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REVIEW

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Coronavirus disease 2019 (Covid-19) vaccination recommendations in special populations and patients with existing comorbidities

Zeinab Mohseni Afshar[1] | Arefeh Babazadeh[2] | Alireza Janbakhsh[1] | Feizollah Mansouri[1] | Terence T. Sio[3] | Mark J. M. Sullman[4,5] | Kristin Carson-Chahhoud[6] | Rezvan Hosseinzadeh[7] | Mohammad Barary[7] | Soheil Ebrahimpour[2]

[1]Clinical Research Development Center, Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran

[2]Infectious Diseases and Tropical Medicine Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

[3]Department of Radiation Oncology, Mayo Clinic, Phoenix, Arizona, USA

[4]Department of Social Sciences, University of Nicosia, Nicosia, Cyprus

[5]Department of Life and Health Sciences, University of Nicosia, Nicosia, Cyprus

[6]Australian Centre for Precision Health, University of South Australia, Adelaide, Australia

[7]Student Research Committee, Babol University of Medical Sciences, Babol, Iran

Correspondence
Soheil Ebrahimpour, Infectious Diseases and Tropical Medicine Research Center, Health Research Institute, Babol University of Medical Sciences, Ganjafrooz Blvd., Babol 4717647745, Iran.
Email: drsoheil1503@yahoo.com

Summary

Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a crucial step in ending the current worldwide pandemic. However, several particularly vulnerable groups in the population were not included in sufficient numbers in coronavirus disease 2019 (Covid-19) vaccine trials. Therefore, as science advances, the advice for vaccinating these special populations against Covid-19 will continue to evolve. This focused review provides the latest recommendations and considerations for these special populations (i.e., patients with rheumatologic and autoimmune disorders, cancer, transplant recipients, chronic liver diseases, end-stage renal disease, neurologic disorders, psychiatric disorders, diabetes mellitus, obesity, cardiovascular diseases, chronic obstructive pulmonary disease, human immunodeficiency virus, current smokers, pregnant and breastfeeding women, the elderly, children, and patients with allergic reactions) using the currently available research evidence.

Abbreviations: ABA, Abatacept; ACE2, Angiotensin-converting enzyme 2; ACIP, Advisory Committee on Immunisation Practices; ACOG, American College of Obstetricians and Gynecologists; ACR, Acute cellular rejection; ASRM, American Society for Reproductive Medicine; BAFF, B cell activation factor; BMI, Body mass index; CAD, Coronary artery disease; CD, Cluster of differentiation; CDC, Centers for Disease Control and Prevention; CIDP, Chronic inflammatory demyelinating polyneuropathy; CLD, Chronic liver disorders; CNS, Central nervous system; COPD, chronic obstructive pulmonary disease; Covid-19, Coronavirus disease 2019; CVD, Cardiovascular disorder; CVID, Common variable immunodeficiency; DMARD, Disease-modifying antirheumatic drug; DMT1, Diabetes mellitus type 1; DMT2, Diabetes mellitus type 2; DMTs, Disease-modifying therapies; ESRD, End-stage renal disease; EUA, Emergency Use Authorisation; FDA, Food and Drug Administration; GBS, Guillain-Barré syndrome; HBV, Hepatitis B virus; HCC, Hepatocellular carcinoma; HCV, Hepatitis C virus; HIV, Human immunodeficiency virus; HSCT, Haematopoietic stem cell transplant; ICI, Immune checkpoint inhibitors; ICU, Intensive care unit; IL, Interleukin; IRAE, Immune-related adverse event; ISRR, Immunisation stress-related response; JAK, Janus kinase; JCVI, Joint Committee on Vaccination and Immunisation; MELD, Model for End-stage Liver Disease; MERS, Middle East respiratory syndrome; MHRA, Medicines and Healthcare Products Regulatory Agency; MIS-C, Multisystem inflammatory syndrome in children; MTX, Methotrexate; NMD, Neuromuscular disorder; NYHA, New York Heart Association; PAD, Peripheral arterial disease; PBC, Primary biliary cholangitis; PD, Peritoneal dialysis; PEG, Polyethylene glycol; PI3K, Phosphatidylinositol 3-kinases; PNES, Psychogenic non-epileptic seizures; RBD, Receptor-binding domain; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; SLE, Systemic lupus erythematosus; SOT, Solid-organ transplant; TCZ, Tocilizumab; TNF, tumour necrosis factor; WHO, World Health Organisation.

KEYWORDS
Covid-19, efficacy, immunocompromise, safety, SARS-CoV-2, vaccination

1 | INTRODUCTION

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has resulted in many individuals becoming infected, more than four million deaths, and has placed an unprecedented burden on public health services worldwide.[1-3] Vaccinations against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a crucial step in ending the current worldwide pandemic. However, several particularly vulnerable groups in the population were not included in sufficient numbers in coronavirus disease 2019 (Covid-19) vaccine trials.[4] Table 1 summarises the current Covid-19 vaccination recommendations in these special populations and patients with existing comorbidities. Therefore, as science advances, the advice for vaccinating these special populations against Covid-19 will continue to evolve. This focused review provides the latest recommendations and considerations for these special populations using available research evidence.

