The Saudi thoracic society guidelines for vaccinations in adult patients with chronic respiratory diseases

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Abstract:

Adult patients with chronic respiratory diseases (CRDs) are considered high risk group who are more likely to experience worse clinical outcomes if they acquire viral or bacterial infections. Vaccination is the best preventive tool to reduce the risk of infection and disease occurrence and to reduce the level of severity of complications associated with the various vaccine-preventable infections. These guidelines were developed by the Saudi Thoracic Society task force to emphasize the critical importance of improving the vaccine coverage rates in adult patients with CRD. They are intended to serve as a reference for healthcare practitioners managing CRD patients. The guidelines aimed to review the current knowledge related to vaccination efficacy in adult patients with CRD, based on the recent evidence and recommendations. Integrating the administration of the recommended vaccines in routine healthcare, such as during outpatient visits or before hospital discharge, is crucial for improving the vaccination rates in high-risk patients. The key strategies to address this public health priority include simplifying vaccination guidelines to enhance their accessibility and implementation by healthcare providers, increasing awareness in both the patients and healthcare providers that vaccines are not only intended for children. Additional strategies include maintaining continuous surveillance and advance research to discover novel vaccines. This approach aims to expand the range of preventable diseases and improve overall health and well-being. Vaccine hesitancy remains a significant challenge that necessitates a clear understanding of the community concerns. Providing appropriate education and communication, as well as addressing these concerns, are the crucial steps toward improving vaccine acceptance and uptake. By implementing these guidelines and multifaceted strategies, healthcare systems can optimize vaccine coverage and protection for patients with CRD, reduce the burden of vaccine-preventable complications, and improve the clinical outcomes in this vulnerable population.

Keywords:

Adults, chronic obstructive pulmonary disease, chronic respiratory diseases, COVID-19, herpes zoster, influenza, pneumococcal, respiratory syncytial vaccine, vaccine

Introduction

Chronic respiratory diseases (CRDs) are noncommunicable diseases of the respiratory system. The examples of CRD are chronic obstructive pulmonary disease (COPD), bronchiectasis, idiopathic pulmonary fibrosis (IPF), obstructive sleep apnea, and other non-IPF interstitial lung diseases.[1] In addition, CRD includes chronic asthma, hypoxic hypercapnic respiratory failure, patients requiring home oxygen, and noninvasive ventilatory support as well as chronically ventilated patients [Table 1].

Patients with CRD account for a substantial number of hospital admissions and

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Table 1: Chronic respiratory diseases (CRD)

COPD
Bronchiectasis
ILD
OSA
Chronic asthma
Hypoxic hypercapnic respiratory failure
Patients requiring long-term home oxygen or NIV support
Chronically ventilated patients

COPD=Chronic obstructive pulmonary disease, ILD=Interstitial lung diseases, OSA=Obstructive sleep apnea, NIV=Noninvasive ventilatory

emergency room visits in Saudi Arabia, resulting in a high morbidity and mortality rate. Smoking, exposure to indoor and outdoor pollutants, dust, sandstorms, and air pollution are the environmental problems in Saudi Arabia which may contribute to the CRD.

In 2019, CRD was the third reason for mortality in the world.[2] Approximately 4 million people died prematurely from CRD globally in that year.[3] Although the overall morbidity and mortality of CRD in Saudi Arabia have not yet been fully assessed, it is expected to reflect the global trend. In a study of the Middle East and North Africa, which which includes Saudi Arabia, CRD ranked as the 6th cause of mortality in 2019, rising from 12th position in 1990. Globally, CRD accounted for 4% of total mortality of all causes and 2.9% of disability-adjusted life years (DALYs).[4] in Saudi Arabia, CRD was the 11th cause of DALYs in 2017 compared to the 15th position in 1990.[5]

patients with CRDs are more susceptible to viral and bacterial infections which attributed to the poor muco-ciliary clearance, the consumption of inhaled corticosteroids (ICS), and the release of adhesion molecules that enhance the attachment of organisms to the airways, facilitating bacterial colonization.[6] Viral and bacterial infections significantly contribute to respiratory deterioration in patients with CRD, leading to worsening outcomes, and complications, with a considerable impact on morbidity and mortality.[7,8] Lower respiratory tract infections (LRTIs) considered as the 4th cause of mortality among females and 6th among males. In 2019, LRTI ranked the 13th leading cause of disability globally, accounting for 1.8% of DALYs.[9]

Pneumonia is a prevalent complication in patients with CRD, and the rate of pneumococcal pneumonia increases with increased age. For instance, there is 2.7 times higher risk of pneumococcal pneumonia among healthy people above 65 years old, in comparison to healthy people below 65 years old. Moreover, there is 7.7 times higher risk of pneumococcal pneumonia in patients 65 years and older with CRD.[10] In patients with COPD, pneumonia significantly impacts morbidity, mortality, and healthcare costs,[11,12] with 20 times higher risk compared to non-COPD individuals.[13] Such higher rate of pneumonia attributed to smoking consumption as well as the higher use of ICS. COPD exacerbations result in a 2.5% to 14% increase in mortality for hospitalized patients, which rises to 30% for patients admitted to the ICU.[14] Infectious causes account for two-thirds of these exacerbations.[15] The most common virus associated with COPD exacerbation is the rhinovirus followed by the influenza virus with a prevalence rate of 2.5%–11.6%.[16] Patients with asthma reported two times higher rate of pneumococcal infection than general population.[17]

