

Childhood Vaccinations

Top 14 questions answered with the nuance you may be looking for

Are childhood vaccines safer than the diseases themselves?

1

Yes, the **benefits continue to outweigh the risks** for routine vaccine-preventable diseases. For example, the risks of side effects from a measles-mumps-rubella (MMR) vaccination are very small, especially compared to the effects of a measles infection, as shown below.

Complications from 10,000 children getting measles infections:

- **2,000** hospitalizations
 - **10** cases of brain swelling
 - **10-30** child deaths
- **1,000** ear infections with potential permanent hearing loss
- **500** cases of pneumonia

Complications from 10,000 children getting the MMR vaccine:

- **3** fever-related seizures
- **0-1** cases of abnormal blood clotting
- **0.035** allergic reactions

Do children *really* need vaccinations, even if the disease is not still around?

2

Although many diseases, like measles, are no longer widespread in most U.S. communities, children still need vaccines to maintain their immunity. These diseases are still alive and well in other parts of the world. In the U.S., we have cases of rubella, for example, but only from international travelers.

Think of population immunity like a water dam built to prevent flooding. Once it's built, we won't have flooding anymore. But if the next generation comes along and says, "Hey, there's no flooding anymore—do we really need this dam?" and decides to get rid of it, the flooding would return quickly. Your probability of encountering measles or polio is low because so many people around you are vaccinated.

Protecting against flooding is most important for people who can't save themselves—babies, the elderly, and the sick. When adults and kids are vaccinated against common diseases, it helps protect people whose immune system isn't fully functioning or who haven't been able to be vaccinated yet.



How do we know vaccines are safe? Are they ever taken off of the market?

Rigorous, ongoing scrutiny of vaccine safety continues long after clinical trials conclude. This is important because even among the largest trials involving tens of thousands of volunteers, scientists may not detect a very rare safety concern that may emerge only after millions of doses.

The U.S. has a few monitoring systems to watch for the ongoing safety of vaccines:

- Anyone can submit a report to the **Vaccine Adverse Event Reporting System (VAERS)**, which requires careful follow-up and additional study to figure out what if any, role vaccines played in the reported medical conditions. VAERS reports are frequently misrepresented as proof of vaccine safety issues, but they are unconfirmed reports that provide potential directions. If enough reports are submitted, the U.S. does a far more rigorous follow-up study using VSD (see next bullet).
- **Vaccine Safety Datalink (VSD)** is a national network of medical records from healthcare organizations and insurers that allows us to examine whether there is a link between vaccinations and safety signals.
- **V-safe** is a new program that started during the COVID-19 pandemic in which people text CDC more actively after a vaccine about how they feel and follow up weeks and months afterward. This allows CDC to watch for safety signals proactively.

Other monitoring systems exist, including **FDA BEST**. We also don't rely solely on U.S. data. The same vaccines are used worldwide, and other countries can flag potential safety issues that we can interrogate.

Example of catching a safety signal quickly: In 1999, an approved vaccine against rotavirus, a common cause of severe gastrointestinal illness in children, was found to be associated with a potentially fatal intestinal blockage. Within months of the vaccine's approval in 1998, reports to VAERS suggested a possible association. The vaccine was halted while the issue was investigated, and following confirmation of a link, the CDC withdrew its recommendation that infants receive the vaccine. It was never used again.

Example of how sensitive our systems are: During the COVID-19 pandemic, these systems also contributed to rapidly identifying blood clots associated with the Johnson & Johnson COVID-19 vaccine, ultimately leading to recommendations against its use and eventual withdrawal from the U.S. market. This safety signal was detected after 6 cases (out of 6.8 million doses given).

Children receive so many more vaccines these days. Why? Is this okay?

4



This is true; Children born before the 1990s received far fewer vaccines than today's kids. However, **over the years, we have gotten better at developing vaccines in two ways.**

We target immune protection far more efficiently. Over the years, scientists got smarter at targeting viruses and bacteria—exposing children to fewer and fewer parts of the microbe (antigens) to stimulate the immune system.

Mid 1980's

Children under 2 received vaccines against **7 diseases.**

These vaccine formulas were safe and effective but complex, targeting more than **3,000 antigens.**

TODAY

Children under 2 receive vaccines against **15 diseases.**

These vaccine formulas target **180 antigens** and therefore ask 'less' of the immune system.

This is one way scientists and physicians know that the number of childhood vaccines cannot 'overwhelm' immune systems. Also, this number of antigens is far less than the germs our immune systems marshal a response to every day, almost always without us even knowing it. That's the immune system doing its job!

Advances in medical research have also led to many new vaccines that have further reduced childhood illnesses. For example, a safe and effective Haemophilus influenza type b ("HiB") vaccine was developed in the late 1980s. It has dramatically lowered rates of childhood meningitis (brain infections), pneumonia, and epiglottitis (infection of the epiglottis that prevents kids from breathing). The same can be said for vaccines against varicella, pneumonia, rotavirus, and others capable of causing severe illness and deaths of children.

Do we need to be reinfected to keep the immune system active? What about boosters?

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Contrary to rumors, we don't need to get reinfected over and over for our immune systems to be ready to respond. Everything in our life—our house, pets, our own body—is filled with microbes. Although most of these microbes aren't harmful, they keep our immune systems active and ready to defend against dangerous foreign invaders.

That said, to stay protected from certain diseases (like pertussis, aka “whooping cough”, or tetanus, aka “lockjaw”), you may need a vaccine booster. This is for a few reasons:

1. **Catching these diseases usually acts as a natural booster but would also put you and your family at risk.**
2. **Even if you got infected, boosters can help.** For example, a tetanus infection will not give you any immunity—the dose of toxin is too low to activate an antibody response; you have no protection from getting tetanus a second time if you are infected. A vaccine can help.
3. **Some diseases need annual booster shots because viruses change quickly.** For example, the flu virus changes from year to year, so each year's shot targets a different version of the virus. Scientists are hard at work figuring out the details of how to make current vaccines work better, but until those mysteries are unraveled, boosters it is.



