EDUCATIONAL OBJECTIVES
After participating in this activity, pharmacists will be able to:
- Describe vaccine hesitancy and barriers to vaccination
- Recognize how the determinants of vaccine hesitancy contribute to behavioral outcomes
- Recall anti-vaccine claims and rebuttals
- Discuss situation-appropriate intervention strategies

After participating in this activity, pharmacy technicians will be able to:
- Recall the benefits of vaccination
- Recognize the various determinants of vaccine hesitancy
- List ways to promote vaccine acceptance

ABSTRACT: Vaccines are responsible for reducing the incidence of vaccine-preventable diseases. While most people receive routine recommended vaccinations, a small portion of the population does not. Vaccine hesitancy and refusal are complex behaviors and the consequences of choosing not to vaccinate jeopardize both individual and societal health and safety. Pharmacists and pharmacy technicians must know the determinants and factors that contribute to vaccine hesitancy before they address and manage it appropriately. A comprehensive understanding of such influences can help pharmacists and pharmacy technicians identify and communicate with hesitant individuals better. Pharmacists and technicians are also able to screen patients for missing immunizations, provide patient education and support, and offer guidance.

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FACULTY DISCLOSURE: Ms. MacDonald and Prof. Wick have no actual or potential conflicts of interest associated with this article.

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INTRODUCTION
Vaccines benefit both the individual and the public by preventing the spread and reducing the incidence of vaccine-preventable diseases within a population.1 In developed countries, vaccines are responsible for diminishing the threat of vaccine-preventable diseases,2,3 particularly vaccine-preventable diseases that once plagued infants and children.4,5 A successful vaccination program is contingent on the majority of the population receiving recommended vaccinations as scheduled to ensure both individual and community protection.1,6 This creates “herd immunity.” For most vaccine preventable diseases, more than 85% of the population needs to be vaccinated to reach a level consistent with herd immunity. But some experts indicate that exceeding 90% is prudent since some patients may be unable to receive vaccines. To ensure community protection and patient safety, healthcare providers should see all visits that do not risk patient and provider exposure as opportunities for patients to catch up on any missing or late vaccinations. As the global coronavirus pandemic continues to change our routines and activities, this practice will allow patients who have delayed vaccination appointments to be appropriately vaccinated.

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Nonadherence to vaccine recommendations, such as vaccination delay or refusal, undermines individual and public health initiatives. Pharmacists and technicians must also be aware that researchers may not have tested the efficacy of alternative vaccine schedules; such schedules may not produce an adequate immune response. Vaccine-preventable disease outbreaks are a consequence of under-vaccination and are a prevalent threat even in the U.S. In 2019, more than 1,000 people across 31 states contracted measles, marking the largest measles outbreak in 30 years. The CDC determined that the majority of cases occurred in unvaccinated patients, while 73% of all cases were associated with recent local measles outbreaks in New York. Although vaccine-related concerns are common even among vaccine acceptors, several factors still motivate a minority of the population to delay or decline vaccination.

What is Vaccine Hesitancy?
A panel of World Health organization (WHO) immunization experts describe vaccine hesitancy as the “delay in acceptance or refusal of vaccines despite availability of vaccination services. Vaccine hesitancy is complex and context-specific; that means it varies across time, place, and vaccines. It is influenced by factors such as complacency, convenience, and confidence.”

It is important to understand that this definition recognizes only reluctant individuals’ possible decisions. In reality, hesitancy exists on a continuum. It ranges from complete refusal of all vaccines to complete acceptance without any concern; in between are intermediate decisions such as refusal of some vaccines and acceptance of others, and full acceptance although the individual is unsure. The spectrum of possible outcomes implies that the process of reaching a decision is complicated and guided by external and internal components. Identifying the factors that influence an individual’s behavior are essential to understand the reasons for vaccine hesitancy. Knowing the specifics also helps determine the most appropriate intervention.

Understanding Vaccine Hesitancy
The terms complacency, convenience, and confidence used in the WHO definition of vaccine hesitancy are the foundation of the “3 Cs” model as described in Table 1.