Infectious causes are the primary cause for acute ILD exacerbations with organisms often remaining unidentified despite extensive workup.[18,19] Patients with ILD reported five times higher rate of pneumonia than the general population, this increased incidence did not correlate with the risk of death.[17]

Influenza and pneumococcal diseases are prevalent among patients with bronchiectasis which contribute significantly to acute exacerbation of the disease, frequents admissions, and ultimately death.[20]

COVID-19 caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is usually self-limited with mild respiratory symptoms, and most patients recover with no need for special medical care. However, the severe outcome of COVID-19 infection is significantly more in the old ages as well as in individuals with chronic medical diseases.[21] Asthma and COPD are predominant comorbidities among hospitalized patients with COVID-19 infection.[22,23] Because CRD patients are having reduced respiratory reserve, any decline in respiratory function can be detrimental.[24] The use of corticosteroids to treat CRD may increase susceptibility to infections and heighten the risk of COVID-19 complications.[24] Ultimately, such individuals with CRD are at higher rate of severe outcomes, complications, and death.[25,26]

This occurs because the virus penetrates the cells by attaching to the angiotensin converting enzyme 2 receptors. This receptor is abundantly present in the lung of patients with CRD and smokers.[27,28]

Respiratory syncytial virus (RSV) accounts for 10% of admissions due to pneumonia, 11% for COPD, and 7% for asthma.[29,30] Hospitalized patients with RSV infections experience a significant healthcare burden due to comorbidities, multiple inpatient admissions, and high costs.[31] RSV infection is associated with higher odds of hospital stays lasting seven days or more, pneumonia, ICU admissions, exacerbation of COPD, and increased mortality within one year of admission.[29,31] In a Saudi retrospective study, most patients with RSV-related

community-acquired pneumonia were elderly with comorbidities, one in four patients admitted to ICU, with death rate of 32%,[32] RSV should be considered as a possible etiology of respiratory symptoms in elderly individuals.

Given the seriousness of infectious complications among patients with CRD, implementing a preventative strategy is crucial. This approach provides substantial benefits to both patients and the healthcare system. The best method to prevent and reduce infectious complications, as well as protecting patients, is the administration of the recommended vaccines. Vaccines against respiratory infections are an essential preventative strategy for managing patients with CRD. Influenza and pneumococcal vaccines (PCVs) are significantly associated with a reduction in COPD exacerbations.[33-35]

The influenza vaccine significantly reduced complications related to the illness such as pneumonia, hospitalization, and death (Evidence C).[36] There was one-third reduction in admission due to pneumonia, 17% reduction in office visits, and a 6.4% reduction in visits due to any respiratory condition due to influenza vaccine (Evidence A).[37]

Among Chinese patients with COPD, the vaccine effectiveness to reduce exacerbations was 70% for the influenza vaccine alone, 54% for the 23-pneumococcal polysaccharide vaccine (PPSV-23) alone, and 72% for both vaccines together. The effectiveness of the vaccines to reduce pneumonia was 59% for the influenza vaccine alone, 53% for the PPSV-23 alone, and 73% for both vaccines together. The effectiveness of the vaccines to reduce admission was 58% for the influenza vaccine alone, 46% for the PPSV-23 alone, and 69% for both vaccines together (Evidence C).[38] The influenza vaccine reduced the all causes of death by 41% in COPD patients (Evidence C).[39] In other retrospective study among COPD patients, the influenza and pneumococcal vaccinations alone or combined together showed significant reduction in COPD exacerbations (Evidence C).[40] In a randomized trial involving 167 adult patients with CRD including bronchiectasis, the group receiving both vaccines experienced fewer acute infectious exacerbations in comparison to the group receiving only the influenza vaccine (Evidence A).[41]

COVID-19 vaccination is the primary prevention measure, not only protecting against acute infection but also significantly reducing the likelihood of developing the long-COVID symptoms (Evidence A).[42,43] COVID-19 vaccination is highly effective in preventing serious complications in patients with CRD (Evidence A).[44] In addition, COPD patients infected with COVID-19 are more likely to experience severe exacerbations, poor outcomes, and mortality.[45] However, there is observed reduced effectiveness of COVID-19 vaccine in COPD patients which attributed to viral mutations from one season to the next, as well as health-seeking behavior as vaccinated individuals typically have more access to healthcare compared to the unvaccinated.[46]

Hospitalizations and mortality rates of COVID-19 reduced internationally, largely due to a high immunity from increased vaccination coverage among people and herd immunity.[47] The World Health Organization (WHO) anticipates continuous evolving of the virus without becoming more virulent. Regular updated vaccine doses will be required, especially in high-risk populations, to prevent transmission spikes as immunity wanes over time. Currently, the virus is still spreading and undergoing genetic changes, particularly in the critical regions of its spike protein.[48]