2 | RHEUMATOLOGIC AND AUTOIMMUNE DISORDERS

Individuals on immunosuppressive therapies are among those most susceptible to Covid-19-related morbidity and mortality. Although vaccinating these populations should be a high priority for healthcare providers and governments, they have mostly been excluded from vaccine trials.[5] The most important reason behind such exclusions is that immunosuppressive therapies can impair the vaccine-induced humoral and cellular immune responses, making it difficult to measure its effectiveness on the immune system.[6] It is important to note that there are many such diseases, and we do not fully understand the pathogenesis of any of them. Thus, it is essential to consider the diseases and the treatments for them when considering vaccination. For example, does the disease or treatment suppress T cell or B cell responses, and will this differ according to the vaccine used? In the following section, we discuss the impact of several immunosuppressive agents on vaccine response. It is essential to know that some of the information has been generalised from experiences with influenza, pneumococcal, and tetanus vaccines.

The effect of corticosteroids on vaccine-induced antibody production is dose-dependent. Prednisolone doses higher than 10 mg daily, or equivalent doses of other corticosteroids, impair vaccine response, and thus, tapering the dose around the time of vaccination would appear necessary.[7] Disease-modifying antirheumatic drugs (DMARDs) are agents used for decreasing inflammation in rheumatic disorders. Methotrexate (MTX), hydroxychloroquine, sulfasalazine, leflunomide, cyclophosphamide, mycophenolate, and azathioprine are examples of these agents.[8] All DMARDs can affect antibody responses, but none of them, except MTX and cyclophosphamide, lower immunologic responses below the threshold of seroprotection.[8] In addition, MTX suppresses humoral response by interacting with the B cell activation factor (BAFF).[9] Thus, it is reasonable to withhold MTX for at least two weeks before and after vaccination. However, withholding the medication for more than two weeks may lead to a flare-up in the underlying disease.[10] Thus, the timing of withholding medication should be carefully monitored to lower the risk of adverse events.

Anti-tumour necrosis factors (TNFs) and interleukin (IL)-17 blockers seem to have no significant effect on vaccine-induced immunity unless used concurrently with MTX.[11,12] IL-6 inhibitors, such as tocilizumab (TCZ), seem to have no substantial effect on vaccine-induced seroprotection unless co-administered with MTX.[13] However, while some studies have reported there should be at least 12 weeks between tocilizumab administration and vaccination to have the ideal antibody response,[13] other research has shown that TCZ does not impair antibody production for other types of vaccines (not Covid-19).[14] Information about the impact of IL-1 antagonists, including anakinra, and canakinumab, on vaccine-induced seroprotection, is scarce, and more studies are urgently needed.[15] Janus kinase (JAK) inhibitors, such as baricitinib and tofacitinib, might trigger drug interactions with mRNA vaccines, primarily when used concurrently with MTX.[16] Therefore, it is better to withhold JAK inhibitors for 1–2 weeks on either side of the vaccination date.[16] Anti-CD20 agents (e.g., rituximab) impair B cell production, making patients prone to severe forms of Covid-19. These agents are also believed to profoundly affect vaccine-induced antibody responses, even several months after their use.[17] Therefore, it is recommended that their use be limited only to essential cases or administered with a minimum gap of four weeks before and six months after vaccination.[17] The impact of T-cell lymphocyte activation inhibitors, such as abatacept (ABA), on vaccine-induced immunity, is controversial and more studies are needed to clarify any interactions.[18]

In general, TNF inhibitors, such as TCZ, ABA, and IL-17 antagonists, seem to impact vaccine efficacy negatively. The Centers for Disease Control and Prevention (CDC) recommends at least a two-week spacing between administration of these agents and vaccination.[14] Thus, the decision to vaccinate rheumatologic patients who use the medications mentioned above should be individually made since it appears that low-dose immunosuppressive agents do not significantly affect the vaccine-induced antibody response.[14] Overall, it appears best to vaccinate these patients when their underlying disease is under control.[14] It is also noteworthy that allergic reactions in these patients may happen following vaccination, especially in patients with systemic lupus erythematosus (SLE), necessitating a more extended period (at least 2 h) of monitoring following vaccination.[14]

Another important consideration is the safety profile of the Covid-19 vaccines in rheumatology patients, which do not seem to be contraindicated since none of the treatments attenuate vaccines.[19] However, it is currently unknown whether Covid-19 vaccines can

TABLE 1 Summary of existing Covid-19 vaccination recommendations in special populations and in patients with existing comorbidities

