

ARTICLE

Deciphering the Mysteries: Seasonal Influenza and the Role of Flu Vaccines in Public Health

Nima Mostafa, Arman Mohsen, Shahrad Mardin, and Ameen Elyas*

(Received: 14 August 2022; Revised: 22 October 2022; Accepted: 30 December 2022; Published: 12 January 2023)

Abstract

Seasonal influenza remains a significant public health concern, causing widespread illness, hospitalizations, and deaths annually. The virus undergoes frequent genetic changes, leading to new strains that challenge public health responses. Understanding the complexities of influenza transmission, pathogenesis, and the body's immune response is crucial for effective prevention and control. Flu vaccines play a pivotal role in mitigating the impact of seasonal influenza. They are formulated annually to match circulating strains, thereby enhancing their effectiveness. Vaccination reduces the severity of illness, prevents complications, and decreases the overall burden on healthcare systems. Despite challenges such as vaccine hesitancy and varying effectiveness, widespread vaccination remains the most effective strategy for controlling influenza outbreaks. Ongoing research aims to develop universal vaccines that offer broader and longer-lasting protection. Deciphering the mysteries of seasonal influenza and improving flu vaccine strategies are essential for safeguarding public health and reducing the global impact of this persistent viral threat.

Keywords: Flu Vaccines; Genetic Changes; Immune Response; Influenza Transmission; Public Health; Seasonal Influenza; Vaccine Effectiveness

Abbreviations: CDC: Centers for Disease Control and Prevention, HCW: Healthcare worker, OSHA: Occupational Safety and Health Administration, VAERS: Vaccine Adverse Event Reporting System, VE: Vaccine effectiveness, VSD: Vaccine Safety Datalink, WHO: World Health Organization

1. Introduction

Influenza, a highly contagious respiratory illness, exacts a heavy toll worldwide each year. With approximately 1 billion cases annually, including 3-5 million severe ones leading to 290,000-650,000 deaths, this viral infection poses a significant public health challenge. While influenza can affect individuals of all ages, certain groups like young children, older adults, pregnant women, and those with chronic conditions such as diabetes, heart disease, or compromised immunity face heightened risks of severe complications like pneumonia [1, 2, 3, 4, 5]. Seasonal flu vaccines offer the most effective protection against this ever-mutating virus. This comprehensive guide delves into the transmission dynamics, symptoms, and prevention strategies for influenza, emphasizing the crucial role of vaccination. We explore vaccine effectiveness, benefits for healthcare workers and high-risk groups, employer strategies for promoting immunization, optimal timing for vaccination, and addressing common safety concerns. Additionally, we examine influenza surveillance and monitoring efforts by global health organizations like the World Health Organization (WHO) to enhance preparedness and response capacities against potential outbreaks [6, 7, 8, 9].

^{© 2023} The Author(s). Published by Fusion of Multidisciplinary Research, An International Journal (FMR), Netherlands, under the (Creative Commons Attribution 4.0 International License (CC BY 4.0)

2. Influenza Transmission and Symptoms

Influenza viruses are highly contagious and can spread rapidly through respiratory droplets expelled when an infected person coughs, sneezes, or talks. These droplets can travel up to six feet and infect others who inhale them or come into contact with contaminated surfaces. Healthcare workers, due to their frequent close contact with sick patients, are at an elevated risk of exposure to influenza viruses [10, 11, 12, 13] (Fig. 1).

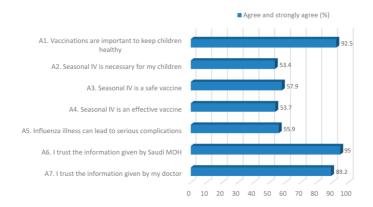


Figure 1. Attitudes and behaviors regarding the influenza vaccine.

