,12,5,24
	Healthy bodies belief	9	2,12,16,23
	Social norms	6	2,11,19,1,5
	Vaccination not a priority	6	14,15,4,29,16,8
	Against vaccination in general	6	27,4,29,5,18,24
	Alternative prevention methods	5	20,22,16,5,8
	Diseases are beneficial	4	2,12,16,5
	Fear of injection	4	11,26,5,28
	Previous negative experiences	4	2,29,16,8
	Humans too weak to fight vaccines	3	2,10,5
	Responsibility if something bad happens	2	10
Vaccine and vaccination specific issues	No medical need	9	11,14,21,27,13,29,5,18,8
	Access	7	14,19,1,22,4,24,8
	Financial cost	6	26,1,22,29,23,28
	Lack of recommendation from providers	4	4,18,24
	Vaccine novelty	2	22,5
	Inconsistent advice from providers	2	3,22

**Determinants can be recorded more than once in an article (e.g. different types of conspiracy theories mentioned)*

Figure 2. Determinants of vaccine hesitancy by category and number of times recorded



Interventions, their target audience and evaluation

Hesitant audiences targeted

Interventions to reduce vaccine hesitancy were found to be specific to the vaccine and target audience. Interventions targeting the influenza vaccine, for instance, have mostly been focused on healthcare workers [27,17,18,25], high risk groups [21,22,27,4,29,25], and the elderly [27,25]. The ones aiming to improve childhood vaccines coverage rates have focused on parents [2,11,25,6,9]; and those targeting the HPV and rubella vaccines have focused on young people [26] and their parents [27,29,5,25].

Settings

Interventions to reduce vaccine hesitancy were found to take place in healthcare facilities such as hospitals [21,25], primary care centres [22,17,23,25,9], or nursing homes [25]. Only a small number of interventions were reported in schools [26,25], in the workplace [18,25] or in the community [26,25]. The choice of setting was found to be determined by the specific needs and requirements of the country or region where the intervention took place [11]. For instance, Oscarsson recommends that in countries where young people have very little contact with healthcare professionals, HPV vaccination training and educational campaigns should take place within youth centres or schools [26].

Virtual on-line settings provide a means of targeting multiple hesitant groups at the same time and/or to respond to each groups' particular demands and claims [20,7]. According to the United Nations Children's Fund (UNICEF), online communication strategies appear to be most effective when combined with more traditional methods such as face-to-face interactions or the use of leaflets and posters [20].

Content of communication strategies

Some of the articles identified by the rapid literature review looked into the content of messages and communications strategies aimed at reducing vaccine hesitancy (see Table 3). These studies advised decision-makers and vaccination policy implementers to design communication campaigns targeted at patients and healthcare workers with informational and educational messages on: the risk and consequences of diseases, the risk of not being vaccinated, the safety of vaccines, effects of vaccines on the immune system, and alternative modes of prevention and how they compare to vaccination [2,22,5,18,23]. However, Sampson and Cairns both recognised that this list is not exclusive and content has to be specific and adapted to the identified determinants of vaccine hesitancy of various populations [18,25]. Various studies recommend using health needs assessments to look into what type of information people would like to receive on vaccination, and using existing national or regional social networks to tailor communication strategies [3,11,4]. Oscarsson and Kardas recommended involving hesitant populations in the design and implementation of communication strategies, through co-operative and interactive discussions. They also noted the importance of creating clear and effective messages, which are easy to find for everyone [26,23]. One study insisted that in order to achieve successful results, it is essential to organise a continuous provision of information to the public, with regular updates and monitoring [22].

UNICEF provides some guidelines for the development of online communication campaigns and interventions. In terms of content of messages, UNICEF advises not criticising hesitant populations but rather empowering them to ask doctors questions, and providing them with clear and easy-to-understand facts on vaccination. They also stress the importance of highlighting parents' ability to protect children in their environment and region, and of underlining that they have the right but also the responsibility of choosing to vaccinate their children. UNICEF's report also provides recommendations on the design of such strategies. For instance, they suggest multiple methods, including search engine optimisation, to improve visibility and ensure content can be easily found online. They also advise that information is provided in a transparent manner, acknowledging past errors and vaccine side effects, and giving examples of current successful cases, such as the elimination of certain diseases. Finally, UNICEF stresses the importance of monitoring hesitant populations and websites continuously in order to detect potential changes in beliefs and the development of new determinants of vaccination refusals [20].

Table 3. Summary of recommendations for content of communication strategies and interventions

	Recommendations	Reference
Design	Tailor content by conducting health needs assessments and by making use of existing social networks	3,11,4
	Involve hesitant populations in design	26,23
	For online communication campaigns: use search engine optimisation to improve visibility	20
Format	Specific and adapted to determinants identified in targeted audience	4,25
	Clear, effective, and easy to find	26,23
	Continuous information, with regular updates and monitoring	22
	For online communication campaigns: transparent and monitoring hesitant populations	20
Content	The risk and consequences of diseases	2,22,5,18,23
	The risk of not being vaccinated	2,22,5,18,23
	Effects of vaccines on the immune system	2,22,5,18,23
	Alternative modes of prevention and how they compare to vaccination	2,22,5,18,23
	For online communication campaigns: avoid criticising hesitant populations, empower individuals to ask doctors the right questions, clear and easy-to-understand facts on vaccination, ability and responsibility to protect others (children)	20

Communication methods available

Three main types of communication interventions aimed at reducing vaccine hesitancy were identified. The first one involves setting up a **mass communication campaign**, which consists of the distribution of comprehensive but non-specific information, to the entire population. No particular hesitant group are targeted and the content of these campaigns can include a wide range of messages, from specific information on the need for the influenza vaccine for example, to the benefits of vaccination in general [17,18,25].

A more **personalised communication campaign** is another approach, which targets specific hesitant populations and their needs or requirements. This can include individually addressed correspondence, and was often found to entail direct contact with hesitant individuals, for instance through medical consultations [20,23,25].

Training and educational interventions are another alternative for relevant stakeholders. These focus on training and informing hesitant populations and health professionals such as vaccines providers on the needs for vaccination, as well as addressing concerns of hesitant populations and determinants of vaccine refusal. These can be implemented at an individual or population level [25].

Cairns notes that these interventions will most likely not be effective by themselves and an effective communication strategy targeting vaccine hesitancy would have to combine all three types of campaigns [25]. Although no channel (posters, letters, leaflets, online tools) of communication was found to be more effective than another when used independently, d'Alessandro stresses that the targeted audience should receive information continuously, from various stakeholders and channels [22].

Evaluation of interventions

The review of selected studies found mixed evidence on the effectiveness of interventions targeting vaccine hesitancy. This is partly due to the specificity of such interventions to the audience, particular culture, country and vaccine. An intervention to improve influenza vaccination might be successful in a particular country, population, or even time frame (outbreak of pandemic influenza) but unsuccessful in another [26,27,25]. Interventions which solely promoted favourable attitudes to vaccination were not found to improve attitudes [25]. Furthermore, strategies aimed at improving knowledge (education and training) were successful in general but the effect on vaccine uptake was not always positive [25]. Finally, interventions focusing on improving knowledge of healthcare workers were mostly found to have a positive impact on vaccine uptake [17,25,6,7,9]. Opel also confirmed that communications from providers of vaccination are more successful when they are presumptive (assuming that patients will get vaccinated) rather than participatory (asking patients how they feel about vaccination) [6].

