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What are the factors that contribute to parental vaccine-hesitancy and what can we do about it?

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Abbreviations: vaccine-hesitant parents, VHPs; human papillomavirus, HPV; measles, mumps, and rubella vaccine (MMR).

Parental refusal or delay of childhood vaccines is increasing. Barriers to vaccination among this population have been described, yet less is known regarding motivating factors. Researchers are beginning to evaluate various approaches to address the concerns of "vaccine-hesitant" parents, but few studies have evaluated the effect of interventions on timely vaccine uptake. Several models for communicating with vaccine-hesitant parents have been reported for healthcare providers; however, the effectiveness and utility of these strategies has not been quantified. This article reviews the known barriers to vaccination reported by vaccine-hesitant parents and the current evidence on strategies to address parental vaccine hesitancy.

Introduction

Increasing numbers or parents have concerns about vaccination for their children. Recent US data has shown a rise in the rate of vaccine exemptions for kindergarteners,[1,2] as well as an increase in the use of alternative vaccination schedules.[3,4] While some areas of the US are more affected than others, the proportion of children with incomplete primary vaccine series by 35 mo of age and or upon kindergarten entrance is below the Healthy People 2020 goal in most regions.[5,6] Unvaccinated children have been linked to an increased incidence of vaccine preventable diseases and outbreaks of diseases throughout the US and internationally.[7-11]

Parents who follow alternative vaccine schedules or refuse one or more childhood vaccinations are frequently referred to as "vaccine-hesitant" parents (VHPs).[12-14] VHPs may have acquired misinformation about the risks and benefits of childhood vaccines through social networks[15] or the internet.[14,16] Yet, health care providers are consistently cited as the most important resource for vaccine information by VHPs, and provider recommendation for vaccination is one of the most important factors to improve vaccine uptake.[17] Providers report numerous challenges associated with providing care to children of VHPs, such as time needed to address questions during clinic visits,[18] frustration with the lack of perceived trust in the provider's recommendations, or the struggle over whether to refuse to treat children of VHPs due to the risk of disease exposure to other patients.[19]

Effective strategies which provide VHPs with accurate vaccine information to support their ability to make informed vaccination decisions are needed. This article reviews the most common reasons why parents report delaying or refusing childhood vaccines as well as current data on outcome-based interventions to improve vaccine acceptance. Because healthcare providers are the primary source for trusted vaccine information, several suggested strategies for providers to communicate with VHPs are also presented along with the future research needs to tackle this growing problem.

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Barriers to Vaccination

In health services research, a barrier is an obstacle that prevents an individual from adopting a particular health action.[20] For VHPs, barriers to vaccination have been well described,[13,18,21-38] and most barriers are centered on concerns about vaccine safety. Surveys or interviews conducted with VHPs have found that VHPs are more likely to state that vaccines are not safe. Using the Health Belief Model (HBM) as a theoretical guide to identify constructs which vary between individuals and predict engagement in health related behaviors, concerns about vaccine safety map onto the perceived benefits vs. perceived barriers construct.[20] Also mapping onto this construct, VHPs are also more likely to believe that children receive too many vaccines, that their child may have a serious side effect from a vaccine, and that vaccines may negatively impact the child's immune system. Despite several well conducted epidemiological studies refuting any increased risk of developing autism following vaccination, some VHPs still report this as a concern. Also, even though thimerosal is no longer used as a preservative for any recommended childhood vaccines (with the exception of multidose influenza vaccine), some VHPs still report concerns about "mercury" or thimerosal in vaccines.

Studies have shown that VHPs also question the necessity of vaccinations, which maps onto the perceived seriousness or perceived susceptibility (perceived threat) construct within the HBM. Some VHPs prefer their child acquire the natural disease rather than develop immunity through vaccination, or believe that the human body can protect itself from the serious complications of the vaccine preventable diseases. Others believe that some vaccine preventable diseases are not dangerous or easily treatable,

or that their child is not at risk for the disease. Further, some VHPs do not want their child to receive a vaccination because they question vaccine efficacy.