The primary symptoms of influenza include:

- Fever
- Cough
- · Sore throat
- Runny or stuffy nose
- · Muscle or body aches
- Headaches
- Fatigue

These symptoms typically appear suddenly and can range from mild to severe, depending on the individual's age, overall health, and the specific strain of the virus. Influenza can also lead to more severe complications, such as pneumonia, which can be life-threatening, especially for high-risk groups like young children, older adults, and individuals with underlying medical conditions [14, 15, 16]. It's important to note that influenza symptoms can sometimes be confused with those of the common cold, but influenza is generally more severe and accompanied by a higher fever and more severe body aches. Prompt diagnosis and treatment are crucial in managing influenza and preventing further transmission [17, 18, 19, 20].

3. Vaccine Effectiveness

Vaccination is a safe and effective way to prevent influenza infection, reduce the severity and duration of illness, and decrease the spread of the virus to others. The effectiveness of flu vaccines typically ranges from 40-60% when the vaccine composition is well-matched to the circulating strains

[21]. For healthcare workers (HCWs), influenza vaccination has been shown to be effective in protecting them from infection, reducing both symptomatic and asymptomatic cases. Furthermore, vaccinating HCWs may provide a protective effect for patients, reducing mortality by 29% and influenzalike illness episodes by 42% (Fig. 2) [22].

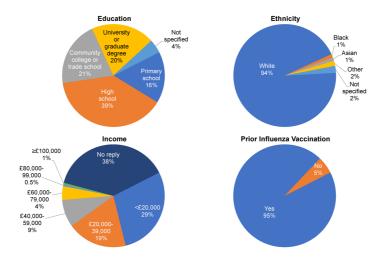


Figure 2. Demographics of the patient population (n = 185).

Vaccine effectiveness (VE) studies allow an assessment of the positive effects of influenza vaccines in real-world settings. Several factors influence VE, including:

- · Age of vaccinees
- Match between vaccine strain and circulating virus
- Egg-adaptations during vaccine production
- · Subject's history of previous vaccination

In children, VE varies from moderate to effective, depending on the influenza season and age group. For adults and the elderly, vaccination provides an overall protective effect, although VE can fluctuate across different seasons and virus types/subtypes [23]. While the flu vaccine is not 100% effective, it can significantly lower the risk of contracting the flu and reduce the severity of illness and risk of serious complications if infected. Reviews of past studies have found that the flu vaccine lowers the risk of flu illness by 40% to 60% when the vaccine matches the spreading flu viruses. Even when the vaccine doesn't completely prevent the flu, it may lessen the severity of illness and lower the risk of serious complications and hospitalization [24, 25, 26, 27, 28, 29, 30].

The flu vaccine is developed annually to protect against the most commonly circulating influenza strains, available as either trivalent (protects against 3 flu viruses) or quadrivalent (protects against 4 flu viruses). It takes about 2 weeks after vaccination for the body to develop antibodies and provide protection, during which time individuals remain vulnerable to the flu. The vaccine's effectiveness decreases over time, so it's recommended to get vaccinated before flu season starts, ideally by the end of October. Factors impacting vaccine effectiveness include the match between the vaccine and circulating strains, as well as age; a high-dose vaccine is recommended for those 65 and older [31, 32, 33, 34, 35, 36].

4. Vaccination Benefits for Healthcare Workers

Vaccination against influenza is especially crucial for healthcare workers (HCWs) who have frequent close contact with patients or work in high-risk settings like hospitals, clinics, and nursing homes. Employers have a responsibility to create a safe work environment and should actively encourage all workers, particularly HCWs, to receive the flu vaccine [37, 38].

The Centers for Disease Control and Prevention (CDC) and the Joint Commission recommend strategies to improve vaccination rates among healthcare personnel, such as:

- 1. Making the vaccine readily available to workers during their normal shifts.
- Providing education and promotional campaigns to address vaccine hesitancy and misconceptions.
- 3. Implementing mandatory vaccination policies or requiring declination statements from those who refuse vaccination.

These strategies have been found to be effective in increasing vaccination rates among HCWs, with some facilities achieving coverage exceeding 94% [39, 40, 41].

Workers have the right to a safe workplace and to receive information and training about workplace hazards and how to prevent them. If they believe there is a serious hazard or their employer is not following Occupational Safety and Health Administration (OSHA) rules, workers can file a complaint with OSHA. Additionally, workers have the right to exercise their rights without retaliation as explained in Table 1 [42].

