Respiration

Clinical Investigations

Respiration
DOI: 10.1159/000544919

Received: November 29, 2024
Accepted: February 13, 2025
Published online: March 9, 2025

Vaccination Strategies in Respiratory Diseases: Recommendation from AIPO-ITS/ETS, SIMIT, SIP/IRS, and SItI

Claudio Micheletto[a] Stefano Aliberti[b, c] Massimo Andreoni[d] Francesco Blasi[e, f] Fabiano Di Marco[g] Rosa Di Matteo[h] Giovanni Gabutti[i] Sergio Harari[j, k] Ivan Gentile[l] Roberto Parrella[m] Roberta Siliquini[n] Laura Sticchi[o]

on behalf of Associazione Italiana Pneumologi Ospedalieri – Italian Thoracic Society (AIPO-ITS/ETS), Società Italiana di Malattie Infettive e Tropicali (SIMIT), Società Italiana di Pneumologia/Italian Respiratory Society (SIP/IRS), Società Italiana di Igiene Medicina Preventiva e Sanità Pubblica (SItI)

[a]Respiratory Unit, Integrated University Hospital of Verona, Verona, Italy; [b]Department of Biomedical Sciences, Humanitas University, Milan, Italy; [c]Respiratory Unit, IRCCS Humanitas Research Hospital, Milan, Italy; [d]Department of System Medicine, Infectious Disease Clinic, University of Tor Vergata, Rome, Italy; [e]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; [f]Respiratory Unit and Cystic Fibrosis Center, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy; [g]Department of Health Science, University of Milan, ASST Papa Giovanni XXIII, Bergamo, Italy; [h]Respiratory Unit, Hospital Antonio Cardarelli, Naples, Italy; [i]National Coordinator Working Group Vaccines and Immunization Policies, Italian Scientific Society of Hygiene, Preventive Medicine and Public Health (SItI), Cogorno, Italy; [j]Division of Pulmonary and Respiratory Intermediate Care Unit, MultiMedica IRCCS, Milan, Italy; [k]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [l]Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy; [m]Respiratory Infection Diseases Unit, Cotugno Hospital, AORN Ospedali dei Colli, Naples, Italy; [n]University of Torino, AOU Città della Salute e della Scienza, Torino, Italy; [o]University of Genoa, IRCCS Ospedale Policlinico San Martino, Genoa, Italy

Keywords
Respiratory diseases · Vaccination strategies · Chronic respiratory infections · Preventive healthcare · Immunization recommendations

Abstract
Background: Chronic respiratory diseases, including asthma, chronic obstructive pulmonary disease, and bronchiectasis, are significant global health concerns associated with recurrent exacerbations, hospitalization, and increased mortality. Preventive strategies, particularly vaccination, play a crucial role in managing these diseases by reducing

karger@karger.com
www.karger.com/res

Correspondence to:
Claudio Micheletto, claudio.micheletto@aovr.veneto.it

infection-related exacerbations and stabilizing lung function. ***Summary:*** This review summarizes the recommendations provided by four major Italian scientific societies on vaccination against key respiratory pathogens, including respiratory syncytial virus, influenza, SARS-CoV-2, *Streptococcus pneumoniae*, and varicella zoster virus, which pose serious risks to individuals with chronic respiratory conditions. Evidence supporting the role of vaccines in minimizing exacerbations and improving patient outcomes in asthma, chronic obstructive pulmonary disease, and bronchiectasis is highlighted, alongside recent advancements in vaccine technology and recommendations for high-risk populations. This expert-led, multidisciplinary approach underlines the necessity of targeted immunization strategies to mitigate complications, lower healthcare costs, and enhance the quality of life for patients with respiratory diseases. ***Key Messages:*** By collecting the latest evidence-based recommendations, this article aims to guide healthcare providers in adopting optimal vaccination strategies for respiratory disease management and contribute to the broader public health effort to reduce the burden of respiratory infections.

Introduction

Chronic respiratory diseases, such as asthma, chronic obstructive pulmonary disease (COPD), and bronchiectasis, are significant and growing health concerns globally. According to the Global Burden of Disease study, COPD is now the third leading cause of death worldwide. At the same time, asthma affects over 350 million people, contributing to substantial healthcare costs and reduced quality of life [1, 2]. These diseases are characterized by recurrent exacerbations that have severe implications for disease progression, lung function decline, and overall prognosis [3–5].

Exacerbation is frequently triggered by respiratory infections, which act as primary environmental stressors in susceptible individuals. Respiratory viruses, such as influenza, respiratory syncytial virus (RSV), and SARS-CoV-2, are particularly common culprits, while bacterial infections, particularly *Streptococcus pneumoniae*, are also significant contributors [6–8]. In patients with asthma, COPD, and bronchiectasis, these infections not only precipitate exacerbations but also increase the risk of hospitalization, mechanical ventilation, and mortality [9–12].

Given the pivotal role of infections in exacerbating respiratory diseases, preventive strategies are essential for maintaining stable lung function and reducing healthcare utilization. Vaccination is a cornerstone of such preventive measures, offering protection against common respiratory pathogens and thereby reducing the frequency and severity of exacerbations [13]. For instance, seasonal influenza vaccination can reduce exacerbations in COPD patients by up to 40%, while pneumococcal vaccination significantly decreases the risk of invasive pneumococcal disease and community-acquired pneumonia [14].

The COVID-19 pandemic has further underscored the importance of respiratory infection control, particularly in vulnerable populations such as individuals with asthma, COPD, and bronchiectasis [15]. Vaccination against SARS-CoV-2 has become a priority, as evidence indicates that individuals with these conditions are at a higher risk of severe outcomes if infected with the virus [16, 17]. Additionally, new advancements in RSV vaccines for older adults and those with chronic conditions represent promising tools to prevent viral-induced exacerbations [18].

While much attention has been focused on respiratory pathogens, there is growing recognition of the importance of preventing non-respiratory infections, such as herpes zoster (HZ), in individuals with chronic respiratory diseases. Patients with asthma and COPD are at increased risk of HZ due to impaired immune responses associated with these conditions, the use of corticosteroids, and the overall burden of chronic disease [19]. HZ reactivation can not only lead to severe complications, such as post-herpetic neuralgia (PHN) but also indirectly exacerbate underlying respiratory conditions through systemic inflammation and prolonged recovery periods. Vaccination against HZ, particularly with the recombinant zoster vaccine (RZV), is an essential tool in preventing these outcomes and improving the overall health and quality of life for patients with chronic respiratory diseases.

Recognizing the crucial role of vaccination in managing patients with these infections, four leading Italian scientific societies have provided recommendations on vaccination against five key pathogens: RSV, influenza, SARS-CoV-2, *S. pneumoniae*, and varicella zoster virus. These recommendations aim to optimize preventive care and improve outcomes for individuals with asthma, COPD, and bronchiectasis, who are particularly vulnerable to infections and their complications.

Risk Groups for Vaccination

Individuals at higher risk of severe respiratory infections and complications should be prioritized for vaccination. These include people with chronic diseases,

immunosuppressive conditions, and lifestyle factors that increase their susceptibility to infections. The primary risk conditions that warrant specific vaccination strategies are the following:

- Chronic respiratory diseases: patients with COPD, asthma, bronchiectasis, and interstitial lung diseases are at increased risk of exacerbations and complications from respiratory infections [20].
- Cardiovascular diseases: conditions such as heart failure, ischemic heart disease, and hypertension have been associated with a higher risk of severe outcomes from respiratory infections [21, 22].
- Diabetes mellitus: both type 1 and type 2 diabetes increase susceptibility to infections due to immune system dysfunction [23].
- Immunosuppressive conditions: patients with cancer, those undergoing chemotherapy, organ transplant recipients, and individuals with HIV have impaired immune responses, making them more vulnerable to severe infections [24].
- Chronic kidney and liver diseases: chronic kidney disease and cirrhosis are associated with increased risk of invasive bacterial infections, including pneumococcal and viral infections [25].
- Neurological diseases: neuromuscular disorders that impair respiratory function, such as amyotrophic lateral sclerosis and multiple sclerosis, elevate the risk of complications from respiratory infections [26].
- Tobacco smoking: active smoking impairs mucosal defenses and increases susceptibility to infections, such as influenza, pneumococcus, and RSV [27].
- Occupational exposure: healthcare workers and individuals exposed to industrial pollutants are at higher risk of respiratory infections due to prolonged exposure to airborne pathogens [28].

Methods

A multidisciplinary board of experts in respiratory, infectious diseases, and public health was established to promote best practices in preventing hazardous infection in subjects with asthma and COPD. The final goal was to create a document that collects recommendations, providing a valuable review to facilitate knowledge exchange.

The project comprised different phases, during which the experts met to define the roles of each participant and establish the research objectives. The aim was to select the best practices for inclusion in the project, relying on the participants' expertise in respiratory diseases. During the meeting's brainstorming, each scientific board member presented their approach to patient management, including therapy and vaccination, and hypothesized a model for future prevention.

Relevant literature in the field was selected by conducting a PubMed/MEDLINE search based on the following research strategies: "respiratory diseases" AND "infections" OR "SARS-CoV-2" OR "HZV" OR "RSV" OR "influenza" OR "pneumococcus." The search was updated within 5 years (2019–2024).

Respiratory Syncytial Virus

Background

Respiratory syncytial virus (RSV) poses a significant risk to specific populations due to various predisposing factors. Severe RSV infection primarily affects infants under 1 year of age and older adults, particularly those aged 60 years and older. Individuals with chronic respiratory diseases, such as COPD, asthma, and bronchiectasis, are at increased risk of severe outcomes. Comorbidities, including cardiovascular diseases, diabetes, renal insufficiency, and compromised immune systems due to conditions, such as HIV or cancer, also heighten susceptibility to RSV infections. Additionally, immunosuppressed individuals, such as those undergoing chemotherapy, organ transplant recipients, or those on long-term corticosteroid therapy, are more prone to complications. Premature infants and those with low birth weight have underdeveloped lungs and immune systems, making them particularly vulnerable to RSV. Socioeconomic factors, such as overcrowded living conditions and limited access to healthcare, further contribute to increased exposure and risk of infection [29, 30]. RSV is the most frequent cause of respiratory infections in children, accounting for about 60% of acute respiratory infections in children under 5 and more than 80% in infants under 1 year of age [31]. In healthy adults, RSV typically causes mild respiratory symptoms; however, severe or even fatal forms are observed in individuals at higher risk due to advanced age or comorbidities. In Europe, RSV causes around 3 million cases of acute respiratory syndrome, 465,000 hospitalizations, and 33,000 hospital deaths annually among individuals over 60 years of age [21].

Since the 2019–2020 season, Italy has implemented RSV surveillance through the "RespiVirNet" system. The RSV season coincides with the flu season, starting in October or November and peaking between December and February. In adults and older individuals (≥60 years),

Table 1. Main risk conditions for respiratory infections

Risk factor/condition	Description	Indication for vaccination
Chronic respiratory diseases	COPD, asthma, bronchiectasis, interstitial lung diseases	High risk for severe outcomes
Cardiovascular diseases	Heart failure, ischemic heart disease, hypertension	Higher risk of complications
Diabetes mellitus	Type 1 and type 2 diabetes	Increased susceptibility to infections
Immunosuppressive conditions	Cancer, organ transplantation, HIV	Require vaccination to reduce risk of severe disease
Chronic kidney and liver diseases	Chronic kidney disease, cirrhosis	Elevated risk of invasive infections
Tobacco smoking	Active smokers	Increased susceptibility to respiratory infections
Occupational exposure	Healthcare workers, individual exposed to industrial pollutants	Higher exposure risk to respiratory pathogens
Degree of bronchial obstruction	FEV_1 <50%	Higher risk of severe respiratory infections

RSV significantly increases hospitalizations (three to five times), emergency visits, and outpatient visits, particularly among those with chronic conditions such as heart failure, asthma, and COPD. These conditions also increase the risk of severe outcomes and exacerbations [21, 22].