Example of an effective intervention

The Parent Attitudes About Childhood Vaccines (PACV) Survey was designed by Opel et al to measure vaccine hesitancy in parents of the general population. It includes three major categories of questions: immunisation behaviour, safety and efficacy, and general attitudes and trust (see Table 4). Parents' responses to these questions allow the calculation of the 'PACV score' by assigning two points for every 'hesitant response', one point for 'don't know' or 'not sure' answers and 0 point for 'non-hesitant responses'. Points are then summed up and converted to a scale from 0–100 to provide the PACV score, which is then compared to delay in immunisation. Based on this tool of vaccine hesitancy measurement, the research group designed an intervention to respond to hesitancy. The intervention, which was proven successful, consisted of administrating the PACV survey to parents before appointments with health supervision visits. The PACV score, easily calculated, would then be used to inform healthcare providers on the possible hesitancy of parents. It allows healthcare workers to tailor and adapt their messages and communication strategies to address specific claims and inform patients on areas of misperceptions [6,9].

Table 4. Questions of the PACV survey, by category (adapted from Opel 2011 [26])

Immunisation behaviour
Have you ever delayed having your child get a shot for reasons other than illness or allergy?
Have you ever decided not to have your child get a shot for reasons other than illness or allergy?
How sure are you that following the recommended shot schedule is a good idea for your child?
It is my role as a parent to question shots.
If you had another infant today, would you want him/her to get all the recommended shots?
Overall, how hesitant about childhood shots would you consider yourself to be?
Beliefs about vaccine safety and efficacy
Children get more shots than are good for them.
I believe that many of the illnesses shots prevent are severe.
It is better for my child to develop immunity by getting sick than to get a shot.
It is better for children to get fewer vaccines at the same time.
How concerned are you that your child might have a serious side effect from a shot?
How concerned are you that any one of the childhood shots might not be safe?
How concerned are you that a shot might not prevent the disease?
Do you know of anyone who has had a bad reaction to a shot?
General attitudes and trust
The only reason I have my child get shots is so they can enter daycare or school.
I trust the information I receive about shots.
I am able to openly discuss my concerns about shots with my child's doctor.
All things considered, how much do you trust your child's doctor?

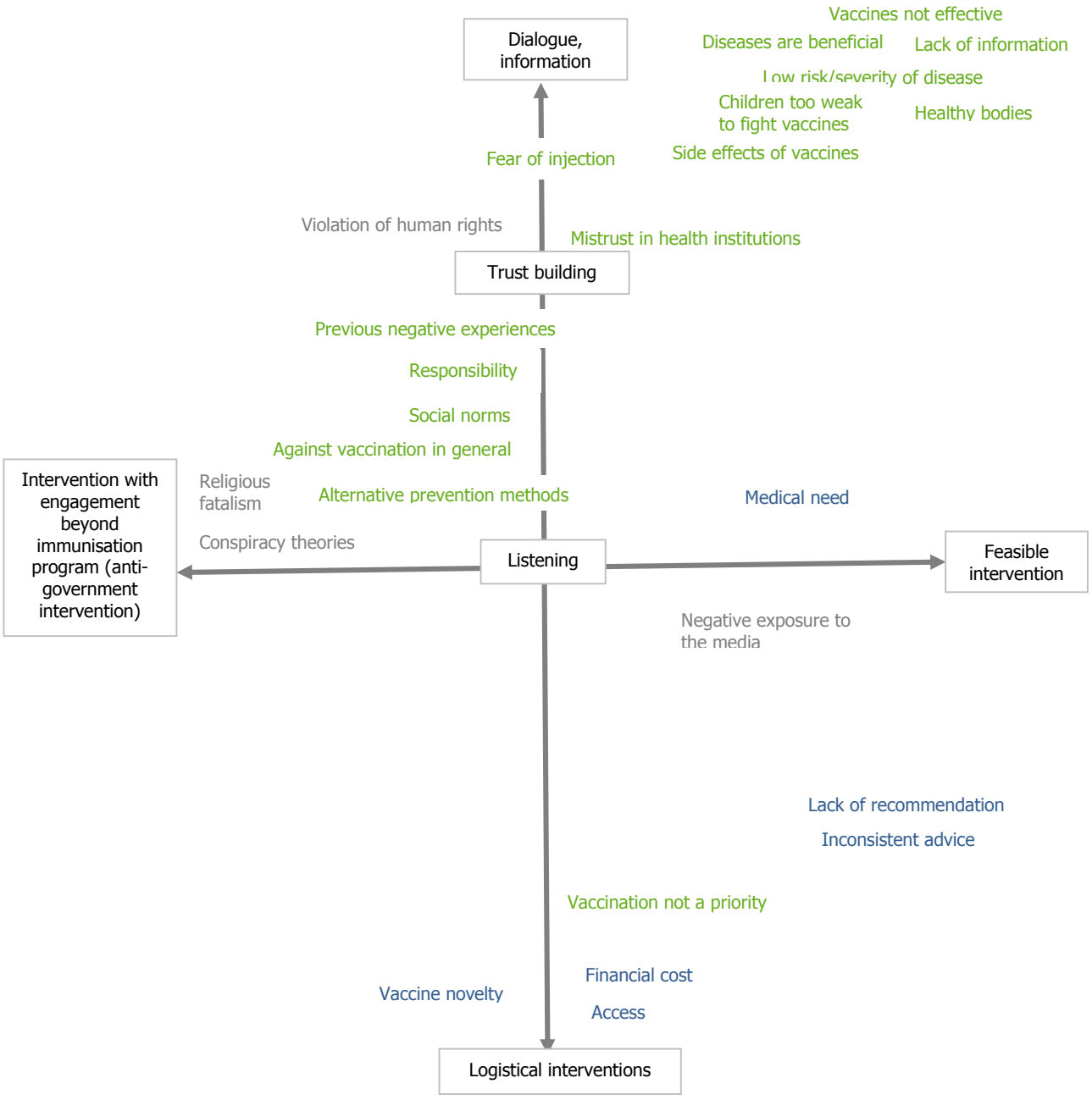
Discussion and general recommendations for developing interventions to reduce vaccine hesitancy

The articles selected for review recommend every communication intervention to be based on clear and comprehensive frameworks combining an array of concepts: knowledge, attitudes, acceptance, perceptions, beliefs, or behaviour. They advise prioritising interventions that can target the most common population groups and behaviour, and leave smaller scale interventions to fill the gaps and address specific hesitant populations. Various studies agree that messengers have to be perceived as credible and trusted sources by hesitant populations and this trust needs to be reinforced by using effective and transparent arguments [2,3,11,20]. Boedeker and Cairns note that ideally, vaccine providers are to be used as advocates of vaccination, but interventions can use a range of stakeholders as long as they have expertise in communication design, delivery, and evaluation [21,25]. They also mention that optimally, healthcare workers are to be included as receivers of information, training and education.

Determinants of vaccine hesitancy need to be addressed specifically and use methods and types of interventions relevant to the issue and the context. Based on its own extensive experience and the work of well-known experts in the field such as Brendan Nyhan, the Vaccine Confidence Project has developed a matrix to help and inform the design of interventions based on these determinants (see Figure 3). Certain determinants such as individual beliefs in risks of vaccination and low risk of getting the disease can be addressed through discussions, information, and educational interventions. Others, such as mistrust in institutions, require interventions that will build trust in health systems and vaccines. Certain determinants simply require logistical interventions: for instance, reducing costs or improving access.

The challenge lies in hesitant populations with determinants and beliefs which are difficult to control or alter. These include religious beliefs or people with conspiracy theories. Although there are ways to work with these populations, for instance, by collaborating with religious or community leaders, these determinants are based on strongly rooted ideologies which constitutes one of the most difficult type of behaviour change. These type of behaviour might not be tackled effectively by short-term, general interventions.