The WHO has set the international target rate for influenza vaccine coverage at 75%,[49] while, the Centers for Disease Control and Prevention set pneumococcal vaccination coverage rate at 60%.[49] However, most countries have not met these targets. For instance, in the United Kingdom (UK), the coverage rate for influenza vaccination in COPD was 23%[40] while influenza vaccination rates were 30.5% in Italy,[50] 36.5% in Turkey,[51] and 46.5% in Germany.[52] Regarding pneumococcal vaccination, the coverage rates were 10.8% in the UK,[40] 13.3% in Italy,[50] 14.1% in Turkey,[51] and 14.6% in Germany.[52]

In Saudi Arabia, the actual vaccination coverage rate in individuals with CRD is not documented and varies by vaccine type, patient population, and region. Despite increased public health awareness of these infections, vaccination programs primarily focus on influenza and PCVs. Although the delivery of the influenza vaccine is on the rise, coverage for other vaccines remains significantly lower. Vaccination rates depend on several factors, including vaccine accessibility and availability, healthcare worker awareness, and patient acceptance. Specific studies assessing the vaccination and effectivness for each CRD subtype are scant or limited to COPD, with most knowledge derived from observational studies or real-world data. In addition, current international recommendations are based on the consensus and expert opinion targeting all CRD in general.

Over the years, the burden of infectious diseases in patients with CRD has increased. Regardless of the primary lung disease, patients with CRD are considered a high-risk category for infectious complications, with significant morbidity and mortality. Consequently, such patients should receive all the currently recommended and updated vaccines. Healthcare authorities and workers must make every effort to increase the awareness

about the vaccinations and to encourage and improve the vaccination rates in CRD patients. The recommended vaccines should be available and accessible in every healthcare facility and offered to every patient with CRD as part of their routine management. The vaccination status and types of vaccines received by patients with CRD should be documented and easily accessible in their medical records.

The current guidelines were developed by the Saudi Thoracic Society (STS) task force to serve as a reference for healthcare practitioners managing patients with CRD. In addition, they can guide policymakers in establishing vaccination programs. The guidelines incorporate the latest advancements and changes in vaccinology, integrating expert opinions, and evidence-based recommendations. The STS selected a panel of nine clinicians and researchers with expertise in chronic respiratory and infectious diseases to develop these guidelines.

Methodology

The panel members systematically searched the literature, similar guidelines, and systematic reviews. The relevant publications were reviewed, and analyzed. Recommendations, Assessment, Development, and Evaluation (GRADE) was the tool used for grading the evidence. The panel members conducted several physical and online meetings, focusing on reviewing the literature, grading the evidence and formulating evidence-based recommendations.

Evidence A is a systematic reviews or meta-analysis or randomized controlled trials (RCT). Limited RCT were considered as Evidence B. Noninterventional studies were considered as Evidence C and panel personal opinion and agreement was considered as Evidence D.

The following vaccines are available in Saudi Arabia and recommended for adults with chronic respiratory diseases [Table 2].

Influenza Vaccine

Influenza infection is primarily caused by two main types of influenza viruses (A virus and B virus). Influenza A virus is classified into hemagglutinin (HA) and neuraminidase (NA) antigens. Three antigens of HA (H1, H2, and H3) and two antigens of NA (N1, N2) are responsible for widespread outbreaks in humans. Influenza B viruses are classified as Yamagata B and Victoria B lineages.

The seasonal influenza vaccine component is manufactured annually taken in consideration the effectiveness of the vaccine of proceeding year and prevalent viral strains. The WHO recommends strains for both the northern (which includes Saudi Arabia) or southern hemispheres, with the aim of providing protection against the anticipated circulating influenza viruses.[53] The strain in Saudi Arabia is produced in February each year and distributed in August. Patients with CRD are in the category of high-risk populations for severe influenza outcomes.

Trivalent influenza vaccine (TIV) typically includes A (H1N1) and A (H3N2) antigens from influenza A and Victoria B antigen from influenza B. In contrast, quadrivalent influenza vaccine (QIV) typically includes A (H1N1) and A (H3N2) antigens from influenza A and both Victoria B and Yamagata B antigens from influenza B. The influenza vaccine for next year will be trivalent (TIV).[53]

Types of influenza vaccines

1. Inactivated influenza vaccine (IIV)
   a. Description: Egg-based influenza vaccine that contains inactivated (killed) influenza viruses. These viruses are no longer infectious but can stimulate an immune response
   b. Administration: 0.5 ml administered in the deltoid muscle
   c. Population: Adult patients above the age of 19 years with CRD (Evidence A).[54]

Table 2: The recommended available vaccines in Saudi Arabia for patients with chronic respiratory diseases