Currently, no specific antiviral drugs are available for RSV; however, passive immunoprophylaxis with monoclonal antibodies and active vaccination are effective preventive strategies. In the pre-fusion configuration, the F protein is the target antigen for both monoclonal antibodies and vaccines [32].

Several countries have already introduced RSV vaccination programs. In the USA, the Centers for Disease Control and Prevention (CDC) recommend a single dose of the RSV vaccine for all adults aged 75 years or older, as well as for adults aged 60–74 years who are at increased risk of severe RSV disease [33].

In the UK, the Joint Committee on Vaccination and Immunisation recommends RSV immunization for both newborns and adults over 75 years old [34]. In Ireland, the National Immunisation Advisory Committee (NIAC) recommends vaccination for individuals over 65 years old [35]. In Germany, the vaccination is recommended for adults aged 75 years or older, as well as for adults aged 60–74 who are at increased risk of severe RSV disease [36]. Austria, France, Norway, Sweden, Belgium, and Poland have also implemented similar vaccination guidelines for adults over 60 years and individuals at high risk [37–42].

In Italy, the Life Calendar Board recently issued a position paper advocating RSV vaccination in older individuals and high-risk adults. This proactive approach recommends vaccinating individuals over 60 years old with chronic diseases, as well as those over 75 years of age, to ensure immediate protection [43].

Target Population

RSV vaccination is recommended for adults aged 60 years and older, particularly those with chronic respiratory diseases, cardiovascular diseases, diabetes, or immunosuppression. Vaccination is also advised for younger adults with chronic conditions that increase their risk of severe RSV infections, as well as for pregnant women to protect newborns (Table 1) [44].

Available Vaccines

Recently, three vaccines for RSV have been approved by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). They are now available for use in high-risk populations, particularly among older adults.

The first available vaccine is a recombinant monovalent vaccine targeting RSV A, adjuvanted with AS01E. In a phase III trial, this vaccine exhibited an efficacy of 82.6% in preventing RSV-associated lower respiratory disease in individuals over 60 years of age. Notably, it showed 81% efficacy in people aged 60–69 years, 93.8% in those aged 70–79 years, and 94.6% in individuals with at least one comorbidity [18]. Furthermore, the vaccine

demonstrated an efficacy of 67.2% over two RSV seasons and of 62.9% over three seasons, maintaining significant protection against severe lower respiratory tract disease caused by RSV [18, 45]. The vaccination resulted in high coverage among older subjects with chronic cardiorespiratory or endocrine/metabolic comorbidities. Efficacy against respiratory syncytial virus – acute respiratory infections (RSV-ARI) was 81.0% in participants with ≥1 condition of interest (88.1% for cardiorespiratory, 79.4% for endocrine/metabolic conditions) and 88.0% in participants with ≥2 conditions of interest [46]. Postvaccination neutralizing titers were at least as high in participants with ≥1 condition of interest as in those without [37]. The vaccine not only prevented RSV infection but also reduced the severity of symptoms in cases of breakthrough infection, with a 42% decrease in symptom severity compared with placebo during the first season (1.07 vs. 1.86, $p = 0.0258$) [47].

The second vaccine is a recombinant bivalent non-adjuvanted vaccine containing the pre-fusion F protein from both RSV A and RSV B strains. This vaccine is approved for passive immunization of newborns, protecting them against lower respiratory tract disease caused by RSV during the first 6 months of life, following maternal immunization during pregnancy [48]. Additionally, it is approved for active immunization in adults aged 60 years and older to prevent RSV-related lower respiratory tract infections. The efficacy of the vaccine for active immunization in individuals aged 60 years and older for the prevention of lower respiratory tract disease caused by RSV was evaluated in a phase III clinical trial (RENOIR Study) [49]. The efficacy was found to be 65.1% against the first episode of RSV-associated lower respiratory tract infection with more than two symptoms and 88.9% against the first episode with more than three symptoms. The vaccine demonstrated efficacy over two RSV seasons [50]. No safety concerns were reported.

Additionally, an mRNA-based RSV vaccine has recently been approved by the FDA and EMA. This vaccine encodes the pre-fusion F protein of RSV A, intended for use in adults aged 60 years and older. Trials have shown promising results, with 83.7% efficacy in preventing RSV-related lower respiratory tract disease with two or more symptoms and 82.4% efficacy in cases involving three or more symptoms, with a median follow-up of 3.7 months. This vaccine has been generally well tolerated, with no major safety issues observed during the clinical trials [51]. The main characteristics of the three RSV vaccines are reported in Table 2 [52–54].

Adverse Effects and Management

The most commonly reported adverse effects for RSV vaccines include mild-to-moderate local reactions at the injection site (e.g., pain, redness, and swelling) and systemic symptoms such as fatigue, headache, and fever. Serious adverse effects, including severe allergic reactions, are rare. The relative risk of severe adverse events is estimated to be below 1 in 100,000 doses [52–55].

Appropriateness of Use

The Life Calendar Board recommends RSV vaccination for individuals aged 75 years and older, as this group is more likely to have chronic conditions, which significantly increase the risk of severe RSV-related complications. Likewise, RSV vaccination is recommended for individuals aged 60 years and older with chronic illnesses. The board encourages the inclusion of RSV vaccination in the routine immunization schedule for adults, focusing on individuals over 60 years with comorbidities, as well as older adults over 75 years of age. The objective was to offer immediate protection to these high-risk groups, ensuring they are shielded from severe RSV infections [43].

At present, there are no well-defined criteria for selecting a specific RSV vaccine based on patient characteristics. However, the central recommendation is to optimize and equitably use the available vaccines to prevent complications, hospitalizations, and mortality from RSV, particularly among vulnerable populations.

Recently, the first effectiveness results of protein-based vaccines have been published. These data show that RSV vaccination was effective in preventing RSV-associated hospitalizations (VE: 80%) and emergency department visits (VE: 77%) among adults aged 60 years and older in the USA during the 2023–2024 RSV season, the first season following RSV vaccine approval [56, 57].

Experts' Insight

RSV vaccination is currently authorized in patients aged 60 years or older, as they are considered at the highest risk of RSV disease and because current evidence is limited to this population. However, RSV vaccination may also be appropriate in adult patients younger than 60 years who suffer from pre-existing clinical conditions that are associated with a higher risk of severe RSV infection. These include patients with lung disease (such as COPD, asthma, and bronchiectasis), patients with cardiac, renal, hepatic, endocrine, metabolic, or neurological underlying diseases, oncologic patients, patients moderately severely immunocompromised and those with

Table 2. Main characteristics of RSV vaccines

Vaccine	RSVPreF3 (Arexvy® GSK) [52]	RSVpreF (Abrysvo® Pfizer) [53]	RSVpreF mRNA (mRESVIA® Moderna) [54]
Technology	Recombinant monovalent adjuvanted with AS01E	Recombinant bivalent non-adjuvanted	mRNA-based
Antigen	RSV recombinant glycoprotein F in pre-fusion conformation	Recombinant pre-fusion glycoprotein F from RSV A and RSV B	RSV glycoprotein F in pre-fusion form encoded by an mRNA sequence
Indication to use RCP (approved by EMA, November 2024)	Active immunization to prevent lower respiratory tract disease caused by RSV in adults aged 60+ years and in adults aged 50+ years at increased risk of severe RSV disease	Passive protection against RSV lower respiratory tract disease in newborns (up to 6 months) via maternal immunization during pregnancy. Active immunization for adults aged 60+ years against RSV lower respiratory tract disease	Active immunization to prevent lower respiratory tract disease caused by RSV in adults aged 60+ years
Presentation	Powder and suspension to be reconstituted before administration	To be reconstituted by adding the entire contents of a pre-filled syringe to the powder vial using a designated adapter	Pre-filled syringe, ready to use
Storage	Store in refrigerator (2–8°C)	Store in refrigerator (2–8°C)	Stored at −40°C to −15°C. After removal from the freezer, it can be stored at 2–8°C for up to 90 days
Adverse effects	Injection site reactions, fatigue, headache	Fever, muscle pain, nausea	Injection site swelling, fatigue

other underlying conditions that might increase the risk of severe respiratory disease (e.g., frailty, advanced age, residence in a nursing home).

Influenza

Background

The World Health Organization (WHO) recommends annual influenza vaccination as the primary means of preventing the disease, given the antigenic variability of the virus and the decline in immunity over time [58]. In Italy, annual influenza vaccination represents a critical preventive measure, particularly for individuals at high risk, such as those over 60 years old or with chronic respiratory conditions (including severe asthma, bronchopulmonary dysplasia, cystic fibrosis, and COPD [59, 60]).

Vaccination against influenza is a crucial strategy for reducing overall disease transmission and protecting vulnerable populations. The effectiveness of the vaccine depends on the antigenic match between vaccine strains and circulating viruses, which is why WHO determines the vaccine composition for each influenza season [58, 59]. High vaccination coverage rates are essential to achieving these preventive goals, with Italy targeting 75% as the minimum coverage and 95% as the optimal target for individuals aged 65 years or older. The goal is to reduce the individual risk of disease, hospitalization, and death, to minimize the risk of transmission to people at high risk of complications, and to lower the social and economic burden of influenza [60].

Target Population

Influenza vaccination is recommended annually for individuals aged 60 years and older and for children aged 2–18 years, as well as those with chronic respiratory diseases (e.g., COPD, asthma, bronchiectasis) and other comorbidities such as cardiovascular diseases, diabetes, or immunosuppression. Additionally, vaccination is advised for pregnant women, healthcare workers, and individuals living in long-term care facilities (Table 1) [60, 61].

Available Vaccines

In Italy, all influenza vaccines meet the required standards for efficacy, immunogenicity, tolerability, and safety and are authorized by the EMA and the Italian Medicines Agency (AIFA). Influenza vaccines are

categorized into inactivated and live attenuated vaccines, with specific formulations (trivalent or quadrivalent [QIV]) and recommendations for different age groups and risk categories.

Inactivated vaccines include those produced in embryonated chicken eggs, cell cultures, or recombinant technologies. These vaccines are further divided into split or subunit vaccines. The inactivated vaccines (QIV) derived from embryonated chicken eggs can be used in individuals aged 6 months and older, including pregnant women at any stage of pregnancy. Children under 9 years old who have not been previously vaccinated should receive two doses at least 4 weeks apart, while older individuals and those previously vaccinated require only one dose [60].

Vaccines produced in cell cultures (ccQIVs) are authorized from 2 years of age and follow similar dosing regimens, with two doses recommended for vaccine-naive children between 2 and 9 years of age. Recombinant vaccines (rQIVs), produced using DNA technology, are available for individuals aged 18 years and older and require a single dose [60].

High-dose inactivated vaccines contain a higher concentration of hemagglutinin to enhance immune responses and are specifically recommended for people aged 60 years and older. Adjuvanted inactivated vaccines, which contain the MF59 adjuvant, are designed to elicit stronger immune responses with smaller antigen quantities and are indicated for individuals aged 50 years and older [60].

The live attenuated vaccine is administered intranasally and authorized for use in children aged 2–18 years. Starting from the 2024 to 2025 season, this vaccine will be available in a trivalent form, following the decision to phase out the B/Yamagata lineage due to its cessation of circulation [61]. Two doses are recommended for children aged 2–9 years who have not previously been vaccinated, while a single dose is sufficient for those already immunized.