Figure 3. Matrix of vaccine hesitancy determinants and interventions



Current knowledge gaps and suggestions of themes for future qualitative research

Some knowledge gaps which might be addressed in future studies were identified across all articles. Two studies mentioned the need for more information on the influence of demographic factors on vaccine hesitancy rather than vaccine uptake, such as: gender [1,10,26,27], socioeconomic status [11,26,27,16], educational level [12], or age [27]. ECDC also underlines the need for such type of demographic information on a country and European level when comparing hesitancy across countries [27]. Some researchers mentioned that it is important to include both parents who refused and parents who accepted vaccination in order to ensure a balanced discussion [10,26]. Studies on influenza also acknowledge the potential interest of conducting more research on the link between hesitancy for pandemic and seasonal influenza vaccination [15,27], and to measure trends in hesitancy as it changes over time [12,7] as well as before and after pandemics [22]. More practical barriers also require further research such as forgetfulness, distance between individuals and health centres, or registration with local health institutions [2,19,29]. Regarding population groups, further studies could be conducted on individuals who do not receive Western medicine [11], and who for instance opt for homeopathic therapies, or traditional Chinese medicine. These populations are not included in studies identifying study participants through health centres.

Many researchers agreed that results from interviews or focus groups should be quantified in some manner, for instance, by asking individuals to rank factors that might affect their decision-making by order of importance [12,16]. This will allow a deeper understanding of which determinants are most important and should be prioritised during interventions. In terms of interventions, more research was requested on the potential need to tailor communication strategies to hesitant populations [2,12] or social groups [11], as well as on how communication strategies can address beliefs and hesitancy and how they can make use of social networks and digital interactive technologies [25,7]. Sadaf mentions that there is insufficient evidence on the link between hesitancy and quantifiable outcomes such as vaccination rates, intent to vaccinate or change in attitudes [7]. Finally, Larson stressed the importance of conducting more research into multi-level factors which can contribute to vaccine hesitancy and whether hesitant behaviours are influenced by individual or a collection of factors. She also highlights the lack of research on contextual factors and the lack of established metrics which could assess the presence or impact of vaccine hesitancy [1].

Based on the gaps in knowledge mentioned above, and the tools for measurement of vaccine hesitancy used across all studies, the Vaccine Trust Group identified themes and areas which could be included in a future European comprehensive qualitative research in vaccine hesitancy (see Box 3). These themes were grouped according to the following categories: 'demographic information', 'immunisation behaviour', 'information sources and content', 'attitudes', and 'trust'.

In conclusion, two main themes and areas for actions emerged from the literature review. Based on the reviewed articles, the most common determinant of vaccine hesitancy in Europe is concerns or fears about vaccine safety. This includes many specific beliefs, such as the fear of adjuvants or side effects, but is overall a problem of risk perception. Qualitative studies addressing vaccine safety and risk perception in Europe would bring considerable value and benefits to currently available evidence. The second issue identified was the problem of hesitant vaccine providers and healthcare workers. There is a lack of information on the proportion of hesitant providers across European countries and its link to the perceived individual trust in providers as a source of information. More studies are therefore needed on the complex interaction between providers and individuals in terms of vaccine hesitancy. Questions to be addressed could include: What is the impact of provider hesitancy on vaccine uptake? Are providers hesitant to specific vaccines, and if so, which ones? How can interventions address this issue and improve vaccine uptake amongst both hesitant providers and individuals?

Box 3. Identified themes for a qualitative study

Demographic information and family composition

- Vaccination status of previous generations
- Role of different family members

Immunisation behaviour

- Who makes the decision (mother, father, grandparents, religious leaders, etc.), was it a difficult or straightforward decision, was it the same for all children
- Factors and reasons (single or combination) influencing decision to vaccinate (with rank of importance for each)
- Behaviour in normal times versus time of epidemic
- Practical barriers

Information sources and content

- Need for information
- Sources of information for vaccination (trusted and non-trusted) and content provided by each source (who do they ask)
- Other important sources of information (not health related) such as religious leaders, teachers or community leaders
- What makes them decide to trust the information they read/hear?
- Role of culture and religion
- What is the impression vaccine providers gave about their own beliefs/hesitancy?
- Is vaccination a topic of conversation (with whom in their social networks?) and what do they talk about
- Severity of vaccine preventable diseases, thoughts about risk of getting the disease, importance of vaccination in protecting the community, how would they feel if vaccination programmes were to stop? Would that increase their sense of risk or not?
- Interactions with doctors: how would they prefer to discuss vaccination issues with providers, what do they value more (well-informed doctors, conviction, conflict of interests)

Attitudes

- Beliefs about vaccine safety and risk perception: Concern, worries, doubts about vaccination and potential side effects as well as previous experience of adverse effects (including self, others and anecdotal reports)
- Concerns about specific vaccines vs vaccination in general
- Perception about new vaccines
- Personal protection measures against disease (other than vaccination)
- Circumstances in which they might change their opinions about some or all vaccines
- Why do they believe vaccines are recommended and how would they react if everyone would stop vaccinating

Trust

- Perceived positive and negative aspects of the national immunisation programme
- Trust in and satisfaction with health system, health services, immunisation services, doctors/nurses
- Trust in stakeholders recommending vaccination such as National immunisation technical advisory groups

References

1. Larson HJ, Jarrett C, Eckersberger E, Smith D, Paterson P. Understanding vaccine hesitancy around vaccines and vaccination from a global perspective: A systematic review of published literature, 2007–2012. Vaccine 2014, 32: 2150-2159
2. Hamsen IA, Mollema L, Ruiter RAC, Paulussen TGW, Melker HE, Kok G. Why parents refuse childhood vaccination: a qualitative study using online focus groups. 2013. BMC Public Health 13:1183
3. Stefanoff P, Mamelund S-E, Robinson M, Netterlid E, Tuells J, Bergsaker MAR, Heijbel H, Yarwood J. Tracking parental attitudes on vaccination across European countries: the vaccine safety, attitudes, training and communication project (VACSATC). 2010. Vaccine 28(35), 5731-5737
4. Sampson R, Wong L, MacVicar R. Parental reasons for non-uptake of influenza vaccination in young at-risk groups: a qualitative study. 2011 British Journal of General Practice 61(588): e386-391.
5. Grandahl M, Oscarsson M, Stenhammer C, Neveus T, Westerling R, Tyden T. Not the right time: Why parents refuse to let their daughters have the human papillomavirus vaccination. 2014. Acta Paediatrica, International Journal of Paediatrics 103(4): 436-441.
6. Opel DJ, Mangione-Smith R, Taylor JA, Korfiatis C, Wiese C, CatZ S, and Marting DP. Development of a survey to identify vaccine-hesitant parents: The parent attitudes about Childhood Vaccines Survey. 2011. Human Vaccines 7(4), 419-425
7. Sadaf A, Richards JL, Glanz J, Salmon DA, Omer SB. A systematic review of interventions for reducing parental vaccine refusal and vaccine hesitancy. 2013. Vaccine. 2013 Sep 13;31(40):4293-304
8. Larson H, Schulz W, Tucker J, Smith D. Measuring Vaccine Confidence: Introducing a Global Vaccine Confidence Index. 2015. PLoS Currents Outbreaks. 25 Feb. Edition 1.
9. Opel DJ, Taylor JA, Zhou C, Catz S, Myaing M, Mangione-Smith R. The relationship between parent attitudes about childhood vaccines survey scores and future child immunisation status: a validation survey. Jama Pediatr; 2013. 167(11):1065-1071.
10. Craciun C. and Baban A. Who will take the blame?: understanding the reasons why Romanian mothers decline HPV vaccination for their daughters. 2012. Vaccine 30(48): 6789-6793.
11. Henderson L, Millet C, Thorogood N. Perceptions of childhood immunization in a minority community. 2008. J R Soc Med 101:244-261.
12. Harmsen IA, Ruiter RAC, Paulussen TGW, Mollema L, Kok G, de Melker HE. Factors that influence vaccination decision-making by parents who visit an anthroposophical child welfare center: a focus group study. 2012. Advances in Preventive Medicine, 1-7. (thesis)
13. Ruijs WLM, Hautvast J, Van Ijzendoon, Wilke JC, van der welden K, Hulscher M. How orthodox protestant parents decide on the vaccination of their children: a qualitative study. 2012 BMC Public Health 12.
14. Chen S, Hawkins G, Aspinall E, Patel N. Factors influencing uptake of influenza A (H1N1) vaccine amongst healthcare workers in a regional pediatric centre: lessons for improving vaccination rates. 2012 Vaccine 30(2): 493-497.
15. Smedley J, Poole J, Waclowski E, Stevens A, Harrison J, Watson J et al.. Influenza immunisation: Attitudes and beliefs of UK healthcare workers. 2007. Occupational and Environmental Medicine 64(4): 223-227.
16. Lehmann BA, Ruiter R, Wicker S, van Dam D, Kok G. I don't see an added value for myself: a qualitative study exploring the social cognitive variables associated with influenza vaccination of Belgian, Dutch and German healthcare personnel. 2014. BMC Public Health 14.
17. Dedoukou X, Nicolopoulos G, Maragos A, Giannoulidou S, Maltezou H.. Attitudes towards vaccination against seasonal influenza of health-care workers in primary health-care settings in Greece. 2010. Vaccine 28(37): 5931-5933
18. Ishola DA Jr, Permaloo N, Cordery R, Anderson S. Midwives' influenza vaccine uptake and their views on vaccination of pregnant women. 2013. Journal of Public Health 35(4): 570-577.
19. Harmsen IA, Bos H, Ruiter RAC, Paulussen TGW, Kok G, de Melker HE, Mollema L. Vaccination decision-making of immigrant parents in the Netherlands. 2014. (thesis)
20. UNICEF Tracking anti-vaccination sentiment in Eastern European Social Media. New York. 2013.
21. Boedeker B, Walter D, Reiter S, Wichmann O. Cross-sectional study on factors associated with influenza vaccine uptake and pertussis vaccination status among pregnant women in Germany. 2014. Vaccine 32(33): 4131-4139.
22. d'Alessandro, Hubert D, Launey O, Bassinet L, Lortholary O, Jaffre Y et al.. Determinants of refusal of A/H1N1 pandemic vaccination in a high risk population: A qualitative approach. 2012 PLoS ONE 7(4).
23. Kardas P, Zasawska A, Dec A, Starchuska MReasons for low influenza vaccination coverage: Crosssectional survey in Poland. 2011. Croatian Medical Journal 52(2): 126-133.