Healthcare Worker Role	Influenza Vaccination Coverage
Physicians	94.5%
Hospital Settings	85.7%
Assistants/Aides	62.8%
Long-Term Care and Home Health Care Settings	68.3%

Table 1. Healthcare Worker Role and coverage

The data highlights the need for targeted efforts to improve vaccination rates among certain HCW roles and settings, such as assistants/aides and long-term care facilities. Employer vaccination requirements have been strongly associated with higher influenza and COVID-19 vaccination uptake among HCWs [43].

5. Employer Strategies for Promoting Vaccination

Employers can take several proactive steps to promote influenza vaccination among their workforce. Firstly, securing senior management buy-in and framing flu vaccination as a business priority is crucial. Employers should identify a dedicated flu vaccination coordinator or team with well-defined roles and responsibilities. They should also determine whether contracting with an external provider for vaccination services is necessary [22].

Engaging employees and labor representatives in the planning process can help gauge demand and ensure sufficient access. Scheduling the vaccination clinic during peak flu season, typically in the fall, is recommended to maximize employee participation. Employers should strive to provide ample and accessible vaccination opportunities across multiple business locations [23].

To encourage participation, employers can:

- Allow employees to attend the on-site clinic during work hours.
- · Consider offering flu vaccination to employees' families.
- Set annual goals to improve the percentage of vaccinated employees.
- Utilize incentives such as offering the vaccine at no or low cost, providing refreshments, or holding contests.
- Promote the clinic through various channels, including posters, company communications, leadership messaging, and social media [11].
- Ensure a comfortable and convenient location for the vaccination clinic.
- Encourage managers and leaders to get vaccinated first, setting an example for others.

Alternatively, employers can partner with nearby pharmacies or clinics to arrange employee vaccinations [13]. If sharing a building, employers can explore the possibility of the property manager hosting a clinic for all tenants' employees.

Other effective strategies include:

- Designating a dedicated Flu Campaign Coordinator to plan and implement the program.
- Purchasing enough vaccine to vaccinate all employees.
- Making the vaccine easily accessible through flexible hours, multiple locations, or mobile carts.
- Offering the vaccine throughout the flu season until the supply is exhausted.
- Determining who will cover the cost of immunizations and how employees will pay.
- Developing a smooth workflow and registration process for the clinic.
- Soliciting feedback from employees and the vaccination provider to improve future efforts.
- Reminding employees that their health insurance may cover flu shots at doctors' offices or pharmacies.
- Providing educational materials on where to find flu vaccination clinics in the community.
- Implementing an Influenza Prevention and Illness Policy.

The Centers for Disease Control and Prevention (CDC) recommends two main strategies for businesses and employers: hosting workplace flu vaccination clinics and promoting flu vaccination in the community. Hosting on-site clinics involves offering seasonal flu vaccination to employees at no or low cost, often by contracting with pharmacies or community vaccinators. Promoting community vaccination involves ensuring employees know where they and their families can access seasonal flu vaccines and partnering with local providers [19].

6. High-Risk Groups for Complications

Influenza is a vaccine-preventable disease, and vaccination remains the most effective method of controlling morbidity and mortality of seasonal influenza, especially for high-risk groups. The Centers for Disease Control and Prevention (CDC) recommends the flu vaccine for everyone 6 months and older, with particular emphasis on those at higher risk of flu complications:

The Elderly: As people age, their immune systems weaken, making it harder for their bodies to
fight off infections like the flu. The CDC recommends annual flu vaccination for everyone aged
65 and older.

- 2. **People with Chronic Medical Conditions**: Individuals with chronic conditions like asthma, diabetes, heart disease, or compromised immunity are at increased risk of developing severe complications from the flu. Vaccination is crucial for this group.
- 3. **Pregnant Women**: Influenza poses a higher risk of severe illness for pregnant people and can potentially harm the developing baby. The CDC strongly recommends that all pregnant individuals receive the flu vaccine during any trimester of their pregnancy.
 - Millions of doses of flu vaccines have been safely administered to pregnant people for over 50 years.
 - Getting the flu vaccine while pregnant can also help protect the baby after birth [18].
- 4. **Young Children**: Children under 5 years old, especially those younger than 2, are at high risk of developing serious flu-related complications. The CDC recommends annual vaccination for all children aged 6 months and older.
 - Children under 6 months cannot receive the flu vaccine, so it's important for their caregivers to get vaccinated to provide indirect 'herd immunity' protection.
- 5. **Healthcare Workers**: Due to their frequent close contact with sick patients, healthcare workers are at an elevated risk of exposure to influenza viruses. Vaccination helps protect them and reduces the risk of transmitting the virus to vulnerable patients.