	Vaccine platform	
	mRNA	**Adenoviral vector**
Most common side effects	Fatigue, headache, chills, muscle pain, fever. Worsen after the second dose.	Injection site pain, fever, muscle aches, headache, fatigue. Worsen after the second dose.
Who should not be vaccinated	People with a history of allergic reactions to vaccine ingredients, including polyethylene glycol, and anyone with a history of allergic reactions to polysorbate.[a]	Anyone with a severe allergic reaction to an ingredient in the vaccine.[a]
Significant side effects (rare)	Pfizer/BioNTech and Moderna: Anaphylaxis, Bell's palsy, autoimmune hepatitis, myocarditis, pericarditis	Janssen: VITT, demyelinating Oxford/AstraZeneca: VITT, transverse myelitis, demyelinating
Rheumatologic and autoimmune diseases	• Corticosteroids: Taper to <10 mg/day prior to vaccination. • MTX: Withhold 2 weeks before and after vaccination. • Anti-TNF and IL-17 medications: No specific dose reduction is required. • Anti-IL-6 medications: Vaccination should be 12 weeks before/after TCZ administration. • JAK inhibitors: Withhold 1–2 weeks before and after vaccination. • Anti-CD20 medications: Withhold 4 weeks before until 6 months after vaccination. • ABA: Data are not yet available.	• Corticosteroids: Taper to <10 mg/day prior to vaccination. • MTX: Withhold 2 weeks before and after vaccination. • Anti-TNF and IL-17: No specific dose reduction is required. • Anti-IL-6: Vaccination should be 12 weeks before/after TCZ administration. • JAK inhibitors: Withhold 1–2 weeks before and after vaccination. • Anti-CD20 medications: Withhold 4 weeks before until 6 months after vaccination. • ABA: Data are not yet available.
Cancer	• Anti-CD20 or cytotoxic therapies inactivate the mRNA vaccine. • Cytotoxic chemotherapy: Start chemotherapy courses 2 weeks after vaccination. • If chemotherapy is already initiated, vaccination should be given between courses of chemotherapy. • Lymphocyte or plasma cell-depleting regimens: Vaccination should be 2 weeks before or 3 months after the end of treatment.	• Cytotoxic chemotherapy: 2 weeks after vaccination • If chemotherapy has already been given, vaccination should be given between courses of chemotherapy. • Lymphocyte or plasma cell-depleting regimens: Vaccination should be 2 weeks before or 3 months after the end of treatment.
Transplant patients	• Vaccination is recommended early in the course of the underlying disease. • After transplantation, postpone vaccination for 3–6 months. • If the first dose is received before the transplantation, the second dose should be administered at least 4 weeks after transplantation • A third dose may be warranted for optimal immunity.	• Vaccination is recommended early in the course of the underlying disease. • After transplantation, postpone vaccination for 3–6 months. • If the first dose is received before the transplantation, the second dose should be administered at least 4 weeks after transplantation • A third dose may be warranted for optimal immunity.
CLD	• Recommended, with priority given to patients with higher MELD scores. • Vaccination of patients with CLD undergoing treatment for HBV, HCV, PBC, and autoimmune hepatitis should be performed without discontinuing their therapy. • Vaccination is safe and recommended for patients with HCC. • Patients on the transplant list should receive two doses of the vaccine before the transplant.	• Recommended, with priority given to patients with higher MELD scores. • Vaccination of patients with CLD undergoing treatment for HBV, HCV, PBC, and autoimmune hepatitis should be performed without discontinuing their therapy. • Vaccination is safe and recommended for patients with HCC. • Patients on the transplant list should receive two doses of the vaccine before the transplant.

(Continues)

TABLE 1 (Continued)

	Vaccine platform	
	mRNA	**Adenoviral vector**
	• If the patient received the first dose before the transplant, the next dose could be given to him/her at 6 weeks to 3 months after the transplant.	• If the patient received the first dose before the transplant, the next dose could be given to him/her at 6 weeks to 3 months after the transplant.
	• Vaccination should be withheld in liver transplant recipients with active ACR or those receiving high-dose corticosteroids until the condition is resolved.	• Vaccination should be withheld in liver transplant recipients with active ACR or those receiving high-dose corticosteroids until the condition is resolved.
ESRD	• Taper steroid doses below 20 mg prednisone equivalent daily before vaccination.	• Taper steroid doses below 20 mg prednisone equivalent daily before vaccination.
	• If the patient received anti-CD20 medication, vaccination should be delayed for at least 6 months after the last dose of the therapy.	• If the patient received anti-CD20 medication, vaccination should be delayed for at least 6 months after the last dose of the therapy.
	• If an active underlying disease is present in these patients, immunosuppressive therapy is prioritised over vaccination.	• If an active underlying disease is present in these patients, immunosuppressive therapy is prioritised over vaccination.
Neurologic disorders	• Vaccination is recommended for MS patients.	• Vaccination is recommended for MS patients.
	• MS patients receiving ocrelizumab can receive the vaccine 4–6 weeks before starting the treatment or 4–6 months after ending the treatment.	• MS patients receiving ocrelizumab can receive the vaccine 4–6 weeks before starting the treatment or 4–6 months after ending the treatment.
	• DMTs for MS can reduce the antibody response of vaccines.	• DMTs for MS can reduce the antibody response of vaccines.
	• Patients receiving IRT, including alemtuzumab, rituximab, and ocrelizumab, can be vaccinated 6 months after the treatment.	• Patients receiving IRT, including alemtuzumab, rituximab, and ocrelizumab, can be vaccinated 6 months after the treatment.
	• In high-dose or long-term treatments with corticosteroids, vaccination is allowed 4–6 weeks after cessation of the treatment.	• In high-dose or long-term treatments with corticosteroids, vaccination 4 to 6 weeks after cessation of treatment
	• CDC recommended mRNA vaccines for GBS patients.	• For GBS patients, data are not yet available.
Psychiatric disorders	• Recommended, but no studies have been performed solely on the Covid-19 vaccines and neuropsychiatric disorders.	• Recommended, but no studies have been performed solely on the Covid-19 vaccines and neuropsychiatric disorders.
	• Antipsychotic agents suppress vaccine-induced antibody formation.	• Antipsychotic agents suppress vaccine-induced antibody formation.
	• Antidepressant therapy would normalise the vaccine-induced immune response.	• Antidepressant therapy would normalise the vaccine-induced immune response.
DM	Recommended. Patients with DMT2 are prioritised higher than patients with DMT1.	Recommended. Patients with DMT2 are prioritised higher than patients with DMT1.
Obesity	Recommended	Recommended
CVD	Recommended	Recommended
HIV	Recommended	Data not yet available.
COPD	Recommended	Recommended
Current smokers	Recommended	Recommended
Pregnancy and breastfeeding	Recommended	Janssen: Individualised risk/benefit assessment should be performed before vaccination. Oxford/AstraZeneca: Data are not yet available.
Elderly	Recommended	Recommended
Children	Pfizer/BioNTech: FDA recommends this vaccine for adolescents 12–18 years of age. Moderna: Data are not yet available.	Data is not yet available.