All vaccines should not be administered to children under 6 months old or individuals with a history of Guillain-Barré Syndrome after previous influenza vaccinations. The live attenuated vaccine is contraindicated during pregnancy and in individuals with severe asthma, active dyspnea, or severe immunosuppression. Coadministration with other vaccines is allowed for inactivated vaccines, whereas for live attenuated vaccines, a 4-week interval is recommended if another live vaccine is administered separately [60, 62]. With the shift to trivalent vaccines for the 2025–2026 season, the vaccines will contain two influenza A strains (H1N1 and H3N2) and 1 B strain (B/Victoria lineage), reflecting changes in circulating virus strains [61, 63, 64].

Adverse Effects and Management

The most common adverse effects of influenza vaccines are mild local reactions such as injection site pain, redness, and swelling. Systemic symptoms, including fever, headache, and muscle aches, can also occur, particularly in individuals receiving high-dose or adjuvanted vaccines. Serious adverse events, including Guillain-Barré syndrome, are very rare, with an estimated relative risk of 1–2 cases per million doses.

Management of local reactions includes using analgesics, such as acetaminophen or ibuprofen, to relieve pain and fever. Severe allergic reactions are extremely rare but require immediate medical attention, including the administration of epinephrine [60].

Appropriateness of Use

All authorized vaccines meet the required standards for efficacy, safety, and immunogenicity but differ in composition, target populations, and immune response capabilities. Therefore, appropriate vaccine use is crucial, particularly in a country such as Italy, which has a significantly older population and a high prevalence of comorbidities. The immune response in older individuals is often weaker due to immunosenescence, which means that traditional vaccines may not achieve their full preventive potential [59].

Although studies evaluating the relative effectiveness of vaccines specifically designed for older populations, such as adjuvanted and high-dose vaccines, show significant variation from season to season – due to epidemiological fluctuations, predominant circulating strains, and the match between vaccine strains and circulating viruses – numerous studies indicate that adjuvanted and high-dose vaccines perform better than standard vaccines in older adults [62, 65]. These vaccines, tailored to the specific needs of older populations, have demonstrated greater efficacy in reducing complications, hospitalizations, and mortality than standard vaccines.

The vaccine choice should be based on the characteristics of the individual being immunized, with particular consideration for those at higher risk. Ensuring the optimal use of available resources and selecting the most appropriate vaccine for each individual are essential to maximizing public health benefits and minimizing the burden on healthcare systems [59].

Experts' Insight

Patients with COPD or bronchiectasis and severe asthma should be vaccinated against influenza viruses, preferably with an inactivated vaccine. This is because inactivated influenza vaccines, which contain viral

components, cannot cause infection. These vaccines are safe for individuals with chronic respiratory diseases, who may be at higher risk of severe complications from live viral vaccines due to their compromised immune response. Inactivated vaccines elicit an immune response without posing a risk of viral replication, making them suitable for high-risk populations. Patients with mild-moderate asthma should also receive the influenza vaccination at least annually or as required by local immunization schedules.

SARS-CoV-2

Background

SARS-CoV-2 vaccination has been a crucial tool in combating the pandemic. It is estimated that in the first year of the vaccination campaign alone, approximately 14 million lives were saved [66]. Despite WHO declaring the end of the pandemic on 5 May 2023, COVID-19 continues to cause significant morbidity and mortality, particularly among vulnerable populations. While vaccination has demonstrated a favorable impact across all high-risk groups, immunocompromised patients tend to benefit less from active immunization due to a weaker immune response [67].

Furthermore, the 2023–2024 COVID-19 vaccination season was marked by low vaccine uptake in several countries worldwide. In Italy, for example, it is estimated that only 4% of the population was vaccinated as of September 2023 [68]. In this context, it is important to consider the ongoing evolution of SARS-CoV-2, which continues to present successive waves, not yet synchronized with the colder months but coinciding with the emergence of major variants characterized by immune evasion and sufficient viral fitness [69].

Target Population

SARS-CoV-2 vaccination is recommended for all individuals, with priority given to older adults, immunocompromised patients, pregnant women, healthcare workers, and individuals with chronic diseases. In particular, patients with chronic respiratory diseases (COPDs, asthma) should be prioritized due to the increased risk of severe outcomes from COVID-19 [70] (Table 1).

Available Vaccines

The updated vaccines for the 2024–2025 season, including the Comirnaty (Pfizer-BioNTech) COVID-19 vaccine – mRNA (2024–2025 formula), the Spikevax (Moderna) COVID-19 vaccine – mRNA (2024–2025 formula), and the Nuvaxoid (Novavax) COVID-19 vaccine – recombinant protein (2024–2025 formula), are based on a subvariant. Comirnaty and Spikevax are mRNA-based vaccines authorized for individuals aged 6 months or older, while Nuvaxoid is a protein-based vaccine authorized for individuals aged 12 years or older [71, 72].

The safety and efficacy of COVID-19 vaccines have been extensively demonstrated through large-scale clinical trials [71, 72]. There are limited data in the literature on the latest vaccines available. However, based on recent seasons, vaccines have been shown to provide significant protection, particularly within the first 2 months after vaccination. For instance, they have demonstrated around 51–53% effectiveness in preventing emergency department visits and hospitalizations due to COVID-19. However, immunity tends to wane over time, with effectiveness declining to approximately 39–50% after 60–120 days, highlighting the potential need for booster doses to maintain high levels of protection [73, 74]. Nuvaxoid has been shown to elicit strong neutralizing antibody responses, such as its mRNA counterparts. This makes Nuvaxovid a suitable option for individuals who prefer non-mRNA vaccines or cannot receive them. Furthermore, both Comirnaty and Spikevax, mRNA-based vaccines, have been adapted to match the evolving virus, with trials demonstrating a robust immune response against JN.1 and KP.2 [75–79].

Evolution of COVID-19 Vaccination and Variant-Specific Vaccines

The rapid development of COVID-19 vaccines has been instrumental in mitigating the global impact of the pandemic. However, the continuous emergence of new SARS-CoV-2 variants necessitates the evolution of vaccination strategies to maintain effectiveness [80].

Variant-Specific COVID-19 Vaccines

The emergence of highly transmissible and immune-evasive variants, such as Delta, Omicron, and their sublineages, has driven the development of updated vaccines targeting these variants. mRNA platforms, such as those used in Comirnaty (Pfizer-BioNTech) and Spikevax (Moderna), have enabled rapid updates to vaccine formulations, ensuring they match the antigenic profiles of circulating strains. Protein-based vaccines, such as Nuvaxoid (Novavax), provide an additional option for variant-specific prophylaxis [80].

The Role of Genome Sequencing

Genome sequencing has been critical in identifying emerging variants and monitoring their spread. This technology enables early detection of mutations that

Table 3. Summary of COVID vaccine recommendations (2024–2025)

Target group	Vaccination recommendation
People aged ≥60 years	An updated dose with an updated vaccine[a] is recommended once a year or at least 3 months after infection
Long-term care facility residents	Same as above
Pregnant and postpartum women	Recommended at any stage of pregnancy or postpartum, including breastfeeding
Healthcare workers	Recommended for healthcare, social workers, and healthcare students to protect vulnerable populations
People aged 6 months – 59 years with high-risk conditions	Includes individuals with chronic respiratory diseases (e.g., severe asthma, COPD), cardiovascular diseases, diabetes, immunosuppression, and other specified conditions

[a]Currently, only the COVID-19 vaccine Comirnaty JN.1 is available in Italy [61]. See the text for additional details.

could impact vaccine efficacy or therapeutic interventions. Sequencing data have been pivotal in guiding the design of variant-specific vaccines, as well as in identifying targets for monoclonal antibody therapies.

The importance of genome sequencing is underscored by its ability to support both prophylaxis and therapy. Studies, such as the one by Zella et al. [81] (2021), highlight its role in accelerating the development of effective interventions.

Ongoing Updates to COVID-19 Vaccines

Given the dynamic nature of SARS-CoV-2 evolution, annual updates to vaccine formulations are anticipated, similar to the approach taken for influenza vaccines. These updates are essential to maintaining protection in high-risk populations, particularly older adults and those with chronic conditions or immunosuppression.

Adverse Effects and Management

The most frequently reported adverse effects of SARS-CoV-2 vaccines include injection site pain, fatigue, headache, muscle pain, and fever. These effects are typically mild and resolve within a few days. Rare adverse events include myocarditis and pericarditis, particularly in younger males after the second dose of mRNA vaccines, with an estimated risk of 1 in 10,000–1 in 20,000 doses.

Management of mild-to-moderate symptoms includes rest, hydration, and the use of antipyretics or analgesics. In case of myocarditis or pericarditis, patients should seek immediate medical care and avoid strenuous physical activity until symptoms resolve [82].

Appropriateness of Use

In Italy, during the 2024–2025 season, following the authorization of COVID-19 vaccines by the EMA and AIFA, only the COVID-19 vaccine Comirnaty JN.1 has been approved so far [83], and specific recommendations have been issued (Table 3).

Vaccination is also strongly recommended for family members, cohabitants, and caregivers of individuals with severe vulnerabilities, ensuring that these individuals are well-protected against COVID-19. Priority for vaccination is given to those aged 80 and older, residents of long-term care facilities, individuals with high vulnerability – particularly those with significant immune system impairments – and healthcare and social workers. However, eligibility for vaccination should not be strictly limited to these categories but rather assessed on a case-by-case basis, considering the risk-benefit ratio for each patient. This personalized approach allows for broader protection, regardless of the specific categories identified as high priority.

Vaccination can also be offered to individuals who do not fall into the recommended categories, depending on availability and demand. Concerning the time of re-vaccination, the dose provides protection from severe disease for approximately 6–12 months. For individuals receiving a dose of Comirnaty JN.1, it is recommended to be administered at least once a year, regardless of the number of doses previously received or infections experienced. This time interval could be reduced in immunocompromised patients to ensure greater response and efficacy [84]. In fact, in cases where clinical necessity requires vaccination before the 12-month interval, the SPC for Comirnaty permits vaccination as early as 3 months after the most recent COVID-19 vaccine dose [74].

People who recently had COVID-19 may delay receiving a COVID-19 vaccine for 3 months [84]. The coadministration of updated COVID-19 vaccines with other vaccines, particularly the flu vaccine, is generally allowed unless specific clinical evaluations suggest otherwise. This flexible approach to vaccine administration ensures broad immunization coverage against multiple infectious diseases during the same period and helps streamline efforts to protect public health during flu season and the ongoing fight against COVID-19.

Expert's Insight

In a post-pandemic time, it is important to emphasize the value of COVID-19 vaccination in protecting at-risk populations from deterioration, hospitalization, intensive care unit admission, and death. People living with chronic pulmonary disease are at high risk of progression. However, even during the pandemic era, vaccination uptake among patients with COPD, asthma, and bronchiectasis was not satisfactory due to vaccine hesitancy [85–87].

We advocate for using educational approaches, as they have been shown to increase vaccine uptake, particularly among patients with COPD [88]. Concerning guidelines, COVID-19 vaccination is advised in patients with COPD and with asthma [20]. COVID-19 vaccination is considered safe in patients with asthma, as allergic reactions are rare and no evidence of adverse asthma-related effects has been reported, even in patients with severe disease [86]. In patients with severe asthma under biological treatment, the first dose of the biologic agent should not be given on the same day of the COVID-19 vaccination to help identify possible adverse events associated with either the vaccine or the biologic. Conversely, COVID-19 vaccination can be given on the same day as influenza vaccine [89]. In frankly immunosuppressed patients, it should be considered the possibility of administering more than one dose during the year [84], at least once every 6 months, instead of one per year.