Why can't pharmaceutical companies be sued for vaccine injury?

This varies by country. In the U.S., you cannot immediately sue the pharmaceutical company. **You have to go through the NCVIA first.**

The National Childhood Vaccine Injury Act (NCVIA) was enacted in 1986, after parent activists who believed their children were harmed by vaccines engaged in a series of lawsuits against pharmaceutical companies seeking compensation for damages. While there weren't any major wins on the part of these groups, the cost of these trials eventually reached a point where it was more than what vaccine manufacturers were earning from their products. Consequently, many vaccine manufacturers stopped making vaccines; it didn't make financial sense for them to do so—and the handful that remained were contemplating doing the same.

At that point, Congress stepped in with the National Childhood Vaccine Injury Act (NCVIA), which created the **National Vaccine Injury Compensation Program**. This act granted pharmaceutical companies certain legal protections and established a no-fault compensation system operated by the Department of Health and Human Services with a reduced burden of proof for petitioners who felt they had been harmed by vaccines. The system is paid for by an excise tax on each vaccine dose. The program also established a table of known vaccine-related adverse events—all of them quite rare—for which compensation is provided expeditiously.

This act also established a number of important oversights, including the previously mentioned Vaccine Adverse Effects Reporting System and a non-governmental committee to determine vaccine safety.

This system is imperfect, but it ensures that people harmed by vaccines have a path to compensation and that we still have access to lifesaving vaccines.

Why does the U.S. have different recommendations than other countries?

7



Country-to-country differences tend to be pretty minor overall. When there are differences, they reflect (a) differences in manufacturing capabilities, (b) differences in the patterns of disease, and (c) differences in the payment and distribution systems. Here are a few examples:

- **Behavioral:** Universal vaccination recommendations work better than targeted vaccinations because of convenience and education. The U.S. used to have targeted hepatitis B vaccine recommendations, but uptake was poor. After a universal recommendation, there was a big decline in disease, and many lives (and livers) were saved. The same happened with the flu vaccine; universal recommendations increased uptake among high-risk groups.
- **Financial:** Most countries' governments pay for vaccines through national healthcare systems with fixed budgets, so the cost-benefit analysis is a big consideration when making policy decisions—for some countries, it would be too expensive for the government to vaccinate everyone, so they try to find where the money will have the biggest impact. Sometimes, this can have unexpected results. For example, modeling data suggests that when resources are constrained, prioritizing school-aged children for flu vaccination has the greatest benefit in minimizing flu deaths, even though the majority of deaths occur in the elderly (because this would have the biggest effect on transmission). The U.S. is fortunate in that, rather than having to pick and choose from a place of limited resources, it can offer the vaccine to everyone.
- **Safety net:** The U.S. has much less wiggle room because of worse healthcare access, social support, healthcare capacity, and health. Casting a larger net through universal vaccine recommendations is more critical than in other countries.
- **Availability and accessibility:** Some countries use the oral polio vaccine instead of the inactivated polio vaccine because the oral kind is easier to administer (you don't need people trained in giving injections), cheaper, and stops transmission better. The oral polio vaccine has a different number and timing of doses than the inactivated polio vaccine. However, because the oral vaccine contains actual poliovirus and can revert to paralytic polio if it circulates in the environment, use of the oral vaccine is considered only in places where there is a lot of polio (although even this is being reconsidered).
- **Epidemiological:** Though the diseases themselves are the same, their behavior within a particular country might differ. For example, meningitis caused by meningococcal B tends to occur in adolescents and young adults (and in particular in congregant living settings like college dorms), but throughout Europe, invasive meningococcal disease due to these bacteria is more common among infants. For this reason, many European countries have a recommendation for a meningococcal B vaccination in infancy, whereas the U.S. does not.

Do doctors get paid an incentive for vaccinations?

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Physicians do not get paid by pharmaceutical companies for vaccinations. Vaccination is often billed to insurance companies. But these administration fees are rarely worth it. Surveys of pediatricians report that **most break even or even lose money from vaccination**—because the costs of vaccine storage, handling, and the doses themselves are so high. Some insurers have regional programs offering small financial incentives to pediatric practices for maintaining a certain level of vaccine uptake in their practices, but these programs are not universal, and the incentives are indeed small. The cost of vaccinating kids has gotten so high that some pediatric practices have stopped offering recommended vaccines.

How do we know that the rise in autism is not linked to vaccines?

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First, it's important to note that a lot of research is still needed to evaluate the cause of autism. The data we do have suggests that it is primarily the result of genetics.

What is clear is that vaccines, particularly MMR vaccines, do not cause autism. We know this because of a few reasons:

1. This rumor became prominent in the mid-1990s after a fraudulent scientific study was published by a scientist with conflicts of interest (trying to make his own measles vaccine) who eventually lost his medical license.
2. Huge, robust studies (spanning millions of children across many countries) have not found a link between autism and vaccines.
3. Scientists have learned that the hallmark of autism is dysregulation of brain development starting in the prenatal period before childhood vaccines are introduced.
4. Autism rates have increased over time. This increase is partially explained by factors like changes in diagnosis. Scientists continue to explore the data behind this trend.



Why do babies need the hepatitis B vaccine if they aren't high-risk?

The highest risk factor for hepatitis B (or HBV) is a history of sexually transmitted infections or multiple sex partners. So, if you've only had one partner for a decade, is this even applicable to your baby?

Yes, because the hepatitis B virus is a tricky booger:

1. **The majority of people with HBV globally are unaware they have it.** Many who do have it don't know how they contracted it. If we only give it to people who believe they are high-risk, we will miss many cases. Remember: it can take decades from the time you contract hepatitis B virus before symptoms become apparent.
2. **Hepatitis B virus requires only a very tiny dose to cause infections,** which means that even though it is bloodborne and sexually transmitted, it can be spread casually, like through sharing a toothbrush or even through being bitten by an infected person (such as at daycare).
3. **It's very stable in the environment,** capable of remaining infectious for weeks and even months on surfaces.
4. **The outcomes can be severe.** Mother-to-baby transmission at birth is the most common cause of chronic HBV infection, which can lead to liver cancer, liver failure, and death. If babies contract hepatitis B disease near birth, 95% develop the chronic form.

