

SEASONAL FLU SHOTS: YOUR BEST DEFENSE AGAINST ANNUAL INFLUENZA VARIANTS

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Abstract:

Influenza, commonly known as the flu, is a seasonal viral infection that impacts millions each year and can lead to severe illness or even death. This article aims to illuminate the crucial role of seasonal flu shots in preventing infection from annual influenza variants. Vaccination offers multifaceted benefits including personal protection, reduced transmission rates, and a lesser burden on healthcare systems. Contrary to popular belief, the vaccine has a well-established safety profile and can significantly reduce the severity of illness even if one contracts the flu post-vaccination. Moreover, the Centers for Disease Control and Prevention recommend annual vaccination due to the virus's frequent mutations. The article also clarifies common misconceptions about the vaccine's safety and effectiveness, advocating that a flu shot is the best defense against influenza for the majority of the population.

Keywords: Influenza, Seasonal Flu Shots, Vaccination, Annual Variants, CDC, Protection, Healthcare Resources, Safety, Effectiveness.

1- Introduction:

Influenza, more commonly known as the flu, is not just a bothersome illness that can sideline you for a few days—it's a significant global public health issue with the potential for severe outcomes. Despite its widespread nature, affecting millions annually, it is often underestimated for its ability to disrupt lives and strain healthcare systems. Each year, the flu leads to a staggering number of hospital admissions, medical complications, and unfortunately, fatalities¹. This impact is particularly devastating among high-risk groups such as infants, elderly individuals, pregnant women, and those with underlying health conditions. For these populations, a seemingly harmless flu can rapidly progress into life-threatening complications, including pneumonia, organ failure, and secondary bacterial infections².

The complexity of managing influenza is heightened by the virus's capacity for frequent mutations. Because of these mutations, the flu virus yields new strains almost every season. The recurring changes mean that any immunity acquired from past infections or vaccinations diminishes in effectiveness, requiring people to get vaccinated each year for continued protection³. Yet, despite persistent public health advisories and voluminous data affirming the benefits of flu shots, a significant proportion of the population skips their annual vaccination. Various factors contribute to this lapse, ranging from ingrained myths about the vaccine's safety to a lackadaisical attitude regarding the flu's potential severity.

This article aims to delve into the imperative of seasonal flu shots as the frontline defense against the ever-changing landscape of annual influenza variants. We will explore the manifold benefits of getting vaccinated, from personal protection to societal impact. We will also address some of the most common misconceptions and concerns that people have about the flu vaccine. By equipping you with this knowledge, we hope to emphasize the critical role that each of us plays in fostering a healthier, safer community through annual vaccinations.

The seasonal flu vaccine is the product of meticulous scientific research and continuous surveillance, created to combat the strains projected to be most prevalent during the upcoming season⁴. Before being released to the public, these vaccines are subjected to rigorous testing and safety evaluations. The benefits of getting a flu shot are manifold, not just limiting to individual health. A vaccinated person is less likely to transmit the virus to others, thereby serving as a linchpin in the collective effort to contain outbreaks⁵. This becomes even more critical in times of healthcare crises, where systems are already burdened and resources are scarce.

The objective of this article is to shine a spotlight on the urgent need for seasonal flu shots as the first line of defense against the mutable and recurrent annual influenza variants. We will delve into the numerous advantages of vaccination, from safeguarding one's own health to contributing to broader societal well-being. Additionally, we will tackle prevalent misconceptions and uncertainties surrounding the flu vaccine, providing evidence-based insights to counteract these concerns. Armed with this information, the aim is to underscore the vital role each individual plays in constructing a healthier, more resilient community by committing to annual vaccinations.

2- Understanding Influenza

The seasonal flu, or seasonal influenza, is a contagious respiratory illness caused by influenza viruses. It typically occurs annually, with outbreaks most common during the fall and winter months, although the timing and duration of flu seasons can vary⁶. The illness is characterized by a sudden onset of symptoms that can include fever, chills, cough, sore throat, muscle aches, and fatigue.

Influenza viruses primarily spread through respiratory droplets when an infected person coughs, sneezes, or talks. It can also spread by touching surfaces contaminated with the virus and then touching one's mouth, nose, or eyes. While most people who contract the flu will recover within a week or two without requiring medical treatment, the illness can lead to severe complications like pneumonia, bronchitis, and ear and sinus infections⁷. In extreme cases, influenza can result in hospitalization or death, particularly among high-risk groups like young children, the elderly, and people with chronic health conditions.