Streptococcus pneumoniae

Background

S. pneumoniae, a major cause of lower respiratory tract infections, poses a significant health risk, especially in young children and older adults. With over 100 different serotypes identified, its polysaccharide capsule serves as the primary virulence factor, making pneumococcus responsible for a range of diseases, from noninvasive infections, such as sinusitis and pneumonia, to invasive diseases, such as bacteremia and meningitis [90]. WHO has recognized pneumococcal vaccination as a crucial intervention. In Italy, the NIP 2023–2025 recommends routine vaccination for at-risk groups, particularly those aged 65 years and older, as well as individuals with underlying chronic conditions [91–93]. Vaccination not only reduces the spread of disease but also offers both direct protection and herd immunity, with the aim of achieving over 75% coverage among adults aged 65 and older [93]. The available vaccines, including polysaccharides and conjugate ones, are authorized by the EMA and offer protection based on their serotype content. The choice between these vaccines depends on their characteristics and immune responses, with conjugate vaccines (PCVs) generally preferred for primary prevention [94].

Target Population

Pneumococcal vaccination is recommended for all adults aged 65 years and older and for individuals with chronic conditions, including COPD, asthma, diabetes, and immunosuppressive disorders [95] (Table 1).

Available Vaccines

All pneumococcal vaccines available in Italy meet the required standards for efficacy, immunogenicity, tolerability, and safety and are authorized by the EMA and/or AIFA. Pneumococcal vaccines can be categorized as either polysaccharide vaccines (PPSVs) or PCV. These vaccines differ in their serotype content, with antibodies directed against the capsule providing protection. However, the immune response is generally serotype-specific, making it crucial to use vaccines that target the most prevalent circulating serotypes.

According to national surveillance data on invasive bacterial diseases, the most prevalent pneumococcal serotypes in Italy in 2022 were 3, 8, 19A, 23B, 6C, 9N, 19F, 11A, 15A, 23A, 14, and 35F in adults over 64 years of age [96]. PPSV, such as the 23-valent pneumococcal polysaccharide vaccine (PPSV23), are thymus-independent and, therefore, ineffective in children under 2 years of age. They do not induce immune memory or prolonged protection over time, and repeated doses can lead to tolerance or hypo responsiveness. PPSV23 is recommended for active immunization against pneumococcal infections in individuals aged 2 years and older. While it is protective against invasive forms of pneumococcal disease, its efficacy against pneumonia varies depending on the clinical trials evaluated [97]. The immunization schedule includes one dose, with revaccination considered for high-risk individuals after at least 5 years.

However, repeated doses are generally limited to two due to the risk of reduced immunogenicity after multiple administrations [94, 98].

In contrast, PCVs are preferred for primary prevention due to their ability to induce immune memory, prevent carriage, and provide herd immunity. Available PCVs include the 10-valent, 13-valent, 15-valent, and 20-valent PCVs. PCV10 and PCV13 are indicated for active immunization against invasive diseases and pneumonia in children, while PCV13 is also approved for adults aged 18 and older [99]. PCV15 and PCV20, including additional serotypes, are suitable for broader protection against invasive diseases and pneumonia in both children and adults. Based on their characteristics and available data, these vaccines are considered the first choice for primary prevention against pneumococcal infections, also for individuals with underlying conditions, and they can be used sequentially with PPSV23 to maximize coverage against pneumococcal serotypes [73, 93, 100].

Adverse Effects and Management

Common adverse effects of pneumococcal vaccines include injection site pain, swelling, and redness. Systemic symptoms, such as fever, fatigue, and muscle pain, are also reported. Severe adverse events, including febrile seizures and anaphylaxis, are extremely rare, with a relative risk of less than 1 in 100,000 doses.

Local reactions can be managed with analgesics and cold compresses. Systemic reactions typically resolve within a few days. Severe allergic reactions require immediate emergency care and the administration of epinephrine [101].

Appropriateness of Use

According to the Italian NIP 2023–2025, the primary focus is vaccinating the 65-year-old cohort using a sequential vaccination strategy that includes both PCVs and PPSVs (PPSV23). This approach ensures broader serotype coverage and extended protection, particularly for high-risk individuals [93]. PCVs, such as PCV15 and PCV20, offer enhanced protection due to their broader serotype coverage and the ability to induce immune memory [93, 100, 102].

The CDC has developed pneumococcal vaccination recommendations for adults aged 19 and older, which vary based on age, previous vaccination status, and risk factors [73]. Table 4 provides a summary of these recommendations, focusing on adults aged 19 years and older, stratified by age and risk profile.

The use of PCVs, followed by PPSV23, ensures comprehensive coverage against *S. pneumoniae*. By integrating these vaccines into a rational strategy, healthcare providers can maximize protection for both high-risk adults and older populations [73, 94].

Experts' Insight

In accordance with the Italian NIP 2023–2025, pneumococcal vaccination is strongly recommended for all subjects with one or more risk conditions, i.e., for those with an increased probability of developing pneumococcal disease if infected. In particular, the recommendation applies to individuals of any age who are at risk and have chronic lung diseases, among other pathologies or predisposing conditions. In at-risk subjects who have never been vaccinated, it is necessary to determine the most appropriate vaccination schedule based on age. For at-risk individuals with risk conditions who have previously been vaccinated, if they have received only one dose of a conjugated vaccine (−7, −10, −13, or −15 valent), the administration of a dose of PCV20 is recommended. This dose can be followed by a dose of PPSV23 after at least 8 weeks, with the possibility of repeating this vaccination only once after 5 years. In at-risk subjects for disease and those aged over 18 years who have received vaccination with only the polysaccharide preparation (PPSV23), the administration of a dose of PCV20 is recommended 1 year after the last vaccination.

Pneumococcal vaccination is recommended in patients with COPD (PCV20 or PCV15 followed by PPSV23) [104] and bronchiectasis [105]. The 2024 GINA main report states that "people with asthma, particularly children and older individuals, are at high risk of pneumococcal disease. The pneumococcal vaccine protects against invasive pneumococcal infection, but asthma alone is not a specific indication for pneumococcal vaccination." GINA advice is to "encourage children, adults, and older individuals with asthma to follow their local immunization schedule, including for pneumococcal vaccination" [106].

Varicella Zoster Virus

Background

The risk of HZ, also known as shingles, increases with age. In Italy, the incidence is estimated at 6.42 cases per 1,000 person-years in individuals over 50 years of age [107]. Conditions such as chronic respiratory diseases (e.g., COPD and asthma) exacerbate the risk because of their effects on cell-mediated immunity. For instance, COPD is associated with reduced systemic immunity and the use of corticosteroids, which further suppress

Table 4. CDC pneumococcal vaccination recommendations for adults (19+ years)

Population	Vaccine recommendation
Adults ≥65 years, no previous vaccination	Administer 1 dose of PCV20 or 1 dose of PCV15 followed by PPSV23 at least 1 year later (8 weeks for high-risk patients)
Adults ≥65 years, previously immunized with PPSV23	Administer 1 dose of PCV20 or 1 dose of PCV15 at least 1 year after the last PPSV23 dose
Adults ≥65 years, previously immunized with PCV13	Administer 1 dose of PCV20 or 1 dose of PPSV23 at least 1 year later (8 weeks for high-risk patients)
Adults ≥65 years, previously received PCV13 at any age and PPSV23 before 65	Administer 1 dose of PCV20 or PPSV23 after 5 years (intervals vary for special cases)
Adults ≥65 years, completed PCV13 at any age + PPSV23 after 65	Consider PCV20 at least 5 years after the last PPSV23 dose
Adults 19–64 years, immunocompromised, no previous vaccination	Administer 1 dose of PCV20 or 1 dose of PCV15 followed by PPSV23 at least 8 weeks later
Adults 19–64 years, immunocompromised, previously vaccinated with PPSV23	Administer 1 dose of PCV20 or PCV15 after at least 1 year
Adults 19–64 years, immunocompromised, previously vaccinated with PCV13	Administer 1 dose of PCV20 after 1 year or PPSV23 after 8 weeks, followed by another PPSV23 dose after 5 years
Adults 19–64 years, immunocompromised, previously vaccinated with PCV13 and 1 dose of PPSV23	Administer 1 dose of PCV20 or alternatively 1 dose of PPSV23, at least after 5 years. Vaccination recommendations will be reevaluated when the subject turns 65 years of age
Adults 19–64 years, immunocompromised, previously vaccinated with PCV13 and 2 doses of PPSV23	Administer 1 dose of PCV20, at least after 5 years. In this case, no alternative intervention is envisaged, and the vaccination recommendations will need to be reevaluated when the subject turns 65 years of age
Adults 19–64 years, with comorbidities (chronic diseases), no previous vaccination	Administer 1 dose of PCV20 or PCV15, followed by PPSV23 at least 1 year later
Adults with comorbidities who completed PCV13 + PPSV23 schedule	No further intervention required until reevaluation at age 65
Adults with comorbidities previously immunized exclusively with PPSV23	Administer either 1 dose of PCV20 or 1 dose of PCV15 after at least 1 year
Adults with comorbidities previously immunized exclusively with PCV13	Administer either 1 dose of PCV20 or 1 dose of PPSV23 at least after 1 year, reevaluating the vaccination recommendations when the subject turns 65 years of age

Source: [73, 103].

immune function [108, 109]. Similarly, asthma's altered immune responses, including a Th1/Th2 imbalance, increase susceptibility to HZ and its complications, such as PHN and ophthalmic zoster [110].

Vaccination plays a key role in preventing shingles, particularly among at-risk populations. The first vaccine available was a live attenuated zoster vaccine (ZVL), which showed an efficacy of 51% in reducing HZ incidence and 67% in preventing PHN. However, its efficacy waned over time and decreased significantly in older age groups [111, 112]. More recently, RZV, licensed in 2017 by the FDA and in 2018 by the EMA, has demonstrated significantly higher efficacy. In two major clinical trials, RZV was found to be 97.2% effective in individuals over 50 years of age and 91.3% effective in those over 70 years, with long-term protection extending up to 10 years [113, 114]. Notably, RZV is suitable for immunocompromised individuals, offering critical protection where ZVL could not be used [115].

Given the higher risk of shingles among individuals with chronic respiratory diseases, many national immunization plans now recommend shingles vaccination for those with conditions such as COPD and asthma. The Italian NIP 2023–2025 also advocates for vaccination in

these groups, reinforcing the importance of RZV for individuals with immunodeficiency or undergoing immunosuppressive treatments [93].

Target Population

Varicella zoster vaccination is recommended for individuals aged 50 years and older, with a particular focus on those aged 65 and older and those with chronic conditions such as COPD, asthma, diabetes, and immunosuppression. Vaccination with recombinant adjuvanted vaccine is also indicated for immunocompromised individuals 18 years and older at increased risk of HZ (shingles) and its complications [116] (Table 1).

Available Vaccines

Several live attenuated vaccines for preventing HZ have been developed over time [115, 117–119]. The first licensed vaccine was the single-dose live-ZVL or Zovastax, approved by the FDA in 2006 for adults over 60 years of age and by the EMA in 2012 for those over 50 years, aimed at preventing HZ and PHN [111, 120]. In the Shingles Prevention Study, a randomized, multicenter, placebo-controlled, double-blind clinical trial involving 38,546 immunocompetent individuals aged 60 and older, ZVL reduced zoster incidence by 51% and PHN by 67% [117]. In a separate study involving 22,439 subjects aged 50–59, the efficacy of ZVL in preventing HZ was 69.8% (no data on PHN prevention) [121]. However, the efficacy profile declined with age and waned over time. In the 60–69-year age group, vaccine efficacy was 64%, dropping to 41% in individuals aged 70–79 years and further down to 18% in those aged 80 and older [111]. Vaccine effectiveness against shingles was 49.1%, decreasing from 67.5% in the first year after vaccination to 47.2% in the second year and 31.8% by 8 years post-vaccination [112].