These components are interlinked and influenced by vaccine hesitancy’s determinants (e.g., specific factors that influence an individual’s behavior; see Table 2) to ultimately affect vaccine-related decisions. Clinicians can use the determinants of vaccine hesitancy to determine an individual’s beliefs and opinions regarding vaccines and vaccination.

| Confidence: Trust in vaccine effectiveness and safety; the system that delivers them, including the reliability and competence of health services and health professionals; and the motivations of policy makers who decide on needed vaccines. |
| Complacency: The perceived risks of vaccine preventable diseases are low and vaccination is not deemed a necessary preventive action. |
| Convenience: A significant factor when physical availability, affordability and willingness to pay, geographical accessibility, ability to understand (language and health literacy), and appeal of immunization services affect uptake. |

Contextual Influences
Communication and Media Environment. The three most commonly referenced sources for vaccine-related information are healthcare providers, friends and family, and the media (primarily the Internet). Although healthcare providers encourage patients to seek knowledge about vaccines from reputable sources when making vaccine-related decisions, misinformation regarding vaccines is prevalent. Unfortunately, the widespread presence of incorrect information and the universal use of the Internet and social media outlets can result in pervasive transmission of anti-vaccine messages. The pharmacy team also needs to be aware that they need to repeat vaccine-promoting messages even if they perceive that the patient or parent is well-educated; across the U.S., we have areas of highly educated individuals who are vaccine refusers.

Exposure to anti-vaccine ideals can contribute to vaccine hesitancy through confirmation bias. Confirmation bias occurs when individuals accept only the information that supports and validates what they already believe, which perpetuates underlying bias. For example, if a person believes that all vaccines contain mercury, he or she will preferentially read or listen to messages that confirm that incorrect information (vaccines do not contain mercury). The consequences of misinformation are twofold: misinformation contributes to how individuals and groups make vaccine-related decisions and provokes distrust of healthcare providers.
Religion. Faith and religion can have a profound impact on health-related behaviors, with pig (pork or porcine) consumption a particular important consideration for people who are members of faiths that prohibit pork.\(^18\) (Note that some vegetarians and vegans also have concerns.) This belief does not impede many interventions, as pharmacists and other health care providers can recommend and many individuals will accept an alternative that does not contain porcine derivatives.

A few manufacturers use porcine gelatin as a stabilizer in some vaccine formulations (listed in Table 3).\(^19\) Its presence may be the sole reason that members of some religions refuse certain vaccines.\(^18\) If an appropriate substitute vaccine is available, pharmacy immunizers should offer this option.

### Individual and Group Influences

**Health system and providers: trust and personal experience.** The patient-provider relationship is a central element of the vaccine decision-making process for many individuals.\(^20,21\) Patients hold healthcare providers—as educators and trusted health authorities—responsible for the outcomes of vaccine hesitancy and refusal-related conversations. The provider’s approach often influences the patient’s decision to vaccinate.

If the relationship between patient and provider is built on cooperation, trust, and respect, patients are more likely to consider the provider a dependable resource and consider the provider’s behavior as an example of best health practices.\(^11\) This dynamic permits healthcare professionals to engage in constructive discussion when approached with concerns, or to clarify misinformation that may obstruct the patient’s perspective on vaccines.\(^22\) From this vantage point, providers can advocate for vaccination acceptance while maintaining a patient-centered dialogue.\(^5,11\)

### Table 2. Determinants of Vaccine Hesitancy\(^13\)

<table>
<thead>
<tr>
<th>Influence Category</th>
<th>Source of Influence</th>
<th>Determinants (factors that affect outcome)</th>
</tr>
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</table>
| Contextual influences | Influences arising due to historic, socio-cultural, environmental, health system, institutional, economic, or political factors | • Communication and media environment  
• Influential leaders, immunization program gatekeepers, and anti-or pro-vaccination lobbies  
• Historic influences  
• Religion/culture/gender/socio-economic influences  
• Politics/policies  
• Geographic barriers  
• Perception of the pharmaceutical industry |
| Individual and group influences | Influences arising from personal perception of the vaccine or influences of the social/peer environment | • Personal, family, and/or community members’ experience with vaccination, including pain  
• Beliefs, attitudes about health and prevention  
• Knowledge/awareness  
• Health system and providers (trust and personal experience)  
• Risk/benefit (perceived, heuristic [meaning learned from one’s own experiences])  
• Immunization as a social norm as opposed to the perception they are not |
| Vaccine/vaccination-specific issues | Directly related to vaccine or vaccinations | • Risk/benefit (epidemiological and scientific evidence)  
• Introduction of a new vaccine, a new formulation, or a new recommendation for an existing vaccine  
• Mode of administration  
• Design of vaccination program/mode of delivery (e.g., routine program or mass vaccination campaign)  
• Reliability and/or source of supply of vaccine and/or vaccination equipment  
• Vaccination schedule  
• Costs  
• The strength of the recommendation and/or healthcare professionals’ knowledge base and/or attitudes |