The HBV vaccine induces protective immune responses in nearly everyone (80-100%). The vaccine risks are **extremely low**—the only safety signal found is rare allergic reactions (one severe allergic reaction for every 2-3 million doses).

Are there any long-term studies on whether the HPV vaccine impacts fertility?

11

Some of these concerns stemmed from a case series that was published in 2012, describing six girls who developed primary ovarian insufficiency (POI) from 8 months to 2 years after they received the first human papilloma virus (HPV) vaccine dose. This stirred public concern that the HPV vaccine could cause infertility.

However, case series often generate more questions than answers because they can't assess causality (correlation doesn't equal causation). Fortunately, **no rigorous lab or epidemiological follow-up studies have found a link:**

- No effect of HPV vaccination on fertility has been found in 3 studies in rodents.
- A strong study in North America followed women planning on getting pregnant. Some of the women (and their partners) had their HPV vaccines, some of them didn't. The scientists found **no difference in infertility**. In fact, in some groups, vaccinated women had higher fertility.
- Another large study found that 120 of 199,078 female patients at hospitals had POI. There was **no difference** between those with the HPV vaccine and those without.

It is also critical to note that **being infected by the HPV virus can harm fertility** because of the procedures involved in treating HPV-related cancers. Some evidence has also suggested that HPV itself may reduce male fertility.

Why do some children still get sick with a disease after being vaccinated?

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Vaccines significantly reduce the likelihood of getting sick from infectious diseases and, in many cases also greatly reduce transmission. For example, since the chickenpox vaccination program began in the United States, there has been an over **97% decrease in chickenpox cases**. For whooping cough, nearly all children (98 in 100) were protected within a year of their last shot and about 7 in 10 children were protected five years after getting the last DTaP shot. Most vaccines, however, do not completely eliminate the risk of becoming infected with the disease.

Upon infection, vaccines can also **lessen the severity of several diseases**. Most recently, this has been demonstrated in a number of COVID-19 vaccine studies, which have found that vaccinated individuals, compared with unvaccinated individuals, are less likely to become severely ill.

For many vaccine-preventable diseases, immunity from an infection can be imperfect- it may still make sense to get vaccinated even after recovering to help prevent serious illness from reinfection and to reduce spread.

Do kids really get 72 doses of vaccines?

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This number comes up a lot, and it's understandable to have questions about it. By the time a child turns 18, they're recommended to receive vaccines that protect against 17 potentially serious diseases, including:

- Measles, mumps, rubella (MMR)
- Polio
- Tetanus, diphtheria, pertussis (whooping cough)
- Hepatitis A and B
- Varicella (chickenpox)
- Pneumococcal disease
- Meningococcal disease
- Rotavirus
- Hib (Haemophilus influenzae type b)
- HPV (human papillomavirus)
- COVID-19
- Influenza (flu)

Because some of these vaccines require more than one dose, the total over time adds up to:

- 28 doses by two years old (which includes yearly flu shots)
- 35 doses by five years old (which includes yearly flu shots)
- 54 doses by age 18, with a third coming from yearly flu vaccines.

Some counts—like the commonly cited 72—include every yearly flu and COVID shot through age 18, and sometimes count combination vaccines (like MMR, which protects against three diseases) as three separate doses. Others may even include vaccines given to pregnant mothers, which are intended to protect newborns in the first weeks of life.

The exact number of doses a child receives can vary based on timing, catch-up schedules, health conditions, and which vaccine formulations are available.

It helps to remember that little kids are exposed to a lot of illness: on average, they have 6–8 viral infections per year, and often more if they're in daycare. Vaccines can't prevent every illness, but they do offer protection from some of the most serious ones—helping reduce the risk of complications, hospitalizations, and long-term effects.

What can I do to protect myself and others if vaccines are not an option for me?

We understand that vaccines may not be accessible to everyone—and we still want you to stay safe. While vaccines are among the most effective tools we have to prevent serious illness, there are additional layers of protection that can help reduce your risk and protect those around you:

- **Wash your hands with soap**, especially before eating or touching your face, and after being in public spaces.
- **Improve air flow** indoors by opening windows or using air purifiers
- **Wear a well-fitting mask**, especially in high-risk settings like crowded indoor spaces or during outbreaks

If you get symptoms, **call your physician**. For some infections, antibiotics or antivirals may be available. Also, be sure to stay home when you're sick to avoid spreading the infection to others.

That said, some of these measures may not be enough on their own—many viruses and bacteria, especially those that affect young children, are incredibly contagious and can spread quickly even when people are doing their best to stay cautious.

While not as effective as vaccines, there are some things that you can do to support your immune system once you're sick:

- **Sleep is critical**, as this is when the immune system executes most of its repair processes.
- **Hydration**. Proper fluid balance ensures your body can transport nutrients and immune cells and remove pathogens and waste products.
- **Staying healthy** – including a balanced, nutrient-dense diet and exercise – benefits your health in many ways, including reducing risk of comorbidities that can put you at higher risk from infections.

It's important to know that diet and exercise alone do not guarantee protection against infections. Many other immune health remedies you may see on social media are either very weak (they may help a little bit, but likely not much) or have no evidence of helping fight off infections when studied across large groups of people. See [this guide](#) for more information.