Being a live vaccine, ZVL is contraindicated in immunocompromised individuals (e.g., patients with malignancies, HIV infection, or immunosuppressive therapy) and during pregnancy [111]. The adjuvanted RZV or Shingrix was approved by the FDA in 2017 for use in adults over 50 years [122]. In 2021, the FDA expanded the indication to include adults aged 18 years and older at increased risk of HZ due to immunodeficiency or immunosuppression caused by known diseases or therapies [122]. The EMA approved RZV for use in adults over 50 in 2018 and for immunocompromised adults over 18 in 2020 [123]. RZV consists of the glycoprotein E antigen and the AS01B adjuvant system, designed to induce a strong cellular and humoral immune response [122]. Unlike ZVL, RZV is administered in two doses and is not contraindicated in immunocompromised patients.

Two pivotal studies demonstrated the efficacy of RZV at 97.2% and 91.3% in preventing HZ in adults aged 50 years and older (ZOE-50) and 70 years and older (ZOE-70), respectively [113, 114]. Pooled data from these studies showed a vaccine efficacy of 91.2% against PHN in individuals aged over 50 and 88.8% in those aged over 70 years [114]. RZV has also shown an acceptable safety profile, with the most common adverse events being injection site pain, myalgia, fatigue, and headache [123].

In a real-world retrospective cohort study of immunocompetent individuals over 50 enrolled in the Kaiser Permanente Hawaii Health Plan (11,864 individuals who received two doses of RZV), the vaccine was found to be 83.5% effective against HZ (95% CI, 74.9–89.2) and 93.3% effective against HZO (95% CI, 48.7–99.1) [124]. An extension study of ZOE-50 and ZOE-70 assessing long-term protection found that efficacy against HZ remained high 10 years after initial vaccination, with the safety profile remaining clinically acceptable. This suggests that RZV provides long-term clinical benefits in individuals aged over 50 years [125].

Adverse Effects and Management

The most common adverse effects of the RZV (Shingrix) vaccine include injection site pain, swelling, and redness, as well as fatigue, fever, and muscle aches. These reactions are generally mild and resolve within a few days. Rare serious adverse effects include anaphylaxis, with an estimated risk of less than 1 in 100,000 doses.

Management includes the use of over-the-counter analgesics for pain and fever. Severe allergic reactions require immediate administration of epinephrine and emergency medical care [126].

Appropriateness of Use

According to the NIP 2023–2025, vaccination against HZ is recommended for the 65-year-old cohort, with a one- or two-dose schedule according to the used vaccine. Besides, the vaccination is recommended for subjects affected by diabetes mellitus, cardiovascular diseases (excluding isolated hypertension) after a risk assessment, COPD and asthma. RZV should be used in individuals with congenital/acquired immunodeficiency, those who are candidates for immunosuppressive therapy, individuals with chronic kidney failure or those on dialysis, and individuals with recurrent or particularly severe previous cases of shingles [93]. The live attenuated

Table 5. HZ vaccination recommendations for adults

Age group	Vaccine	Doses	Schedule	Notes
Adults aged 50 years and older	Shingrix (RZV)	2 doses	2–6 months apart	Recommended regardless of prior HZ or varicella history. ZVL is no longer available
Adults aged 18 years and older with a weakened immune system	Shingrix (RZV)	2 doses	Typically, 2–6 months apart, but in some cases, it can be 1–2 months apart	Recommended for those who are immunodeficient or immunosuppressed due to disease or therapy. It can be given during antiviral treatment if necessary
Individuals previously vaccinated with Zostavax (ZVL)	Shingrix (RZV)	2 doses	Minimum 8 weeks after Zostavax	ZVLs protection wanes over time, so RZV is recommended even for those previously vaccinated with ZVL
Coadministration with other vaccines	Shingrix (RZV)	N/A	It can be given with other vaccines	RZV can be administered alongside non-adjuvanted flu, pneumococcal, COVID-19 and diphtheria-tetanus-pertussis vaccines at different anatomic sites

Source [129].

vaccine (ZVL) has demonstrated moderate efficacy in preventing HZ, although studies indicate reduced effectiveness in certain high-risk populations, such as individuals with type 2 diabetes or a prior history of HZ infection [23].

RZV, which provides a longer lasting efficacy than ZVL, is indicated for the prevention of HZ and PHN in adults over 50 years and adults over 18 years at increased risk of HZ, including those with chronic diseases such as asthma and COPD. It has been shown to maintain high efficacy across all groups, including individuals with respiratory diseases and other comorbidities, making it the preferred option for HZ prevention [127]. Coadministration with non-adjuvanted influenza, pneumococcal, COVID-19, and diphtheria-tetanus-pertussis vaccines is permitted to allow for streamlined immunization during flu season [128].

As with other vaccines, patient adherence to the full vaccination schedule is crucial (Table 5). In particular, the two-dose regimen for RZV should be completed typically within a 6-month period to ensure optimal immunity. Conversely, for subjects who are or will be immunodeficient or immunosuppressed and who would benefit from completing the series in a shorter period, the second dose can be administered 1–2 months after the first [129]. However, studies have noted lower adherence rates among older adults and those with chronic conditions, underscoring the need for increased awareness and education among healthcare professionals and patients regarding the importance of completing the vaccination series [109, 130, 131].

Expert's Insight

The rationale and motivations for the prevention of HZ through vaccination derive from the significant epidemiological impact, the frequent and debilitating complications (especially PHN), the negative impact on the quality of life of affected people, the suboptimal possibility of treatment of complications, and the costs for the diagnostic and clinical-therapeutic management of the patient with acute HZ, hospitalizations, complications, and social costs related to HZ. In addition to the older age group, vaccination is recommended in the presence of comorbidities and in subjects intended for immunosuppressive therapy. Based on efficacy and duration of protection data, adjuvanted recombinant vaccine (RZV) is preferentially recommended and should be considered the only option in subjects at risk aged 18 years and older with chronic diseases, as well as patients with congenital and/or acquired immunosuppression.

The GOLD 2024 document recommends HZ vaccination in COPD patients. Recent evidence suggests that HZ vaccination should be considered a valuable prevention tool for patients with asthma [132].

Concluding Remarks

The prevention of exacerbations is considered a fundamental aspect of the overall management of respiratory diseases, particularly chronic obstructive diseases. COPD patients with frequent exacerbations experience a severe decline in lung function and increased mortality. A progressive worsening of spirometry values following

infectious exacerbations has also been confirmed in patients with bronchial asthma.

For this reason, international documents recommend vaccination as a fundamental tool in the management of these chronic diseases. The GOLD document [104] recommends anti-flu, anti-SARS-CoV-2, anti-pneumococcal, anti-RSV, and anti-whooping cough vaccinations for patients suffering from COPD who were not vaccinated during adolescence and anti-zoster.

The GINA document encourages children, adults, and older individuals to adhere to their local immunization schedule, including vaccinations for pneumococcal, pertussis, influenza, RSV, and COVID-19 [133]. This document, representing the recommendations of four Italian scientific societies, summarizes the scientific evidence and provides guidance for an appropriate vaccination strategy in respiratory patients.

Acknowledgments

Editorial assistance was provided by Raffaella Gatta, PhD, Aashni Shah and Valentina Attanasio (Polistudium SRL, Milan, Italy) and AIPO Ricerche Edizioni (AIPO Ricerche, Milan, Italy). Graphical assistance was provided by Massimiliano Pianta (Polistudium SRL, Milan, Italy).

Conflict of Interest Statement

C.M. received payment or honoraria as a speaker from A. Menarini, AstraZeneca, Berlin Chemie, Boehringer Ingelheim, Chiesi, Firma, GlaxoSmithKline, Laboratori Guidotti, Novartis, Roche, Sanofi and Zambon and consultation fees from AstraZeneca, Chiesi, and GlaxoSmithKline. S.A. reports grants or contracts from any entity from Physioassist S.A.S., Moderna Italy, Moderna T.X., Boehringer Ingelheim, Chiesi Farmaceutici S.P.A., GlaxoSmithKline S.p.A., Insmed Incorporated, Insmed Netherlands B.V., Insmed Italy, Zambon, AN2 Therapeutics, Vertex Pharmaceuticals, Fondazione Internazionale Menarini, AstraZeneca, Brahms G.M.B.H., Verona Pharma plc, Pfizer Srl. M.A. reports having participated at GlaxoSmithKline, Gilead, and AstraZeneca Advisory Boards. F.B. reports grants and personal fees from AstraZeneca, personal fees from Boehringer Ingelheim, personal fees from Chiesi, personal fees from GlaxoSmithKline, personal fees from Grifols, grants and personal fees from Insmed, personal fees from Menarini, personal fees from O.M. pharma, personal fees from Pfizer, personal fees from Sanofi, personal fees from Vertex, personal fees from Viatris, personal fees from Zambon, outside the submitted work. F.D.M. declares personal fees and support for research from AstraZeneca, Boehringer Ingelheim, Chiesi, Eurodrugs Laboratories, Laboratori Guidotti, GlaxoSmithKline, Levante Pharma, Menarini, Sanofi, Zambon. R.D.M. has no conflicts to declare. GG reports having received personal fees for advisory board membership and/or consultancy and/or lectures from Emergent Biosolutions, GlaxoSmithKline, M.S.D., Sanofi Pasteur, Pfizer, Moderna, Novavax, Viatris, and Seqirus. S.H. has no conflicts to declare. I.G. declares personal fees from Abbvie, Abbott, Advanz, AstraZeneca, GlaxoSmithKline, M.S.D., Gilead, Pfizer, Infectopharm, Angelini, S.O.B.I., Basilea, Mundipharma, and Shionogi. R.P. reports having received personal fees for advisory board membership and/or consultancy and/or lectures and/or research from Insmed, GlaxoSmithKline, AstraZeneca, and Tillots Pharma. R.S. reports having received personal fees for advisory board membership and/or consultancy and/or lectures and/or research from M.S.D., Pfizer, GlaxoSmithKline, Sanofi Pasteur, Seqirus, AstraZeneca, Moderna, Viatris. L.S. reports having received personal fees for advisory board membership and/or consultancy and/or lectures and/or research from M.S.D., Pfizer, GlaxoSmithKline, Sanofi Pasteur, Seqirus, AstraZeneca, A.j. Vaccines, Moderna, Novavax.

Funding Sources

This manuscript was made possible thanks to a donation from GlaxoSmithKline Spa. GlaxoSmithKline Spa had no role in the preparation of the manuscript.

Author Contributions

Study conception and design: C.M., M.A., G.G., I.G., and L.S.; collection and interpretation of data: C.M., F.D.M.; manuscript drafting: C.M., M.A., F.D.M., G.G., I.G., and L.S.; manuscript editing: C.M., M.A., F.B., G.G., I.G., R.P., and L.S.; approval to submit: C.M., S.A., M.A., F.B., F.D.M., R.D.M., G.G., S.H., I.G., R.P., R.S., and L.S.