Type of vaccine	Adult dose and mode of delivery	Age per year: 18–49	50–59	60–64	≥65
IIV	0.5 mL IM Annually	Recommended	Recommended	Recommended	Recommended
HD-IIV	0.7 mL IM Annually	Not recommended	Not recommended	Not recommended	Recommended
Pneumococcal vaccines	0.5 mL IM	Recommended [Table 3]	Recommended [Table 3]	Recommended [Table 3]	Recommended [Table 3]
COVID-19 vaccine (mRNA vaccines)	0.3 mL Pfizer-BioNTech 0.5 mL moderna COVID-19 IM	Recommended (see text)	Recommended (see text)	Recommended (see text)	Recommended (see text)
RSV vaccines	0.5 mL IM	Not recommended (see text)	Not recommended	Recommended	Recommended
RZV	Two-doses (0.5 mL IM), 2–6 months apart	Conditional recommendation (see text)	Recommended	Recommended	Recommended

IIV=Inactivated influenza vaccine, HD-IIV=High-dose IIV, IM=Intramuscular, RSV=Respiratory syncytial virus, RZV=Recombinant zoster vaccine

2. High dose IIV (HD-IIV)
   a. Description: Egg-based that contains higher antigens (four times) than the standard dose IIV
   b. Administration: 0.7 ml administered in the deltoid muscle
   c. Population: Adult patients 65 years and older with CRD (Evidence A).[55,56]
3. Live attenuated influenza vaccine (LAIV): Not yet available in Saudi Arabia
4. Recombinant influenza vaccine (RIV): Not yet available in Saudi Arabia
5. Cell Culture-based Vaccine (CCIV): Not yet available in Saudi Arabia.

The vaccine preferably to be administered in September each year. Nevertheless, the vaccine can be given at any time during the season. Most influenza vaccines are designed to provide effective immunity with a single dose.

Precautions and contraindications

- In sick patient with acute illness, the vaccine should be postpended till the time of complete recovery from the acute illness
- History of previous anaphylactic reaction is the only absolute contraindication for influenza vaccine
- In patient with allergy to eggs, the vaccine can be safely administered (not contraindicated)
- History of Guillain-Barre syndrome (GBS) is not contraindication for influenza vaccine; however, the vaccine should be avoided in patients who had GBS after receiving the previous vaccine (up to 6 weeks)
- Healthcare workers who provide the vaccine to their patients should be able to manage possible but rare allergic reactions including anaphylaxis to the vaccine.

Immunogenicity and effectiveness

Immunogenicity

Serum antibodies against hemagglutinins are a correlate of vaccine-induced protection for IIV and the protection against influenza infection after the vaccine is usually shorter than 1 year.[57]

Effectiveness

Numerous studies demonstrated the efficacy of influenza vaccines in preventing the influenza infection and reducing complications among individuals 19 and older with CRD.[58-61] Many factors determine the vaccine effectiveness including age of the patient, coexisting chronic medical diseases and history of previous influenza vaccinations, however, influenza vaccines have been especially beneficial in reducing the complications from influenza infection in individuals with CRD (Evidence A).[59] Vaccine has been proven in preventing complications (e.g., pneumonia and worsening underlying respiratory conditions), reducing severity (e.g., reduce symptom severity and improve recovery), enhancing community herd immunity and reducing morbidity and mortality (Evidence C).[60]

Common adverse events

Mild and transient local pain and redness at the injection site usually mild and transient which may persist for several hours to few days. Fever and other systemic symptoms such as fatigue are mild and lasting for a few days and usually more common with HD-IIV compared to the standard dose of IIV.

Uncommon and rare adverse events

- Severe allergic anaphylaxis reaction: Severe adverse reactions to influenza vaccines are exceptionally rare. Anaphylaxis is a serious and life-threatening condition that can manifested as shortness of breath, tachycardia, and hypotension[61]
- Guillain-Barré syndrome (GBS): The incidence is about 1 case per million vaccinated individuals, while the risk of GBS is 17 cases per million individuals with influenza infection[55]
- Oculorespiratory syndrome: It is rare allergic reaction to influenza vaccine manifested by bilateral red eyes with or without respiratory symptoms. Patients who developed red eyes without respiratory symptoms can be revaccinated with influenza vaccine in future while patients who developed red eyes with respiratory symptoms should not be vaccinated with influenza vaccine in future.

Pneumococcal Vaccination

Pneumococci are classified in distinct serotypes based on the unique composition of the virulent capsular polysaccharide. More than 100 serotypes were identified.[62] Among these serotypes, 24 pneumococcal serotypes are culprit for pneumococcal diseases.

Types of pneumococcal vaccines

- Valent pneumococcal conjugate vaccines (PCV13,15,20,21)
- 23-Pneumococcal polysaccharide vaccine (PPSV23).

Mode of administration and dose

0.5 ml administered in the upper arm (deltoid muscle) for all vaccine types.

Indications

All adults with CRD (above the age of 19).

