

# Toward Comprehensive Immunization: The Role of Combined COVID-19 and Influenza Vaccines in Public Health

Satish Kumar Sarankar<sup>1,\*</sup>, Santosh Ojha<sup>2</sup>, Neetu Sahu<sup>2</sup>, Monika Pawar<sup>3</sup>, Priyanka Shrivastava<sup>3</sup>

## Abstract

*The emergence of multi-pathogen vaccines, particularly those combining protection against COVID-19 and influenza, marks a significant advancement in immunization efforts. These combination vaccines have the potential to streamline vaccination processes, improve vaccine uptake, and reduce the burden on healthcare systems by offering a single dose that targets both viruses. COVID-19 and seasonal influenza are major public health concerns, with overlapping symptoms and seasonal patterns that justify the rationale for a combined vaccine approach. Recent technological advancements, especially mRNA and viral vector platforms, have paved the way for the rapid development of these combination vaccines. This review explores the current progress in developing COVID-19 and flu combo vaccines, highlighting key players, clinical trials, and the potential public health benefits. It also addresses the challenges, such as immune interference, manufacturing complexities, and regulatory hurdles that must be overcome for successful implementation. Furthermore, the implications for public health, including increased vaccination rates, cost-effectiveness, and reduced strain on healthcare systems, are discussed. Ensuring equitable global access and distribution of these vaccines is crucial to their impact, especially in resource-limited settings. Looking forward, the review touches on future innovations, including the development of vaccines targeting other respiratory pathogens and the potential for universal vaccines. The combined COVID-19 and flu vaccine represents a promising step toward more comprehensive and efficient vaccination strategies, contributing to improved global health outcomes.*

**Keywords:** COVID-19, influenza, multi-pathogen vaccines, mRNA vaccine technology, public health immunization

### \*Author for Correspondence

Satish Kumar Sarankar

E-mail: satish\_sarankar@yahoo.co.in

<sup>1</sup>Professor & Principal, Faculty of Pharmacy, Mansarovar Global University, Sehore, Madhya Pradesh, India

<sup>2</sup>Associate Professor, Faculty of Pharmacy, Mansarovar Global University, Sehore, Madhya Pradesh, India

<sup>3</sup>Assistant Professor, Faculty of Pharmacy, Mansarovar Global University, Sehore, Madhya Pradesh, India

Received Date: September 23, 2024

Accepted Date: October 09, 2024

Published Date: November 16, 2024

**Citation:** Satish Kumar Sarankar, Santosh Ojha, Neetu Sahu, Monika Pawar, Priyanka Shrivastava. Toward Comprehensive Immunization: The Role of Combined COVID-19 and Influenza Vaccines in Public Health. International Journal of Vaccines. 2025; 2(1): 9–17p.

## INTRODUCTION

COVID-19 and influenza are two of the most significant respiratory illnesses affecting global public health. Both diseases pose serious health threats, leading to high morbidity, mortality, and substantial economic and social disruption. Although they are caused by different viruses—SARS-CoV-2 for COVID-19 and the influenza virus for flu, they share several clinical features, including fever, cough, and respiratory distress [1]. The overlapping symptoms and their potential to cause widespread outbreaks make it essential to address both diseases concurrently, especially during the flu season when the simultaneous circulation of these viruses can overwhelm healthcare systems [2].