References

1 GBD 2019 Chronic Respiratory Diseases Collaborators; Moghaddam SS, Ghamari S-H, Rad EM, Rezaei N, Shobeiri P. Global burden of chronic respiratory diseases and risk factors, 1990–2019: an update from the Global Burden of Disease Study 2019. eClinicalMedicine. 2023;59:101936. https://doi.org/10.1016/j.eclinm.2023.101936

2 Nigro M, Laska IF, Traversi L, Simonetta E, Polverino E. Epidemiology of bronchiectasis. Eur Respir Rev. 2024;33(174):240091. https://doi.org/10.1183/16000617.0091-2024

3 Lommatzsch M, Speer T, Herr C, Jörres RA, Watz H, Müller A, et al. IgE is associated with exacerbations and lung function decline in COPD. Respir Res. 2022;23(1):1. https://doi.org/10.1186/s12931-021-01847-0

4 Viniol C, Vogelmeier CF. Exacerbations of COPD. Eur Respir Rev. 2018;27(147):170103. https://doi.org/10.1183/16000617.0103-2017

5 Choi H, McShane PJ, Aliberti S, Chalmers JD. Bronchiectasis management in adults: state of the art and future directions. Eur Respir J. 2024;63(6):2400518. https://doi.org/10.1183/13993003.00518-2024

6 Bourzac K. Respiratory syncytial virus co-infections might conspire to worsen disease. Nature. 2023;621(7980):S60–1. https://doi.org/10.1038/d41586-023-02959-x

7 Hedberg P, Johansson N, Ternhag A, Abdel-Halim L, Hedlund J, Nauclér P. Bacterial co-infections in community-acquired pneumonia caused by SARS-CoV-2, influenza virus and respiratory syncytial virus. BMC Infect Dis. 2022;22(1):108. https://doi.org/10.1186/s12879-022-07089-9

8 Cilloniz C, Luna CM, Hurtado JC, Marcos MÁ, Torres A. Respiratory viruses: their importance and lessons learned from COVID-19. Eur Respir Rev. 2022;31(166): 220051. https://doi.org/10.1183/16000617.0051-2022
9 Gerayeli FV, Milne S, Cheung C, Li X, Yang CWT, Tam A, et al. COPD and the risk of poor outcomes in COVID-19: a systematic review and meta-analysis. EClinicalMedicine. 2021;33:100789. https://doi.org/10.1016/j.eclinm.2021.100789
10 Izquierdo JL, Rodríguez JM, Almonacid C, Benavent M, Arroyo-Espliguero R, Agustí A. Real-life burden of hospitalisations due to COPD exacerbations in Spain. ERJ Open Res. 2022;8(3):00141-2022. https://doi.org/10.1183/23120541.00141-2022
11 Kartsiouni E, Chatzipanagiotou S, Tamvakeras P, Douros K. The role of viral infections in pulmonary exacerbations of patients with non-cystic fibrosis bronchiectasis: a systematic review. Respir Investig. 2022;60(5):625–32. https://doi.org/10.1016/j.resinv.2022.06.002
12 Aliberti S, Gramegna A, Zucchetti S, Simonetta E, Amati F, Castelli D, et al. Respiratory viruses in stable bronchiectasis: a multicenter evaluation in Northern Italy. Respir Med. 2022;205:107056. https://doi.org/10.1016/j.rmed.2022.107056
13 Agustí A, Calverley P, Decramer M, Stockley R, Wedzicha J. Prevention of exacerbations in chronic obstructive pulmonary disease: knowns and unknowns. J COPD F. 2014;1(2):166–84. https://doi.org/10.15326/jcopdf.1.2.2014.0134
14 Fekete M, Pako J, Nemeth AN, Tarantini S, Varga JT. Prevalence of influenza and pneumococcal vaccination in chronic obstructive pulmonary disease patients in association with the occurrence of acute exacerbations. J Thorac Dis. 2020;12(8):4233–42. https://doi.org/10.21037/jtd-20-814
15 Shteinberg M, Sibila O, Stein N, Faner R, Jordan A, Olvera N, et al. Risk of SARS-CoV-2 infection and disease severity among people with bronchiectasis: analysis of three population registries. Chest. 2024;165(1):79–83. https://doi.org/10.1016/j.chest.2023.08.007
16 Pardhan S, Wood S, Vaughan M, Trott M. The risk of COVID-19 related hospitalsation, intensive care unit admission and mortality in people with underlying asthma or COPD: a systematic review and meta-analysis. Front Med. 2021;8:668808. https://doi.org/10.3389/fmed.2021.668808
17 Meng M, Wei R, Wu Y, Zeng R, Luo D, Ma Y, et al. Long-term risks of respiratory diseases in patients infected with SARS-CoV-2: a longitudinal, population-based cohort study. eClinicalMedicine. 2024;69:102500. https://doi.org/10.1016/j.eclinm.2024.102500
18 Papi A, Ison MG, Langley JM, Lee D-G, Leroux-Roels I, Martinon-Torres F, et al. Respiratory syncytial virus prefusion F protein vaccine in older adults. N Engl J Med. 2023;388(7):595–608. https://doi.org/10.1056/NEJMoa2209604
19 Gershon AS, McGihon RE, Thiruchelvam D, To T, Wu R, Bell CM, et al. Medication discontinuation in adults with COPD discharged from the hospital: a population-based cohort study. Chest. 2021;159(3):975–84. https://doi.org/10.1016/j.chest.2020.09.254
20 Available from: https://goldcopd.org/gold-covid-19-guidance/
21 Savic M, Penders Y, Shi T, Branche A, Pirçon J. Respiratory syncytial virus disease burden in adults aged 60 years and older in high-income countries: a systematic literature review and meta-analysis. Influenza Resp Viruses. 2023;17(1):e13031. https://doi.org/10.1111/irv.13031
22 Osei-Yeboah R, Spreeuwenberg P, Del Riccio M, Fischer TK, Egeskov-Cavling AM, Bøås H, et al. Estimation of the number of respiratory syncytial virus–associated hospitalizations in adults in the European union. J Infect Dis. 2023;228(11):1539–48. https://doi.org/10.1093/infdis/jiad189
23 Bollaerts K, Alexandridou M, Verstraeten T. Risk factors for modified vaccine effectiveness of the live attenuated zoster vaccine among the elderly in England. Vaccin X. 2019;1:100007. https://doi.org/10.1016/j.jvacx.2019.100007
24 Bertaglia V, Morelli AM, Solinas C, Aiello MM, Manunta S, Denaro N, et al. Infections in lung cancer patients undergoing immunotherapy and targeted therapy: an overview on the current scenario. Crit Rev Oncol Hematol. 2023;184:103954. https://doi.org/10.1016/j.critrevonc.2023.103954
25 Pant P, Baniya S, Jha A. Prevalence of respiratory manifestations in chronic kidney diseases; A descriptive cross-sectional study in A tertiary care hospital of Nepal. JNMA J Nepal Med Assoc. 2019;57(216):80–3. https://doi.org/10.31729/jnma.4284
26 Pascual Martinez N, Mira Padilla E, Gómez Rebollo C, Muñoz Corroto C, García Lovera P, Lesaga López E, et al. Risk factors for respiratory infections in als patients. 02 02 - Noninvasive ventilatory support. 2022:2450. https://doi.org/10.1183/13993003.congress-2022.2450
27 Jiang C, Chen Q, Xie M. Smoking increases the risk of infectious diseases: a narrative review. Tob Induc Dis. 2020;18:60. https://doi.org/10.18332/tid/123845
28 Monoson A, Schott E, Ard K, Kilburg-Basnyat B, Tighe RM, Pannu S, et al. Air pollution and respiratory infections: the past, present, and future. Toxicol Sci. 2023;192(1):3–14. https://doi.org/10.1093/toxsci/kfad003
29 Shi T, McAllister DA, O'Brien KL, Simoes EAF, Madhi SA, Gessner BD, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. Lancet. 2017;390(10098):946–58. https://doi.org/10.1016/S0140-6736(17)30938-8
30 Rozenbaum MH, Begier E, Kurosky SK, Whelan J, Bem D, Pouwels KB, et al. Incidence of respiratory syncytial virus infection in older adults: limitations of current data. Infect Dis Ther. 2023;12(6):1487–504. https://doi.org/10.1007/s40121-023-00802-4
31 Addo M, Cornely O, Denkinger M, Ertl G, Herold S, Pletz M, et al. RSV vaccination strategies for high-risk patients 2023: a collaborative position paper by leading German medical societies and organizations. Infection. 2024;52(1):285–8. https://doi.org/10.1007/s15010-023-02141-5
32 Wildenbeest JG, Lowe DM, Standing JF, Butler CC. Respiratory syncytial virus infections in adults: a narrative review. Lancet Respir Med. 2024;12(10):822–36. https://doi.org/10.1016/S2213-2600(24)00255-8
33 Britton A, Roper LE, Kotton CN, Hutton DW, Fleming-Dutra KE, Godfrey M, et al. Use of respiratory syncytial virus vaccines in adults aged ≥60 Years: updated recommendations of the advisory committee on immunization practices — United States, 2024. MMWR Morb Mortal Wkly Rep. 2024;73(32):696–702. https://doi.org/10.15585/mmwr.mm7332e1
34 Respiratory syncytial virus (RSV) immunisation programme for infants and older adults: JCVI full statement, 11 September 2023. https://www.gov.uk/government/publications/rsv-immunisation-programme-jcvi-advice-7-june-2023/respiratory-syncytial-virus-rsv-immunisation-programme-for-infants-and-older-adults-jcvi-full-statement-11-september-2023
35 Ireland. Immunisation guidelines for Ireland. Available from: https://www.rcpi.ie/Healthcare-Leadership/NIAC/Immunisation-Guidelines-for-Ireland
36 Germany. STIKO Epidemiologisches Bull. 2024:1–32. Available from: https://www.rki.de/DE/Aktuelles/Publikationen/Epidemiologisches-Bulletin/2024/32_24.pdf?__blob=publicationFile&v=3
37 Bundesministeriums für Soziales Gesundheit Pflege. Impfplan Österreich 2023/2024. 2023. CDC. Interim effectiveness of updated 2023–2024 COVID-19 vaccines. MMWR (Morb Mortal Wkly Rep). 2023. Available from: https://www.cdc.gov/mmwr/volumes/73/wr/mm7312a5.htm
38 France: Haute Autorité de Santé. Available from: https://www.has-sante.fr/upload/docs/application/pdf/2024-10/recommandation_strategie_de_vaccination_contre_les_infections_par_le_vrs_chez_ladulte_age_de_60_ans_et_plus_place_du_vaccin_.pdf