TABLE 1 (Continued)

	Vaccine platform	
	mRNA	Adenoviral vector
Allergic diseases	Recommended unless a prior history of allergy to PEG or positive skin test for this agent is present.	Recommended unless a prior history of allergy to polysorbate or positive skin test for this agent is present.

Abbreviations: ABA, abatacept; ACR, acute cellular rejection; CDC, Centers for Disease Control and Prevention; CLD, chronic liver disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular diseases; DMT1, diabetes mellitus type 1; DMT2, diabetes mellitus type 2; DMT, disease-modifying therapy; ESRD, end-stage renal disease; FDA, Food and Drug Administration; GBS, Guillain-Barré syndrome; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IRAEs, immune-related adverse events; IRT, immune-reconstitution therapies; MELD, model for end-stage liver disease; MS, multiple sclerosis; PBC, primary biliary cholangitis; PEG, polyethylene glycol; SLE, systemic lupus erythematosus; VITT, vaccine-induced immune thrombotic thrombocytopenia.

[a]For more information about vaccine ingredients, please see: CDC.gov.

trigger autoimmunity by direct immune-activating or non-specific adjuvant effects, leading to the exacerbation of rheumatologic or autoimmune disorders. Such events may follow the Pfizer/BioNTech vaccine administration.[19] Nonetheless, as the benefits of vaccinating vulnerable individuals outweigh the risk of exacerbating rheumatic disorders, the American College of Rheumatology recommends vaccination against Covid-19 in all eligible rheumatologic patients.[20] Some have hypothesised that protein subunit-based vaccines, such as the Novavax vaccine candidate, will have better efficacy and safety profiles for rheumatologic, autoimmune, and autoinflammatory patients.[21]

3 | CANCER

Patients with cancer are particularly vulnerable to adverse outcomes from moderate and severe Covid-19 infections, which may be due to their underlying malignancy, cytotoxic chemotherapy, radiotherapy, other existing comorbidities, and advanced age.[22] We must consider the diseases and their treatments when considering vaccination. For example, some treatments may impair cellular or humoral immunity to affect the overall vaccine response. It should also be noted that these effects might differ according to the vaccine used. Leukaemia, non-Hodgkin's lymphoma, and lung cancer are the most commonly seen malignancies related to severe Covid-19 cases.[22] Therefore, owing to the relatively high fatality rate of Covid-19 in active cancer patients, this group is among the most highly prioritised to be vaccinated against the disease.[22] Currently, there is no preferred Covid-19 vaccine for these patients, and so these individuals can receive any approved vaccine under their physician's supervision.

In general, although it is believed that the natural- or vaccine-induced antibody response in cancer patients is suboptimal, especially among those with haematologic malignancies, there are no absolute contraindications to the Covid-19 vaccine in cancer patients undergoing glucocorticoid therapy, chemotherapy, radiotherapy, hormonal therapy, immunotherapy, or surgery.[23] The efficacy of mRNA vaccines in patients with solid tumours and haematological malignancies has been reported to be 83% and 72%, respectively. Anti-CD20 or cytotoxic therapies in these patients is thought to be the reason for the lower-than-expected immune response in cancer patients, making mRNA vaccines less effective in these patients.[24] However, the T-cell response induced by current vaccines is strong enough to recommend immunisation in these patients, except during the intensive phase of chemotherapy.[24] Thus, carefully considering the timing and interval between the vaccine and the last cycle of chemotherapy would be an essential factor in the adequate vaccine immune response in this population.[24] For patients planning to start cytotoxic chemotherapy, it is better to administer the first dose of the vaccine at least two weeks before initiating the first chemotherapy cycle. However, for those already on cytotoxic chemotherapy, the first dose of the vaccine can be administered between chemotherapy cycles.[25] Furthermore, since these immunocompromised patients mount insufficient antibody response after natural SARS-CoV-2 infection and consequently shed the virus for a more extended period, vaccinating these individuals is vital in arresting the virus cycle,[26] further validating the importance of vaccinating as many cancer patients in the community as possible.

Several potential concerns regarding using checkpoint inhibitors and targeted therapies, such as tyrosine kinase inhibitors, including erlotinib and imatinib, and its potential interference with viral vaccines exist.[27] However, there is no reported data at this time. The prevalence of immune-related adverse events (IRAEs) following vaccination is unknown for checkpoint inhibitors, yet this side effect may occur within 2–3 days following vaccination.[27] Therefore, avoiding vaccination may be reasonable in cases of significant concern.[28] Patients receiving lymphocyte or plasma cell-depleting regimens should delay Covid-19 vaccination for at least 3 months following the end of their immunotherapeutic treatment to get the best antibody response. However, if they are about to start these regimens, it is reasonable to administer the first dose of the vaccine at least two weeks before starting the immunotherapy course.[24] It is also believed that the Covid-19 vaccine is safe and effective in patients undergoing radiation therapy.[25] At the beginning of the pandemic, there were significant concerns regarding clinical resource distribution and keeping patients safe from Covid-19 infections.[29] However, the clinical burden has substantially reduced since vaccines became available.

Another important issue in patients receiving active systemic therapies is the occurrence of post-vaccination fever. However, any fever should not necessarily be attributed to vaccine response since

other differential diagnoses, like neutropenic fever, Covid-19 infection, post-surgical complications, and underlying cancer relapse may also be responsible. In addition, it is possible that the vaccinated individuals, including immunocompromised patients, may acquire SARS-CoV-2 with or without prior infection history. Therefore, adhering to preventive measures, such as hand hygiene, face coverings, and social distancing, are still likely to be necessary for everyone in the foreseeable future.