The novel coronavirus SARS-CoV-2 has caused the COVID-19 pandemic which quickly spread around the world at the end of this year. COVID-19 primarily spreads through respiratory droplets and close contact, though airborne transmission can occur, particularly in poorly ventilated spaces. Acute Respiratory Distress Syndrome (ARDS) acute pneumonia and quiet symptoms are various symptoms that may occur together with this disease [3]. In severe cases, COVID-19 can lead to multiorgan failure and death, especially in older adults and individuals with preexisting health conditions. COVID-19 has a notable impact on global health due to its high transmissibility and the potential for severe disease outcomes. Public health measures, such as wearing a mask social distancing and lockdown have been taken to prevent the spread of the virus. However, these measures have social and financial implications. Reducing the severity of COVID-19 And much of this reduction in transmission has been made possible by the rapid development and distribution of vaccines. However, with the virus continually evolving, new variants pose a challenge to long-term control efforts. Therefore, achieving high vaccination coverage and developing strategies to manage future variants are crucial [4] influenza virus. In particular, strains A and B are seasonal causes of influenza. Also known as the flu. It affects millions of people worldwide annually, leading to a significant number of hospitalizations and deaths, particularly among the elderly, young children, and individuals with underlying health conditions. When an infected person coughs, sneezes, or talks, respiratory droplets are released into the air. This causes influenza to be incredibly contagious. Symptoms include fever, cough, sore throat, and body aches and tired. It is the most common symptom. While most people recover within a few weeks, influenza can cause severe complications, such as pneumonia, bronchitis, and worsening of chronic health problems [5]. Influenza's seasonal nature and the virus's capacity to mutate frequently through antigenic drift and shift-poses a unique challenge for public health. Although the efficacy of annual flu vaccinations varies, they are produced based on estimates of circulating strains. The need for yearly vaccination, coupled with vaccine hesitancy in some populations, often results in suboptimal coverage. Despite the availability of antiviral medications, their effectiveness is highest when administered early in the course of illness, and they do not replace the need for vaccination as the primary preventive measure [6].

The simultaneous circulation of COVID-19 and influenza poses a dual threat, particularly during the flu season. Both viruses can lead to respiratory illnesses that strain healthcare resources, increase hospitalizations, and cause significant mortality, especially among vulnerable populations [7]. The co-occurrence of these diseases can lead to diagnostic challenges due to their overlapping symptoms, complicating clinical management and increasing the risk of severe outcomes if patients contract both infections simultaneously [8].

A combined COVID-19 and influenza vaccine represents a strategic advancement in public health efforts. It can simplify vaccination efforts by reducing the number of healthcare visits required, improving vaccine coverage, and enhancing population immunity against both viruses. By leveraging advanced vaccine technologies like mRNA and viral vectors, scientists aim to create an effective and safe multi-pathogen vaccine that provides broad protection with a single dose [9]. Such a combined approach can mitigate the seasonal and pandemic threats posed by these respiratory viruses, ultimately reducing the burden on healthcare systems and improving health outcomes globally.

## **BACKGROUND ON COVID-19 AND INFLUENZA**

Both COVID-19, caused by the SARS-CoV-2 virus, and influenza, caused by the influenza virus, are respiratory diseases that spread through airborne droplets. They share similar symptoms, including fever, cough, and fatigue, but differ in severity, with COVID-19 generally posing a greater threat due to its higher transmission rate and severity in vulnerable populations.

*COVID-19:* The pandemic, which began in late 2019, has caused millions of deaths worldwide, prompting an unprecedented global vaccine development effort. A notable scientific achievement has been the rapid development and commercialization of COVID-19 vaccines, especially mRNA vaccines like those produced by Moderna and Pfizer-Biontech [10].

*Influenza:* Influenza, on the other hand, is a more familiar but still serious disease, particularly during the flu season. The World Health Organization (WHO) estimates that seasonal influenza kills up to 650,000 people and causes 3–5 million serious illnesses each year. Annual flu vaccination is a cornerstone of preventing this seasonal burden, but flu vaccines must be updated regularly due to the virus's frequent mutations [11].

Given the shared seasonality of these two illnesses and the ongoing COVID-19 pandemic, the rationale for developing a combined vaccine is strong. It could simplify the vaccination process, improve compliance, and reduce logistical challenges.

## **SCIENTIFIC FOUNDATIONS OF MODERN VACCINE TECHNOLOGIES**

Conventional vaccine technologies, such as inactivated and live-attenuated vaccines, have been the foundation of immunization for decades. These vaccines rely on using killed or weakened forms of pathogens to stimulate an immune response, offering effective protection against diseases like measles, polio, and influenza. While successful, conventional methods often require lengthy production times, complex storage conditions, and multiple doses to ensure long-lasting immunity. Additionally, they are sometimes less adaptable to rapidly evolving pathogens like COVID-19. The need for advanced vaccine technologies has emerged to address these limitations. Innovations, such as mRNA and viral vector vaccines offer faster development, more targeted immune responses, and greater adaptability, making them essential tools in combating modern infectious diseases and pandemics.