Additional barriers that have been reported by VHPs align with the cues to action construct within the HBM, such as the mandatory vaccination requirements for day care centers or schools. Vaccine accepting parents are more likely than VHPs to report that they have a good relationship with their child's primary healthcare provider and to trust that the provider has their child's best interest at heart. Certain religious or moral barriers to vaccination have also been described, including concerns about prior use of fetal tissues in the manufacturing of vaccines. Finally, some VHPs distrust the government as the licensing body for vaccine recommendations and/or the pharmaceutical companies as the manufacturers of the vaccines.

Barriers specifically related to the human papillomavirus (HPV) vaccine were recently reported in a systematic review of the literature.[39] Although some barriers are similar to other childhood vaccines, such as concerns about vaccine safety or potential adverse events, other barriers appear to be specific to the HPV vaccine. For example, some parents have concerns about the effect the HPV vaccine will have on their child's sexual behavior. As with other recommended childhood vaccines, physician recommendation of HPV vaccine was an important component to parental support for vaccination.

Despite a thorough collection of knowledge regarding the most frequently reported barriers to vaccination among VHPs, very little is known about motivating factors for vaccination in this population. In contrast to a barrier, a motivator is a factor which encourages, influences, and guides goal-oriented behavior.[20] Motivational factors are believed to be important components of successful behavioral change interventions and could serve as worthy resources to encourage vaccination. Although provider recommendation for vaccination has been demonstrated as a motivator in several studies, there is currently a lack of research toward understanding of additional factors that may positively influence vaccination among VHPs. This deficiency may hinder the development of successful interventions.

Identifying Interventions in VHPs to Encourage Childhood Vaccination

Studies of behavioral or educational interventions to improve the attitudes and vaccine intentions of parents regarding childhood vaccinations and/or the vaccination rates of the children of VHPs have been reported. To identify relevant articles describing interventions for parents, or providers who provide care to VHPs, with quantifiable results, a PubMed search was conducted using specific combinations of medical subject heading (Mesh) terms (parents, vaccines, vaccinations, refusal to participate, parental consent, attitude, communication, health communication, intervention studies) as well as a search of the titles and abstracts for these Mesh terms. A search of titles and abstracts of articles for additional terms not available as Mesh (vaccine hesitancy, vaccine hesitant, vaccine-hesitant, opt out, exemption, barrier, and confidence) was also conducted. The search was limited to publications in the English language published over the prior 10 y (i.e., 2003–2013). This search strategy resulted in 374 articles.

Abstracts for all articles were reviewed. Articles describing interventions to address vaccine hesitancy were included if they specifically addressed the vaccine-hesitant population (parents who voluntarily refuse or delay recommended childhood vaccines for their child for reasons other than financial limitations, health care access or basic health care knowledge about the availability of vaccines for specific diseases), or focused on changing parental intentions or attitudes toward vaccines, and identified an intervention which was quantitatively evaluated to improve either attitudes, vaccination intent, or vaccine uptake of children for a licensed vaccine recommended by the Advisory Committee on Immunization Practices at the time of the study. Commentaries and editorials were excluded, as were studies reporting only the results of qualitative research (focus groups, interviews). References were reviewed for all relevant articles and new articles meeting the above specified criteria were included. Seven studies were found which focused on overall childhood vaccines, while 8 studies were found focusing on HPV vaccine.

Interventions Focused on Routine Childhood Vaccines (Table 1)

Few studies evaluating interventions for VHPs have specifically identified and enrolled parents as vaccine-hesitant prior to the intervention. However, Williams et al. conducted an educational intervention for VHPs and identified VHPs for participation through the use of a 15-question survey developed by Opel et al.[40] Our study assessed change in parental attitudes regarding childhood vaccines among VHPs of 2-wk-old infants following an educational intervention.[41] The three-part intervention consisted of (1) an 8 min video focused on common concerns of VHPs as well as 3 first-person parental accounts of vaccine preventable diseases, (2) a handout on common myths regarding vaccines, and (3) a handout on finding accurate vaccine information online. The intervention resulted in a significant improvement in parental attitude about childhood vaccines in the intervention arm compared with the control arm at the 2 mo well visit (median difference 6.7 on 100 point scale, $P = 0.049$). There was no significant difference in the infant vaccination rates between the control and intervention arm at 12 wk of age. Gowda et al. developed and evaluated a tailored, web-based educational intervention to improve vaccination intent of children of VHPs with the measles, mumps, and rubella vaccine (MMR).[42] Participants were classified as vaccine-hesitant prior to the intervention using a survey broadly assessing vaccine hesitancy developed by Gust et al.[34] The tailoring included images consistent with the self-reported race of the parent, addressed specific concerns or specific prior experiences with MMR vaccination, and included the first name of the child. The tailored intervention was compared with untailored educational information. Although not statistically significant, the researchers found that a