### Table 3. US Vaccines Containing Porcine Gelatin\(^19\)

<table>
<thead>
<tr>
<th>Porcine gelatin-containing vaccines</th>
<th>Non-porcine vaccine alternatives</th>
</tr>
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<tbody>
<tr>
<td>Influenza (FluMist) Quadrivalent</td>
<td>Flulaval, Fluvirin, Agriflu, Fluzone</td>
</tr>
<tr>
<td>Zoster (Shingles) (Zostavax) Frozen and refrigerator stable</td>
<td>Shingrix</td>
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<tr>
<td>MMR (MMR-II)</td>
<td></td>
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<tr>
<td>MMRV (ProQuad)</td>
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Frozen: recombinant albumin
Conversely, an interaction’s outcome may instead be detrimental to the patient-provider relationship. Examples include when a provider assumes a patient’s reasons for hesitancy, or if a provider’s response does not meet the patient’s expectations. Misguided interventions often have the patient’s best interest in mind yet neglecting a patient-centered approach will fall short of encouraging a reciprocal patient-provider relationship. Such an outcome can occur when a provider’s response to reluctance is providing information and education without first listening to the patient’s concerns (see the section on motivational interviewing on page 5). For example, providers who don’t ask patients why they refuse vaccines and simply present evidenced-based information immediately come across as authoritarian and inflexible. Providers should not consider vaccine acceptance in this context—vaccine acceptance because the patient feels pressured or bullied—to be a successful intervention. Other outcomes are also possible. The patient may misinterpret the provider’s efforts as patronizing and in turn, dismiss the provider’s recommendations. Alternatively, patients may become distrustful. If they feel pressured by the provider to accept vaccination or believe the provider ignored or dismissed their concerns, they may consequently avoid future communication and possibly vaccination.

**Perceived risk/benefit.** Vaccine hesitancy is not only specific to vaccines—it also includes disease-specific concerns. If individuals believe that they are at risk for contracting a disease, they are more likely to seek and accept a vaccine to prevent that disease. However, this same risk/benefit analysis can produce the opposite outcome if the perceived risk of vaccination is greater than that of disease. It’s critical to explain how dangerous vaccine-preventable diseases are.

Vaccines are responsible for minimizing the incidence of many once-common vaccine-preventable diseases, which has altered many peoples’ perception of their disease susceptibility. That is, people think that now-rare diseases are unlikely to circulate. This unintended consequence has masked the risks and complications of many debilitating diseases, such as the measles. In turn some people have transferred the fears they previously held toward the disease to concerns regarding safety and the need for vaccines. A vaccine’s potential adverse health events may present a greater perceived risk than the disease, contributing to vaccine-hesitant beliefs and behaviors.

**Knowledge/awareness.** Although research confirms that vaccines are safe and effective, anti-vaccine sentiments take a variety of forms, as described in Table 4.