4 | TRANSPLANT PATIENTS

Transplant recipients are another at-risk group that should be prioritised for getting vaccinated since they have an increased risk of infection and developing more severe forms of Covid-19.[30] However, these patients have not been included in the vaccine trials to date, and therefore vaccine safety, efficacy, and durability profiles have not been measured in these patients.[31] Nevertheless, considering the consequences of severe Covid-19 in this population and the previous experiences with other vaccines, such as influenza vaccines, in stable transplant patients, the benefits of vaccination outweigh the possible side effects.[32] Therefore, SARS-CoV-2 vaccination is strongly recommended for these patients.[32] Nonetheless, it is also probable that the immunosuppressed condition in these patients may cause a lower anti-SARS-CoV-2 antibody response, depending on the period since the transplantation, the intensity of the immunosuppression, and the type of transplantation.[33]

The conditioning and maintenance of immunosuppressive regimens and their dosing and intensity vary significantly between solid organ transplant (SOT) recipients and haematopoietic stem cell transplant (HSCT) recipients.[34] It has been suggested that antimetabolite maintenance therapy can lead to a weaker post-vaccination antibody response than other regimens.[34] Therefore, those patients should be vaccinated early in the course of their underlying disease, as the timing of vaccination is a significant factor in determining its effectiveness.[35] Also, it is better to postpone vaccination to at least 3–6 months after transplantation when the immunosuppression is lower.[36] Nevertheless, if the first dose of the vaccine is received before transplantation, the second dose should be postponed until at least four weeks post-transplant.[36]

Some experts believe that a third dose is needed in transplant patients, considering shorter longevity and lower antibodies' efficacy.[37] A recent randomised placebo-controlled trial showed that a third dose of the mRNA-1273 (Moderna) vaccine could significantly increase the anti-receptor-binding domain (RBD) antibody levels and anti-SARS-CoV-2-specific T-cell counts in transplant patients, indicating a higher humoral and cellular immunity triggered after a third dose of the vaccine.[37] There is also evidence of a difference in the antibody response from different vaccines, with the mRNA-1273 (Moderna) vaccine being found to result in a more significant immune response in transplant recipients.[38] In general, vaccination is not contraindicated in stable transplant recipients, except live-attenuated vaccines, which might lead to disseminated infection, especially when their immunosuppression condition is highest, usually occurring in the first 3–6 months after the transplant.[38] Fortunately, none of the current Covid-19 vaccines are live-attenuated, meaning it is possible to administer the vaccine to this vulnerable population.[38] Apart from vaccine-related efficacy, durability, and safety issues, vaccine-associated allograft rejection is a unique concern in this population, although this has not been reported with any Covid-19 vaccines.[38] Nevertheless, although extremely rare, there would appear to be a slight chance of stimulating immunologic rejection reactions via the vaccination-induced immune response.[38]

5 | CHRONIC LIVER DISEASES

Patients with chronic liver disorders (CLD), including cirrhosis, hepatobiliary malignancies, and transplant candidates (or recipients), are vulnerable populations at risk of more severe forms of Covid-19 and higher mortality.[39] This population needs special attention due to their underlying disease, and many operations or treatments were delayed due to the hospitals being overwhelmed or not wanting to put patients at more risk.[39] Therefore, vaccination should also be a priority for these patients.[39] Vaccination seems to be safe in stable CLDs, such as compensated cirrhosis and viral hepatitis.[39] Moreover, individuals with decompensated cirrhosis, liver malignancies, and liver transplant patients should also be prioritised for vaccination using the Child-Turcotte-Pugh or the Model for End-stage Liver Disease (MELD) scores.[40] The higher the scores, the sooner they should get the vaccine. However, the extent of the vaccine-induced immune response is unknown and expected to be suboptimal in these patients due to their underlying disease and the medications they use. It is also noteworthy that mRNA Covid-19 vaccines are expected to have favourable safety and efficacy profiles in these patients.

Patients with CLD who are on medical treatment for hepatitis B virus (HBV), hepatitis C virus (HCV), primary biliary cholangitis (PBC), or autoimmune hepatitis do not need to stop therapy in order to receive Covid-19 vaccines.[41] Moreover, patients with hepatocellular carcinoma (HCC) on locoregional (i.e., imaging-guided liver tumour-directed procedures) or systemic therapy can also be vaccinated without pausing their treatment.[41] Nevertheless, in recent infections or fever cases, vaccination should be delayed until the condition is stable.[41] However, the use of immune checkpoint inhibitors (ICI) in patients with some liver diseases (e.g., HCC) is still a concern that should be further studied since immune-related adverse reactions are a possible result of vaccine interactions with ICI.[41] Moreover, the timing of the vaccination in hepatobiliary cancer patients is heavily dependent on the stage of the malignancy, types of medication, and concomitant comorbidities.[41] Patients with CLD on the waiting list for transplantation should receive two doses of the vaccine, preferably before the transplant. However, they should be encouraged to receive the vaccine even if their second is scheduled after the

liver transplant.[30] However, for these patients, the time interval between the two doses of the vaccine does not necessarily need to be four weeks, and the second dose should be planned after transplant (e.g., within 6 weeks).[30] Moreover, following liver transplantation, the best time to be vaccinated would be when the immunosuppression has been attenuated and other prophylactic medications are withheld, ideally six weeks to three months post-liver transplantation.[30] In order to prevent acute cellular rejection (ACR), liver transplant recipients should not discontinue their immunosuppressive medications solely to achieve a favourable immune response after vaccination. Moreover, Covid-19 vaccinations should be withheld in liver transplant recipients with active ACR or those receiving high-dose corticosteroids until the condition is resolved.