Influenza is a viral infection that primarily attacks the respiratory system, including the nose, throat, and sometimes the lungs. Often confused with the common cold, true influenza is far more severe and can lead to significant complications, such as pneumonia, or even death in certain vulnerable populations⁸. The illness is caused by influenza viruses, which come in three main types: A, B, and C.

Influenza A is the most common and potentially severe type, responsible for most flu epidemics. These viruses are zoonotic, meaning they can infect animals as well as humans. They have a high propensity for mutation, leading to the frequent emergence of new strains⁹. This variability makes it challenging for scientists to predict which strains will be most prevalent in any given year, and it is also the reason why new vaccines need to be formulated annually.

Influenza B viruses, by contrast, are primarily a human illness. Though they can lead to outbreaks, they are generally less severe than their Type A counterparts¹⁰. Unlike Type A, Type B viruses do not cause pandemics but can still be quite serious and lead to hospitalizations.

Influenza C is the mildest type and usually causes mild respiratory symptoms. Infections are less common and typically result in milder illnesses compared to Types A and B¹¹. Because of this, Type C influenza is less of a public health concern and is not targeted by seasonal flu vaccines.

It's important to note that influenza viruses are highly contagious. They are usually transmitted through droplets when an infected person coughs or sneezes, but they can also be spread by touching surfaces contaminated with the virus¹². Once infected, symptoms usually appear within one to four days, and a person may be contagious a day before showing symptoms and up to a week after becoming sick.

The hallmark signs of influenza include fever, cough, sore throat, runny or stuffy nose, body aches, headaches, and fatigue. Some people may also experience vomiting and diarrhea, though this is more common in children. Because the virus strains change so frequently and can lead to severe complications, getting vaccinated every year is considered the best defense against this ever-changing foe.

3- Why Flu Shots are Important

Flu shots serve as the primary line of defense against the seasonal influenza virus, offering benefits that extend far beyond individual well-being. Even though influenza may seem like a benign inconvenience to some, the reality is that it poses a real threat to public health. The vaccine not only safeguards against the physical toll of the illness but also lessens the social and economic impacts of influenza outbreaks¹³.

One of the most straightforward benefits of getting a flu shot is personal protection. Influenza can lead to severe illness, hospitalization, and even death, particularly in vulnerable populations such as children, the elderly, and those with compromised immune systems¹¹. Being vaccinated significantly reduces the risk of contracting the virus, and if you do fall ill, the symptoms are generally milder than they would be without the vaccine.

But the benefits of getting vaccinated don't stop at the individual level; they have a communal impact as well. A concept known as herd immunity comes into play. Herd immunity occurs when a sufficient percentage of a population becomes immune to a disease, either through vaccination or previous infections, thereby providing a measure of protection for those who are not immune¹⁴. This is particularly crucial for those who cannot receive vaccinations, like people with certain allergies or immune system disorders. Your decision to get vaccinated contributes to this broader community defense, making it less likely for the virus to spread.

Furthermore, flu shots help reduce the severity and duration of illness among those who do get infected after vaccination. Data has shown that vaccinated individuals who still contract the flu are less likely to need hospitalization and experience fewer complications¹⁵. They recover more quickly, which is beneficial not only for the patient but also for healthcare providers, who face a lower burden of treating severe flu cases.

There's also an economic aspect to consider. Widespread flu can lead to increased absenteeism in workplaces and schools, resulting in a loss of productivity. When a large portion of the community is vaccinated, this loss is mitigated.

Finally, getting vaccinated is particularly important during times of broader healthcare crises, such as other viral pandemics, when medical resources are stretched thin. Reducing the number of severe flu cases allows healthcare systems to allocate resources more effectively to other urgent needs¹⁶.

In summary, flu shots are not merely a personal health choice but a social responsibility. They offer a robust defense mechanism against the yearly threat of influenza, safeguarding individual and public health while easing the strain on healthcare systems.