References

1

1. **Bester, Johan Christiaan (2016). Measles and Measles Vaccination. JAMA Pediatrics, doi:10.1001/jamapediatrics.2016.1787.** This work directly compares the risks of measles infection to measles vaccination based on the strongest available evidence for the outcomes of each as well as their incidence, finding that the chance of a serious adverse event from measles vaccination (via MMR vaccine) is drastically lower than the risks posed by measles infection itself (in many cases by over 1000-fold).
2. **Institute of Medicine. Adverse effects of vaccines: evidence and causality. Washington, DC: National Academies Press, 2012, doi: 10.17226/13164.** This monograph from the National Academies examines the vaccines routinely administered on the childhood vaccination schedule and all evidence available to date on possible adverse events that may occur with vaccination to determine whether or not there is evidence for a given adverse event being caused by the vaccines. In the vast majority of cases, the adverse events in question are either not linked or the adverse events themselves are too rare to determine conclusively that a link is present, both of which support the exceptional safety record of vaccines.
3. **Hotez, P.J. and Marsh, B. (2020) You are unvaccinated and got sick. these are your odds., The New York Times. Available at: <https://www.nytimes.com/2020/01/09/opinion/vaccine-hesitancy.html> .** A great example of data visualization covering several vaccines and infectious diseases, which also explains the sources of these data, again demonstrating that the risks of the infectious diseases are much greater.
4. **Talbird SE, Carrico J, La EM, et al. Impact of Routine Childhood Immunization in Reducing Vaccine-Preventable Diseases in the United States. Pediatrics 2022; 150. DOI:<https://doi.org/10.1542/peds.2021-056013>.** This reference is focused on how the routine childhood vaccination schedule has helped to control the threat of vaccine-preventable diseases. A discussion about whether or not to vaccinate must not neglect the benefits of vaccination, in addition to the risks.

2

1. **Paul Fine, Ken Eames, David L. Heymann, "Herd Immunity": A Rough Guide, Clinical Infectious Diseases, Volume 52, Issue 7, 1 April 2011, 911–916 1.** This review summarizes the concept of herd immunity and explains its mathematical basis. In brief, a given infectious disease has a threshold for herd immunity that results in transmission stopping for that disease which increases with the contagiousness of the disease, and should immunity dip below that threshold (such as through lower vaccination rates), the growth of the infectious disease within the population becomes exponential (each case will on average produce more than 1 additional case).
2. **A. McDermott, Herd immunity is an important—and often misunderstood—public health phenomenon, Proc. Natl. Acad. Sci. U.S.A. 118 (21) e2107692118, <https://doi.org/10.1073/pnas.2107692118> (2021).** This article discusses provides clarification on the meaning of herd immunity and provides a historical overview of how the concept came to be and evolved over the years, focusing on COVID-19 as an important case for illustrating the complexity of herd immunity and why the messaging around herd immunity to COVID-19 has changed with time. Key points include that the determination of whether or not herd immunity is possible to achieve requires knowledge of what the population's current state of immunity is, and, critically, requires knowledge of how well the vaccine for the disease in question prevents transmission, which is not necessarily the same as how well it prevents disease and is much harder to study.

3. **V. A. A. Jansen et al. Measles Outbreaks in a Population with Declining Vaccine Uptake. Science 301,804–804(2003).DOI:10.1126/science.1086726.** Using data from the United Kingdom, the effect of measles vaccine uptake is compared with the effective reproductive number of measles, demonstrating that there is an extremely robust relationship between declines in measles vaccine uptake and outbreaks of measles, with the note that continued poor uptake of MMR would result in the re-establishment of measles as an endemic disease within the United Kingdom.
4. **Crowcroft NS, Britto J. Whooping cough--a continuing problem. BMJ. 2002 Jun 29;324(7353):1537-8. doi: 10.1136/bmj.324.7353.1537. PMID: 12089076; PMCID: PMC1123488.** Pertussis (whooping cough) has experienced resurgences globally despite, in many cases, the use of effective vaccines. Options for controlling pertussis and their limitations are discussed.
5. **Craig AT, Heywood AE, Worth H. Measles epidemic in Samoa and other Pacific islands. The Lancet Infectious Diseases 2020; 20: 273–5.** This provides an account of the 2019 Samoan measles outbreak and in particular why the outcome was so different from other Pacific islands, during which Samoa experienced 83 deaths due to measles, with 72 of those deaths in children under 5. Despite inter-Pacific Island travel being common, other Pacific islands did not experience measles outbreaks and measles has been eliminated from many of these due to high vaccination uptake.
6. **Rane MS, Wakefield J, Rohani P, M. Elizabeth Halloran. Association between pertussis vaccination coverage and other sociodemographic factors and pertussis incidence using surveillance data. Epidemics 2023; 44: 100689–9.** This paper emphasizes the fact that herd immunity is a local phenomenon meaning that in understanding risks posed by an infectious disease, it is much more about what vaccination rates are like within your community than what they may be at the national level, with pertussis being a critical example. As pertussis vaccination coverage dropped, pertussis became more likely to become endemic.
7. **Phadke VK, Bednarczyk RA, Salmon DA, Omer SB. Association Between Vaccine Refusal and Vaccine-Preventable Diseases in the United States. JAMA 2016; 315: 1149– 58.** This study compares the risks of contracting measles and pertussis based on vaccination status, finding that those with vaccine exemptions have a 20-fold higher risk of developing pertussis and are 35 times more likely to develop measles.
8. **Maldonado YA, O’Leary S, Hotez P. Vaccine Exemptions and the Risk of Continued Disease Outbreaks. Pediatrics 2021; 149. DOI:https://doi.org/10.1542/peds.2021- 054369.** This article summarizes the data on how vaccine refusal contributes to outbreaks with reference to COVID-19 and a recent study examining how vaccine exemptions changed following California’s ban on non-medical exemptions to measles vaccination and the effect on the potential for measles outbreaks.