<table>
<thead>
<tr>
<th>Anti-vaccine claim</th>
<th>Pro-vaccine rebuttal</th>
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<tr>
<td>“Hot lots” of vaccines are responsible for more serious adverse outcomes</td>
<td>VAERS is used to report adverse events that occur after vaccination; this does not mean that the event was absolutely related to the vaccine. Members of the pharmacy team need to be able to explain the difference between an adverse reaction—something expected and mild—and an adverse event—an unexpected and serious issue. Most issues related to vaccines are “side effects” (expected adverse reactions).</td>
</tr>
<tr>
<td>● Some people believe that some Hot Lots of vaccines cause more side effects or vaccine injuries than other vaccine lots. People who perpetuate this myth apply data from the Vaccine Adverse Reports System (VAERS) inappropriately.</td>
<td>No scientific evidence supports this claim. Additionally, children are exposed to significantly more antigens at birth than through vaccines. Thirtys years ago, vaccines used 3,000 antigens to protect against eight diseases by age two. Today, vaccines use 305 antigens to protect against 14 diseases by age two.</td>
</tr>
<tr>
<td>Antigenic overload occurs in children because their immune systems are unable to manage the number of antigens that vaccines introduce adequately, or...</td>
<td>Infection-induced immunity may elicit a superior immune response. However, the risks and complications associated with infection are significantly greater than those of vaccines. Vaccine-induced immunity is able to prevent infection successfully. Contracting some diseases—such as measles—wipes out other acquired immunities.</td>
</tr>
<tr>
<td>Antigenic overload causes a “cytokine storm” that predisposes children to adverse events and vaccine-induced complications.</td>
<td></td>
</tr>
<tr>
<td>Natural immunity from an infection is safer than immunity from a vaccine.</td>
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<tr>
<td>Vaccines are responsible for the development of autoimmune diseases such as type 1 diabetes mellitus, multiple sclerosis, and Guillain-Barre syndrome. This argument is based on a theory that the immune system is unable to discriminate between intrinsic antigens and the vaccine’s antigens, causing antibodies to bind the intrinsic antigens selectively, eliciting an autoimmune response.</td>
<td>Multiple efforts have been made to review this claim. A panel of experts from the Institute of Medicine reviewed more than 12,000 published reports and several high-quality studies; none established a connection between vaccines and autoimmune diseases.</td>
</tr>
</tbody>
</table>
Intervention Strategies: A Personalized Approach

Patients and healthcare professionals need to work together—that is, collaborate and share decision-making—to adhere to vaccination programs and can do so after they take certain steps:

- Understand the risks and benefits of vaccination.
- Explain the vaccine-preventable disease and the consequences of contracting it.
- Make evidence-based decisions (such as adhering to the recommended vaccine schedules) for patients. This means accessing the CDC patient web sites if patients need more information than the healthcare provider can provide.
- Accept accountability for the health and safety of individuals who are unable to be vaccinated; patients who are healthy and robust need to understand that their failure to “join the herd” of vaccinated people puts others at risk.
- Advocate for health equity (the concept that everyone should have a fair opportunity to attain their full health potential and that no one should be disadvantaged from achieving this potential) regarding the access to vaccine-related resources and the elimination of barriers.

Efforts that involve patients and providers working collaboratively—sharing evidence, understanding each others’ points of view, and working toward good health for our entire society, not just the individual—depends on two things. First, providers must consider vaccine-hesitant patients’ needs and how they affect public health and safety needs. Second, providers need to consider their other patients; some practices will not see patients who refuse vaccines because they would potentially expose other patients to vaccine-preventable disease. Although the laws surrounding patient dismissal in this situation are not straightforward, there are ethical concerns, such as negligence, that can manifest as legal troubles or disciplinary actions from the provider’s regulatory authority.

Beliefs and behaviors that relate to vaccine hesitancy vary at an individual level; clinicians must individualize strategies to address these concerns and ideally increase vaccine acceptance. Interventions should prioritize the patient’s autonomy, recognize the influence of specific determinants (particularly context and individual determinants), and ameliorate any barriers that may be present. Motivational interviewing (and open-ended questions) can help patients resolve their hesitancy. Immunizers need to listen to patients’ thoughts about change, and what they think change will require. Reflect your understanding (“I know that you have many vaccine-related concerns.”) Then, identify missing or incorrect information, but don’t do it in a confrontational or scolding manner. Ask if you can address an issue directly and do so only if the patient agrees. (“May I tell you something about vaccination that I learned in a continuing education class recently?”) Invite patients to reconsider and summarize and reiterate next steps. (“You said that needle-induced pain is a concern, and we talked about three things that might help—breathing exercises and topical spray that numbs the area. Which of those approaches might you be able to try before giving up?”) Some parents refuse the HPV vaccine for their teens, and after discussion, you might say, “You said that vaccination for HPV would encourage your son to engage in unprotected sexual activity. We agreed that it would be even MORE dangerous if he has unprotected sex without being vaccinated. And we agreed that kids often make risky decisions, and we identified two possible courses of action. You might talk to him about the risks of unprotected sex and ask him what he has heard about the HPV vaccination in health class. Which of those approaches might you be able to try before giving up?”