4- When to Get a Flu Shot

Timing is crucial when it comes to maximizing the effectiveness of your flu shot. The influenza virus typically circulates most actively in the United States from late fall through early spring, although the exact timing can vary¹⁷. In general, it takes about two weeks after receiving the vaccination for the body to develop sufficient antibodies to protect against the flu. Here are some guidelines to consider:

- Before Flu Season Begins

The Centers for Disease Control and Prevention (CDC) recommend that people get a flu vaccine by the end of October, before the flu season really gets underway¹⁸. However, vaccination should continue to be offered throughout the flu season, even into January or later.

- Consider Your Individual Circumstances

Certain populations, such as those who are pregnant, elderly, or have chronic health conditions, may have specific recommendations for when to get vaccinated. It's always advisable to consult your healthcare provider for personalized guidance.

- Children and First-time Vaccination

Children aged 6 months to 8 years may require two doses of the flu vaccine, given at least four weeks apart, to be fully protected⁹. If your child falls into this age range and is getting vaccinated against influenza for the first time, or has only had one flu shot in total before July 1 of the current year, plan on starting the vaccination process earlier to allow time for the second dose before flu season starts.

- Travel Plans

If you are planning to travel, particularly to the Southern Hemisphere where the flu season may be different, consult your healthcare provider about the best time to get your vaccine.

- During Ongoing Healthcare Crises

In times of healthcare emergencies, such as during a COVID-19 surge, it's especially important to get vaccinated against the flu to minimize the burden on healthcare systems. Consult local health advisories to find out if there are any specific recommendations regarding flu shots during such times.

- If You Missed the Ideal Window

Even if you miss the recommended window, getting a flu shot later can still be beneficial. Flu season can last as late as May, and vaccination in December or even later can offer protective benefits.

Remember, the best time to get a flu shot is before flu viruses begin spreading in your community. However, it's better late than never, and getting vaccinated at any point during flu season provides valuable protection against the illness.

5- Types of Flu Vaccines

Understanding the different types of flu vaccines can help you make an informed decision about which option is best for you. Each year, the flu vaccine is updated to protect against the influenza viruses that research indicates will be most common during the upcoming season¹⁸. Here are the main types of flu vaccines currently available:

- **Inactivated Influenza Vaccines (IIV):** The most common type of flu vaccine is the inactivated influenza vaccine (IIV), which uses a killed (inactivated) version of the virus²⁰. It is given via injection and is approved for people 6 months and older. Several variations exist, including trivalent (three-component) and quadrivalent (four-component) versions, designed to protect against three or four different flu viruses, respectively.
- **Live Attenuated Influenza Vaccine (LAIV):** The (LAIV) is a nasal spray that contains a weakened form of the live virus. Unlike IIV, LAIV is generally recommended for healthy individuals between the ages of 2 and 49²¹. It is not recommended for pregnant women or those with certain health conditions.
- **High-Dose Flu Vaccine:** Specifically designed for people 65 years and older, the high-dose flu vaccine contains four times the amount of antigen (the part of the vaccine that stimulates the immune system) compared to regular flu shots²². This makes it more effective for older adults whose immune systems may be weaker.
- **Adjuvanted Flu Vaccine:** This vaccine contains an additive (adjuvant) that helps create a stronger immune response²³. Like the high-dose vaccine, the adjuvanted flu vaccine is approved for people 65 years and older.
- **Cell-Based and Recombinant Flu Vaccines:** Traditionally, flu vaccines have been produced using chicken eggs, but newer technologies involve cell-based and recombinant methods. Cell-based flu vaccines are made by growing the virus in animal cells rather than chicken eggs, which may lead to a better match against circulating viruses²⁴. Recombinant flu vaccines do not use the full virus or chicken eggs in the production process, making them a good option for people with egg allergies.
- **Jet Injector:** For adults between the ages of 18 and 64, the flu vaccine can also be delivered using a jet injector, which uses a high-pressure stream of fluid to inject the vaccine instead of a needle²⁵.

Each type of flu vaccine has its own set of recommendations and contraindications, so it's important to consult with a healthcare provider to determine which is most appropriate for you. Regardless of the type you choose, getting vaccinated is the best way to protect yourself and others from the flu.