24. Opstelten W, van Essen G, Hak E. Determinants of non-compliance with herpes zoster vaccination in the community-dwelling elderly. 2009. Vaccine 27(2): 192-196.

25. Cairns G, MacDonald L, Angus K, Walker L, Cairns-Haylor T, Bowdler T. Systematic literature review of the evidence for effective national immunisation schedule promotional communications. Stockholm: ECDC; 2012.

26. Oscarsson MG, Hannefors A, Tyden T. "Young women's decision-making process for HPV vaccination." Sexual and Reproductive Healthcare. 2012. 3(4): 141-146.

27. European Centre for Disease Prevention and Control. Review of scientific literature on drivers and barriers of seasonal influenza vaccination coverage in the EU/EEA. Stockholm: ECDC; 2013.

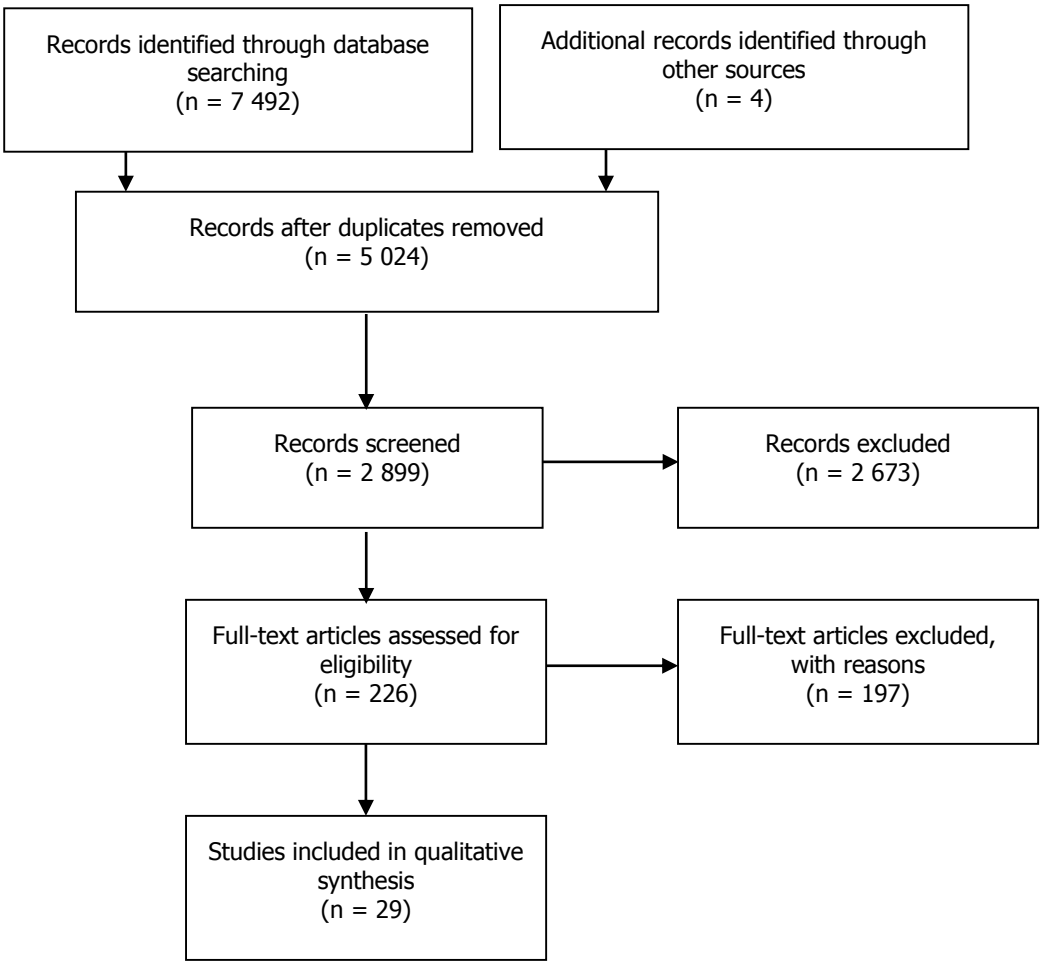
28. Marek E, Dergez T, Krischovicks A, Kovacs K, Rebek-Nagy G, Gocze Ket al.Difficulties in the prevention of cervical cancer: Adults' attitudes towards HPV vaccination 3 years after introducing the vaccine in Hungary. 2011. Vaccine 29(32): 5122-5129.

29. Kroneman M, van Essen G, Paget W. Influenza vaccination coverage and reasons to refrain among high-risk persons in four European countries. 2006. Vaccine 24(5): 622-628.