Recommendations for pneumococcal vaccine types in patients with CRD

- For naïve patients (never received any PCV before)
  - Administer single dose of PCV20

Table 3: Recommendations for pneumococcal vaccines in adult patients (19 years old and above) with chronic respiratory diseases

Patient category	Option A	Option B
Naive patient	PCV20	PCV15 now followed by a PPSV23 with a 1-year interval
PPSV23 was received only	PCV20 after 12 months of the last PPSV23 dose	PCV15 after 12 months of the last PPSV23 dose
PCV13 was received only	PCV20 after 12 months of the last PCV13 dose	PPSV23 after 12 months of the last PCV13 dose
Both PCV13 and PPSV23 received		
a) Current age ≥65 years or immunocompromised and PPSV23 received before the age of 65 years	PCV20 after 5 years of the last PPSV23 dose	PPSV23 after 5 years of the last PPSV23 dose
b) current age >65 yeras or immunocompromised and PPSV23 recivived at age > 65 yeras	PCV20 after 5 years of the last PPSV23 dose	
c) Current age 19–64 years with CRD	No current recommendation	No current recommendation

CRD=Chronic respiratory diseases, PCV=Pneumococcal conjugate vaccine, PPSV23=23-pneumococcal polysaccharide vaccine

  - In case PCV20 is not available: administer single dose of PCV15 now followed by a single dose of PPSV23 after 12 months (8-week interval in immunocompromised patients and revaccinate once after 5 years).
- In case, only PPSV 23 was received (at any age): Wait for 12 months after PPSV23 vaccine then administer a single dose of PCV20 OR single dose of PCV15 (8-week interval in immunocompromised patients and revaccinate once after 5 years)
- In case only PCV13 was received (at any age): Wait for 12 months after of PCV13 vaccine then administer a single dose of PCV20 OR single dose of PPSV23 (8-week interval in immunocompromised patients and revaccinate once after 5 years)
- In case both PCV13 and PPSV23 vaccines were received in the past: Consider the patient's age
  - Patient's age is 19–64 years: No current recommendations
  - Patient's age 65 years and above:
- In case of a history of PCV13 received at any age and PPSV23 received before the age of 65 years: Wait for 5 years after of PPSV23 vaccine then administer a single dose of PCV20 OR a single dose of PPSV23
- In case of a history of PCV13 received at any age and PPSV23 received at age ≥65 years: Wait for 5 years after PPSV23 vaccine then administer a single dose of PCV20 [Table 3].

Note: PCV21 (not yet avaliable in Saudi Arabia) has recently approved by the Advisory Committee on Immunization Practices for elderly populations above age 65 years and for individuals 19–64 years based on their health status. PCV21 includes eight new pneumococcal serotypes that are not contained in currently available PCVs.[63]

Contraindications

- History of previous anaphylactic reaction
- History of allergic reaction to diphtheria toxoid-containing vaccine.

Immunogenicity and effectiveness

Immunogenicity

Both the PPSV23 and PCVs are immunogenic in adults. The efficacy of PPSV23 has been documented in several RCTs (Evidence A)[64,65] and in meta-analysis (Evidence A).[66] pneumococcal polysaccharide antigens in PCV stimulating T-helper cells which subsequently stimulate B-cells to produce antibodies and ultimately make the vaccine be able to create a longer immunity.[67]

PCV13 prevented about half of the occurrences of vaccine-type pneumococcal pneumonia. With efficacy against invasive pneumococcal disease is 75%, against pneumococcal pneumonia is 46% and against nonbacteremic pneumococcal pneumonia is 45% (Evidence A).[68] The immunogenicity of PCV20 has been demonstrated in several double-blind (Evidence A)[69-71] and open label (Evidence A)[72] randomized clinical trials. Pneumonia and death reduced in adults' patients received PCV20 in comparison to PPV23 (Evidence A).[73]

Effectiveness

PCVs reduce both the severity and mortality associated with pneumonia.[73] PCV is one of the recommended vaccines for patients with COPD.[74] In addition, pneumococcal vaccination reduces clinic visit, admission, as well as drug utilization related to the treatment of pneumococcal disease. Pneumococcal vaccination also provides economic value by reducing the incidence of co-morbid conditions and the typical complications that can arise from pneumococcal disease.[75] In addition, the vaccination can support the avoidance of nosocomial infections that may follow hospitalizations for pneumococcal disease.[76]

Common adverse events

Mild and transient pain, swelling, induration, and redness at the injection site.[76] Injection site reaction is self-limiting and resolved with analgesia and a warm

compression. Systemic reactions such as fever, fatigue, myalgias, and headache are mild and last for a few days.[70]

COVID-19 Vaccination

The WHO Technical Advisory Group for COVID-19 Vaccine Composition (TAG-CO-VAC) convenes on the regular basis to evaluate the evolution of the virus on the antigen composition of the vaccine and suggest to the WHO regarding if any modifications to the components of the antigen of COVID-19 vaccines are necessary. For example, the Omicron XBB 1.5 sublineage was included in the 2023 COVID-19 vaccines formulation.[77]