6- Common Concerns and Myths About Flu Vaccines

Despite the scientific consensus on the safety and efficacy of flu vaccines, public perception is sometimes influenced by misconceptions and misinformation. Addressing these concerns is crucial for increasing vaccination rates and enhancing public health. Here are some common myths and concerns about flu vaccines:

- "The Flu Vaccine Can Give You the Flu"

One of the most pervasive myths is that the flu shot can give you the flu. This is untrue. The inactivated influenza vaccine contains only a killed virus, which cannot cause infection²⁶. The live attenuated version contains a weakened virus that also cannot cause the flu. However, some people may experience mild symptoms like a low-grade fever or soreness at the injection site, which are common side effects and not the flu itself.

- "I'm Healthy, So I Don't Need the Vaccine"

Many healthy individuals think they don't need a flu shot, believing they can fight off the virus. While it's true that healthy people are less likely to suffer severe complications from the flu, they can still spread the virus to vulnerable populations. Getting vaccinated helps protect not just yourself, but also others around you.

- "The Vaccine Isn't Effective"

While it's true that the flu vaccine isn't 100% effective, it significantly reduces the risk of infection and severity of illness²⁷. Effectiveness can vary from season to season but generally ranges from 40% to 60%. Even if you contract the flu after vaccination, symptoms are typically milder and less likely to result in hospitalization.

- "I'm Allergic to Eggs, So I Can't Get Vaccinated"

Egg allergies were once considered a contraindication for receiving the flu vaccine because most flu vaccines are produced using chicken eggs. However, there are egg-free vaccines like cell-based and recombinant flu vaccines that are safe for individuals with egg allergies.

- "Natural Immunity is Better"

Some people argue that getting the flu naturally will provide better immunity than vaccination. While it's true that natural infection can lead to immunity, the risks associated with the flu, such as severe illness, hospitalization, and even death, far outweigh the potential benefits of natural immunity²⁸.

- "I Got Vaccinated Last Year, So I'm Good"

The flu virus mutates regularly, and each year's vaccine is formulated to combat the strains expected to be most prevalent during the upcoming season. Therefore, last year's vaccine won't necessarily protect you from this year's virus.

- "Vaccines Contain Harmful Ingredients"

Some people are concerned about ingredients like thimerosal, a mercury-based preservative used in some multi-dose vaccine vials. However, numerous studies have shown thimerosal to be safe, and it does not cause autism or other neurodevelopmental disorders. Furthermore, thimerosal-free formulations are available.

Addressing these concerns and myths is crucial for improving public understanding of the flu vaccine's role in individual and community health. Consult with healthcare providers and rely on credible sources for accurate, evidence-based information.

7- Possible Side Effects

The seasonal flu vaccine is generally considered safe, but some people may experience mild side effects. These are usually short-lived and less severe than the symptoms of an actual influenza infection. Common side effects include soreness at the injection site, low-grade fever, and mild fatigue²⁹. You may also experience a mild headache or general muscle aches that resolve within a day or two. Less commonly, individuals might feel nauseous after receiving the vaccine.

In rare instances, fainting can occur, though this is often a reaction to the needle rather than the vaccine itself. Extremely rare but serious side effects include allergic reactions like hives, difficulty breathing, and swelling around the eyes or lips³⁰. Guillain-Barré Syndrome, an extremely rare neurological disorder that can lead to temporary paralysis, has been associated with the flu vaccine, though the risk is estimated to be about 1 in 1 million and it's still not definitively proven that the flu shot causes it.

For those who opt for the nasal spray version of the vaccine, known as FluMist, side effects may include a runny nose, wheezing, headache, vomiting, muscle aches, and low-grade fever.

If you experience persistent or severe side effects, consult your healthcare provider. It's important to note that experiencing side effects is not the same as contracting the flu from the vaccine. The injectable flu vaccine contains killed or inactivated viruses, and the nasal spray contains weakened viruses, neither of which can cause the flu. Always consult your healthcare provider for personalized medical advice and treatment.

8- Flu Shot vs. Flu Mist

The flu shot and FluMist serve the same essential purpose: to protect against the seasonal flu. However, they differ in several ways.

The flu shot is administered via a needle, usually into the muscle of the upper arm, whereas FluMist is a nasal spray vaccine that requires no needle³¹. In terms of composition, the flu shot is made from inactivated or killed flu viruses, while FluMist contains live but weakened flu viruses.