6 | END-STAGE RENAL DISEASE

Patients with end-stage renal disease (ESRD) are also more prone to infection with Covid-19 due to their regular or occasional dialysis sessions, where they are exposed to a densely populated environment with a high possibility of SARS-CoV-2 transmission.[42] Moreover, these patients may present with atypical manifestations of SARS-CoV-2 infection, leading to a delay in diagnosing the disease.[43] In addition, patients often have multiple comorbidities and higher rates of polypharmacy.[44] Therefore, the risk of developing a severe or lethal SARS-CoV-2 infection is likely higher in this population, and vaccinating them early against Covid-19 is highly recommended.[45] Moreover, although ESRD patients develop seroconversion following vaccination, they are well-established to achieve a less robust and perhaps less durable antibody response.[46] The seropositivity rate after SARS-CoV-2 vaccination does not appear to differ between haemodialysis and peritoneal dialysis (PD) patients.[47] The extent of the immune response to SARS-CoV-2 vaccination depends on the vaccine type, the time spent since ESRD onset, and possibly age, body mass index (BMI), and nutritional status, as indicated by serum albumin and iron levels. With that in mind, several studies have suggested that a third or booster dose of vaccine would be necessary for these individuals to produce an optimal antibody response.[37,48-50]

There does not appear to be a preference for one vaccine type over another, with adenoviral vector vaccines, such as the ChAdOx1 nCoV-19 (Oxford/AstraZeneca) vaccine, and the mRNA vaccines (i.e., Pfizer/BioNTech, and Moderna) used for vaccinating ESRD patients.[49,51] In addition, patients with autoimmune renal diseases (e.g., IgA nephropathy) undergoing anti-CD20 therapy (e.g., rituximab) should replace their immunosuppressive treatment with another non-interfering regimen until a few weeks after vaccination.[52] For example, it is reasonable for these individuals to taper steroid doses below 20 mg prednisone (or equivalent) daily or wait for at least six months after the last rituximab dose before being vaccinated.[52] However, if their underlying disease is active, the immunosuppressive therapy is prioritised over-vaccination,[53] although the activation or relapse of the underlying autoimmune kidney disease has only rarely been reported following vaccination.[54,55]

7 | NEUROLOGIC DISORDERS

Like individuals with many chronic disorders, neurological patients are at increased risk of severe Covid-19 infection, complications, and mortality.[56] Patients with Alzheimer disease, Parkinson disease, motor neuron diseases, central nervous system (CNS) disorders, neuromuscular disorders (NMDs), and autoimmune disorders, including multiple sclerosis (MS), myasthenia gravis (MG), and Guillain-Barré syndrome (GBS), are among the most concerning neurological disorders.[56] Thus, vaccination against Covid-19 is vital for this population,[57] but vaccination risks and adverse events must be carefully monitored. For example, there is some concern that vaccination against SARS-CoV-2 may exacerbate MS by inducing immunological responses and triggering immunological reactions.[58] Nonetheless, vaccines are generally safe in MS patients, and following vaccination, there is a low probability of acute relapse, although there have been some reports of MS symptom aggravation (pseudo-relapse).[58]

Patients with a history of GBS and autoimmune conditions should receive mRNA Covid-19 vaccines, if not contraindicated.[59] However, it is generally believed that some of the disease-modifying therapies (DMTs) used to treat MS could reduce the antibody response following vaccination.[60] Moreover, these medications can affect the safety and efficacy of the vaccines.[61] Patients being treated with β-interferons, glatiramer acetate, teriflunomide dimethyl fumarate, natalizumab, or sphingosine-1-phosphate receptor modulators fingolimod, ozanimod, and siponimod can be vaccinated at any time during their treatment, despite the likely vaccine response attenuation.[62] However, in MS patients scheduled to start ocrelizumab therapy, the two-dose vaccine regimen should be administered at least 4–6 weeks before the initiation of their treatment course, or at least 4–6 months after the treatment course last ocrelizumab infusion.[63] In patients treated with immune-reconstitution therapies, including alemtuzumab, and oral cladribine, it is better to delay vaccination until at least six months after the last course of treatment.[64] In patients on high-dose or long-term corticosteroids, vaccination should be delayed until 4–6 weeks after treatment.[65] Nonetheless, if these patients are not on DMTs, they should receive the SARS-CoV-2 vaccine as soon as possible.

There are theoretical concerns that mRNA-based Covid-19 vaccines may trigger the development of de novo neurodegenerative or neurologic disorders, such as demyelinating diseases or fever-induced seizures. In this case, the potential vaccine-induced adverse reaction could be even more debilitating than the viral infection.[66,67] The adjuvants used in vaccines, including anti-SARS-CoV-2, might be responsible for potential neurologic adverse effects.[68] Another potential neurological adverse event that may result from vaccination is the immunisation stress-related response (ISRR), which manifests itself as psychogenic non-epileptic seizures (PNES).[69] Transverse

myelitis,[70-72] GBS,[73,74] and Bell's palsy[75] are other potential neurological consequences of the Covid-19 vaccination reported so far. Another potential adverse effect of these vaccines might be an exacerbation of MG and chronic inflammatory demyelinating polyneuropathy (CIDP).[76] The demyelinating disease has most commonly been reported following viral-vector vaccines, which should be further investigated.[77]