High-Risk Group	Rationale for Flu Vaccination
The Elderly	Weakened immune systems
Chronic Conditions	Increased risk of complications
Pregnant Women	Protect mother and developing baby
Young Children	Underdeveloped immune systems
Healthcare Workers	Frequent patient exposure

Table 2. High-Risk Groups

Ensuring high vaccination rates among these high-risk groups is crucial for reducing the overall burden of influenza and preventing severe outcomes, hospitalizations, and fatalities as given in Table 2.

7. Vaccination Timing and Duration of Protection

The Centers for Disease Control and Prevention (CDC) recommends that most people aged 6 months and older get a seasonal flu vaccine each year, ideally by the end of October [19]. Routine annual influenza vaccination is recommended for all persons aged 6 months and above who do not have contraindications. For most adults and pregnant persons, vaccination should ideally be offered during September or October, but can continue throughout the flu season.

Approved ages and dose volumes for intramuscular influenza vaccines (IIV4s and RIV4) are as follows :

- 6 months through 35 months: 0.25 mL
- 3 years and older: 0.5 mL

The live attenuated influenza vaccine (LAIV4) is administered intranasally, with 0.1 mL per nostril (0.2 mL total), for persons aged 2 through 49 years. While vaccination is recommended by the end of October, it can be given as early as July or August for certain groups like children and pregnant women in the third trimester. The flu vaccine is generally available starting in August each year, with

shipments beginning sometime in August. It takes about two weeks after getting the flu vaccine for the body to build up immunity (Fig. 3).

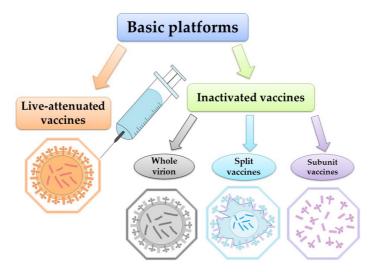


Figure 3. Major influenza vaccine platforms.

The CDC recommends getting the flu vaccine by the end of October, but individuals can still benefit from getting it later in the flu season. This is because flu viruses change quickly, and the vaccine is updated each year to match the viruses expected to be most common that season. The flu vaccine provides protection against four of the influenza viruses expected to be most common during the upcoming flu season.

For the 2022-2023 flu season, there are three flu vaccines that are preferentially recommended for people aged 65 years and older :

- 1. Fluzone High-Dose Quadrivalent
- 2. Flublok Quadrivalent recombinant
- Fluad Quadrivalent adjuvanted

The flu vaccine composition has been updated for the 2022-2023 season, with changes to the H3N2 and B/Victoria lineage components. The flu vaccine supply for the 2022-2023 season is projected to be 156.2 million to 170 million doses. It is safe and recommended to get a COVID-19 vaccine and a flu vaccine at the same visit. Flu activity and severity for the 2022-2023 season are difficult to predict, but flu is expected to circulate along with COVID-19. Coinfection with flu and COVID-19 is possible, and preliminary data suggests it occurred in about 6% of pediatric flu-associated hospitalizations and 16% of pediatric flu-associated deaths in the 2021-2022 season.

8. Addressing Vaccine Safety Concerns

Influenza vaccines are subject to rigorous safety testing and monitoring to ensure their safety for public use. The Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) closely monitor vaccine safety through systems like the Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Datalink (VSD) [27].