Efficacy can also differ between the two. The flu shot is generally considered effective for a wide range of populations and is the more traditional form of the vaccine. FluMist's efficacy can vary; sometimes it performs comparably to the flu shot, but not always²⁰.

Recommendations on who should receive the vaccines also differ. The flu shot is recommended for almost everyone 6 months and older, including pregnant women and those with chronic health conditions. In contrast, FluMist is generally recommended for healthy, non-pregnant people between the ages of 2 and 49.

Side effects for the flu shot are generally mild and may include soreness at the injection site, a low-grade fever, and mild fatigue. FluMist also has mild side effects but they may include a runny nose, wheezing, headache, vomiting, muscle aches, and low-grade fever³².

Lastly, while the flu shot is widely available, FluMist may not be as easily accessible in all locations or for all age groups. Consult your healthcare provider to determine which option is best for you, as individual health needs can significantly influence the most appropriate choice.

Parameter	Flu Shot	FluMist
Method of Administration	Administered via a needle into the upper arm muscle	Administered as a nasal spray, needle-free
Vaccine Composition	Made from inactivated or killed flu viruses	Made from live, but weakened, flu viruses
Efficacy	Generally effective for a broad range of populations	Variable efficacy, sometimes less effective
Age and Health Status	Recommended for almost everyone 6 months and older	Recommended for healthy people between ages 2 and 49
Side Effects	Mild, including soreness at injection site and low-grade fever	May include runny nose, wheezing, and headache
Availability	Widely available	May be less widely available

This table offers a quick overview of the key differences between the flu shot and FluMist, including how they are administered, their composition, efficacy, recommended populations, side effects, and availability. Remember, consult your healthcare provider for personalized medical advice and to determine which option is best for you.

9- Conclusion

Influenza is more than just a seasonal nuisance; it poses serious health risks and can lead to severe illness, hospitalization, and even death. Fortunately, flu vaccines offer a proven method for reducing these risks for individuals and communities alike. From inactivated and live attenuated vaccines to high-dose and adjuvanted versions, there are options to suit various needs and preferences.

However, misinformation and misconceptions about flu vaccines often hinder vaccination efforts. Myths about the flu shot causing the flu, concerns about vaccine ingredients, and misunderstandings about vaccine effectiveness can deter people from getting vaccinated. It's crucial to counter these myths with accurate, evidence-based information to ensure that as many people as possible benefit from flu vaccination.

Vaccination not only protects the individual but also contributes to broader community protection through herd immunity. This becomes especially vital in vulnerable populations and during times when healthcare resources are stretched thin, such as during other viral outbreaks or pandemics.

Timing is also essential, and while getting vaccinated early in the season is ideal, it's never too late to get your flu shot. Even if you've missed the recommended window, vaccination still offers valuable protection.

Consult your healthcare provider for personalized advice and to address any concerns or questions you may have about the flu vaccine. At the end of the day, getting vaccinated is not just a personal health choice but a social responsibility, offering a strong defense against the annual threat of influenza and contributing to the greater good.

References:

- [1]. Tyrrell CS, Allen JLY, Gkrania-Klotsas E. Influenza: epidemiology and hospital management. *Medicine (Abingdon)*. 2021 Dec;49(12):797-804. doi: 10.1016/j.mpmed.2021.09.015. Epub 2021 Nov 12. PMID: 34849086; PMCID: PMC8624711.
- [2]. Morens DM, Taubenberger JK. Influenza Cataclysm, 1918. *N Engl J Med*. 2018 Dec 13;379(24):2285-2287. doi: 10.1056/NEJMp1814447. PMID: 30575465; PMCID: PMC6558650.
- [3]. Pooley N, Abdool Karim SS, Combadière B, Ooi EE, Harris RC, El Guerche Seblain C, Kisomi M, Shaikh N. Durability of Vaccine-Induced and Natural Immunity Against COVID-19: A Narrative Review. *Infect Dis Ther*. 2023 Feb;12(2):367-387. doi: 10.1007/s40121-022-00753-2. Epub 2023 Jan 9. PMID: 36622633; PMCID: PMC9828372.
- [4]. Agor JK, Özalp OY. Models for predicting the evolution of influenza to inform vaccine strain selection. *Hum Vaccin Immunother*. 2018 Mar 4;14(3):678-683. doi: 10.1080/21645515.2017.1423152. Epub 2018 Feb 12. PMID: 29337643; PMCID: PMC5861780.