Annex 1. Search strategy developed on Medline (Ovid)

1. ((vaccin$ or immunis$ or immuniz$) adj5 (anxiety or attitude$ or awareness or behavio?r or belief$ or criticis$ or doubt$ or distrust or dropout$ or exemption$ or fear$ or hesitanc$ or trust or mistrust or perception$ or refus$5 or rejection or rumo?r$ or intent$5 or controvers$ or misconception$ or misinformation or opposition or delay or dilemma$ or objector$ or resist$ or sceptic$)).ti,ab.
2. ((vaccin$ or immunis$ or immuniz$) adj3 (uptake or barrier$ or choice$ or mandatory or compulsory or concern$ or accepta$ or knowledge or parent$ con$)).ti,ab.
3. (((vaccin$ or immunis$ or immuniz$) adj5 confidence) not confidence interval).ti,ab.
4. ((vaccin$ or immunis$ or immuniz$) adj5 decision making).ti,ab.
5. ((vaccin$ or immunis$ or immuniz$) and (anti-vaccin$ or antivaccin$)).ti,ab.
6. 1 or 2 or 3 or 4 or 5
7. exp vaccination/
8. Vaccines/
9. Mass Vaccination/
10. Immunization/
11. exp Immunization Programmes/
12. 7 or 8 or 9 or 10 or 11
13. Public Opinion/
14. Attitude to Health/
15. Attitude/
16. Health Knowledge, Attitudes, Practice/
17. "Patient acceptance of health care"/
18. Treatment Refusal/
19. Parental Consent/
20. Decision Making/
21. Prejudice/
22. Internet/
23. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24. 12 and 23
25. 6 or 24
26. limit 25 to humans
27. europe/ or exp austria/ or exp belgium/ or exp estonia/ or exp latvia/ or exp lithuania/ or exp bulgaria/ or exp croatia/ or exp czech republic/ or exp hungary/ or exp poland/ or exp romania/ or exp slovakia/ or exp slovenia/ or exp finland/ or exp france/ or exp germany/ or exp greece/ or exp iceland/ or exp ireland/ or exp italy/ or exp liechtenstein/ or exp luxembourg/ or exp cyprus/ or exp malta/ or exp portugal/ or exp denmark/ or exp norway/ or exp sweden/ or exp spain/ or exp switzerland/
28. exp great Britain/
29. mediterranean region/
30. mediterranean islands/
31. netherlands/
32. scandinavia/
33. exp European Union/
34. 27 or 28
35. 26 and 29

Annex 2. PRISMA flow diagram



Annex 3. Data extraction tables

Table A1. Data extraction results: countries, target population and vaccine

Reference	Country/region	Target population	Vaccine
1	the Netherlands	Parents who refused to vaccinate their children	Childhood vaccines
2	England, Norway, Poland, Spain and Sweden	Parents of children between 0–3 years old	All vaccines
3	United Kingdom (North East London)	Mothers in orthodox Jewish communities	Childhood vaccines
4	Romania	Women aged 30–50 and mothers of girls in the HPV vaccine target group	HPV
5	United Kingdom (Scotland)	Frontline healthcare workers in a paediatric hospital	Influenza A(H1N1)
6	Sweden	HPV vaccinated young women (17–26 years old)	HPV
7	United Kingdom	Nurses, doctors, laboratory technicians, porters in acute hospitals	Influenza
8	the Netherlands	Parents from anthroposophical child welfare centers	Childhood vaccines
9	the Netherlands	Immigrant mothers, especially from Moroccan or Turkish decent	Childhood vaccines
10	Eastern Europe	Social media users speaking Polish, Russian, Romanian or English	All vaccines
11	Germany	Pregnant women	Pertussis and influenza
12	Global	Parents, primary-care givers, healthcare workers	Childhood vaccines
13	France	Patients with cystic fibrosis	Influenza A(H1N1)
14	Europe	Various	Influenza
15	the Netherlands	Orthodox protestant parents	All vaccines
16	United Kingdom (Scotland)	Parents who refused to vaccinate their children at high risk	Influenza
17	Germany, Poland, Spain and Sweden	High-risk groups	Influenza
18	Belgium, the Netherlands and Germany	Healthcare workers in hospitals	Influenza
19	Sweden	Parents who refused to vaccinate their daughters with the HPV vaccine	HPV
20	Greece	Healthcare workers in primary healthcare centres who refused vaccination	Influenza
21	United Kingdom (London)	Midwives	Influenza
22	Poland	Primary care patients	Influenza
23	Hungary	Male and female adults	HPV
24	the Netherlands	Community-dwelling elderly	Herpes zester and influenza
25	Europe	Various	All vaccines
26	United States	Vaccine hesitant parents	All vaccines
27	Global	Parents	All vaccines
28	Global	Vaccine hesitant parents	All vaccines
29	United States	Parents	Childhood vaccines

Table A2. Data extraction results: measurement and determinants of vaccine hesitancy

Reference	Measurement of vaccine hesitancy	Determinants of vaccine hesitancy
1	**Online focus groups (forums)** • Based on a semi-structured protocol with open-ended and minimal questions • Themes: Family composition; Child welfare centre visited; Perceived positive and negative aspects of the national immunisation program; factors influencing their decision to refuse any or all vaccinations; Need for information on the national immunisation program; Perceptions about new vaccines within the national immunisation program; End discussion and evaluation of the focus group by participants	**Contextual influences** • Previous negative exposure to the media **Individual and group influences** • Social environment: friends and families • Lifestyle: a healthy lifestyle reduces risk of infection (good nutrition) • Immune system not developed to fight vaccines • Low perception of transmission risk and severity of disease • Risk of side effects (and adjuvants): risk > benefits • Vaccines not 100% effective • Advantages to having a disease: building resistance • Previous negative personal experience
2	**Face-to face interviews, telephone interviews, and mail-in questionnaires** • Questionnaire based on the Department of Health England's attitudinal survey • Open questions, questions with answers in the Likert scale, yes/no questions • 10 core questions: What are your main sources of information about vaccination? Overall how satisfied were you with your (last) vaccination appointment? Have you ever chosen not to give your child a vaccine that you have been offered? Have you ever had any doubts about having your child vaccinated? Have you ever had worries about the safety of a vaccination? Would you have your child vaccinated with vaccines offered to you in the future? Who do you trust the most to give health advice and information about vaccination? Are you satisfied with the way in which vaccination is provided? How important are vaccinations in protecting the whole community against diseases? How serious are vaccine-preventable diseases to your child?	**Individual and group influences** • Fear of adverse events (link between autism and MMR) • Fear of vaccine safety and unknown long term effects • Low quality of provision of services • Poor information **Vaccine/Vaccination specific issues** • Benefits of herd immunity • Disagreements between experts on safety of vaccines
3	**Semi-structured interviews** • Questions: Who normally makes decisions about tour children's health (you, your husband, family, etc)? Who do you typically ask if you're not sure what to do? Do you look at leaflets from your GP? Who else do you ask? Where else would you go for advice? What comes into your mind when I say BCG? (image, words, anything at all) Why do you think that comes to mind? Where do you know this from? What comes to mind when I say MMR? Where do you think your ideas come from? Have you ever heard or read anything which has worried you about these immunizations? Can you describe what a 'bad' reaction would be? (If respondent says 'bad reaction') What would this mean? (If respondent says 'bad reaction') Have you heard any positive messages about these two immunizations? On what grounds did you choose to immunize or not to immunize your child? (E.g. was the decision an active and considered choice or simply forgotten). What about your other older children – did you do the same? Was this decision made just as any other health related decision would be? Did you seek any special advice? From where? Was the decision difficult or fairly straightforward to make?	**Contextual influences** • Religious fatalism (trust in God's decisions) **Individual and group influences** • Separation from other communities led to feelings of safety about TB (low transmission risk), leading to no perceived need for vaccine • Anxiety about adverse effects (MMR, whopping cough) • Injection of foreign substances • Social norms