Common side effects of flu vaccines are typically mild and temporary, such as soreness, redness, or swelling at the injection site, low-grade fever, and general body aches . These side effects usu-

ally resolve within a few days and are not cause for concern. Serious adverse events following influenza vaccination are rare. There is a possible small association between injectable flu vaccines and Guillain-Barré syndrome (GBS), with an estimated risk of fewer than 1-2 cases per 1 million people vaccinated. However, the risk of developing GBS is significantly higher after contracting influenza itself than after receiving the flu vaccine (Fig. 4) [29].

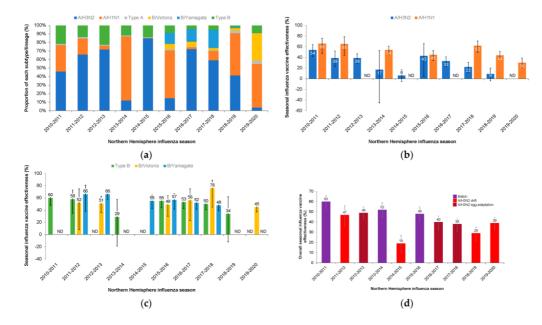


Figure 4. Seasonal influenza vaccine effectiveness.

For individuals with egg allergies, the CDC recommends that they can receive any licensed, age-appropriate influenza vaccine. Numerous studies have consistently demonstrated the safety of influenza vaccination during pregnancy, with no increased risk of miscarriage, stillbirth, or other adverse pregnancy outcomes. Both the CDC's Advisory Committee on Immunization Practices and the American College of Obstetricians and Gynecologists recommend that all pregnant individuals receive the inactivated influenza vaccine.

Influenza vaccines undergo rigorous safety testing and monitoring, with different types tailored for specific age groups and populations:

- Inactivated Influenza Vaccines (IIVs): Have an excellent safety profile and are recommended for children ≥ 6 months, the elderly, asthmatics, and those with high-risk conditions.
- Live Attenuated Influenza Vaccines (LAIVs): Administered intranasally, they induce a broader immune response but are not recommended for the elderly, immunosuppressed, or children < 2 years old due to safety concerns.

While pandemic influenza vaccines may have an incompletely described safety profile, with some associations reported between certain adjuvanted vaccines and increased risk of narcolepsy and anaphylaxis , seasonal influenza vaccines have a well-established safety record, with hundreds of millions of Americans safely receiving them over the past 50 years. It's important to note that the flu vaccine cannot cause influenza illness, as it either contains inactivated virus or a particle designed to mimic the flu virus to trigger an immune response. Healthcare providers and trusted organizations like the CDC, American Academy of Pediatrics, and Vaccine Information Center offer resources and guidance for addressing vaccine safety concerns and promoting vaccine confidence [23].

9. Influenza Surveillance and Monitoring

The World Health Organization (WHO) has established a Global Influenza Surveillance and Response System (GISRS) that has been operational since 1952. GISRS currently comprises institutions in 129 WHO Member States, including:

- National Influenza Centres (NICs)
- WHO Collaborating Centres (WHO CCs)
- WHO H5 Reference Laboratories
- WHO Essential Regulatory Laboratories (ERLs)

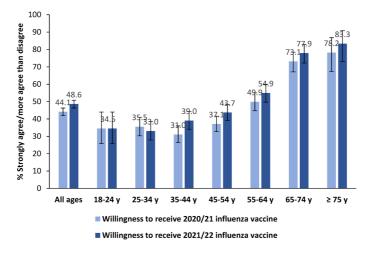


Figure 5. Between-survey comparison of the declared willingness.

FluNet, a global web-based tool for influenza virological surveillance launched in 1997, tracks the movement of influenza viruses globally (Fig. 5). WHO holds regular meetings and consultations to make recommendations on the composition of influenza virus vaccines for the upcoming influenza seasons in both the northern and southern hemispheres. GISRS is described as a unique platform for surveillance, monitoring, and response not only for influenza but also for other respiratory viruses. This global network plays a crucial role in:

- 1. Monitoring the evolution of influenza viruses
- 2. Providing risk assessments
- 3. Recommending vaccine strain selection
- 4. Developing potential pandemic vaccine viruses

In the United States, influenza surveillance is a collaborative effort between the Centers for Disease Control and Prevention (CDC) and its partners. The U.S. influenza surveillance system comprises five main components:

- 1. Virologic Surveillance: Monitoring influenza virus circulation and characterizing the viruses
- 2. Outpatient Illness Surveillance: Monitoring influenza-like illness (ILI) activity
- 3. **Hospitalization Surveillance**: Monitoring laboratory-confirmed influenza-associated hospitalizations
- 4. Mortality Surveillance: Tracking influenza-associated deaths
- Long-Term Care Facility Surveillance: Monitoring influenza activity in residential care settings

This collaborative effort involves public health and clinical laboratories, healthcare providers, hospitals, and state/local health departments. Influenza surveillance data are used to:

- · Determine when and where influenza activity is occurring
- · Monitor changes in influenza viruses
- Inform vaccine strain selection
- Assess the impact of influenza

The data are reported weekly, and the influenza season runs from October to September as given in Table 3.

WHO Influenza Surveillance	U.S. Influenza Surveillance	
Global Influenza Surveillance	Collaborative effort between CDC and partners	
and Response System (GISRS)		
Comprises 129	Involves public health labs, providers, hospitals, and health	
Member States	departments	
FluNet tracks global	Monitors virus circulation, outpatient illness, hospitalizations, mortality,	
virus movement	and long-term care facilities	
Recommends	Informs vaccine strain selection	
vaccine composition		
Monitors respiratory	Focuses on influenza	
viruses		

Table 3. WHO Influenza Surveillance

The regular sharing of quality influenza surveillance and monitoring data by countries allows WHO to provide information about influenza transmission, describe critical epidemiological features, monitor global trends, and support the selection of influenza strains for vaccine production. WHO has defined standard case definitions for influenza-like illness (ILI) and severe acute respiratory infections (SARI) to allow for consistent global surveillance.

10. Conclusion

Influenza remains a formidable public health challenge, exacting a heavy toll worldwide each year. This comprehensive guide has explored the intricate dynamics of this highly contagious respiratory illness, delving into its transmission, symptoms, and the pivotal role of vaccination in mitigating its impact. While vaccination offers the most effective protection against influenza, its effectiveness hinges on factors such as the match between vaccine strains and circulating viruses, as well as individual factors like age and underlying health conditions. Promoting influenza vaccination remains a collective responsibility, involving concerted efforts from healthcare authorities, employers, and individuals alike. By implementing strategies to improve vaccination coverage, particularly among high-risk groups, we can collectively safeguard public health and reduce the burden of this formidable virus. Ongoing surveillance and monitoring efforts by global health organizations further fortify our preparedness and response capabilities, ensuring we stay ahead of this ever-evolving threat.