Table 1. Interventions to improve (1) parental attitudes about childhood vaccines, (2) vaccination intent, or (3) vaccination uptake among vaccine-hesitant parents

First author; pub date	Study period	Study design	Setting(s)	Sample size	Participant characteristics	Intervention	Control	Primary outcome	Effect and significance
General childhood vaccines									
Williams; 12/2013	May 2011–September 2012	Cluster randomized trial	Pediatric primary care clinics (TN, US)	122	Parents/guardians of 2 wk old infants who were screened as vaccine-hesitant using PACV	Educational video with first-person parental accounts, handouts of accurate online vaccine information and common vaccine myths for all childhood vaccines	Received routine care	Change in parental vaccine hesitancy score and on-time vaccination of 2 mo childhood vaccines	6.7 points less vaccine hesitant on 100 point scale in intervention group compared with control ($P = 0.049$)
Wroe; 2005	Not reported	Prospective trial	Prenatal education classes at a hospital (NZ)	100	Pregnant women attending prenatal classes	Intervention provided a 20 page manual on the benefits and risks of childhood vaccinations	Provided with a 19 page less in depth booklet published by the Ministry of Health	On time infant vaccination, vaccine perceptions, parental anxiety and satisfaction with information	There was a significant improvement in the participants' ratings of being satisfied with the information (90 vs 79, $P < 0.001$), clarity of the information, usefulness, and amount of information on the risks of benefits of vaccines in the intervention group compared with the comparison group. There was a significant improvement in the reported likelihood of immunizing in the intervention group post intervention (97 vs. 82, $P < 0.002$); no significant difference was noted in the comparison group. 90% of parents in the intervention group immunized on time compared with the comparison group (70%, $P < 0.05$). Parental anxiety was also significantly lower after the intervention in the intervention arm compared with the comparison.

MMR vaccine									
Gowda; 2/2012	June–December 2011	Randomized trial	Pediatric primary care clinics (MI, US)	77	Parents/guardians of children < 6 y of age hesitant to vaccinate against MMR using a broad measure of vaccine hesitancy	Culturally and individually tailored web-based intervention focused on MMR vaccine	Web pages similar in appearance to the intervention but untailored	MMR vaccination intent	A greater proportion of parents in the tailored than untailored arm had positive vaccination intentions after intervention (58% vs. 46%; NS)
Jackson; 6/2011	May–July 2006	Cluster randomized trial	Primary healthcare centers and childcare organizations (UK)	142	Parents with children eligible for MMR (1st or 2nd dose)	Attended one 2 h parent meeting co-facilitated by researcher and parent which included provision of balanced information, group discussion and coaching, and received MMR vaccine informational pamphlet	Received the pamphlet only	Decisional conflict as measured by Decisional Conflict Scale and self-reported decision/attitudes about MMR vaccine	Decisional conflict decreased for both arms at one week (effect estimate = –0.54, $P < 0.001$) and 3 mo (effect estimate = –0.60, $P < 0.001$) post-intervention; no significant difference between arms. Significantly more parents in the intervention group reported vaccinating their child with MMR (93% vs. 73%, $P = 0.04$).
Shourie; 12/2013	May 2009–September 2010	Cluster randomized trial	General Practices (UK)	220	First time parents with child eligible for 1st MMR dose	Three-arm cluster randomized trial; Intervention arms included (1) MMR decision aid plus usual practice, and (2) MMR leaflet plus usual practice	Usual practice only	Decisional conflict	Decreased decisional conflict post-intervention for both intervention arms ($P < 0.001$; decision aid effect estimate = 1.09, 95% CI -1.36 to -0.82; information leaflet effect estimate = –0.67, 95% CI –0.88 to –0.46).