Providers must maintain a welcoming and patient-centered environment by remaining attentive and empathetic to the patient’s concerns and questions. To ensure this dynamic and encourage a cooperative and honest patient-provider relationship, providers should ask for the patient’s permission before dispensing advice or information if possible. This helps providers to direct their input toward specific issues and thus prevent overwhelming the patient with unsolicited information.
Confront misinformation: Debiasing

If a patient expresses concerns that refer to vaccine misinformation, debiasing may help correct the misconception.33 (Note that these techniques are from social sciences journals and not terms with which most pharmacists or technicians are familiar—they are included here because they help address misinformation.) It is important for providers to first gain an accurate understanding of the patient’s beliefs, as providers can only use debiasing techniques if the patient is receptive to the proposed correction.33 Table 5 defines the potential impact of misinformation and associated intervention strategies. Debiasing requires all who provide counseling to vaccine-hesitant patients to be on the same page. Many healthcare systems handle this in part by refusing to hire anyone who will not promote vaccinations—all employees need to be vaccinated and deliver the facts about vaccination unabashedly. Clinicians should note that if an individual’s beliefs are strongly influenced by misinformation, clinicians should avoid debiasing strategies.33

### Table 5. Misinformation Debiasing Strategies

<table>
<thead>
<tr>
<th>Effect(S) of misinformation</th>
<th>Debiasing techniques</th>
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<tr>
<td>Misinformation, regardless of a correction, has continued influence over beliefs and behaviors.</td>
<td>Clinicians create an information gap when they simply correct a misconception; provide an alternative and evidence-based explanation to fill such gap(s).</td>
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<tr>
<td>Familiarity backfire occurs when beliefs about misinformation are strengthened through its repetition.</td>
<td>Start with the facts and introduce the misinformation only after you cover the facts.</td>
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<td>• In other words, in some cases, healthcare providers show vaccine-hesitant patients information that proves that a belief is false. After some time passes, these patients may be likely to remember the myth itself, rather than evidence that disproves it. These patients may be more likely to believe the myth—meaning the provider’s efforts backfired.</td>
<td>Before mentioning any misinformation, explicitly state that the information that you are about to discuss is false. It can help to explain why it can is misleading, and why people may believe it although it is false. Correct all misinformation immediately after you mention it. Include a reasonable explanation to replace the original myth. Avoid repeating misinformation and then saying that it is not true. Focus on the correct explanation instead. If you must repeat misinformation, emphasize that it is NOT true.</td>
</tr>
<tr>
<td>Overkill backfire refers to when it is easier for patients to understand and accept misinformation, which makes the truth seem comparatively unrealistic and complicated.</td>
<td>Keep corrections straightforward and short—less is more. A hesitant patient believes that childhood vaccination is responsible for type 1 diabetes, though this claim has not been proven. The provider decides to explain that the cause of type 1 diabetes is not completely understood and launches into an elaborate description of the disease’s pathology. While the provider’s response is intended to correct the misinformation, it may instead overcomplicate the issue from the patient’s perspective. If the patient is unable to make sense of the provider’s statement, the patient may dismiss the correction as science fiction and continue to believe the misinformation—to accept vaccines as the cause of type 1 diabetes is less of an intuitive leap for the patient than to reconcile with a convoluted correction.</td>
</tr>
<tr>
<td>Worldview backfire occurs when a personal belief is threatened by the truth and misinformation is reinforced.</td>
<td>Affirm worldview with corrections that support the individual’s values and concentrate on positive facts, such as benefits and opportunities.</td>
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Persistent refusal: Standby Strategies. Patients and parents may be unresponsive to vaccine-promoting interventions. If an individual continues to refuse vaccination, it is most important to acknowledge and honor the right to decline.¹⁶,²³ Immunizers shouldn’t discount these interactions or label them as failures, but instead consider them an opportunity to try again later. Providers should encourage future contact if the patient should have more questions or if they change their mind regarding vaccination.²³,³⁶