3

1. **Jacqueline E. Tate, Catherine Yen, Claudia A. Steiner, Margaret M. Cortese, Umesh D. Parashar; Intussusception Rates Before and After the Introduction of Rotavirus Vaccine. Pediatrics September 2016; 138 (3): e20161082. 10.1542/peds.2016-1082**

The rotavirus vaccine is critical for preventing a severe form of gastroenteritis mainly affecting infants, but the first-generation vaccine rarely could cause a condition known as intussusception where the bowel telescopes over itself and cuts off blood flow to that region, which was too rare to be detected in pre-licensure studies. This adverse event was detected via VAERS, the vaccine was removed, and next-generation vaccines have now been introduced which are associated with a very small increased risk of intussusception hospitalization between 8 and 11 weeks, but at a rate far lower than hospitalizations by rotavirus (which the vaccine prevents).

2. **CDC. How Vaccine Safety Monitoring Works. Vaccine Safety Systems. 2024; Available from: <https://www.cdc.gov/vaccine-safety-systems/about/monitoring.html>**

This article presents an overview of the process by which the US tracks vaccine safety with links to specific safety monitoring systems provided within.

3. **Alimchandani M. Overview of Postmarketing Safety Monitoring. ACCV. Available from: <https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/vaccines/accv03082024-fda-update.pdf>**

This is a presentation delivered to the Advisory Committee on Childhood Vaccines describing how vaccine safety is monitored once a vaccine has been licensed for use in the US with a detailed discussion of the data sources for vaccine safety monitoring.

4. FDA and CDC Lift Recommended Pause on Johnson & Johnson (Janssen) COVID-19 Vaccine Use Following Thorough Safety Review. FDA. 2021; Available from: <https://www.fda.gov/news-events/press-announcements/fda-and-cdc-liftrecommended-pause-johnson-johnson-janssen-covid-19-vaccine-use-following-thorough>

Describes the process by which a serious adverse event (thrombosis with thrombocytopenia syndrome, a blood clotting disorder) was detected following use of the Janssen vaccine through just 6 cases in 6.8 million doses, demonstrating the extreme sensitivity of our current safety monitoring systems to detect serious adverse events and also explains that after a thorough risk-benefit evaluation, it was determined that the danger posed by COVID-19 meant that the risks of not vaccinating with the Janssen vaccine were much greater than vaccinating, which means the vaccine's use should continue.

5. CDC. About CDC's Vaccine Safety Monitoring Program. Vaccine Safety Systems. 2024; Available from: <https://www.cdc.gov/vaccine-safety-systems/about/cdcmonitoring-program.html>

Provides an overview of how CDC monitors vaccine safety and the different purposes of the safety monitoring systems and the strategies used by CDC to continuously evaluate the safety of vaccines well after they are released to the public and to make adjustments to recommendations accordingly.

6. National Immunization Technical Advisory Groups (NITAGs). www.who.int. Available from: [https://www.who.int/europe/groups/national-immunization-technical-advisory-groups-\(nitags\)](https://www.who.int/europe/groups/national-immunization-technical-advisory-groups-(nitags))

The process of vaccine safety monitoring occurs globally, and in almost every country there are national immunization technical advisory groups (NITAGs) comprising multidisciplinary experts tasked with making recommendations about the use of vaccines. NITAGs may collaborate with the WHO to help align recommendations as needed with WHO recommendations.

7. Rudolph A, Mitchell J, Barrett J, et al. Global safety monitoring of COVID-19 vaccines: how pharmacovigilance rose to the challenge. Therapeutic Advances in Drug Safety 2022;13:204209862211189.

Describes the advances in safety monitoring that rapidly came about from the COVID-19 pandemic and release of vaccines including pre-emptive measures such as creating a list and diagnostic criteria for adverse events of special interest (AESIs) to monitor before vaccine release, and underscores the need for continued transparency of safety monitoring systems even after the end of the pandemic.

4

1. Offit PA, Quarles J, Gerber MA, et al. Addressing Parents' Concerns: Do Multiple Vaccines Overwhelm or Weaken the Infant's Immune System? PEDIATRICS 2002; 109: 124–9.

Discusses the immunology of receiving multiple vaccines, demonstrating that in fact, despite more vaccines on the schedule over time (and therefore more diseases we can protect children from) the burden on the immune system is actually lessened because the number of antigens in the vaccines has declined.

2. CDC. Multiple Vaccines at Once. Vaccine Safety. 2024. <https://www.cdc.gov/vaccine-safety/about/multiples.html>.

Explains the reason that children get so many vaccines while so young; the major reason is that children are born without immunity to these diseases and so long as they aren't immune, they are at major risk for contracting these serious illnesses. Also summarizes the data demonstrating that multiple vaccines at the same time is safe and has been thoroughly tested, and CDC and FDA together are continuing to actively monitor the safety of vaccines well after they are released.

3. CDC. Your child needs vaccines as they grow! Vaccines & Immunizations. 2024. <https://www.cdc.gov/vaccines/imz-schedules/child-easyread.html>.

Describes the childhood immunization schedule to show the timeline of each vaccination, demonstrating how many diseases we can protect children against today that we could not in the past. Note that many of the vaccines exist as combination vaccines, which reduces the number of injections needed e.g., instead of separate vaccines for polio, Haemophilus influenzae type B, hepatitis B, diphtheria, tetanus, and pertussis, these can be given via a single injection of a single vaccine product.

4. CDC. Chapter 8: Haemophilus influenzae. Epidemiology and Prevention of Vaccine-Preventable Diseases. 2024; published online Sept 30. https://www.cdc.gov/pinkbook/hcp/table-of-contents/chapter-8-haemophilus-influenzae.html#cdc_report_pub_study_section_6-secular-trends-in-the-united-states (accessed Nov 22, 2024).

This details how the introduction of vaccines against Hib have resulted in major declines in the rates of epiglottitis and meningitis in children (this example is referenced in the answer to the question).

5

1. World Health Organization. Tetanus. Who.int. 2024; published online July 12. <https://www.who.int/news-room/fact-sheets/detail/tetanus>.

Describes immunity to tetanus, noting that recovery from tetanus does not result in protection from an additional episode of tetanus.