As of April 2024, over 94% of the genetic sequences of the virus found in publicly accessible sources originate from JN.1. These variants are consistently replacing the previous XBB lineage variants, such as EG.5.[78] Multiple JN.1 variants (JN.1.13.1, JN.1.11.1, KP. 2) have undergone separate evolutionary modifications in the spike protein. These substitutions occur within the epitopes targeted by the neutralizing antibodies. The neutralization titers against JN.1 are generally 2–5 times lower compared to the titers against the XBB.1.5 antigen. Compared to vaccines with an older antigen, an extra dose of an updated vaccine causes a 40% increase in the antibodies to the variant.[48] Statistical modeling suggests that an updated vaccine antigen may increase the efficiency of a vaccine dose by around 23%–33% against severe illness and by 11%–25% against symptomatic disease.[78]

Current SARS-CoV-2 evolution trends point to JN.1 as the most probable immediate ancestor of SARS-CoV-2 variations.[48] More data are needed regarding the public health implications of newly emerging variants, as well as their exact timing, antigenic features, and particular mutations.[78] Based on the results of early relative vaccine effectiveness studies targeting JN.1, the effectiveness of the XBB.1.5 vaccine will be reduced if SARS-CoV-2 evolves further from JN.1. According to the TAG-CO-VAC, one strategy is to employ JN.1 lineage for the coming 2024–2025 season.[77] The US FDA Vaccine Advisory Committee recommended a monovalent JN.1-lineage. The committee preferred JN.1-lineage for the coming year to be the KP. 2 strain.[79]

Types of vaccines

- Messenger RNA (mRNA) vaccines: used in Saudi Arabia for patients 12 years and above with CRD. The two available mRNA vaccines are:
  - Pfizer-BioNTech COVID-19 vaccine
  - Moderna COVID-19 vaccine.
- Protein subunit vaccine (Novavax COVID-19 Vaccine): Not available in Saudi Arabia.

Administration

- Pfizer-BioNTech COVID-19 vaccine: 0.3 ml intramuscular
- Moderna COVID-19 vaccine: 0.5 ml intramuscular.

COVID-19 vaccine recommendations for adults with CRD (Evidence B and C)

- Adults with CRD are high-risk group and should be vaccinated with single dose if they did not receive the vaccine before and should be re-vaccinated after 1 year of the previous vaccine
- Re-vaccination after 6–12 months of the previous dose is recommended for the oldest adults (>70 years) with CRD
- The minimal interval for additional vaccine doses is 3 months for immunocompetent individuals and 2 months for immunocompromised individuals
- The updated COVID-19 vaccine should be considered for both the initial and re-vaccination doses
- The omicron BA.4/BA.5 and the original vaccines are not recommended anymore as they are replaced by the updated COVID-19 vaccine
- Testing for the antibodies is not needed after receiving COVID-19 vaccinations or to determine whether a person needs to be vaccinated
- The vaccination should be integrated into primary, secondary, and tertiary healthcare services to ensure vaccine delivery, especially for the high-risk groups, preferably before the winter season
- Tests for the virus will not be impacted by the prior administration of the vaccine.

Contraindications

History of previous anaphylactic reaction is the only absolute contraindication for COVID-19 vaccine.

Precautions[78]

- In sick patient with acute illness, the vaccine should be postpended till time of complete recovery from the acute illness
- If patient had nonsevere reaction to one type of the vaccine, an alternate COVID-19 vaccine type may be administered
- Vaccination may be considered after 3 months of complete recovery following the diagnosis of multisystem inflammatory syndrome in adults
- Patient who developed myocarditis or pericarditis secondary to previous COVID-19 vaccine should not be given new COVID-19 vaccine
- In patient who had acute symptomatic COVID-19 infection or asymptomatic positive test, the vaccine must be postpended for at least 3 months.

Messenger RNA vaccine-related adverse events

- Local pain, redness which usually mild and transient which may persist for several hours to few days

- Fever and other systemic symptoms such as fatigue are mild and lasting for a few days
- Axillary lymph nodes enlargement on the same side of the vaccinated arm
- Myocarditis and pericarditis which developed in the week after the vaccination particularly in young male patients. Most cases are mild, and patients respond well to treatment, which may include analgesics. For severe cases, hospitalization may be required with the majority of patients recovering fully with appropriate medical care. The risk of developing these conditions after COVID-19 infection is higher than the risk of developing these conditions following COVID-19 vaccination
- Rarely, anaphylactic reactions occur after receiving the COVID-19 vaccination
- The observation period after vaccination is usually 15 min, due to the risk of syncope (fainting). However, this period should be extended to 30 min in persons with a previous history of mild-to-moderate reaction to COVID-19 vaccine
- In Saudi Arabia, health-care workers are required to document and report any potential side effect or reaction attributed to the vaccine. This reporting is important to recognize any concerns and it is not intended to determine if a vaccination is to be blamed for an adverse event, it can recognize "signals" that could point to potential safety issues that need more investigation.[80]