8 | PSYCHIATRIC DISORDERS

Patients with psychiatric disorders, especially those with severe mental disorders, such as bipolar, schizophrenia, and major depressive disorders, are at increased risk of being infected with Covid-19. Those with severe mental illnesses who were taking antipsychotics were at increased risk of mortality from Covid-19,[78] which may be associated with patients' different lifestyles, habits, cognitive impairment, difficulties in adhering to infection control measures, and these population's socioeconomic status.[79,80] In addition, neuropsychiatric disorders and inflammation correlate, which could be a risk factor for more morbidity and mortality in these patients.[81] Therefore, these patients should be prioritised for Covid-19 vaccination to minimise the risk of infection and transmission to other people. However, comorbid mental disorders have often been overlooked and underestimated in research evaluating the predictors of the severity and mortality from Covid-19.[82] In many countries, institutionalised patients are listed high in the vaccination list, second only to healthcare personnel.[83]

It must be noted that vaccinating patients with psychiatric disorders may also cause some concerns, as the efficacy, safety, and durability of the Covid-19 vaccine are not yet known in these patients. Moreover, vaccinating these patients may also give them the false belief that they are fully protected against the disease, and thus, they may be more likely to ignore hygiene protocols.[83] Previous studies have shown a diminished antibody response to influenza and hepatitis vaccines in those with severe mental health issues.[84,85] Nevertheless, there are currently no published studies about the efficacy of Covid-19 vaccines among patients with neuropsychiatric disorders. The relationship between vaccine response and psychotropic medications seems paradoxical. For example, antipsychotic agents (e.g., clozapine) might be associated with a syndrome resembling common variable immunodeficiency (CVID) in some patients that may lead to the suppression of vaccine-induced antibody formation.[86] At the same time, antidepressant treatment might normalise the vaccine-induced immune response.[87]

9 | DIABETES MELLITUS

Patients with diabetes mellitus, due to their comorbidities and acquired immunodeficiency, are at increased Covid-19-related morbidity and mortality.[88] Diabetes is one of the comorbidities most associated with adverse outcomes in Covid-19 patients. However, there seems to be no difference in the severity or mortality of SARS-CoV-2 infection, based on whether they have diabetes type 2 (DMT2) or type 1 (DMT1).[89] Nonetheless, the CDC prioritised vaccination among patients with DMT2 over those with DMT1.[90] Therefore, vaccination is critical and necessary for this population, and endocrinologists should encourage their patients to be vaccinated as soon as possible.[91] It appears that the immune response following Covid-19 vaccination is not affected by the serum glucose levels, as diabetic patients show an optimal antibody response.[92] Furthermore, Covid-19 infected patients are at increased risk of developing new-onset diabetes. Therefore, vaccination can also help to prevent an increase in diabetes mellitus in the community.[93]

10 | OBESITY

The association between obesity and viral infections was first demonstrated during the H1N1 epidemic in 2009, with the more body fat, the higher the risks of developing more severe illness and more extended hospitalisation in an intensive care unit (ICU).[94-96] The reason behind this association was thought to be the impairment of humoral and cellular immunity, along with lower vaccine-induced immunity in these patients.[97] Another reason could be the marked rise of angiotensin-converting enzyme 2 (ACE2) expression associated with high-fat diets.[98] Another factor that plays a crucial role in making obese children more susceptible to infections, such as Covid-19, is hyperinsulinism, which is due to the compensatory mechanisms of their pancreatic β cells to overcome insulin resistance in their body.[99] Thus, when higher amounts of insulin are required in intense metabolic activity, such as activating immune cells in response to the SARS-CoV-2 infection, their β cells cannot produce more insulin, as they are already working near their limit.[100] Moreover, SARS-CoV-2 can enter the pancreatic β cells via ACE2 receptors, causing virus-triggered cell death or immune-mediated loss of infected pancreatic β cell mass.[100,101] Insulin resistance in these patients can also impair the anti-inflammatory and vasoactive characteristics of nitric oxide (NO) by reducing phosphatidylinositol 3-kinases (PI3K).[102]

Previous research has shown obesity as prevalent comorbidity among patients admitted into the ICU, especially among children and adolescents.[103,104] This research shows that a higher BMI may increase the likelihood of getting a severe disease.[105] Furthermore, a high BMI correlated with an increased need for mechanical ventilation in Covid-19 patients, with about 85% of patients with a BMI > 35 kg/m^2 requiring mechanical ventilation.[106] It is noteworthy that this correlation was independent of age, gender, or the presence of any other comorbidities[106] and has been confirmed elsewhere.[107-112] Thus, it is recommended that obese individuals, especially those with higher BMIs, be prioritised for Covid-19 vaccination.

11 | CARDIOVASCULAR DISEASES

Cardiovascular disorders (CVD) and hypertension are among the comorbidities with the highest risks of adverse outcomes from SARS-CoV-2 since most of these patients are of advanced age and have metabolic or other underlying diseases.[113] Therefore, this group should also be prioritised for Covid-19 vaccination. Patients who have had a recent hospitalisation, primarily in the previous six months, those with NYHA III-IV pulmonary hypertension, high grade peripheral arterial disease (PAD), morbid obesity, stage C heart failure, 1- or 2-vessel obstructive coronary artery disease (CAD) with angina, and poorly controlled diabetes, are among the most critical group of cardiovascular patients for vaccination.[114] There have been no published studies on the type of Covid-19 vaccine most suitable for these patients.