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Table 1. Interventions to improve (1) parental attitudes about childhood vaccines, (2) vaccination intent, or (3) vaccination uptake among vaccine-hesitant parents *(Continued)*

First author; pub date	Study period	Study design	Setting(s)	Sample size	Participant characteristics	Intervention	Control	Primary outcome	Effect and significance
					Influenza vaccine				
Frew; 10/2013	September 2011–May 2012	Randomized trial	Venue-based sampling (GA, US)	261	Pregnant women	Comparison of gain- and loss-frame message effects on intent to vaccinate infant for influenza	Control messages	Intent to vaccinate infant against influenza	Both gain (OR = 2.13, 90% CI: [1.12, 4.05]) and loss-frame messages (OR = 2.02, 90% CI: [1.08, 3.79]) were significantly associated intent to immunize infants against influenza compared with the control
Sales; 11/2011	April–September 2008	Prospective trial	Middle and High Schools (GA, US)	324	Middle and high school parents and their children	A multi-component school-based influenza vaccination intervention (County 1) OR a multi-component provider-based influenza vaccination condition (County 2); both arms consisted of a *structural component* (provision of influenza vaccination in schools or provider offices) and an *educational component* (a tailored brochure for parents and a live in-school presentation for students)	Standard of care (County 3)	Change in attitudes/ beliefs regarding influenza vaccination and influenza vaccination intent and uptake	Significant differences were found for perceived benefits ($P < 0.001$), perceived barriers ($P < 0.001$), and social norms of vaccination $P = 0.01$) between the 3 study arms at 1 y following intervention; the provider-based county had significantly higher perceived benefits scores and significantly lower perceived barrier scores than school-based or control counties. Both intervention counties' rates of influenza vaccination significantly increased from baseline to follow-up at 1 y ($P = 0.04$, and $P < 0.001$, respectively), with no significant increase in the control county ($P = 0.49$). Similarly, adolescent influenza vaccine intent for the coming year in both intervention counties showed significant increases (school-based, $P = 0.047$, provider-based, $P = 0.006$), but the control group did not ($P = 0.44$).

larger percentage of parents who received the tailored educational tool intended to have their child vaccinated against MMR compared with the untailored arm.

Among studies in which parents were not specifically identified as vaccine-hesitant prior to the intervention, Frew et al. evaluated the effect of using gain or loss-frame messaging to improve intent for infant influenza vaccination.[43] Framing health messages in terms of gains or losses can influence health decisions. Loss-framed messages are traditionally more effective for detecting illness while gain-framed messages are more effective with preventative health behaviors.[20] Although this study did not specifically enroll mothers who were vaccine-hesitant, it did find that both types of messages (gain and loss-framed) were positively associated with maternal intent to immunize their infants against influenza (gain-frame OR = 2.13 [90% CI: 1.1–4.1], loss-frame OR = 2.02 [90% CI: 1.1–3.8]). A cluster randomized trial reported by Jackson et al. evaluated the impact of a multicomponent intervention on parental decisional conflict, vaccination intent, and vaccination with MMR.[44] Parents in the intervention arm participated in a group meeting focused on MMR. The purpose of the meeting was to provide balanced vaccine information, group discussion, and coaching. The group was facilitated by one researcher and one parent. Both arms received a leaflet addressing MMR specific questions. Although enrolled parents were not specifically identified as vaccine-hesitant pre-intervention, significantly more parents in the intervention arm reported vaccinating their child (93% vs. 73%, $P = 0.04$). Shourie et al. conducted a three-arm cluster randomized trial comparing the use of a MMR decision aid, to a MMR informational leaflet, to usual care.[45] Decisional conflict was reduced in both intervention arms; children whose parents were in the leaflet arm were less likely to be vaccinated with MMR (91%) compared with the decision aid (100%) and control (99%) arms ($P = 0.017$). Wroe et al. conducted a prospective interventional trial comparing the impact of a 20 page manual on the benefits and risks of childhood vaccinations to support vaccination decisions (intervention) to a less in depth 19 page leaflet published by the Ministry of Health (control).[46] Women in the intervention group were significantly more likely to immunize their infants on time compared with the control group (90% vs. 70%, respectively; $P < 0.05$). Sales et al. evaluated changes in parental attitudes and vaccination intent after a school-based educational intervention on influenza vaccine by surveying parents before and after the intervention.[47] The intervention included a brochure mailed to the child's home and a school presentation on influenza vaccination for the students. Parents who participated in the intervention reported significantly higher influenza vaccination rates in their adolescents relative to a control group. Again, participants in this study and were not specifically identified as vaccine-hesitant prior to participation.