Over the past few decades, vaccine technology has advanced significantly, shifting from traditional methods to more sophisticated and targeted approaches. Here is an in-depth exploration of the various vaccine platforms, along with their scientific rationale:

### **Inactivated Vaccines**

Inactivated vaccines contain germs which are bacteria or viruses that are killed or killed to prevent disease. Usually, heat or chemical agents like formaldehyde are used in the inactivation process. By exposing the immune system to the pathogen's structural elements without running the danger of spreading the disease, these vaccinations elicit an immunological response. These substances are recognized as foreign by the immune system, which stimulates the production of antibodies. In case the body encounters the virus again. This response helps identify and eliminate the virus. Inactivated vaccines that are safe for people with compromised immune systems are easy to store and very stable [12]. When the immune system recognizes these substances as foreign antibodies are created. If the virus comes back to spread again. This response helps the body recognize and eliminate the virus. Inactivated vaccines are reasonably stable and easy to store. This makes it safe for use in patients with compromised immune systems.

### **Live-Attenuated Vaccines**

Live vaccines use weakened or attenuated viruses or bacteria. When germs are modified to be less virulent and able to spread. A powerful immune response is stimulated live vaccines closely mimic the real disease and stimulates a strong and durable immune response. Exposure of the immune system to potential organisms. Even though there is a risk of germs, the organism causes a strong induction of the body's immune response (using antibodies) and cells live vaccines generally induce a strong and long-lasting immune response. They usually provide lifelong immunity after just one or two doses [13, 14]. However, they are not suitable for immunocompromised individuals, as even a weakened pathogen can pose health risks. Additionally, they require careful storage to maintain their viability, often needing refrigeration to remain effective.

### **Subunit, Recombinant, and Conjugate Vaccines**

These vaccines include only parts of the pathogen (subunits), such as proteins, that are sufficient to stimulate an immune response. Recombinant vaccines use genetically engineered technology to

produce these proteins in a lab setting. Conjugate vaccines increase immunogenicity by attaching the polysaccharides of the pathogen to a carrier protein. By using specific components of the pathogen, these vaccines focus the immune system's response on key antigens critical for protection. With this focused strategy, less chance of adverse reactions while still stimulating a strong immune response. Subunit, recombinant, and conjugate vaccines are safer because they do not use live components of the pathogen. They can also be tailored to provoke a strong immune response against specific parts of the pathogen. However, they may require the use of adjuvants (substances that enhance the immune response) and multiple doses to achieve sufficient immunity [15, 16]. Additionally, they are often less effective in young children unless conjugated with a carrier protein to enhance their immunogenicity.

### **Messenger RNA Vaccines or mRNA-Driven Immunization**

Messenger RNA vaccines (mRNA vaccines) use a segment of the genetic code (mRNA) that encodes a viral protein, typically the spike protein of SARS-CoV-2 in the case of COVID-19 vaccines. This mRNA is delivered into cells, where it is used as a template to produce the viral protein, which in turn stimulates an immune response. Like traditional vaccines, mRNA vaccines do not use live virus particles. Instead, they harness the body's cellular machinery to produce the antigen, which is then recognized by the immune system as foreign [17]. Consequences include T-cell activation and the production of neutralizing antibodies. mRNA vaccines can be rapidly developed and easily adapted to target different strains or new pathogens, offering flexibility in response to emerging health threats. mRNA vaccines offer the advantages of a rapid development and manufacturing process, along with a high safety profile since they do not involve the use of a live virus. It also stimulates a powerful and focused immune response. However, these vaccines require ultra-cold storage, which complicates distribution in areas lacking advanced refrigeration facilities [18]. Additionally, long-term data on the duration of immunity and potential side effects are still being studied.

### **Viral Vector Vaccines**

Viral vaccines recruit harmless viruses (vectors) to pass on genes that encode antigens upon infection. The vector enters the cell and teaches it how to make an antigen, which triggers an immune response. Examples include the AstraZeneca and Johnson & Johnson COVID-19 vaccines, which use adenoviruses as vectors [19]. By using a viral vector to introduce genetic material into the body, these vaccines induce a robust immune response. The vector acts as a delivery system, allowing the body to produce the antigen internally and trigger a natural immune response, including both antibody production and T-cell activation. Viral vector vaccines are designed to provoke a strong immune memory, offering long-lasting protection [20]. Viral vector vaccines can induce strong, long-lasting immunity with just a single dose and have the capacity to deliver large quantities of antigen genes. However, their efficacy can be reduced if there is preexisting immunity to the viral vector in the population. Additionally, they may face more complex regulatory approval processes due to the use of a live virus vector.