39 FHI. RS-virusvaksine - veileder for helsepersonell. 2024. Available from: https://www.fhi.no/va/vaksinasjonshandboka/vaksiner-mot-de-enkelte-sykdommene/rs-virusvaksine/?term=
40 Folkhälsomyndigheten. Vaccination mot RS-virus. Sweden: Folkhälsomyndigheten; 2023. Available from: https://www.folkhalsomyndigheten.se/smittskydd-beredskap/vaccinationer/vacciner-som-anvands-i-sverige/vaccin-mot-rs-virus/
41 Superior Health Council. Vaccination against adults. Belgium: Superior Health Council; 2023. Available from: https://www.health.belgium.be/sites/default/files/uploads/fields/fpshealth_theme_file/20230918_shc-9725_rsv_vaccination_adults_vweb_1.pdf
42 Poland. Official journal of the minister of health - protective vaccination program. 2023. Available from: https://dziennikmz.mz.gov.pl/DUM_MZ/2023/87/akt.pdf
43 Board del Calendario per la Vita. Raccomandazioni del Board del Calendario per la Vita sulla vaccinazione contro Virus Respiratorio Sinciziale (VRS o RSV) nella popolazione anziana e negli adulti a rischio. Gennaio. 2024. Available from: https://www.igienistionline.it/docs/2024/19cdv.pdf
44 Available from: https://www.cdc.gov/rsv/hcp/vaccine-clinical-guidance/older-adults.html
45 Ison MG, Papi A, Langley JM, Lee DG, Leroux-Roels I, Martinon-Torres F, et al. The efficacy of a single dose of the respiratory syncytial virus prefusion F protein vaccine in adults ≥60 years of age over 3 RSV seasons. Abstract presented at: Chest. 2024.
46 Feldman RG, Antonelli-Incalzi R, Steenackers K, Lee D-G, Papi A, Ison MG, et al. Respiratory syncytial virus prefusion F protein vaccine is efficacious in older adults with underlying medical conditions. Clin Infect Dis. 2024;78(1):202–9. https://doi.org/10.1093/cid/ciad471
47 Curran D, Matthews S, Cabrera ES, Pérez SN, Breva LP, Rämet M, et al. The respiratory syncytial virus prefusion F protein vaccine attenuates the severity of respiratory syncytial virus-associated disease in breakthrough infections in adults ≥60 years of age. Influenza Resp Viruses. 2024;18(2):e13236. https://doi.org/10.1111/irv.13236
48 Kampmann B, Madhi SA, Munjal I, Simões EAF, Pahud BA, Llapur C, et al. Bivalent prefusion F vaccine in pregnancy to prevent RSV illness in infants. N Engl J Med. 2023;388(16):1451–64. https://doi.org/10.1056/NEJMoa2216480
49 Walsh EE, Pérez Marc G, Zareba AM, Falsey AR, Jiang Q, Patton M, et al. Efficacy and safety of a bivalent RSV prefusion F vaccine in older adults. N Engl J Med. 2023;388(16):1465–77. https://doi.org/10.1056/NEJMoa2213836
50 Walsh EE, Pérez Marc G, Falsey AR, Jiang Q, Eiras D, Patton M, et al. RENOIR trial — RSVpreF vaccine efficacy over two seasons. N Engl J Med. 2024;391(15):1459–60. https://doi.org/10.1056/NEJMc2311560
51 Wilson E, Goswami J, Baqui AH, Doreski PA, Perez-Marc G, Zaman K, et al. Efficacy and safety of an mRNA-based RSV PreF vaccine in older adults. N Engl J Med. 2023;389(24):2233–44. https://doi.org/10.1056/NEJMoa2307079
52 Arexvy SmPC. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/arexvy
53 Abrysvo SmPC. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/abrysvo
54 mResvia SmPC. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/mresvia
55 Ison MG, Papi A, Athan E, Feldman RG, Langley JM, Lee D-G, et al. Efficacy and safety of respiratory syncytial virus (RSV) prefusion F protein vaccine (RSVPreF3 OA) in older adults over 2 RSV seasons. Clin Infect Dis. 2024;78(6):1732–44. https://doi.org/10.1093/cid/ciae010
56 Surie D, Self WH, Zhu Y, Yuengling KA, Johnson CA, Grijalva CG, et al. RSV vaccine effectiveness against hospitalization among US adults 60 Years and older. JAMA. 2024;332(13):1105–7. https://doi.org/10.1001/jama.2024.15775
57 Payne AB, Watts JA, Mitchell PK, Dascomb K, Irving SA, Klein NP, et al. Respiratory syncytial virus (RSV) vaccine effectiveness against RSV-associated hospitalisations and emergency department encounters among adults aged 60 years and older in the USA, October, 2023, to March, 2024: a test-negative design analysis. Lancet. 2024;404(10462):1547–59. https://doi.org/10.1016/S0140-6736(24)01738-0
58 WHO. Vaccines against influenza: WHO position paper-May2022. Wkly Epidemiol Rec. 2022;19:185–208.
59 Antonelli Incalzi R, Consoli A, Lopalco P, Maggi S, Sesti G, Veronese N, et al. Influenza vaccination for elderly, vulnerable and high-risk subjects: a narrative review and expert opinion. Intern Emerg Med. 2024;19(3):619–40. https://doi.org/10.1007/s11739-023-03456-9
60 Ministero della Salute. Prevenzione e controllo dell'influenza: raccomandazioni per la stagione 2024-2025. Available from: https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2024&codLeg=100738&parte=1%20&serie=null
61 WHO. Recommended composition of influenza virus vaccines for use in the 2024-2025 northern hemisphere influenza season. Available from: https://cdn.who.int/media/docs/default-source/influenza/who-influenza-recommendations/vcm-northern-hemisphere-recommendation-2024-2025/recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2024-2025-northern-hemisphere-influenza-season.pdf?sfvrsn=2e9d2194_7&download=true
62 Calabrò GE, Boccalini S, Panatto D, Rizzo C, Di Pietro ML, Abreha FM, et al. The new quadrivalent adjuvanted influenza vaccine for the Italian elderly: a health technology assessment. IJERPH. 2022;19(7):4166. https://doi.org/10.3390/ijerph19074166
63 Available from: https://www.ema.europa.eu/en/news/eu-recommendations-2024-2025-seasonal-flu-vaccine-composition
64 Available from: https://www.cdc.gov/flu/spotlights/2023-2024/trivalent-vaccines-2024-2025.htm
65 Systematic review update on the efficacy, effectiveness and safety of newer and enhanced seasonal influenza vaccines for the prevention of laboratory confirmed influenza in individuals aged 18 years and over. Stockholm: ECDC; 2024. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/Systematic-review-update-enhanced-seasonal%20flu-vaccines.pdf
66 Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. Lancet Infect Dis. 2022;22(9):1293–302. https://doi.org/10.1016/S1473-3099(22)00320-6
67 Lee ARYB, Wong SY, Chai LYA, Lee SC, Lee MX, Muthiah MD, et al. Efficacy of covid-19 vaccines in immunocompromised patients: systematic review and meta-analysis. BMJ. 2022;376:e068632. https://doi.org/10.1136/bmj-2021-068632
68 ECDC 2024. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/COVID-19-interim-vaccination-coverage-EU-EEA-2023-2024.pdf
69 Available from: https://www.cdc.gov/mmwr/volumes/73/wr/mm7337e2.htm
70 Russo AG, Decarli A, Valsecchi MG. Strategy to identify priority groups for COVID-19 vaccination: a population based cohort study. Vaccine. 2021;39(18):2517–25. https://doi.org/10.1016/j.vaccine.2021.03.076
71 European Medicines Agency (EMA). ETF recommends updating COVID-19 vaccines to target new JN.1 variant. 2024. Available from: https://www.ema.europa.eu/en/news/etf-recommends-updating-covid-19-vaccines-target-new-jn1-variant
72 World health organization (WHO) statement on the antigen composition of COVID-19 vaccines. Available from: https://www.who.int/news/item/26-04-2024-statement-on-the-antigen-composition-of-covid-19-vaccines
73 Kobayashi M, Pilishvili T, Farrar JL, Leidner AJ, Gierke R, Prasad N, et al. Pneumococcal vaccine for adults aged >19 years: recommendations of the advisory committee on immunization practices, United States, 2023. MMWR (Morb Mortal Wkly Rep). 2023;72(3):1–39. https://doi.org/10.15585/mmwr.rr7203a1

74 EMA. 2023. https://www.ema.europa.eu/en/news/ema-and-ecdc-statement-updating-covid-19-vaccines-target-new-sars-cov-2-virus-variants
75 Vaccines and related biological products advisory committee june 5, 2024 meeting presentation- pfizer/BioNTech clinical and preclinical supportive data 2024-2025 COVID19 vaccine formula. https://www.fda.gov/media/179144/download (Accessed Oct 26, 2024).
76 EMA confirms its recommendation to update the antigenic composition of authorized COVID-19 vaccines for 2024-2025. Available from: https://www.ema.europa.eu/en/documents/other/ema-confirms-its-recommendation-update-antigenic-composition-authorised-covid-19-vaccines-2024-2025_en.pdf
77 Moderna Clinical Trial Data Confirm Its Updated COVID-19 Vaccine Generates Robust Immune Response in Humans Against Widely Circulating Variants. https://investors.modernatx.com/news/news-details/2023/Moderna-Clinical-Trial-Data-Confirm-Its-Updated-COVID-19-Vaccine-Generates-Robust-Immune-Response-in-Humans-Against-Widely-Circulating-Variants/default.aspx
78 Nham E, Sohn JW, Choi WS, Wie S-H, Lee J, Lee J-S, et al. Effectiveness of COVID-19 XBB.1.5 monovalent mRNA vaccine in Korea: interim analysis. Front Immunol. 2024;15:1382944. https://doi.org/10.3389/fimmu.2024.1382944
79 DeCuir J, Payne AB, Self WH, Rowley EAK, Dascomb K, DeSilva MB, et al. Interim effectiveness of updated 2023–2024 (monovalent XBB.1.5) COVID-19 vaccines against COVID-19–associated emergency department and urgent care encounters and hospitalization among immunocompetent adults aged ≥18 Years — VISION and IVY networks, september 2023–january 2024. MMWR Morb Mortal Wkly Rep. 2024;73(8):180–8. https://doi.org/10.15585/mmwr.mm7308a5
80 McLean G, Kamil J, Lee B, Moore P, Schulz TF, Muik A, et al. The impact of evolving SARS-CoV-2 mutations and variants on COVID-19 vaccines. mBio. 2022;13(2):e0297921. https://doi.org/10.1128/mbio.02979-21
81 Zella D, Giovanetti M, Cella E, Borsetti A, Ciotti M, Ceccarelli G, et al. The importance of genomic analysis in cracking the coronavirus pandemic. Expert Rev Mol Diagn. 2021;21(6):547–62. https://doi.org/10.1080/14737159.2021.1917998
82 Goddard K, Hanson KE, Lewis N, Weintraub E, Fireman B, Klein NP. Incidence of myocarditis/pericarditis following mRNA COVID-19 vaccination among children and younger adults in the United States. Ann Intern Med. 2022;175(12):1169–771. https://doi.org/10.7326/M22-2274
83 Circolare Ministeriale del 17/09/2024 - "Prevenzione e controllo dell'influenza: raccomandazioni per la stagione 2024-2025", DETERMINA AIFA del 16 luglio 2024. Classificazione, ai sensi dell'articolo 12, comma 5, della legge 8 novembre 2012, n. 189, del medicinale per uso umano, a base di bretovameran, «Comirnaty JN.1». (Determina n. 306/2024). (24A03900) (GU Serie Generale n.182 del 05-08-2024). Disponibile al link: https://www.gazzettaufficiale.it/eli/id/2024/08/05/24A03900/sg
84 ACIP vaccine reccommendations and guidelines 2024. https://www.cdc.gov/acip/vaccine-recommendations/index.html
85 Fasehun OO, Adedoyin O, Iheagwara C, Ofuase-Lasekan IH, Manandhar S, Akoto NA, et al. COVID-19 vaccination rates and predictors of vaccine uptake among adults with chronic obstructive pulmonary disease: insights from the 2022 national health interview survey. Cureus. 2024;16(4):e59230. https://doi.org/10.7759/cureus.59230
86 Bossios A, Bacon AM, Eger K, Paróczai D, Schleich F, Hanon S, et al. COVID-19 vaccination acceptance, safety and side-effects in European patients with severe asthma. ERJ Open Res. 2023;9(6):00590–2023. https://doi.org/10.1183/23120541.00590-2023
87 Fekete M, Horvath A, Santa B, Tomisa G, Szollosi G, Ungvari Z, et al. COVID-19 vaccination coverage in patients with chronic obstructive pulmonary disease – a cross-sectional study in Hungary. Vaccine. 2023;41(1):193–200. https://doi.org/10.1016/j.vaccine.2022.11.020
88 Misra R, Kirk B, Shawley-Brzoska S, Totzkay D, Morton C, Kuhn S, et al. Educational intervention to increase COVID-19 vaccine uptake in rural patients with chronic diseases: lessons learned from an innovative academic–community partnership. IJERPH. 2024;21(1):71. https://doi.org/10.3390/ijerph21010071
89 Available from: https://ginasthma.org/wp-content/uploads/2023/07/GINA-2023-Full-report-23_07_06-WMS.pdf
90 ECDC. Factsheet about pneumococcal disease. https://www.ecdc.europa.eu/en/pneumococcal-disease/facts
91 WHO. Pneumococcal conjugate vaccines in infants and children under 5 years of age: WHO position paper-February 2019. Weekly Epidemiol Rec. 2019;8:85–104.
92 WHO. Considerations for pneumococcal vaccination in older adults. Weekly Epidemiol Rec. 2021;23:217–28.
93 Presidenza del Consiglio dei Ministri Conferenza permanente per i rapporti tra lo stato le regioni e le province autonome, Intesa Governo, Regioni e Province autonome di Trento e di Bolzano sul "Piano nazionale di prevenzione vaccinale (PNPV) 2023 -2025" e sul "Calendario nazionale vaccinale". Intesa 02 agosto 2023, n.193. G.U. Serie Generale, n. 194. https://www.trovanorme.salute.gov.it/norme/dettaglioAtto.spring?id=95963&page=newsett
94 Davies LRL, Cizmeci D, Guo W, Luedemann C, Alexander-Parrish R, Grant L, et al. Polysaccharide and conjugate vaccines to *Streptococcus pneumoniae* generate distinct humoral responses. Sci Transl Med. 2022;14(656):eabm4065. https://doi.org/10.1126/scitranslmed.abm4065
95 Fletcher MA, Vojicic J, Daigle D, Taysi B, Haridy H, Abalos MG, et al. National recommendations for adult pneumococcal vaccination in countries of the WHO regions of americas, africa, eastern mediterranean, south east asia, and western pacific. Vaccine. 2024;42(26):126390. https://doi.org/10.1016/j.vaccine.2024.126390
96 Istituto Superiore di Sanità. Sorveglianza nazionale delle malattie batteriche invasive. Dati 2020-2022. Available from: https://www.iss.it/documents/20126/6703853/RIS-2_2023.pdf/ab5becbe-d2d8-ca12-b756-1e348b80c5a1?t=1698390273826
97 Pneumovax (vaccino pneumoccico polisaccaridico). Riassunto delle caratteristiche dl prodotto. Available from: https://msdsalute.it/product/pneumovax/
98 Calendario Vaccinale per la Vita. 4a edizione, 2019. su: https://www.igienistionline.it/docs/2019/21cvplv.pdf
99 Prevenar 13. EPAR-product information. 2024. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/prevenar-13
100 Vaxneuvance. EPAR-product information. 2024. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/vaxneuvance
101 El-Beyrouty C, Buckler R, Mitchell M, Phillips S, Groome S. Pneumococcal vaccination-A literature review and practice guideline update. Pharmacotherapy. 2022;42(9):724–40. https://doi.org/10.1002/phar.2723
102 Bonanni P, Villani A, Scotti S, Biasci P, Russo R, Maio T, et al. The recommended lifetime immunization schedule from the board of vaccination calendar for life in Italy: a continuing example of impact on public health policies. Vaccine. 2021;39(8):1183–6. https://doi.org/10.1016/j.vaccine.2021.01.019
103 CDC. Pneumococcal vaccine timing for adults. Available from: https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/index.html
104 GOLD guidelines stress the importance of vaccines for patients with COPD. Available from: https://www.pulmonologyadvisor.com/features/2024-gold-guidelines-recommend-patients-with-copd-receive-all-vaccines/
105 Hill AT, Sullivan AL, Chalmers JD, De Soyza A, Elborn SJ, Floto AR, et al. British thoracic society guideline for bronchiectasis in adults. Thorax. 2019;74(Suppl 1):1–69. https://doi.org/10.1136/thoraxjnl-2018-212463
106 Available from: https://ginasthma.org/2024-report