References

- [1] R Edgar Hope-Simpson. *The transmission of epidemic influenza*. Springer Science & Business Media, 2013.
- [2] Ottar N Bjørnstad and Cecile Viboud. "Timing and periodicity of influenza epidemics". In: *Proceedings of the National Academy of Sciences* 113.46 (2016), pp. 12899–12901.
- [3] David M Morens and Jeffery K Taubenberger. "Pandemic influenza: certain uncertainties". In: *Reviews in medical virology* 21.5 (2011), pp. 262–284.
- [4] Oliver Ava, Muhammad Oscar, and Tommy George. "The Impact and Prevention of Latch-up in CMOS in VLSI Design". In: Fusion of Multidisciplinary Research, An International Journal (FMR) 1.1 (2020), pp. 1–13.
- [5] Alain Gagnon, Matthew S Miller, Stacey A Hallman, Robert Bourbeau, D Ann Herring, David JD Earn, and Joaquin Madrenas. "Age-specific mortality during the 1918 influenza pandemic: unravelling the mystery of high young adult mortality". In: *PloS one* 8.8 (2013), e69586.
- [6] Eric CJ Claas, Albert DME Osterhaus, Ruud Van Beek, Jan C De Jong, Guus F Rimmelzwaan, Dennis A Senne, Scott Krauss, Kennedy F Shortridge, and Robert G Webster. "Human influenza A H5N1 virus related to a highly pathogenic avian influenza virus". In: *The Lancet* 351.9101 (1998), pp. 472–477.
- [7] David JD Earn, Jonathan Dushoff, and Simon A Levin. "Ecology and evolution of the flu". In: *Trends in ecology & evolution* 17.7 (2002), pp. 334–340.
- [8] Alexandre Gabriel, Claude Charles, Louis Andre, and Charlotte Antoine. "Navigating the Future of Wearable Devices with Flexible Electronics". In: Fusion of Multidisciplinary Research, An International Journal (FMR) 1.2 (2020), pp. 63–72.
- [9] Declan Butler. "Mutations explain poor showing of 2012 flu vaccine". In: Nature News 27 (2014).
- [10] John M Barry. The great influenza: The story of the deadliest pandemic in history. Penguin Uk, 2020.
- [11] Claire Wilson. Influenza and Bird Flu: Examining the Flu. Enslow Publishing, LLC, 2014.
- [12] Henry H. James, Razu Pawel, and Gawin Saduf. "Autonomous Vehicles and Robust Decision-Making in Dynamic Environments". In: Fusion of Multidisciplinary Research, An International Journal (FMR) 1.2 (2020), pp. 110–121.
- [13] Michaela E Nickol and Jason Kindrachuk. "A year of terror and a century of reflection: perspectives on the great influenza pandemic of 1918–1919". In: *BMC infectious diseases* 19 (2019), pp. 1–10.
- [14] Jeremy Brown. *Influenza: the hundred-year hunt to cure the 1918 Spanish flu pandemic.* Simon and Schuster, 2018.
- [15] JC de de Jong, ECJ Claas, Albert DME Osterhaus, Robert G Webster, and WL Lim. "A pandemic warning?" In: *Nature* 389.6651 (1997), pp. 554–554.
- [16] Jimeno Estanislau, Federico Hermogenes, and Bernardo Clemente. "Battery Energy Transformation and Unravelling the Thermodynamics of Energy Storage and Conversion". In: Fusion of Multidisciplinary Research, An International Journal (FMR) 2.1 (2021), pp. 122–135.
- [17] Adam J Kucharski. "Immunity's illusion". In: Scientific American 311.6 (2014), pp. 80–85.
- [18] J Banks, E Speidel, and DJ Alexander. "Characterisation of an avian influenza A virus isolated from a human–is an intermediate host necessary for the emergence of pandemic influenza viruses?" In: *Archives of virology* 143 (1998), pp. 781–787.
- [19] Lone Simonsen, Cécile Viboud, Robert J Taylor, and Mark A Miller. "The epidemiology of influenza and its control". In: *Influenza vaccines for the future* (2011), pp. 27–54.
- [20] Bauyrzhan Satipaldy, Taigan Marzhan, Ulugbek Zhenis, and Gulbadam Damira. "Geotechnology in the Age of AI: The Convergence of Geotechnical Data Analytics and Machine Learning". In: Fusion of Multidisciplinary Research, An International Journal (FMR) 2.1 (2021), pp. 136–151.