### **Protein Subunit Vaccines**

These vaccines contain harmless pieces of the virus (often proteins) that stimulate the immune system without causing disease. Novavax's COVID-19 vaccine, which uses the spike protein of SARS-CoV-2, is an example. Protein subunit vaccines reduce the chance of side effects by containing only the essential antigens needed to trigger an immune response. They target specific parts of the virus that are critical for immune recognition, often resulting in high levels of neutralizing antibodies [21]. Protein subunit vaccines are safer because they do not contain live pathogens and are suitable for individuals with weakened immune systems. Boosters and multiple doses are often required to guarantee an adequate immune response. Additionally, their production can be complex and time-consuming.

### **DNA Vaccines**

DNA vaccines involve injecting genetic material (DNA) that codes for antigens directly into cells. Using this DNA, antigens produced by cells trigger a subsequent immune response. DNA vaccines

show great potential for treating various diseases, including COVID-19. They represent an innovative approach by directly delivering the genetic blueprint for the antigen into the body's cells, enabling these cells to produce the antigen themselves [22]. This internal production can trigger a strong immune response, activating both B cells and T cells. Additionally, DNA vaccines are stable, easy to manufacture, and can be quickly designed and adapted to target emerging pathogens. However, they have historically demonstrated lower immunogenicity in humans compared to animal models, and the efficient delivery of DNA into human cells remains a significant technical challenge [23].

Each of these vaccine technologies offers unique benefits and drawbacks, and their use depends on the specific pathogen, target population, and logistical considerations. The development of multi-pathogen vaccines, such as the combination of COVID-19 and flu vaccines, particularly benefits from platforms like mRNA and viral vectors due to their flexibility, rapid development, and ability to target multiple antigens simultaneously.

## **DEVELOPMENT OF A COMBINATION VACCINE TO PREVENT COVID-19 AND INFLUENZA**

Several pharmaceutical companies and research institutions are already exploring the possibility of combining COVID-19 and flu vaccines into a single shot. Although clinical trials are underway to evaluate the safety and efficacy of the new combination vaccine, this development is still in its early stages.

### **Current Progress**

In 2021, Moderna announced its plans to develop a combined mRNA vaccine that targets both COVID-19 and seasonal flu. This initiative aims to streamline annual vaccination by offering protection against both diseases in a single dose. Moderna's mRNA platform, which proved highly effective in the COVID-19 vaccine, offers flexibility in updating the vaccine to match circulating flu strains and emerging COVID-19 variants [24]. Another key player is Novavax, which has begun clinical trials of its own COVID-19 and flu combination vaccine. Novavax's candidate uses a protein-based approach, combining their COVID-19 vaccine with their experimental flu vaccine.

### **Clinical Trials**

Preliminary trials focus on determining whether these vaccines can induce a robust immune response to both viruses simultaneously. Early results are promising, with some studies showing that individuals receiving the combined vaccine have immune responses comparable to those receiving the vaccines separately.

The ability to protect against multiple pathogens in a single vaccine could be particularly advantageous for older adults and other high-risk populations who already face a heavy vaccination burden [25].

## **CHALLENGES IN DEVELOPING COMBINATION VACCINES**

Developing a vaccine that effectively targets two different pathogens poses several challenges. In addition to the technical aspects, these issues also include logistics and regulations.

### **Immune Interference**

One of the primary biological challenges is the potential for immune interference. When multiple antigens are included in a single vaccine, the immune system may not respond equally to all of them. This could result in a weaker immune response to one or both pathogens. Scientists must carefully balance the immune-stimulating components to ensure that both the flu and COVID-19 components elicit strong and protective immune responses [26].

### **Manufacturing Complexities**

Producing combination vaccines is more complex than manufacturing single-pathogen vaccines. This is especially true of mRNA vaccines, which require special handling and storage procedures.

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Ensuring that the vaccine remains stable and effective during production, distribution, and administration is crucial.

*Regulatory barriers:* To ensure safe and effective combination vaccinations regulatory agencies, such as the European Medicines Agency and the US Food and Drug Administration require extensive testing. The approval process for combination vaccines can be longer than for single vaccines, as regulatory bodies must assess the safety of delivering multiple antigens at once [27].