Reference	Measurement of vaccine hesitancy	Determinants of vaccine hesitancy
4	**Focus groups and semi-structured interviews** • Themes: attitudes towards the vaccines, intentions, knowledge and behaviour • Questions: Where would you go if you needed to find some health information? What about if you needed information specifically for the prevention of cervical cancer? What is your opinion about the recently introduced vaccine for the prevention of the HPV virus (and the prevention of cervical cancer)? (Probes: is it a good thing to have the vaccine, is there anything about it that bothers you?) Where are you hearing information about the vaccine? What would you say about the information you are receiving about the vaccine? Currently, the vaccine is given to young girls and older women who do not have HPV. What will influence your decision about whether you yourself will get vaccinated? What will influence your decision about whether to have your daughter vaccinated? What will influence your decision about whether to have your son vaccinated? Is there anything else that you think is important for us to discuss about the HPV vaccine?	**Contextual influences** • Conspiracy theories: strategy to reduce world population (reinforced by the gratuity of the vaccine) • Vaccine is an experiment serving commercial interests of pharmaceutical companies (east vs west) • Vaccine pushed onto women (without proper information) **Individual and group influences** • Fear of vaccine negative consequences (infertility, cancer). Risk of vaccine > risk of disease • Responsibility for negative side effects (would accept vaccine for themselves but not for children) • Girls are too young for vaccines • Distrust doctors (lack objectivity, commercial interest) • Ineffective healthcare system • Lack of information (how vaccine works, how linked to cervical cancer)
5	**Survey: self-administered, anonymous questionnaires** • Reasons for non-vaccination sought from a list of responses (multiple reasons allowed) with space for additional free text	**Individual and group influences** • Concern about vaccine safety and side effects • Too busy **Vaccine/vaccination specific issues** • Vaccine not needed • No vaccine available • Ease of access to vaccine
6	**Face to face interviews** • They were posed questions within the HBM framework • Questions: Sharing their thoughts about the risk of contracting HPV infection or cervical cancer, estimating how serious they considered an HPV infection or cervical cancer to be, the benefits of and barriers to an HPV vaccination, and what had initiated their HPV vaccination. Finally, they were asked whether they believed their sexual behaviour could be affected by HPV vaccination. • The association between sexual transmission and HPV was explained for those who were unaware of this relationship.	**Individual and group influences** • Trust in health care • Fear side effects (infertility) • Pain of injection • Fear of diseases becoming resistant • Uncertainty of long term effect of vaccine • Limited knowledge of the vaccine **Vaccine/Vaccination specific issues** • Cost
7	**Postal questionnaire** • Questionnaire asking about current and previous uptake of influenza vaccination, reasons for uptake in those who received immunisation, and both barriers to uptake and inducements to accept vaccination in those who had declined.	**Individual and group influences** • Concern about side effects • Belief that the vaccines don't prevent the disease • Lack of time
8	**Focus groups** • Parents were asked to write down what they perceived as positive and negative aspects of the Dutch NIP. • More in-depth questions were asked about which factors influenced their decision whether or not to vaccinate their child, the influence of their social environment in their vaccination decisions, and their need for information.	**Individual and group influences** • Trust in institutions • Perception of health (strong healthy children, strong immune system, good nutrition) • Beliefs about childhood diseases (essential for child development) • Low perceived risk of disease • Low perceived effectiveness of vaccine • Fear of vaccine components

Reference	Measurement of vaccine hesitancy	Determinants of vaccine hesitancy
9	**Focus groups** • All focus groups were semi-structured • Discussion proceeded in three parts: it started with an opening question in which participants introduced themselves and expressed whether or not they visited a CWC. The second part focused on participants' vaccination decision-making process; questions were asked about the influence of social environment, role of culture and religion, role and assessment of received information, knowledge level concerning NIP-vaccinations, and possible practical barriers. In the third part, supplemental information was gathered about the satisfaction of the participants with the NIP, if they would like to see some changes within the NIP, and their opinion about possible future vaccinations within the NIP.	**Contextual influences** • Religious beliefs (Muslim) **Individual and group influences** • Social norm **Vaccine/vaccination specific issues** • Access, language of information
10	**Social media monitoring** • Systematic mapping and content analysis • Record activities of users/events with descriptive analysis (clean and categorise data and analyse into recurring themes, volume of posts, engagement, demographics) AND exploratory analysis (interpret patterns and understand sentiment and attitudes) • Data collection: (1) selection of relevant social media channels, (2) software to gather posts according to language and date, (3) keyword logic and search profiles employed to filter data, (4) archive of relevant articles in database, and (5) empirical application and content analysis	**Contextual influences** • Religious beliefs: God created humans as they should be (with diseases) • Vaccination is a violation of human rights • Conspiracy theory: western plot, promotion by pharmaceutical companies, distrust of governments **Individual and group influences** • Safety and efficacy: live vaccines can mutate and create deadly strains, fear of disease and death from vaccines • Development disabilities: brain injuries, epilepsy, autism, weakened immune system, autoimmune diseases • Chemicals, toxins: insufficient studies about the risks and impact of vaccines, no test on long term side effects • Belief in homeopathy, alternative medicine
11	**Survey: self-administered questionnaires**	**Individual and group influences** • Fear of the vaccine and its side effects **Vaccine/vaccination specific issues** • Vaccine not needed
12	**Systematic review**	**Contextual influences** • Negative exposure to communication and media environment **Individual and group influences** • General health knowledge • Encouragement from others, social norm **Vaccine/vaccination specific issues** • Financial cost • Access (time, administration, accessibility)
13	**Semi-structured, face to face interviews** • An interview outline guide, based on this list, ensured systematic coverage of five main topics: (1) attitudes about vaccination and vaccination history, (2) perception of the risks related to the A/H1N1 vaccine and flu, (3) factors governing the choice about the vaccine, (4) personal preventive measures against the A/H1N1 flu other than the vaccine, and (5) information sources and content.	**Individual and group influences** • Fear of the vaccine: no confidence • Untrustworthy, not 100% safe, fear of side effects • Other options as preventive measures **Vaccine/vaccination specific issues** • Mistrust of new vaccines: new pharmaceutical product, developed in emergency situation, hastily developed, humans treated as guinea pigs • Access

Reference	Measurement of vaccine hesitancy	Determinants of vaccine hesitancy
14	**Systematic review**	**Individual and group influences** • Misperceptions about the vaccine (Individuals with chronic medical conditions) • Low perception of disease transmission risk (parents, adults) • Concerns about safety and efficacy (adjuvants) (parents) • Against vaccination in general (adults) **Vaccine/vaccination specific issues** • Advice from family doctors (adults) • Inconsistent advice from providers (pregnant women) • Cost of vaccines (adults)
15	**In-depth interview** • What is the composition of your family? • Have you had your child/children vaccinated? Why or why not? Can you tell us more about this? Do other things play a role as well? -medical aspects -side effects - importance of having had childhood diseases - religious aspects • When did your decision making take place? Before/during pregnancy? First months of life? Reconsideration with next child or in a new life phase? • Who decides? Roles of husband and wife. - Have you been vaccinated? - And your husband/wife? What does your family think about vaccination? - Has this influenced your decision? What do people in your church think about vaccination? - Has this influenced your decision? - Which church do you belong to? • Did you discuss your decision? Ask for advice? From whom? • Did you find it a difficult decision? Have you ever regretted your decision? Did you previously think differently about vaccination? • For non-vaccinating: What would you do during an epidemic? Polio? What would do in case of an injury? (Tetanus vaccination) What would you do when influenza vaccination is called for? – Age - Medical grounds Specific circumstances : travel, work (hepatitis B and influenza for nursing) • Do you talk about vaccination with your children? Own opinions of older children? What would you think if your children later made a different decision? • What do you think of people who do/do not have their children vaccinated? And if they belong to your own church? • Do you receive reactions to the fact that you are vaccinated/not vaccinated from your surroundings? Do your surroundings know that you have been vaccinated/not been vaccinated? - Topic of conversation? What kinds of reactions do you receive? - From whom? • For non-vaccinating: How do doctors and other organisations react to your non-vaccination? • Do you have anything that has not yet been addressed to add?	**Contextual influences** • Religious beliefs: men should not interfere with divine providence, trust in God **Individual and group influences** • Concerns about vaccine safety and side effects **Vaccine/vaccination specific issues** • Medical need
16	**Self-administered questionnaire followed by second questionnaire (self-administered, telephone, or face to face)**	**Contextual influences** • Exposure to media reporting vaccination scares **Individual and group influences** • Uncertainty about indication for vaccination • Vaccination is not a priority • Health beliefs: about influenza vaccine or vaccination in general, misunderstanding of risk for children with chronic health problems, concerns about the safety of the vaccine (side effects) **Vaccine/vaccination specific issues** • Access (appointment, other illnesses at the time of vaccination) • No invitation