Interventions Focused on Human Papillomavirus (HPV) Vaccine (Table 2)

As certain barriers to HPV vaccination are different from the barriers for other childhood vaccines,[39] strategies and interventions to improve HPV vaccine acceptance are discussed separately.

Providers may be hesitant to recommend the HPV vaccine as strongly as they recommend other childhood vaccines.[48,49] Therefore, interventions for both the family and the provider to improve HPV vaccination have been developed and tested. Fiks et al. developed a family focused clinical decision support system for participants in 22 practice sites through a multisite cluster randomized trial.[50] The system included phone reminders and referrals to an educational website for families of girls eligible for the HPV vaccine. An electronic medical record-based HPV vaccine decision support intervention targeting clinicians, which included immunization alerts, education, and feedback, was also included. The parents who received care at a practice randomized to the clinic-based intervention and were randomized to receive the family-based intervention had increased vaccination rates compared with the group of parents who were randomized to neither intervention (combined intervention group increased the vaccination rates from 16%, 65%, and 63% to 25%, 73% and 76%, for each HPV dose respectively ($P < 0.001$)).[51] Kreuter et al. reported the results of a community based intervention which provided resources for community organizations, and specifically referred community groups and clients to a toll free cancer information number (1-800-CANCER) for additional information about the HPV vaccine.[52] The researchers compared the number of calls to the information line before and after the intervention with the number of calls from a comparison community. Calls increased from an average of 24 calls per month in the year prior to the intervention to 33 calls per month in the year following intervention (+38%), as compared with a decrease of 15% in the comparison community without the intervention in the same months ($P = 0.004$). Call questioning the HPV vaccine or specific questions regarding cervical cancer as the subject of call interactions also increased; however, the small sample size for which the subject of the call was described limited the statistical analysis of this data.

Educational interventions specific for parents or caregivers of children eligible for the HPV vaccine have also been piloted. Spleen and colleagues conducted an educational session to increase HPV vaccine knowledge and vaccination intent for parents and caregivers of HPV vaccine-eligible girls in Appalachia.[53] Intention to vaccinate within 1 mo increased significantly among parents post intervention ($P = 0.002$). Kepka et al. evaluated the effectiveness of a culturally-tailored Spanish HPV vaccine awareness program broadcasted as a "radionovella" through a randomized trial.[54,55] Rural Hispanic parents of adolescents enrolled in the intervention arm had improved HPV attitudes compared with the control arm; however there was no significant improvement in either arm on likelihood of vaccination. Another group published the results of an educational intervention to improve attitudes about HPV vaccine.[56] Kennedy et al. randomized parents of girls aged 11–18 y of age who had not yet received the HPV vaccine to receive an educational pamphlet on HPV, or no intervention, following a pretest on HPV knowledge and attitudes. Parents in the intervention group had significantly improved attitudes on HPV vaccine safety and how to access

Table 2. Interventions to improve (1) parental attitudes about hpv vaccines, (2) vaccination intent, or (3) vaccination uptake among vaccine-hesitant parents