2. Berman M, Rupp R. You still need a flu shot even if you've already been ill. UTMB News. 2022; published online Dec 7. <https://www.utmb.edu/news/article/health-blog/2022/12/07/you-still-need-a-flu-shot-even-if-you-ve-already-been-ill>.

Describes the importance of getting a flu shot even if you have contracted the flu in the current season.

3. Seasonal influenza vaccination strategies. European Centre for Disease Prevention and Control. 2023; published online May 23. <https://www.ecdc.europa.eu/en/seasonal-influenza/prevention-and-control/vaccines/vaccination-strategies>.

Describes the different policies for influenza vaccination across the EU and the basic mechanisms of strain updates to flu vaccines.

6

Vaccine Injury Compensation Programs. History of Vaccines. <https://historyofvaccines.org/vaccines-101/ethical-issues-and-vaccines/vaccine-injury-compensation-programs>.

Explains how vaccine injury compensation programs in the US arose and why they are necessary.

About the National Vaccine Injury Compensation Program | HRSA. [www.hrsa.gov](https://www.hrsa.gov/vaccine-compensation/about).

<https://www.hrsa.gov/vaccine-compensation/about>.

Explains how the current vaccine injury compensation program in the US works, with discussion of objectives, funding, and administration.

Blake V. The National Childhood Vaccine Injury Act and the Supreme Court's Interpretation. AMA Journal of Ethics 2012; 14: 31-4.

Describes the legal basis for the NVICP and the *Brusewitz v. Wyeth* case and Supreme court ruling which details limitations to program concerning what is compensable.

Plan I of M (US) C on R of P in the NV. 1986 National Childhood Vaccine Injury Act (Public Law 99-660). National Academies Press (US), 2010 <https://www.ncbi.nlm.nih.gov/books/NBK220067/>.

The actual text of the 1986 National Childhood Vaccine Injury Act.

Kesselheim A. Safety, Supply, and Suits – Litigation and the Vaccine Industry. New England Journal of Medicine 2011; 364: 1485-7.

Explains strict liability, the meaning of the term "unavoidably unsafe" and the rationale for the Supreme Court ruling of *Brusewitz vs. Wyeth*.

Global Vaccination Schedules. vaccineknowledge.ox.ac.uk. 2022; published online March 9.

<https://vaccineknowledge.ox.ac.uk/vaccination-schedules-other-countries#Why-are-different-vaccination-schedules-used-in-different-countries>.

Explains that differences in how vaccines are recommended across countries reflect differences in the epidemiology of the disease, the way that countries make decisions, the cost of administering the vaccines and the capacity of the health system to add new vaccines.

Guillaume D, Meyer D, Waheed D-N, et al. Factors influencing the prioritization of vaccines by policymakers in low and middle income countries: A scoping review. *Health Policy and Planning* 2022; published online Oct 31.

DOI:<https://doi.org/10.1093/heapol/czac092>.

Discusses the complexities of making vaccine policy decisions in lower- and middle-income countries (LMICs), noting in particular that sociocultural considerations and communication efforts may play a more major role in the decision-making process in LMICs.

Kaur G. Routine Vaccination Coverage – Worldwide, 2022. *MMWR Morbidity and Mortality Weekly Report* 2023; 72. DOI:<https://doi.org/10.15585/mmwr.mm7243a1>.

Explains that the COVID-19 pandemic resulted in major disruptions to the delivery of routine immunizations globally and the coverage still has not recovered to pre-pandemic levels as of the end of 2022, meaning that strategies for catch-up and routine vaccination are needed.

Vaccine Scheduler | ECDC. vaccine-schedule.ecdc.europa.eu. <https://vaccine-schedule.ecdc.europa.eu/Scheduler/ByDisease?SelectedDiseaseId=48&SelectedCountryIdByDisease=-1>.

Demonstrates the vaccination schedule across European countries; for the most part, it is very similar among most of them but there are still differences.

Servadio JL, Choisy M, Thai PQ, Boni MF. Influenza vaccine allocation in tropical settings under constrained resources. *PNAS Nexus* 2024; 3. DOI:<https://doi.org/10.1093/pnasnexus/pgae379>.

An example of how vaccination policy can be counterintuitive through a modeling study on flu vaccination in a setting where a limited number of flu vaccines can be given: though the elderly are at highest risk of fatal influenza, there is a greater reduction in flu deaths by prioritizing schoolchildren for vaccination than for the elderly because schoolchildren play a much bigger role in the spread of influenza.

GPEI-Oral polio vaccine. [Polioeradication.org](https://polioeradication.org). 2024. <https://polioeradication.org/about-polio/the-vaccines/opv/>.

Describes the current use of the oral polio vaccine, including why it may be used in some parts of the world but not others.

Molodecky N, Su R, Er, et al. Evaluation of the 2016 switch from tOPV to bOPV 1 Switch Evaluation Team: Strategy Committee (SC) of the Global Polio Eradication Initiative (GPEI). 2024 <https://polioeradication.org/wp-content/uploads/2024/11/Switch-Report-20240930.pdf> (accessed Nov 22, 2024).

Report from the Global Polio Eradication Initiative describing the effects of switching to an oral polio vaccine (OPV) covering 2 types of polio instead of 3 (because type 1 polio has been eradicated) ultimately noting that the continued use of OPV is a problem because it introduces circulating vaccine-derived polioviruses (cVDPV), underscoring the need to eventually completely withdraw the vaccines despite the strong transmission-reducing effects.

Villena R, Safadi MAP, Valenzuela MT, Torres JP, Finn A, O’Ryan M. Global epidemiology of serogroup B meningococcal disease and opportunities for prevention with novel recombinant protein vaccines. *Human Vaccines & Immunotherapeutics* 2018; 14: 1042–57.

Describes how meningococcal capsule group B disease varies in its epidemiology globally, explaining why many European countries offer a dose of meningococcal B vaccine in infancy, whereas the US does not.