Reference	Measurement of vaccine hesitancy	Determinants of vaccine hesitancy
17	**Questionnaires: face to face interviews and telephone survey** • Questions about vaccine uptake, self-reported chronic conditions, reasons to refrain from vaccination, and whether one had received a personal invitation by a medical professional to have a vaccination. • The questions were defined; no open-ended questions were included.	**Individual and group influences** • Uncertainty about indication/qualification for vaccine • Low risk perception of disease • Vaccination not a priority - forgetfulness • Negative previous experience • Against vaccination in principle **Vaccine/vaccination specific issues** • No medical need • Cost
18	**Semi-structured one-on-one interviews** • General information (i.e., what is your position in this hospital?) • Immunisation status and reasons for vaccination (i.e., did you get vaccinated against influenza in the past season? What are the reasons why you did (not) get vaccinated against influenza in the past season?) • Experiences with influenza vaccination (i.e., what are your experiences with influenza vaccination?) • Intention to get vaccinated (i.e., are you planning to get vaccinated against influenza in the influenza season 2012/13?) • Patient advice (i.e., would you recommend influenza vaccination to your patients and why?).	**Individual and group influences** • Afraid of side effects • Negative previous experience • Health, not at risk of disease • Low perceived effectiveness of vaccine • Access (time) • Lack of knowledge and misconception about who should get vaccinated • Belief a person benefits from getting sick • Other more effective protective measures • Undefined negative emotions of fear
19	**Individual interviews** • The main open-ended question during the interviews was as follows: Can you tell me about your reasons for refusing to let your daughter have the HPV vaccine? • Additional questions were asked to clarify the parents' statements.	**Individual and group influences** • No trust in government, parents know what's best for their children • Mistrust of nurses due to low support • Too young and fragile for vaccine (harmful effect on growing body) • Fear of injection • Inadequate information: about the actual vaccine, why it is needed • Overwhelmed and pressured to make a quick decision (rushed programme) • Recommendation from others (family, friends) • Suspicion about vaccination in general • Vaccination is unnatural • Diseases can improve immune system **Vaccine/vaccination specific issues** • Novelty of the vaccine (unknown side effect, lack of evidence, cause infertility, autoimmune diseases, length of effectiveness) • No medical need
20	**Self-reported questionnaires** • The following data were collected: age, professional characteristics, influenza vaccination in the past, and reason(s) for vaccine uptake.	**Individual and group influences** • Low perceived disease risk • Doubts about vaccine effectiveness • Fear of vaccine adverse effects

Reference	Measurement of vaccine hesitancy	Determinants of vaccine hesitancy
21	**Self-completed semi-structured online survey** • In view of current knowledge about Flu and Flu vaccine, do you personally feel that giving the Flu vaccination to pregnant women is really justified? Have you had the seasonal Flu vaccine since September 2010? Yes/No IF NO: what was your SINGLE most important reason for not having the seasonal Flu vaccine in the 2010/11 Flu season? (Please tick only ONE answer). It was not offered to me/I simply didn't have the time to go for it/The location for vaccination was not convenient for me/Vaccination was offered at inconvenient times of the day/Vaccination was by appointment only. I needed a drop-in session/I intended to have it, but I forgot to go/I did not think that I was eligible to get it/I did not think that I was at risk of getting flu/I did not think that I was at high risk of getting complications of flu, even if I got the illness/I have had Flu vaccine before and it made me feel ill/I was not convinced about its clinical effectiveness/I was worried about side effects/I was concerned that the vaccine itself could cause me to get flu/I have a specific medical contraindication to this vaccine/I was not given enough information about the vaccine/I am very hygienic in my practice, so I present no risk to others and therefore I do not need vaccine/I am a healthy person with a good immune system/I believe that natural infection provides me with stronger immunity than vaccination/I just do not trust vaccines/I was pregnant at the time and was concerned about the vaccine's safety in pregnancy/Other	**Individual and group influences** • Concerns regarding safety, • Uncertainty about effectiveness • Not enough information **Vaccine/vaccination specific issues** • Logistical issues: inconvenient times, no time • Not offered the vaccine • No medical need
22	**Self-administered survey** • The survey was based on a 28-item questionnaire, especially constructed for this purpose • Including questions (in most cases open-ended) assessing patients' knowledge of influenza (12 items, including 8 open-ended questions), attitudes toward influenza vaccination (5 items, including 2 open-ended questions), practice of influenza vaccination (4 items), and patients' characteristics (7 items).	**Individual and group influences** • Good health • Lack of trust in vaccination effectiveness **Vaccine/vaccination specific issues** • Cost of vaccination
23	**Self-administered questionnaire** • The items in the questionnaire inquired about HPV awareness, attitudes and beliefs concerning screening and vaccinating in general, HPV vaccination (importance, financial aspects) in particular.	**Individual and group influences** • No knowledge of disease • Fear of side effects, • Vaccine not effective, lack of evidence • Fear of injection **Vaccine/vaccination specific issues** • Cost
24	**Self-administered questionnaire**	**Individual and group influences** • Unwillingness to comply with physician's advice • Beliefs: low perceived risk of getting disease, low perceived severity of disease • General objection to vaccination • Vaccination weakens ones natural defences **Vaccine/vaccination specific issues** • Lack of recommendation by providers • Access
25	**Systematic review**	**N/A**

Reference	Measurement of vaccine hesitancy	Determinants of vaccine hesitancy
26	**Parent Attitudes about Childhood Vaccines (PACV) Survey** • **Immunisation behaviour:** Have you ever delayed having your child get a shot for reasons other than illness or allergy? Have you ever decided not to have your child get a shot for reasons other than illness or allergy? How sure are you that following the recommended shot schedule is a good idea for your child? It is my role as a parent to question shots. If you had another infant today, would you want him/her to get all the recommended shots? Overall, how hesitant about childhood shots would you consider yourself to be? • **Safety and efficacy:** Children get more shots than are good for them. I believe that many of the illnesses shots prevent are severe. It is better for my child to develop immunity by getting sick than to get a shot. It is better for children to get fewer vaccines at the same time. How concerned are you that your child might have a serious side effect from a shot? How concerned are you that any one of the childhood shots might not be safe? How concerned are you that a shot might not prevent the disease? Do you know of anyone who has had a bad reaction to a shot? • **General attitudes and trust:** The only reason I have my child get shots is so they can enter daycare or school. I trust the information I receive about shots. I am able to openly discuss my concerns about shots with my child's doctor. All things considered, how much do you trust your child's doctor? • PACV score compared to delay in immunisation	**N/A**
27	**Systematic review**	**N/A**
28	**Survey** • In general, how much confidence do you have in immunisation/vaccines? National Health Services (GP surgeries, hospitals, dentists)? Emergency services? Community health workers (health visitors, midwives)? Family planning? • Do you have any children? How old is your youngest child? • Have you ever hesitated/been reluctant to have your youngest child vaccinated? • You said you were reluctant/hesitant to get your youngest child vaccinated but did you eventually have him/her vaccinated or missed the vaccine? (not needed, too far away, timing inconvenient, not possible to leave work, did not think the vaccine was effectives, did not think the vaccine was safe, religious reasons, other beliefs/traditional medicine, bad previous experience or reaction, bad experience with previous vaccinator, someone else told me that their child had a bad reaction, someone else told me that the vaccine was not safe) • In your opinion, how many people in your community get their children immunised? • After the last time you went to the toilet, did you wash your hands with soap, wash them with water, or not wash them at all?	**Contextual influences** • Religious reasons **Individual and group influences** • Vaccine not effective • Vaccine unsafe • Negative previous experience with vaccination or provider • Other prevention methods, traditional medicine • Someone else told them vaccination was not safe • Negative previous experience (from others) **Vaccine/vaccination specific issues** • Access (time, far, work) • No medical need
29	**Parent Attitudes about Childhood Vaccines (PACV) Survey** • See ref 26 • Scoring system to identify vaccine hesitant parents	**Individual and group influences** • Serious adverse effect from vaccination, vaccine is not safe