First author; pub date	Study period	Study design	Setting(s)	Sample size	Participant characteristics	Intervention	Control	Outcome	Effect of interest and significance
Fiks; 6/2013	May 2010–May 2011	Nested cohort study (survey) within cluster randomized trial	Two state, hospital-owned practice-based research network (PA, US)	17 764	Parents of girls aged 11 through 17 eligible for 1 dose of HPV vaccine during study period	Practices were randomized to receive clinician-focused decision support (education, immunization alerts, and feedback); within each practice, families were randomized to receive family-focused decision support (reminder phone calls and referral to a vaccine education website) or no intervention	No intervention	HPV vaccination rates and time to vaccine receipt for doses 1, 2 and 3	The combined intervention group increased the vaccination rates from 16%, 65%, and 63% to 25%, 73% and 76%, for each HPV dose respectively ($P < 0.001$); time to vaccine receipt was shorter with the clinician-focused than the family-focused intervention for HPV dose 1, but the reverse was true for HPV dose 2 and 3
Kreuter; 1/2012	December 2007–July 2008	Feasibility study with prospective cohort for limited efficacy outcome	Community organizations (MO, US)	19 in St. Louis and 9 in Lower Rio Grande Valley	Community organizations serving African American or Hispanic young women or parents of girls aged 9 to 17	Provided availability of a selection of resources to be used by community organizations to promote HPV vaccination in target populations	No intervention provided to proximal areas with similar demographic composition	Demand *for and acceptability of the intervention and* limited efficacy *in increasing calls to 1-800-4-CANCER*	Calls increased by 38%, as compared with a decrease of 15% in the comparison communities in the same months ($P = 0.004$); questions regarding HPV vaccine or cervical cancer also increased (NS)
Spleen; 6/2012	2008–2009	Before and after study	Community sites (PA, US)	117	Parents and caregivers of vaccine eligible girls	60-min PowerPoint presentation on HPV presented by professional health educators	NA	Change in HPV vaccine knowledge and HPV vaccination intent	Intention to vaccinate within 1 mo increased among parents ($P = 0.002$)

Kepka; 12/2011	July–September 2009	Randomized controlled trial	Local community events (WA, US)	90	Hispanic parents or guardians of girls aged 9 – 17 y	Listened to a radionovella on HPV vaccine	Listened to another public service message	Change in HPV vaccine knowledge and attitudes	Intervention group parents were more likely to confirm that their daughter's other parent would want their daughter to receive the HPV vaccine after the intervention (93% compared with 74% before intervention; $P = 0.007$); there was no significance difference in likelihood of HPV vaccine uptake in either group
Kennedy; 3/2011	March 2008	Randomized controlled trial	HealthStyles survey respondents who reported on an initial 2007 survey that their 11- to 18-y-old daughter had not received the HPV vaccine (US)	270	Parents of girls aged 11–18 y of age who had not yet received HPV vaccine and completed pretest survey	Educational flyer on HPV vaccine followed by post-test survey	Received the post-test survey only	Change in HPV vaccine knowledge and attitudes	Mean scores for perceived vaccine safety and access to HPV vaccine information higher at post-test in intervention group (4.9 to 5.5 for safety and 5.6 to 6.7 for information; $P < 0.01$); no significant change in comparison group

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Table 2. Interventions to improve (1) parental attitudes about hpv vaccines, (2) vaccination intent, or (3) vaccination uptake among vaccine-hesitant parents *(Continued)*

First author; pub date	Study period	Study design	Setting(s)	Sample size	Participant characteristics	Intervention	Control	Outcome	Effect of interest and significance
Gillespie; 11/2011	Not reported	Before and after study	pediatric clinic of children's hospital (OH, US)	81	Parents and guardians of children aged 0 to 10 y of age	Educational fact sheet on HPV vaccine	NA	Parental desire for child to receive HPV vaccine	Proportion of parents who wanted their child to receive the HPV vaccine increased from 49% to 70% post intervention ($P = 0.001$)
Bigman; 12/2010	August–September 2007	Randomized trial	Annenberg National Health Communication Survey	334	Participants selected from a previously established research panel designed to be representative of the US population	Participants were randomly assigned to read a short passage about the HPV vaccine that ended with framed vaccine effectiveness information in 1 of 5 ways (positive framed, negative framed, 2 mixed framed, control)	Control condition did not discuss vaccine effectiveness	Opinions regarding HPV vaccine, including efficacy	Respondents exposed to positive framing (70% effective) rated the HPV vaccine as more effective and were more supportive of requiring HPV vaccine than those exposed to the negative frame (30% ineffective) or the control frame; Positive: $M = 4.59$, $SD = 0.71$; Negative: $M = 4.03$, $SD = 1.0$, $P < 0.001$)
Leader; 2/2009	June 2006	Randomized trial	Survey participants were part of a previously established web-enabled research panel (US)	635	Male and female adults	Participants read 1 of 3 short descriptive paragraphs about the vaccine, each of which emphasized a different aspect of the vaccine	NA	HPV vaccine intent in adults who had at least one daughter	Women who read that the vaccine protects only against cervical cancer had significantly higher vaccination intentions (with free or low cost vaccine) compared with women who read the other descriptive paragraphs; $F(2325) = 5.74$, $P = 0.004$