Despite these challenges, the potential benefits of combination vaccines make overcoming these obstacles a high priority for public health organizations and pharmaceutical companies alike.

## **PUBLIC HEALTH CONSIDERATIONS**

A combined COVID-19 and influenza vaccine could have significant implications for public health. By streamlining the vaccination process, it has the potential to increase vaccination rates and enhance protection against both diseases. This approach not only simplifies immunization efforts for individuals but also helps to reduce the burden on healthcare systems during peak infection seasons, ultimately leading to better health outcomes for the population.

### **Increased Uptake**

One of the main advantages of combination vaccines is the convenience for patients. Instead of needing separate appointments or vaccines for flu and COVID-19, individuals could receive one shot that covers both diseases. This is especially important for populations that may be hesitant to get multiple vaccines or who may have difficulty accessing healthcare [28].

### **Cost-Effectiveness**

Administering a single vaccine instead of two separate ones could reduce healthcare costs. Fewer appointments, reduced logistical challenges, and lower storage and transportation costs could lead to significant savings for healthcare systems. Due to limited resources low- and middle-income countries should therefore pay special attention to this issue.

### **Easing Healthcare Burden**

During the flu season, healthcare systems often experience a surge in patients, leading to strain on resources. The addition of COVID-19 exacerbates this burden. A combined vaccine could help alleviate some of the pressure on healthcare systems by reducing the number of appointments and simplifying vaccine administration [29].

## **GLOBAL ACCESS AND DISTRIBUTION**

Ensuring global access to combination vaccines is essential for maximizing their public health impact. However, the distribution of vaccines has often been unequal, particularly for COVID-19.

### **Vaccine Inequality**

Uneven distribution of vaccines has emerged as one of the main problems arising from the COVID-19 pandemic. Rich countries can win majorities. As a result, low-income countries are restricted from access. Ensuring equitable access to combination vaccines will require coordinated efforts between governments, international organizations, and vaccine manufacturers [30].

### **Role of International Organizations**

Organizations like the WHO and GAVI, the Vaccine Alliance, will play a critical role in ensuring that combination vaccines are distributed fairly. Their work in securing and distributing vaccines for low-income countries will be essential for preventing global outbreaks of both COVID-19 and influenza [31].

### **Future Directions and Innovations**

The development of a combined COVID-19 and flu vaccine is just the beginning. As vaccine technologies continue to evolve, the potential for multi-pathogen vaccines grows.

### **Other Pathogens**

Beyond COVID-19 and flu, researchers are exploring the possibility of combining vaccines for other respiratory illnesses like respiratory syncytial virus and pneumococcal infections. These pathogens, along with flu and COVID-19, represent significant public health burdens, particularly for the elderly [32, 33].

### **Advances in Delivery Systems**

Innovations in vaccine delivery systems, such as microneedle patches, could further simplify the vaccination process. These patches could allow individuals to self-administer vaccines, reducing the need for healthcare appointments and increasing accessibility in remote areas [34].

### **Universal Vaccines**

One of the most exciting areas of research is the development of universal vaccines that could provide long-lasting protection against multiple strains or even different types of pathogens. Universal flu vaccines, for example, aim to provide broad protection against all flu strains, potentially eliminating the need for annual updates [35].

## **CONCLUSIONS**

The development of multi-pathogen vaccines, such as a combined COVID-19 and flu vaccine, represents a significant advancement in the field of immunization and public health. By integrating protection against two major respiratory illnesses into a single dose, these vaccines have the potential to simplify vaccination efforts, increase uptake, and ease the burden on healthcare systems globally. The progress made in combining vaccines reflects the remarkable innovations in vaccine technology, particularly with platforms like mRNA and viral vectors. These technologies not only offer a robust immune response but also provide the flexibility needed to address the challenges of combining multiple antigens effectively.

The widespread use of combination vaccinations is hampered, though. Technical challenges, including potential immune interference and manufacturing complexities, must be addressed to ensure that these vaccines are both safe and effective. Additionally, navigating the regulatory landscape and ensuring equitable access across different regions are critical to maximizing the benefits of these vaccines. Looking ahead, the potential for multi-pathogen vaccines extends beyond COVID-19 and influenza. As research progresses, the possibility of combining vaccines for other infectious diseases and developing universal vaccines could further revolutionize public health strategies.

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