Outbreaks on U.S. College Campuses – National Meningitis Association. *National Meningitis Association*. <https://nmaus.org/nma-disease-prevention-information/serogroup-b-meningococcal-disease/outbreaks-on-u-s-college-campuses/>.

Describes US college campuses as high-risk settings for outbreaks of meningococcal B disease.

Allison MA, O'Leary ST, Lindley MC, et al. Financing of Vaccine Delivery in Primary Care Practices. Academic Pediatrics 2017; 17: 770–7.

Explains how vaccine delivery at the point-of-care is financed, noting that in many cases the reimbursement for vaccinations was less than the costs of purchasing and storing the vaccines, with some family medicine and pediatric practices ultimately opting to stop offering vaccines because of the financial burden, and many additional practices seriously considering doing so but ultimately deciding not to.

Coleman MS, Lindley MC, Ekong J, Rodewald L. Net Financial Gain or Loss From Vaccination in Pediatric Medical Practices. Pediatrics 2009; 124: S472–91.

Finds that a majority of surveyed practices broke even or lost money by offering vaccines, with greater losses resulting from higher Medicaid coverage due to poor reimbursement.

Iannelli V. About the Blue Cross Blue Shield Vaccine Bonus for Pediatricians. VAXOPEDIA. 2024; published online July 6. <https://vaxopedia.org/2024/07/06/about-the-blue-cross-blue-shield-vaccine-bonus-for-pediatricians/> (accessed Nov 22, 2024).

Explains the claims about the BCBS vaccine bonus for pediatricians and why it is not the perverse incentive for vaccination some have claimed it to be.

Sandin S, Lichtenstein P, Kuja-Halkola R, Hultman C, Larsson H, Reichenberg A. The Heritability of Autism Spectrum Disorder. JAMA 2017; 318: 1182.

Finds that the majority of autism can be explained by genetic factors, with 83% of the risk of developing autism explainable by genetic factors, consistent with other studies on the question, including twin studies.

Godlee F, Smith J, Marcovitch H. Wakefield's article linking MMR vaccine and autism was fraudulent. BMJ 2011; 342: c7452–2.

Describes the fraud in Andrew Wakefield's case series that suggested a link between MMR vaccination and autism that was subsequently uncovered by investigations by Brian Deer which included falsification of data and failure to disclose major conflicts of interest on the part of Wakefield.

Deer B. Andrew Wakefield's vaccine patent. Brian Deer. <https://briandeer.com/wakefield/vaccine-patent.htm>.

Shows Andrew Wakefield's filed vaccine patent for a single measles vaccine, explaining why he argued that the combination of measles, mumps, and rubella into a single shot was responsible for autism despite no evidence in his fraudulent study to support the claim.

Taylor LE, Swerdfeger AL, Eslick GD. Vaccines are not associated with autism: An evidence-based meta-analysis of case-control and cohort studies. Vaccine 2014; 32: 3623–9.

An analysis of multiple studies examining whether or not vaccines and autism are associated covering over 1 million children, ultimately finding that autism risk is not influenced by vaccination status.

Gerber Jeffrey S, Offit Paul A, Plotkin S. Vaccines and Autism: A Tale of Shifting Hypotheses. Clinical Infectious Diseases 2009; 48: 456–61.

Describes how claims around vaccines and autism have constantly been modified to blame a different factor within vaccines as data consistently fails to demonstrate a link between the vaccines and autism.

Hviid A, Hansen JV, Frisch M, Melbye M. Measles, mumps, rubella vaccination and autism. Annals of Internal Medicine 2019; 170: 513–20.

Massive cohort study of every child born in Denmark from 1999 through 31 December 2010 with follow-up from 1 year of age and through 31 August 2013 looking at whether there is an association between the MMR vaccine and autism, and even having a fully unvaccinated comparison group, demonstrating that no association exists.

Courchesne E, Gazestani VH, Lewis NE. Prenatal Origins of ASD: The When, What, and How of ASD Development. Trends in Neurosciences 2020; 43: 326–42.

Describes the current understanding of how autism may develop, emphasizing that the process is initiated well before children are even born, and therefore before any vaccines have been given.

King M, Bearman P. Diagnostic change and the increased prevalence of autism. International Journal of Epidemiology 2009; 38: 1224–34.

Describes how changes in diagnostic criteria and diagnostic substitution have driven an increase in autism diagnoses.

Brugha TS, McManus S, Bankart J, et al. Epidemiology of autism spectrum disorders in adults in the community in England. Archives of General Psychiatry 2011; 68: 459–65.

Demonstrates that the incidence of autism in adults using updated diagnostic criteria is not significantly different from the rates reported in children, suggesting that the rise in autism diagnoses in children does not reflect a true increase in the rate of autism itself.

10

What causes hepatitis B? Immunization Action Coalition <https://www.immunize.org/wp-content/uploads/catg.d/p4205.pdf>.

Explains how hepatitis B virus (HBV) can be spread and the outcomes of infection, noting that despite the common emphasis on injection drug use and sexual contact as means for transmission, multiple other ways to spread the virus exist.

Achievements in Public Health: Hepatitis B Vaccination --- United States, 1982--2002. Cdc.gov. 2002; published online June 28. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5125a3.htm?mobile=nocontent> (accessed Nov 22, 2024).

Demonstrates the changes in HBV incidence over time in the US, with a precipitous decline shortly following universal vaccination policy.

Gavi Staff. Why a birth dose of hepatitis B vaccine could be life-changing. Gavi.org. 2023.

<https://www.gavi.org/vaccineswork/why-birth-dose-hepatitis-b-vaccine-could-be-life-changing> (accessed Nov 22, 2024).

Explains that while many countries do not do a birth dose of HBV vaccine, this policy is very valuable in helping to address the burden of chronic HBV infections and their consequences, noting that if contracted in infancy, 95% will progress to chronic HBV.

Give Birth to the End of Hep B | Immunize.org. Immunize.org. 2024; published online Aug 23.

<https://www.immunize.org/vaccines/a-z/hepb/end-hepb/>.