HPV vaccine information; the control arm also had improved attitudes but the change was not significant. Gillespie and colleague provided an educational fact sheet about the HPV vaccine to parents or guardians of children less than 10 y of age.[57] Only 49% of participants wanted their young child to receive the HPV vaccine prior to the intervention; this proportion increased to 70% after the intervention ($P = 0.001$).

Two studies evaluating message framing for the HPV vaccine have been conducted. Bigman et al. tested 5 different passages about HPV vaccine effectiveness.[58] The researchers found that participants were more likely to believe that the vaccine is effective, and were more supportive of policies which mandate HPV vaccine, when exposed to positive framed messages (the vaccine is 70% effective) compared with negative framed messages (the vaccine is 30% ineffective). Leader et al. compared different informational messages about the vaccine.[59] Participants who read that the vaccine protects only against cervical cancer were more willing to vaccinate themselves or their daughters, suggesting that framing the information about the protective effects of the vaccine may have more significant effects if not focusing on the fact that HPV is a sexually transmitted disease.

Communication Strategies

Several methods or frameworks for communicating with VHPs have been reported. Unfortunately, there are currently no data to suggest that these methods have been tested for effectiveness. Healy and Pickering have suggested first understanding the specific concerns of the VHP.[60] The authors suggest that an open dialog about the risks of vaccination, followed by provision of additional accurate informational resources may be most effective. The authors also suggest continuing to re-evaluate the vaccination decisions with VHPs over time and to view the process as on ongoing discussion. Another group classifies parents by their beliefs about childhood vaccines (i.e., unquestioning acceptor, cautious acceptor, hesitant, late, or selective vaccinator, or the refuser) and then tailoring the communication style according to their category.[61] Similar categories of parental vaccine acceptance have previously been identified by a research pioneer in vaccine hesitancy, Deborah Gust, et al.[62] For the hesitant, late or selective vaccinators, and refuser groups, the authors suggest guiding the parents to discuss their motivations for vaccinating while avoiding persuasive language and arguments. The C.A.SE approach (Corroborate, About Me, Science, and Explain/Advise) for discussing vaccines has also been suggested.[63] Similar to others, this approach suggests that the provider should begin by discussing the specific concerns of the individual parent. The "About me" portion encourages providers to specifically explain why they are experts on the benefits and risks of vaccinations. Users of this method believe that by first gaining parental trust through conversation, and then sharing the medical information and making a recommendation based on the data, the discussion will be more effective. Supporters of this method also suggest that inclusion of the mnemonic (C.A.S.E.) allows more focused discussions. Shelby and Ernst have suggested that the use of storytelling strategies, similar to strategies used by popular anti-vaccine internet sites, in addition to scientific information about the importance of vaccines may be more effective than scientific information alone.[64]

In addition to potential frameworks to guide discussion about vaccines with VHPs, the importance of provider recommendation for vaccination should be emphasized. There are multiple studies supporting that "physician recommendation" of any vaccine significantly impacts the intent or receipt of a particular vaccine. For instance, a survey of parents of adolescents reported by Gargono, et al. found that physician recommendation was significantly associated with the independent receipt of all adolescent vaccines [(Tdap ($P < 0.001$), MCV4 ($P < 0.001$), and HPV ($P = 0.03$)].[65] The manner in which vaccines are discussed with these parents is also relevant. Opel et al. recently reported a study in which provider-parent clinical visits were videotaped and the provider discussion style regarding vaccinations was compared with vaccine uptake in children of VHPs.[66] The study found that use of a participatory discussion style (e.g., what do you think about childhood shots today?) resulted in a significant higher level of resisting vaccine recommendations (adjusted odds ratio: 17.5; 95% confidence interval: 1.2–253.5) compared with the use of a presumptive discussion style (e.g., your child is going to get shots today).