- [5]. Filip R, Gheorghita Puscaselu R, Anchidin-Norocel L, Dimian M, Savage WK. Global Challenges to Public Health Care Systems during the COVID-19 Pandemic: A Review of Pandemic Measures and Problems. *J Pers Med*. 2022 Aug 7;12(8):1295. doi: 10.3390/jpm12081295. PMID: 36013244; PMCID: PMC9409667.
- [6]. Moghadami M. A Narrative Review of Influenza: A Seasonal and Pandemic Disease. *Iran J Med Sci*. 2017 Jan;42(1):2-13. PMID: 28293045; PMCID: PMC5337761.
- [7]. Alana Biggers, Flu complication facts. Healthline Media LLC. June 4, 2019. <https://www.healthline.com/health/flu-complications#outlook>
- [8]. Mallia P, Johnston SL. Influenza infection and COPD. *Int J Chron Obstruct Pulmon Dis*. 2007;2(1):55-64. doi: 10.2147/copd.2007.2.1.55. PMID: 18044066; PMCID: PMC2692119.
- [9]. Parkhe P, Verma S. Evolution, Interspecies Transmission, and Zoonotic Significance of Animal Coronaviruses. *Front Vet Sci*. 2021 Oct 18;8:719834. doi: 10.3389/fvets.2021.719834. PMID: 34738021; PMCID: PMC8560429.
- [10]. U. Schmitz, L. Lou, C. Roberts, R. Griffith, 7.13 - Ribonucleic Acid Viruses: Antivirals for Influenza A and B, Hepatitis C Virus, and Respiratory Syncytial Virus, Editor(s): John B. Taylor, David J. Trigg, Comprehensive Medicinal Chemistry II, Elsevier, 2007, Pages 373-417, ISBN 9780080450445, <https://doi.org/10.1016/B0-08-045044-X/00214-5>.
- [11]. WHO, Influenza (Seasonal). January 2023, [https://www.who.int/news-room/fact-sheets/detail/influenza-\(seasonal\)](https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal))
- [12]. Dhand R, Li J. Coughs and Sneezes: Their Role in Transmission of Respiratory Viral Infections, Including SARS-CoV-2. *Am J Respir Crit Care Med*. 2020 Sep 1;202(5):651-659. doi: 10.1164/rccm.202004-1263PP. PMID: 32543913; PMCID: PMC7462404.
- [13]. Walsh JA, Maher C. Economic Implications of Influenza and Influenza Vaccine. *Influenza Vaccines for the Future*. 2010 Jun 18:425-40. doi: 10.1007/978-3-0346-0279-2_19. PMCID: PMC7123782.
- [14]. Louis J. Catania, 7 - Immunology: The science of pandemics, infectious disease and COVID-19, Editor(s): Louis J. Catania, The Paradox of the Immune System, Academic Press, 2022, Pages 181-223, ISBN 9780323951876, <https://doi.org/10.1016/B978-0-323-95187-6.00001-7>.
- [15]. Deiss RG, Arnold JC, Chen WJ, Echols S, Fairchok MP, Schofield C, Danaher PJ, McDonough E, Ridoré M, Mor D, Burgess TH, Millar EV. Vaccine-associated reduction in symptom severity among patients with influenza A/H3N2 disease. *Vaccine*. 2015 Dec 16;33(51):7160-7167. doi: 10.1016/j.vaccine.2015.11.004. Epub 2015 Nov 10. PMID: 26562321; PMCID: PMC4684491.
- [16]. Worby CJ, Chang HH. Face mask use in the general population and optimal resource allocation during the COVID-19 pandemic. *medRxiv [Preprint]*. 2020 Apr 7:2020.04.04.20052696. doi: 10.1101/2020.04.04.20052696. Update in: *Nat Commun*. 2020 Aug 13;11(1):4049. PMID: 32511626; PMCID: PMC7276053.
- [17]. Ventola CL. Immunization in the United States: Recommendations, Barriers, and Measures to Improve Compliance: Part 1: Childhood Vaccinations. *P T*. 2016 Jul;41(7):426-36. PMID: 27408519; PMCID: PMC4927017.
- [18]. CDC, Influenza Vaccination: A Summary for Clinicians. National Center for Immunization and Respiratory Diseases (NCIRD) August 25, 2023. <https://www.cdc.gov/flu/professionals/vaccination/vax-summary.htm>