107 Alicino C, Trucchi C, Paganino C, Barberis I, Boccalini S, Martinelli D, et al. Incidence of herpes zoster and post-herpetic neuralgia in Italy: results from a 3-years population-based study. Hum Vaccin Immunother. 2017;13(2):399–404. https://doi.org/10.1080/21645515.2017.1264834

108 Yang Y-W, Chen Y-H, Wang K-H, Wang C-Y, Lin H-W. Risk of herpes zoster among patients with chronic obstructive pulmonary disease: a population-based study. Can Med Assoc J. 2011;183(5):E275–80. https://doi.org/10.1503/cmaj.101137

109 Safonova E, Yawn BP, Welte T, Wang C. Risk factors for herpes zoster: should people with asthma or COPD be vaccinated? Respir Res. 2023;24(1):35. https://doi.org/10.1186/s12931-022-02305-1

110 Shrestha AB, Umar TP, Mohammed YA, Aryal M, Shrestha S, Sapkota UH, et al. Association of asthma and herpes zoster, the role of vaccination: a literature review. Immun Inflamm Dis. 2022;10(11):e718. https://doi.org/10.1002/iid3.718

111 European Medicines Agency. Zostavax: EPAR—product information. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/zostavax (Accessed Jan 14, 2022).

112 Baxter R, Bartlett J, Fireman B, Marks M, Hansen J, Lewis E, et al. Long-term effectiveness of the live zoster vaccine in preventing shingles: a cohort study. Am J Epidemiol. 2018;187(1):161–9. https://doi.org/10.1093/aje/kwx245

113 Lal H, Cunningham AL, Godeaux O, Chlibek R, Diez-Domingo J, Hwang S-J, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med. 2015;372(22):2087–96. https://doi.org/10.1056/NEJMoa1501184

114 Cunningham AL, Lal H, Kovac M, Chlibek R, Hwang S-J, Díez-Domingo J, et al. Efficacy of the herpes zoster subunit vaccine in adults 70 Years of age or older. N Engl J Med. 2016;375(11):1019–32. https://doi.org/10.1056/NEJMoa1603800

115 Parikh R, Widenmaier R, Lecrenier N. A practitioner's guide to the recombinant zoster vaccine: review of national vaccination recommendations. Expert Rev Vaccin. 2021;20(9):1065–75. https://doi.org/10.1080/14760584.2021.1956906

116 Alhothali OS, Alhothali AS, Hanif AA, Bondagji MF, Aljabri HM, Goweda R. A cross-sectional study of the knowledge, practice, and attitude towards herpes zoster vaccination among the general population in the western region of Saudi arabia. Cureus. 2023;15(1):e33508. https://doi.org/10.7759/cureus.33508

117 Oxman MN, Levin MJ, Johnson GR, Schmader KE, Straus SE, Gelb LD, et al. A vaccine to prevent herpes zoster and post-herpetic neuralgia in older adults. N Engl J Med. 2005;352(22):2271–84. https://doi.org/10.1056/NEJMoa051016

118 Ohfuji S, Ito K, Inoue M, Ishibashi M, Kumashiro H, Hirota Y, et al. Safety of live attenuated varicella-zoster vaccine in patients with underlying illnesses compared with healthy adults: a prospective cohort study. BMC Infect Dis. 2019;19(1):95. https://doi.org/10.1186/s12879-019-3719-7

119 Choi WS, Choi JH, Jung DS, Choi HJ, Kim Y-S, Lee J, et al. Immunogenicity and safety of a new live attenuated herpes zoster vaccine (NBP608) compared to Zostavax® in healthy adults aged 50 years and older. Vaccine. 2019;37(27):3605–10. https://doi.org/10.1016/j.vaccine.2019.04.046

120 Centers for Disease Control and Prevention CDC. Update on herpes zoster vaccine: licensure for persons aged 50 through 59 years. MMWR Morb Mortal Wkly Rep. 2011;60(44):1528.

121 Schmader KE, Levin MJ, Gnann JW, McNeil SA, Vesikari T, Betts RF, et al. Efficacy, safety, and tolerability of herpes zoster vaccine in persons aged 50-59 years. Clin Infect Dis. 2012;54(7):922–8. https://doi.org/10.1093/cid/cir970

122 U.S. Food and Drug Administration. Shingrix prescribing information. https://www.fda.gov/media/108597/download (Accessed Jul 14, 2024).

123 Shingrix (package insert): European medicines agency; Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/shingrix

124 Sun Y, Jackson K, Dalmon CA, Shapiro BL, Nie S, Wong C, et al. Effectiveness of the recombinant zoster vaccine among Kaiser Permanente Hawaii enrollees aged 50 and older: a retrospective cohort study. Vaccine. 2021;39(29):3974–82. https://doi.org/10.1016/j.vaccine.2021.05.056

125 Strezova A, Diez-Domingo J, Al Shawafi K, Tinoco JC, Shi M, Pirrotta P, et al. Long-term protection against herpes zoster by the adjuvanted recombinant zoster vaccine: interim efficacy, immunogenicity, and safety results up to 10 Years after initial vaccination. Open Forum Infect Dis. 2022;9(10):ofac485. https://doi.org/10.1093/ofid/ofac485

126 Yih WK, Kulldorff M, Dashevsky I, Maro JC. A broad safety assessment of the recombinant herpes zoster vaccine. Am J Epidemiol. 2022;191(5):957–64. https://doi.org/10.1093/aje/kwac030

127 Oostvogels L, Heineman TC, Johnson RW, Levin MJ, McElhaney JE, Van den Steen P, et al. Medical conditions at enrollment do not impact efficacy and safety of the adjuvanted recombinant zoster vaccine: a pooled post-hoc analysis of two parallel randomized trials. Hum Vaccin Immunother. 2019;15(12):2865–72. https://doi.org/10.1080/21645515.2019.1627818

128 Ali SO, Dessart C, Parikh R. Co-administration of the adjuvanted recombinant zoster vaccine with other adult vaccines: an overview. Vaccine. 2024;42(8):2026–35. https://doi.org/10.1016/j.vaccine.2024.02.035

129 CDC. Shingles vaccine recommendations. Available from: https://www.cdc.gov/shingles/hcp/vaccine-considerations/index.html

130 Ackerson B, Qian L, Sy LS, Bruxvoort K, Wu J, Luo Y, et al. Completion of the two-dose recombinant zoster vaccine series in adults 50 years and older. Vaccine. 2021;39(6):926–32. https://doi.org/10.1016/j.vaccine.2020.12.076

131 Yawn BP, Loskutova NY, Merrill DD, Martinez S, Callen E, Cotton J, et al. Health care professionals' herpes zoster awareness and vaccine recommendations for patients with COPD. Chronic Obstr Pulm Dis. 2022;9(4):562–75. https://doi.org/10.15326/jcopdf.2022.0322

132 Singer D, Thompson-Leduc P, Ma S, Gupta D, Cheng WY, Muthukumar A, et al. Herpes zoster burden in patients with asthma: real-world incidence, healthcare resource utilisation and cost. BMJ Open Resp Res. 2024;11(1):e002130. https://doi.org/10.1136/bmjresp-2023-002130

133 Mallah N, Urbieta AD, Rivero-Calle I, Gonzalez-Barcala F-J, Bigoni T, Papi A, et al. New vaccines for chronic respiratory patients. Arch Bronconeumol. 2024;60(9):565–75. https://doi.org/10.1016/j.arbres.2024.05.026