Respiratory Syncytial Virus Vaccination

The clinical manifestations of RSV infection range from no symptoms to severely symptomatic LRTIs. In temperate climates such as Saudi Arabia, RSV season starts in late fall or early winter.[81] Although it is mainly affecting infants and young children with high morbidity and mortality,[82] RSV is increasingly recognized for its significant impact on the older adult population.[29,83] RSV often presents with respiratory tract infection in infants and is almost always symptomatic in older adults. In fact, 18% of winter respiratory illness visits made by elderly adults were RSV-related.[84] The virus is composed of the surface fusion (F) and attachment (G) glycoproteins that induce antibodies. The function of such proteins is to attach to the cell membrane of the cell and subsequently lead to the characteristic syncytium.[85] Human RSV exists in A and B antigenic subtypes. One subtype usually predominates although both are circulating at the same time.[86]

Respiratory syncytial virus vaccination for adults

The RSV vaccine targets the F surface glycoprotein.[87]

Two respiratory syncytial virus vaccines are available for adult populations

Recombinant monovalent adjuvanted vaccine

This vaccine contains the F protein from the A subtype only. It utilizes the same AS01 adjuvant as the Herpes Zoster (HZ) (recombinant zoster vaccine [RZV], shingles) vaccine. This RSV vaccine licensed for people aged ≥60 years.

Recombinant bivalent nonadjuvanted vaccine

This vaccine contains the F protein from A and from B subtypes, without an adjuvant. This RSV vaccine licensed for people aged ≥60 years, as well as for maternal immunization in weeks 32–36 of gestation.

In 2023, the United States and the European Union granted approval both the RSV vaccines (adjuvanted as well as bivalent) for adults' population 60 years and above.[88,89] In Saudi Arabia, both the adjuvant monovalent vaccine and the nonadjuvant bivalent vaccine were approved for adults' population 60 years and above including patients with CRD. Additionally, the bivalent nonadjuvanted vaccine was also approved for women at 32–36-week gestation.

Dose and route

0.5 ml intramuscular for both vaccines. Vaccination before the peak RSV season is the preferred timing for administering RSV vaccines.

Indications

All adult patients aged ≥60 years with CRD.

Contraindications

- In sick patient with acute illness, the vaccine should be postpended till time of complete recovery from the acute illness
- History of previous anaphylactic reaction.

Vaccine efficacy

Respiratory syncytial virus recombinant monovalent adjuvanted vaccine

The efficacy evidence for this adjuvanted RSV vaccine is based on the analyses of data collected during complete two RSV seasons in both earth hemispheres (Northern and Southern) spanning period from May 2021 to March 2023. The clinical trial involved 24,966 participants randomized into the RSV vaccine arm or the placebo arm with 15 months' mean follow-up period. The efficacy of the RSV vaccine in preventing lower respiratory tract disease was 82.6% and 56.1% during the first year and the second year consecutively. Efficacy of the RSV vaccine over 2 years was 77.5% in preventing medically attended lower respiratory tract disease (Evidence A).[90]

Respiratory syncytial virus recombinant bivalent nonadjuvanted vaccine

The efficacy evidence for this nonadjuvanted RSV vaccine is derived from the data collected during complete one and half seasons of RSV infection (18 months period,

2021–2023). The clinical trial involved 36,862 participants randomized into the RSV vaccine arm or the placebo arm with 12 months' mean follow-up period. The efficacy of the RSV vaccine in preventing lower respiratory tract disease was 88.9% and 78.6% during the first year and the partial second year consecutively. Efficacy of RSV vaccine over 2 years was 81% in preventing medically attended lower respiratory tract disease (Evidence A).[91]

Adverse events

Respiratory syncytial virus recombinant monovalent adjuvanted vaccine

- Local pain and redness which usually mild and transient which may persist for several hours to few days
- Fever and other systemic symptoms such as fatigue are mild and lasting for a few days and are more common in the vaccinated group (3.8%) than the placebo group (0.9%)
- Serious adverse reactions were reported similarly in both arms (4.4% in vaccine arm vs. 4.3% in placebo arm)
- Ten events of atrial fibrillation (0.1%) were reported in the vaccinated arm vs four cases (<0.1%) in placebo arm[92]
- Three inflammatory neurologic events were reported in the vaccinated group.

Respiratory syncytial virus recombinant bivalent nonadjuvanted vaccine

- Local pain and redness which usually mild and transient which may persist for several hours to few days
- Fever and other systemic symptoms such as fatigue are mild and lasting for a few days and are more common in the vaccinated group (1%) than the placebo (0.7%)
- Serious adverse reactions were reported similarly in both arms (4.3% in vaccine arm vs. 4.1% in placebo arm)
- Ten events of atrial fibrillation (<0.1%) were reported in the vaccinated arm vs four cases (<0.1%) in the placebo arm
- Three inflammatory neurologic events were reported in the vaccinated group.[91-94]

Herpes Zoster Vaccination

HZ occurs as result from the reactivation of the varicella-zoster virus (VZV). It is manifested as neuropathic painful skin lesion with blisters, usually appearing unilaterally and following a specific dermatomal pattern.[95,96] HZ affects approximately one in every three people in their lifetime, translating to 30% in the general population.[95,96] Numerous factors impact its incidence, including older age, decrease in immunity, and the prevalence of the VZV in the community. HZ infection has serious complications which can affect the eyes, nerve paralysis, neuromuscular disorders, secondary bacterial infections, and muscle weakness.[97-100] Postherpetic neuralgia (PHN) can be quite debilitating with persistent severe pain that occurs after the fading of a HZ lesion.[101]