Discusses the benefits of a birth dose of HBV vaccine specifically and provides rationale for the policy.

everychildbytwo. Why Infants Should Receive the Hepatitis B Vaccine at Birth – Vaccinate Your Family. Vaccinate Your Family. 2024; published online March 26. <https://vaccinateyourfamily.org/why-infants-should-receive-the-hepatitis-b-vaccine-at-birth/>.

Explains how despite recommendations surrounding testing for HBV during pregnancy, gaps in care may arise, which a universal HBV vaccination policy helps to address.

US) M, Colvin HM, Mitchell AE. Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C- Immunization. Nih.gov. 2010. <https://www.ncbi.nlm.nih.gov/books/NBK220044> (accessed Nov 22, 2024).

Institute of Medicine report on strategies to control viral hepatitis describing current vaccination strategies for HBV and the vaccination series as well as the rationales for it.

CDC. Chapter 10: Hepatitis B. Epidemiology and Prevention of Vaccine-Preventable Diseases. 2024; published online July 10. <https://www.cdc.gov/pinkbook/hcp/table-of-contents/chapter-10-hepatitis-b.html>.

Reviews the biology, epidemiology, and consequences of HBV infection, including the role of chronic infection in the development of liver cancer and cirrhosis.

hepatitis B. Journal of Hepatology 2009; 50: 805–16.

Describes the epidemiology of HBV and the role of vaccination in early childhood to prevent the disease.

Candotti D, Assennato SM, Laperche S, Allain J-P, Levicnik-Stezinar S. Multiple HBV transfusion transmissions from undetected occult infections: revising the minimal infectious dose. Gut 2018; 68: 313–21.

Demonstrates that the minimal infectious dose to develop HBV infection is extremely low, raising concerns about the power of screening to reliably detect and lead to prevention of all HBV cases.

11

McInerney KA, Hatch EE, Wesselink AK, et al. The Effect of Vaccination Against Human Papillomavirus on Fecundability. Paediatric and Perinatal Epidemiology 2017; 31: 531–6.

A study following a cohort of North American pregnancy planners found no relationship between HPV vaccination and the likelihood of having a child.

Naleway AL, Mittendorf KF, Irving SA, et al. Primary Ovarian Insufficiency and Adolescent Vaccination. Pediatrics 2018; 142. DOI:<https://doi.org/10.1542/peds.2018-0943>.

A study of nearly 200,000 female patients identified 120 diagnoses of primary ovarian insufficiency, which had no association with HPV vaccination or other vaccines.

Silvestris E, Paradiso AV, Minoia C, et al. Fertility preservation techniques in cervical carcinoma. Medicine 2022; 101: e29163.

Describes current techniques to preserve fertility in the management of cervical cancer.

Weinberg M, Sar-Shalom Nahshon C, Feferkorn I, Bornstein J. Evaluation of human papilloma virus in semen as a risk factor for low sperm quality and poor in vitro fertilization outcomes: a systematic review and meta-analysis. Fertility and Sterility 2020; 113: 955–969.e4.

A meta-analysis of studies suggesting that HPV infection in males can adversely affect sperm parameters, suggesting that HPV vaccination may enhance male fertility.

Segal L, Wilby OK, Willoughby CR, Veenstra S, Deschamps M. Evaluation of the intramuscular administration of Cervarix™ vaccine on fertility, pre- and post-natal development in rats. Reproductive Toxicology 2011; 31: 111–20.

Developmental and reproductive toxicity study of an HPV vaccine (Cervarix) in rats demonstrating that there was no adverse effect on the development of the litters from treated rats compared with untreated rats.

Wise LD, Pauley CJ, Michael B, Wolf JJ. Lack of effects on male fertility from a quadrivalent HPV vaccine in Sprague-Dawley rats. Birth Defects Research Part B: Developmental and Reproductive Toxicology 2010; 89: 376–81.

An HPV vaccine covering 4 strains of the virus did not demonstrate any effects on male fertility in male rats.

12

Centers for Disease Control and Prevention. Explaining How Vaccines Work. Vaccines & Immunizations. 2024; published online Aug 10. <https://www.cdc.gov/vaccines/basics/explaining-how-vaccines-work.html>.

Provides an overview as to how vaccines work and points where a vaccine could fail to protect against a given disease.

Nirenberg E, Perencevich EN. Understanding and Improving Vaccine Effectiveness Estimates in the Age of Widespread Background Immunity: A Step Toward Improved Science Communication. Clinical Infectious Diseases 2023; 76. DOI:<https://doi.org/10.1093/cid/ciad124>.

Describes specific fallacies in the interpretation of vaccine effectiveness studies with COVID-19 vaccines as a prototype example, demonstrating that the low effectiveness values reported following the emergence of the Omicron variant for various health outcomes does not account for changes in the comparator group.

Andrews N, Tessier E, Stowe J, et al. Duration of Protection against Mild and Severe Disease by Covid-19 Vaccines. New England Journal of Medicine 2022; 386. DOI:<https://doi.org/10.1056/nejmoa2115481>.

Provides a specific example of the point that vaccine elicited protection has to be considered with respect to a specific outcome– COVID-19 vaccines dropped substantially in their ability to protect from mild illness with the emergence of the Omicron variant, but retained robust protection against severe disease in spite of that.

CDC. Chapter 22: Varicella. Epidemiology and Prevention of Vaccine-Preventable Diseases. 2024.

<https://www.cdc.gov/pinkbook/hcp/table-of-contents/chapter-22-varicella.html>.

Reviews the biology, epidemiology, and consequences of varicella (chickenpox), including the role of vaccination in reducing the incidence of varicella in the US.

Cherry JD. The 112-Year Odyssey of Pertussis and Pertussis Vaccines—Mistakes Made and Implications for the Future. Journal of the Pediatric Infectious Diseases Society 2019; 8: 334–41.

Describes the evolution of our understanding of pertussis and pertussis vaccines and ruminates on options to improve control of pertussis.