Healthcare providers must maintain respect and provide direct clinical recommendations for vaccinations.²³ Finally, healthcare providers should inform patients of their responsibilities and vaccine refusal’s potential consequences (see Resources for Pharmacy Staff below to find the CDC document, “If You Choose Not to Vaccinate Your Child, Understand the Risks and Responsibilities” and links to vaccine refusal documentation forms).³⁶

Conclusion
Vaccine hesitancy is a complicated and often an emotional issue. Pharmacists and pharmacy staff can identify the obstacles and barriers to vaccination and its acceptance through education and support, while also offering reliable access to vaccines.⁴ Pharmacies eliminate barriers that prevent access to vaccine delivery services and increase vaccination rates through pharmacist-driven interventions.⁴,³⁷,³⁸ This presence and resultant impact on public health testifies to the importance of pharmacists as trained and certified immunizers.⁴ To maintain the success of pharmacy-based vaccination services, pharmacists and pharmacy staff should have a comprehensive and functional understanding of vaccine hesitancy and the skills to confront it appropriately. The Infographic on the next page summarizes take-away points so you can maximize your effectiveness.

<table>
<thead>
<tr>
<th>Resources for the Pharmacy Staff</th>
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<tbody>
<tr>
<td><strong>Centers for Disease Control and Prevention</strong></td>
</tr>
<tr>
<td>Vaccine Excipient Summary: Excipients Included in U.S. Vaccines, by Vaccine</td>
</tr>
<tr>
<td><strong>U.S. Food and Drug Administration</strong></td>
</tr>
<tr>
<td>Vaccines licensed for use in the US” provides an up-to-date list of excipients used in currently available vaccines.</td>
</tr>
<tr>
<td><a href="www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states">www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states</a></td>
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<td><strong>Centers for Disease Control and Prevention</strong></td>
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<tr>
<td><strong>Centers for Disease Control and Prevention</strong></td>
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<tr>
<td>Current immunization schedules</td>
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<tr>
<td><a href="www.cdc.gov/vaccines/schedules/index.html">www.cdc.gov/vaccines/schedules/index.html</a></td>
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</table>
THE ROAD TO VACCINE ACCEPTANCE

- Number of vaccines given to young children
- Side effects and adverse health events (including misunderstandings including association with autism)
- Vaccine safety (harmful ingredients, insufficient safety testing)
- Vaccine efficacy
- Mandatory childhood vaccines
- Pain at vaccination

Remember that questions and concerns are an opportunity for discussion. Don’t interpret them as defiance or the intent to delay or refuse a vaccine.

Be aware of common concerns and misperceptions

- Accessibility to vaccination services
- Vaccination costs
- Distrust of vaccine
- Distrust of provider administering vaccination
- Perceived need of vaccine
- Gaps in knowledge – such as how vaccines work or about vaccine-preventable diseases
- Misinformation

Effective risk communication must be individualized to the patient's/parents' concerns. Always disclose the potential risks of diseases and benefits of vaccines in an honest, evidence-based, and intelligible manner.

Address pain

- Communication strategies
- Activation strategies

While healthcare providers use various strategies to promote vaccine uptake, an intervention's success is not contingent on whether a patient chooses to vaccinate or not. Instead, immunizers should measure an intervention by its ability to meet the patient's expectations and by the provider's patience and empathy. Keep trying.

Needle-related pain is a common concern for people of all ages. Though recommendations to reducing pain varies between age groups, pain in adults can be minimized with the following recommendations:

- During vaccine administration have the patient sit upright, implement breathing techniques (such as asking the patient to hold their breath)
- Avoid reassurances that convey that the experience will not be painful
- If it is safe and appropriate, suggest a topical anesthetic, such as liposomal lidocaine, amethocaine, or lidocaine-prilocaine. Apply these topicals 20 to 60 minutes before injection or right before vaccination.

Healthcare workers will primarily encounter vaccine-accepting patients. Acknowledge this population's behaviors. To further promote vaccination and recognize the patient's vaccination decisions, remember to commend vaccine acceptors' actions.
REFERENCES