Types of herpes zoster vaccination

1. Recombinant Zoster vaccine (RZV)
   - Description: Recombinant-designed vaccine. This vaccine does not include the live VZV. It uses a specific protein of the HZ virus called glycoprotein E
   - Population: Adults with CRD aged ≥50 years (Evidence B and C)[102,103]
   - Population: Adults with CRD aged 19–49 years with immunodeficiency or immunocompromised due to their disease or due to immunosuppressive drugs (Evidence B and C)[102,103]
   - Administration: Two doses of 0.5 ml IM, 2–6 months apart in immunocompetent patients or within 1–2 months in immunosuppressed patients[104]
   - RZV may be given after 12 months from HZ episode.[102]
2. Live attenuated zoster vaccine: not yet available in Saudi Arabia.

Contraindications

Previous anaphylactic reaction to any part of HZ vaccination.[102-104]

Efficacy

Recombinant zoster vaccine

RZV reduced risk of HZ by 91% and PHN by 88% (Evidence A).[105] In adults aged below 59 years, the efficacy of RZV over 3 years' period is 96.6% against HZ and 100% against PHN while in adults aged from 60 to 69 years, the efficacy of RZV over three years period is 97.4% against HZ (Evidence A).[106,107] This is a crucial impact, especially for individuals with CRD, as they may already experience compromised respiratory function.

Common adverse events

Mild and transient pain, swelling, induration, and transient systemic reactions such as fever and stomach upset are reported as common systemic reactions to RZV. Most of these symptoms are mild and last for few days.[108,109]

Severe adverse events

Severe allergic reactions following RZV vaccination, although rare, are recognized as potential adverse events and could be life threatening. Symptoms of severe reactions include swelling of the face, drop in blood pressure, shortness of breath, and tachycardia.

Healthcare providers administering the vaccine should be vigilant for any signs of anaphylaxis and be prepared to initiate emergency medical procedures promptly.

Co-administration of multiple vaccines

Giving more than one vaccine in one clinic visit in children is a well-established practice but it is not the case in the adult population. The co-administration of more than one vaccine in a single visit is one way to improve the vaccines` uptake in adults and is safe and effective. It also reduces the consultation time and improves compliance with the recommendations.

The co-administration of more than one vaccine in a single visit offers the advantage of optimizing vaccination opportunities. Such practice will reduce the likelihood of missed future opportunities for vaccination. This is particularly relevant for patients with CRD, ensuring they receive comprehensive immunization coverage. In case of the co-administration of more than one vaccine in a single visit, healthcare provider should use different injection sites.

All influenza vaccines can be administered before or after administration another vaccine during the same clinic visit day. The co-administration of PCVs together with the influenza vaccine is immunogenic and safe in adults.[110] Moreover, the co-administration of PCV20 with COVID-19 vaccine (Pfizer-BioNTech) was safe and without any serious concerns, adverse events were not different across the groups and there was no discontinuation of the trial because of concerns related to the vaccine safety[111] No current studies are available in regard to co-administration of other PCVs together with other COVID-19 vaccines.

The immune response of giving RZV and PPSV23 together at the same time is equivalent to the sequential administration of both vaccines at separate occasions with no safety concerns reported.[112] The immune response of giving RZV and QIV together at the same time is equivalent to the sequential administration of both vaccines at separate occasions with no safety concerns reported.[113] The immune responses of giving RZV and PCV 13 together at the same time is equivalent to the sequential administration of both vaccines at separate occasions with no safety concerns reported.[114] Giving high-dose QIV together with COVID-19 vaccine in elderly population is safe and effective. COVID-19 vaccines can be given together with influenza vaccines.[115] The immune response of giving RSV recombinant adjuvanted vaccine and IIV together at the same time is equivalent to IIV or RSV recombinant adjuvanted vaccine administered alone at separate occasions with no safety concerns reported.[116] Although data of giving RSV vaccines together with other vaccines are limited, this practice is considered acceptable pending the accumulation of further real-world experience and safety data.

Given the shared adjuvant component between the RSV-adjuvanted vaccine and RZV vaccine, it is advice to avoid co-administering these two vaccines together during the same clinic visit.

Contraindications for the co-administration of multiple vaccines at the same time will be the same contraindications for each vaccine separately.

Hajj recommendations for vaccinations

Influenza and the updated COVID-19 vaccines are currently among the required vaccinations for performing the Hajj.[117] Other vaccines (Pneumococcal, RSV, and HZ vaccines) are not currently required vaccinations for Hajj. However, patients with CRD are considered a high-risk population and other vaccines (i.e., Pneumococcal, RSV, and HZ vaccines) are strongly encouraged and highly recommended before the Hajj season in this vulnerable population. Ensuring a comprehensive vaccine coverage is crucial for protecting CRD patients during the Hajj.

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Conflicts of interest

There are no conflicts of interest.

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