- [21] Jeffery K Taubenberger, John C Kash, and David M Morens. "The 1918 influenza pandemic: 100 years of questions answered and unanswered". In: *Science translational medicine* 11.502 (2019), eaau5485.
- [22] Svenn-Erik Mamelund. "Influenza, historical". In: Medicine 54 (2008), pp. 361-371.
- [23] Paul Shapshak, Francesco Chiappelli, Charurut Somboonwit, and John Sinnott. "The influenza pandemic of 2009: lessons and implications". In: *Molecular diagnosis & therapy* 15 (2011), pp. 63–81.
- [24] ChoHee Kim, Donghyun Gwan, and Minho Sena Nam. "Beyond the Atmosphere: The Revolution in Hypersonic Flight". In: *Fusion of Multidisciplinary Research, An International Journal (FMR)* 2.1 (2021), pp. 152–163.
- [25] Ronn Pineo. "Four flu pandemics: lessons that need to be learned". In: *Journal of Developing Societies* 37.4 (2021), pp. 398–448.
- [26] Lizabeth Hardman. Influenza Pandemics. Greenhaven Publishing LLC, 2011.
- [27] Philippe RS Lagace-Wiens, Ethan Rubinstein, and Abba Gumel. "Influenza epidemiology—past, present, and future". In: *Critical care medicine* 38 (2010), e1–e9.
- [28] Marc Heylen, Patrick Bossuyt, Philippe Provoost, David Borremans, and Christine Rampelberg. "Making Antennas for 6G". In: Fusion of Multidisciplinary Research, An International Journal (FMR) 3.1 (2022), pp. 235–247.
- [29] John S Oxford and Douglas Gill. "Unanswered questions about the 1918 influenza pandemic: origin, pathology, and the virus itself". In: *The Lancet Infectious Diseases* 18.11 (2018), e348–e354.
- [30] John J Cannell, Michael Zasloff, Cedric F Garland, Robert Scragg, and Edward Giovannucci. "On the epidemiology of influenza". In: *Virology journal* 5 (2008), pp. 1–12.
- [31] Valdemar Johansen, Malthe Rasmussen, and Arne Knudsen. "Dielectric Constants and Their Role in Plasma Simulation". In: Fusion of Multidisciplinary Research, An International Journal (FMR) 3.1 (2022), pp. 248–260.
- [32] Fabio Bagnoli, Barbara Baudner, Ravi PN Mishra, Erika Bartolini, Luigi Fiaschi, Paolo Mariotti, Vincenzo Nardi-Dei, Phil Boucher, and Rino Rappuoli. "Designing the next generation of vaccines for global public health". In: *Omics: a journal of integrative biology* 15.9 (2011), pp. 545–566.
- [33] Mark Glickman and Meena Doshi. "Here's to Your Health: Assessing the Seasonality of Influenza". In: *CHANCE* 24.2 (2011), pp. 53–59.
- [34] Jessica M Donnelly. "" A Serious Matter and Something of a Mystery": 1918 Influenza in the New York Times and the London Times". MA thesis. Idaho State University, 2017.
- [35] Ramandeep Kaur Virk, Vithiagaran Gunalan, and Paul Anantharajah Tambyah. "Influenza infection in human host: challenges in making a better influenza vaccine". In: *Expert review of anti-infective therapy* 14.4 (2016), pp. 365–375.
- [36] Josef Baumgartner, Alexandra Schneider, Ulugbek Zhenis, Franz Jager, and Josef Winkler. "Mastering Neural Network Prediction for Enhanced System Reliability". In: *Fusion of Multidisciplinary Research, An International Journal (FMR)* 3.1 (2022), pp. 261–274.
- [37] Saverio Caini, Winston Andrade, Selim Badur, Angel Balmaseda, Amal Barakat, Antonino Bella, Abderrahman Bimohuen, Lynnette Brammer, Joseph Bresee, Alfredo Bruno, et al. "Temporal patterns of influenza A and B in tropical and temperate countries: what are the lessons for influenza vaccination?" In: *PloS one* 11.3 (2016), e0152310.
- [38] Casimir A Kulikowski. "Pandemics: historically slow "learning curve" leading to biomedical informatics and vaccine breakthroughs". In: *Yearbook of medical informatics* 30.01 (2021), pp. 290–301.
- [39] Michelle Harris. Vaccines: The Truth Behind the Debates. Greenhaven Publishing LLC, 2019.

- [40] William Coetzee, Reiner Khumalo, Brendan Le Roux, and Ebrahim Van Wyk. "Sickle Cell Disease: Causes, Symptoms, and Treatment". In: *Fusion of Multidisciplinary Research, An International Journal (FMR)* 3.1 (2022), pp. 275–286.
- [41] Kunjal Dave and Patricia C Lee. "Global geographical and temporal patterns of seasonal influenza and associated climatic factors". In: *Epidemiologic reviews* 41.1 (2019), pp. 51–68.
- [42] Alison Mack, Eileen R Choffnes, and David A Relman. *The domestic and international impacts of the 2009-H1N1 influenza a pandemic: global challenges, global solutions: workshop summary.* National Academies Press, 2010.
- [43] Carlo Caduff. The pandemic perhaps: dramatic events in a public culture of danger. Univ of California Press, 2015.