Table A3. Data extraction results: Interventions, target audience and evaluation

Reference	Intervention and target audience	Evaluation
1	• Increase information provided to parents on effects of vaccines on the immune system; influence of healthy lifestyles on preventing illnesses; risk and consequences of diseases • Increase access to sources of reliable information.	N/A
2	• In order to successfully deliver public health messages, there is a need to understand sources of information in countries, what population already know about vaccines and what people want to learn about vaccines	N/A
3	• Use the existing social network to communicate positive messages (across countries)	N/A
6	• Young people rarely receive medical care by a physician so information/communication strategies should involve youth centres, schools • Need co-operative discussion - respect of women's views about HPV vaccination	N/A
10	Suggestion for framework on online communication from health workers: • Make content easy to find (search engine optimisation, search marketing to gain visibility), empower parents to ask doctors right questions, do not criticise parents, promote their ability to make the world a safer place for children, highlight individual right and responsibility to choose to vaccinate • Focus on facts on vaccines - transparency is important, take into account past errors (in system and communication) • Present successful cases (near eradication of polio), use countries with favourable public perception of vaccines (Scandinavia) • Monitor	N/A
11	• Gynaecologists should play a major role in communication (HPV)	N/A
13	• Patient education: convey accurate information about disease risks, implement effective tools for communicating vaccine risk benefit ratios, emphasise risk of not being vaccinated and benefits of vaccination, acknowledge safety concerns, compare vaccination to other modes of prevention • Healthcare provider involvement: communicate with patients from professionals involved in implementation of vaccine (GPs) • Message about vaccine: clear and effective about safety, manufacturing, constant updates on infection rates and vaccine safety	N/A
14	**Elderly people:** • Use personalised postcards, letters or phone calls (effective) • Reminder to physicians alone (not effective) • Community pharmacists to advocate flu vaccine (effective) • Have a case manager as part of an interdisciplinary team in a healthcare practice • Lower the age limit for vaccination • Home visits (effective) • Facilitators within the clinics (effective) **Individuals with chronic medical conditions**: • Reminder/recall systems, electronic health reminders • Lead staff members plan the flu campaign (effective) • Written performance report produced during the vaccination campaign with shared results to everyone involved (effective) **Healthcare workers:** • Education or promotion • Improved access to vaccination • Legislation or regulation • Measurement of feedback • More effective if more than one component **Pregnant women:** • Education (and education of providers) • Electronic reminders **Adults in general:** • Electronic reminders (if regular access to internet)	N/A
16	• Better and more targeted information and educational delivery to parents, patients and healthcare providers	N/A

Reference	Intervention and target audience	Evaluation
17	• Information campaign: who qualifies, what is the risk of influenza, problem of relying on natural resistance - targeted at high risk groups (over 65 and chronically ill) • Personally invite high-risk group for vaccination (shown to increase coverage) • Policy measures to reduce financial burden of vaccination for persons in high-risk groups	N/A
19	• More flexible vaccination schedule • More transparent information about the virus and the vaccine and information about who to contact to get the daughter vaccinated at a later date	N/A
20	• Send leaflets, posters, educational material on influenza vaccination to primary healthcare centres • Influenza vaccine offered to all HCWs for free, at their workplace	• Higher coverage than normal but still low
21	• More information on vaccine effectiveness • Employers should deliver more practical and accessible vaccination clinics in the workplace • Special campaigns to promote uptake	N/A
22	• Family physicians are most capable of persuading patients to receive influenza vaccination • Interventions should include both patients and physicians • Use personalised invitations to vaccination at family physician's practices • Make vaccination free of charge • Organise informational campaigns pointing out differences between influenza and other viral respiratory diseases	N/A

Reference	Intervention and target audience	Evaluation
25	**Audiences targeted**: • Healthcare workers (for influenza - improve vaccine uptake in both HCWs and in patient risk group) • Patient at risk groups (for influenza) • Elderly (for influenza) • Parents (for childhood vaccines) • Young people (for HPV, rubella) **Communication methods:** • Mass communication (distribution of universally targeted information to undifferentiated population) • Personalised communication (make a personally relevant appeal to individuals using direct contact or individually addressed correspondence • Training and education • Need a combination of all - only mass communication can be effective by itself • No channel has higher effectiveness (posters, letters, leaflets) • Need multiple contacts rather than one-off with the target audience **Settings:** • Hospitals, nursing homes, general practice centres, and other healthcare facilities • Small number in community or schools **Recommendations and strategic implications:** • Communication interventions should be based on clearly stated theoretical frameworks (vaccine related knowledge, attitudes, perceptions and behaviour are useful indicators of effectiveness) • Communication interventions that can support population scale behaviours are a priority (understand individual choice perspectives as well as social dynamics that shape social norms, values and culture) • Immunisation advocacy: build support and trust in vaccination by using credible and trusted champions for immunisation and visible proof of action. Use informed and motivated healthcare workers as advocates. Multi-method campaigns with various stakeholders • Information provision: knowledge improvement is associated with higher vaccination uptake. Need personalised information exchanges, face to face communication • Communication strategy and information content should be based on formative research and systematic piloting • Education and training for HCWs: effectiveness enhanced when combined with improved service delivery (make vaccines more available) • Expertise in communication: need professional experience in design, delivery and evaluation of promotional communications	• Mixed evidence for all interventions • Intervention promoting favourable attitudes to immunisation • Did not report improvements in attitudes • Message framing had small-scale positive effects • Interventions improving knowledge were successful but did not always have a positive effect on vaccine uptake • Interventions aimed to improve knowledge of HCWs through education and training reported improved rates of vaccine uptake
26	• Let providers be presumptive (it's time to start all those vaccines) rather than participatory (how do you feel about vaccination?)	• Presumptive providers: 26% resists • Participatory providers: 83% resits

Reference	Intervention and target audience	Evaluation
27	**Passage of state laws (introduction of personal belief/philosophical exemption laws for school immunisation requirements)** • Increase in nonmedical exemptions, decrease in proportion of medical exemptions **Statement and school-level implementation of laws (procedural complexities of obtaining nonmedical exemptions and school policies for immunisation requirement)** • Inverse relationship between increasing difficulty of processes for obtaining nonmedical exemptions and exemption rate of state/school **Parent-centred immunisation information or education** • 8/15 studies evaluating impact of educational information on parents' attitudes towards vaccination reported a significant improvement (6 of these tested an educational brochure) • Culturally tailored interventions increased parental acceptance of HPV vaccine but no difference in parents intentions to vaccinate • Web based decision aid: improvement in parents attitudes towards MMR • Out of 10 studies evaluating impact of educational information on parents intention to vaccinate: 5 significant positive impact on intentions (4 tested educational pamphlet, 1 tested a presentation on HPV) • Out of the 5 studies that showed no different in parents intentions: 3 tested brochures, one a multicomponent parent meeting, 1 a "Radionovela"	• No convincing effective interventions • Few studies measure outcomes linked to vaccine refusal, such as vaccination rates, intention to vaccinate, change in attitudes • Most studies scored low on GRADE criteria • Increasing options for obtaining nonmedical exemptions increase overall likelihood of a child obtaining exemptions • Brief educational pamphlets seemed to be the most tested and comprised most of the effective interventions • Need for study: tests effectiveness of delivering information to parents through different media to better inform PH awareness initiatives; develop interventions that can influence perceptions about vaccines; research on changing behaviour
29	• If administered before appointments with health supervision visits, the PACV scores can be used to augment a providers' understanding of where a parent lies on the immunisation acceptance continuum and to shape the discussion positively by allowing providers to structure a visit efficiently to ensure adequate time to discuss concerns and offer tailored advice	• The study assessed that the PACV survey was a valid tool

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