Discussion

Although the reasons why parents are choosing to delay or refuse vaccines for their children have been thoroughly examined, data has demonstrated that the reasons for vaccine delay or refusal may change over time.[16,67,68] Thus it is important to continue to assess the reasons why parents choose to delay or refuse childhood vaccines in order to provide appropriate education to address misinformation. Most previous studies highlight barriers to vaccination among parents who refuse or delay vaccination; there has been little investigation into potential motivating factors for childhood vaccination in this population. In contrast to barriers, motivators are factors which encourage or guide health-related behaviors. For example, if a VHP reports choosing to delay the MMR vaccine for their child because they are concerned about autism, could a potential countering motivator be that severe measles encephalitis can most certainly lead to brain damage, developmental delay or death? A clear understanding of what information, discussion style, or environment may motivate or encourage vaccination should be explored.

Although researchers have begun to develop and evaluate interventions for VHPs, the current data does not support one method for intervention as superiorly effective over others, therefore continued development and evaluation of interventions is needed. Additionally, few interventions have evaluated the ultimate outcome: on-time vaccination of infants or children. Studying actual vaccine uptake in the children of VHPs is more challenging than studying surrogates to this behavior, such as intent, due to the large sample sizes needed to delineate a statistically significant difference. However, if the intention of

interventions is to improve vaccination of children, then this outcome cannot be ignored and research efforts must be directed toward this goal. Luman et al.[69] described a method for evaluating under-vaccination by quantifying total days of under-immunization, rather than just the binomial outcome of on-time vaccination vs. not on-time. This method provides greater power for these types of analyses and has been successfully used by other researchers in this area.[12,40,70]

Most reported interventions are primarily educational in 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. While providing parents with accurate information to counter their misinformed beliefs is important, additional components are likely needed. In our cluster randomized pilot study, we used first-person parental accounts of vaccine preventable diseases in addition to educational information in an effort to enhance the effect of the intervention.[41] The use of such emotionally charged data, provided by parents rather than experts, has been used effectively by persons in "anti-vaccine" messages and may have contributed to the positive results of our intervention. The use of personal narratives and peer-based learning has been employed successfully in behavioral interventions for other health related challenges, such as substance abuse and self-management of diabetes.[71-73] Cultural tailoring and message framing of interventions have also been used successfully in conjunction with educational material for VHPs. Additionally, most behavioral researchers would encourage researchers interested in implementing interventions for behavioral change to utilize a theoretical model to provide a framework for development; however, few of the studies identified in this review discussed the use of a theoretical model. The success of these strategies and others should be considered to optimize future intervention development and testing.

Finally, the effectiveness of suggested provider communication styles should be evaluated. Several of the published communication frameworks suggest discussing vaccines in a gently persuasive, step wise manner. However, recent research by Opel, et al. found that more firm, presumptive discussion styles are more effective than styles in which the parent is participatory. Thus, it is critical to investigate what effect specific communication strategies may have on childhood vaccination rates for children of VHPs in order to determine the most appropriate method for providers to relay vaccine recommendations. Because providers are consistently reported as important sources of vaccine information by VHPs, interventions which include elements addressing *both* provider communication style as well as accurate, individualized and appropriate vaccine information for the VHP may be most beneficial.

Conclusion

The increasing rate of parents who choose to delay or refuse recommended vaccines for their children is a growing problem resulting in resurgence of vaccine preventable diseases. Currently, an understanding of methods to address parental vaccine hesitancy is understudied. Although the barriers to vaccination by these parents have been described, motivating factors for VHPs have not been thoroughly evaluated and may play a key role in effective behavioral interventions for this population. There is a lack of evidence regarding effective strategies to increase vaccine uptake for children of VHPs, and the currently available studies use a wide variety of interventional methods. Few studies identified parents as vaccine-hesitant prior to participation and/or have reported surrogate outcome measures for future vaccination such as attitude and intent, rather than actual vaccine uptake data. Providers play a key role in the vaccination decision-making process for VHPs, yet little data exists on the most effective communication strategies for providers to employ. An evidence-based understanding of the most valuable approaches to address the challenge of parental vaccine hesitancy is needed.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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