- [19]. Li-Kim-Moy J, Yin JK, Patel C, et al. Australian vaccine preventable disease epidemiological review series: influenza 2006 to 2015. *Communicable Diseases Intelligence* 2016;40:E482-95.
- [20]. Wong SS, Webby RJ. Traditional and new influenza vaccines. *Clin Microbiol Rev*. 2013 Jul;26(3):476-92. doi: 10.1128/CMR.00097-12. PMID: 23824369; PMCID: PMC3719499.
- [21]. Giancetti E, Manenti A, Kistner O, Trombetta C, Manini I, Montomoli E. How to assess the effectiveness of nasal influenza vaccines? Role and measurement of sIgA in mucosal secretions. *Influenza Other Respir Viruses*. 2019 Sep;13(5):429-437. doi: 10.1111/irv.12664. Epub 2019 Jun 21. PMID: 31225704; PMCID: PMC6692539.
- [22]. Annalisa Ciabattini, Christine Nardini, Francesco Santoro, Paolo Garagnani, Claudio Franceschi, Donata Medagliani, Vaccination in the elderly: The challenge of immune changes with aging, *Seminars in Immunology*, Volume 40, 2018, Pages 83-94, ISSN 1044-5323, <https://doi.org/10.1016/j.smim.2018.10.010>.
- [23]. Castrodeza-Sanz J, Sanz-Muñoz I, Eiros JM. Adjuvants for COVID-19 Vaccines. *Vaccines (Basel)*. 2023 Apr 26;11(5):902. doi: 10.3390/vaccines11050902. PMID: 37243006; PMCID: PMC1022622.
- [24]. Rockman S, Laurie K, Ong C, Rajaram S, McGovern I, Tran V, Youhanna J. Cell-Based Manufacturing Technology Increases Antigenic Match of Influenza Vaccine and Results in Improved Effectiveness. *Vaccines (Basel)*. 2022 Dec 26;11(1):52. doi: 10.3390/vaccines11010052. PMID: 36679895; PMCID: PMC9861528.
- [25]. Trimzi MA, Ham YB. A Needle-Free Jet Injection System for Controlled Release and Repeated Biopharmaceutical Delivery. *Pharmaceutics*. 2021 Oct 22;13(11):1770. doi: 10.3390/pharmaceutics13111770. PMID: 34834185; PMCID: PMC8620904.
- [26]. CDC, Influenza (Flu) Immunization: Myths and Facts. September 16, 2022, <https://www.healthlinkbc.ca/healthlinkbc-files/influenza-flu-immunization-myths-and-facts>
- [27]. Frentzel E, Jump RLP, Archbald-Pannone L, Nace DA, Schween SJ, Gaur S, Naqvi F, Pandya N, Mercer W; Infection Advisory Subcommittee of AMDA, The Society for Post-Acute and Long-Term Care Medicine. Recommendations for Mandatory Influenza Vaccinations for Health Care Personnel From AMDA's Infection Advisory Subcommittee. *J Am Med Dir Assoc*. 2020 Jan;21(1):25-28.e2. doi: 10.1016/j.jamda.2019.11.008. PMID: 31888863; PMCID: PMC6996022.
- [28]. Wrotek S, LeGrand EK, Dzialuk A, Alcock J. Let fever do its job: The meaning of fever in the pandemic era. *Evol Med Public Health*. 2020 Nov 23;9(1):26-35. doi: 10.1093/emph/eoaa044. PMID: 33738101; PMCID: PMC7717216.
- [29]. Jilani TN, Jamil RT, Siddiqui AH. H1N1 Influenza. [Updated 2022 Oct 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK513241/>

- [30]. CDC, Flu Vaccine Safety Information. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD), August 25, 2023. <https://www.cdc.gov/flu/prevent/general.htm>
- [31]. CDC, Seasonal Flu Vaccines. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD). August 25, 2023. <https://www.cdc.gov/flu/prevent/flushot.htm>
- [32]. CDC, Influenza (Flu)Vaccines. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD). September 30, 2021. <https://www.cdc.gov/vaccinesafety/vaccines/flu-vaccine.html>