12 | CHRONIC OBSTRUCTIVE PULMONARY DISEASE

A 2020 study published in the European Respiratory Journal reported that the ACE2 receptor, a molecule found on the surface of lung cells, is the point of attachment for SARS-CoV-2.[115] People with Chronic Obstructive Pulmonary Disease (COPD) and current smokers have increased airway expression of this enzyme.[115] Although the up-regulation of this receptor is essential in protecting against acute lung injury, it predisposes individuals to increased risk of SARS-CoV-2 infection since this receptor is used as the gateway into the epithelial cells, explaining, at least in part, the increased risk of viral respiratory tract infection in active smokers and virus-related exacerbations in those with COPD.[116] A 2021 systematic review of 59 studies found that having COPD significantly increased the odds of poor clinical outcomes, including the risk of hospitalisation, ICU admission, and mortality.[117] Nevertheless, a review of vaccine-related deaths by the CDC, as of January 8, identified 55 deaths, with COPD being among the most commonly reported comorbidities, alongside hypertension, dementia, diabetes, and heart failure.[118] Of these deaths, 37 were reported among residents of long-term care facilities.[118] However, the report concluded that the benefits of the Covid-19 vaccination outweighed the potential risks in the older frail populations.[118] Therefore, the recommendation is that individuals with COPD be prioritised for Covid-19 vaccination, regardless of age and frailty.

13 | HUMAN IMMUNODEFICIENCY VIRUS

Patients with human immunodeficiency virus (HIV), similar to other comorbidities and immunocompromising conditions, are prone to severe Covid-19.[119] However, the risk is higher in patients with advanced immunosuppression, defined as a $CD4^+$ T cell count of <200/μL.[120] Moreover, if they become infected with SARS-CoV-2, negative impacts on their antiretroviral treatments would also be expected.[121] Unfortunately, few studies have investigated the safety and efficacy of the Covid-19 vaccines in this population. However, one study has reported the mRNA Covid-19 vaccines, such as the BNT162b2 vaccine, to be both immunogenic and safe in patients with HIV.[122] Nevertheless, there remains some level of mistrust in these patients about Covid-19 vaccines, and therefore, discussing this issue with these individuals to address their hesitancy is essential.[123]

14 | CURRENT SMOKERS

It is well established that cigarette smoking causes structural changes in the respiratory tract and decreases immune responsiveness, both systemically and locally within the lungs.[124] Therefore, smoking is a significant risk factor for the proliferation of bacterial and viral infections. Previous studies evaluating the Middle East Respiratory Syndrome—Coronavirus (MERS-Coronavirus) outbreak found higher mortality rates among current smokers than non-smokers and those who had never smoked.[125-127] A 2020 systematic review of five studies from China during the first 2 months of the SARS-CoV-2 pandemic found a possible association between current smokers and Covid-19. This included negative disease progression and adverse outcomes, such as increased ICU admission, the need for mechanical ventilation, and increased mortality when compared to non-smokers.[128] Another recent study confirms these findings, reporting that smokers are overrepresented in fatalities, especially in populations where current smoking is high.[116] The authors suggest that higher rates of Covid-19 would be expected in countries with a higher prevalence of smoking. A more recent study reported that cumulative exposure to cigarette smoke is an independent risk factor for increased hospital admission and death from Covid-19.[129] Given the increased likelihood of contracting SARS-CoV-2 and the propensity for greater disease severity, it concerns that a study from the United Kingdom (UK) found that current smokers were more likely to be undecided or unwilling to be vaccinated against Covid-19.[130] Jackson et al. suggest that due to the disproportionately high number of current smokers among socioeconomically disadvantaged groups, lower vaccination uptake in these clusters could exacerbate the already extant health inequalities.[130] As a result, targeted interventions may be necessary to prevent the compounding of health inequalities in these populations.[130] The recommendation for Covid-19 vaccination among otherwise healthy smokers is that vaccination should occur, and in some cases vaccination is understandably prioritised in this group.

15 | PREGNANCY AND BREASTFEEDING

Covid-19 can manifest itself in its most severe form during pregnancy. Moreover, unfavourable pregnancy outcomes, such as premature labour, myocardial injuries, preeclampsia, perinatal death, and vertical transmission to the foetus, have been reported in pregnant women with Covid-19.[131,132] Therefore, the need to be vaccinated in

this population is extremely important.[133] Although little is known about the efficacy and safety profile of SARS-CoV-2 vaccines in pregnant or lactating mothers, due to their exclusion from vaccine trials, individuals intending to become pregnant and breastfeeding women are advised to receive a Covid-19 vaccine, mainly if they are a member of a high-risk group (e.g., healthcare personnel). However, only the mRNA vaccines are approved in this subsection of the population.[134,135]

Different countries have different policies for vaccinating pregnant women against Covid-19. For example, the American College of Obstetricians and Gynecologists (ACOG) recommends vaccination in pregnant and lactating women.[136] The United States Food and Drug Administration (FDA) and the Advisory Committee on Immunisation Practices (ACIP) have left the option to vaccinate pregnant and lactating women.[137] The South African Society of Obstetricians and Gynecologists has recommended vaccination in those pregnant and breastfeeding women at higher risk of exposure.[138] Canada, Ireland, Germany, and the United Kingdom have left the decision-making to their physician to consider the individualised risk-to-benefit ratio.[139-141] Austria has announced the contraindication of SARS-CoV-2 vaccination for pregnant and nursing women,[142] while the Netherlands and Japan have also recommended vaccination in pregnancy.[143]

Conversely, Israel has prioritised pregnant and lactating women for vaccination,[134] while the Society for Maternal-Foetal Medicine strongly recommends vaccination in pregnant and lactating mothers.[144] The Italian scientific societies have announced that breastfeeding does not interfere with Covid-19 vaccination,[145] and the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) has allowed SARS-CoV-2 vaccination during breastfeeding.[146] However, the Academy of Breastfeeding states insufficient data about the vaccines' entrance into breast milk.[147] The American Society for Reproductive Medicine (ASRM) recommends that pregnant and lactating women, and those undergoing fertility treatment, be vaccinated against SARS-CoV-2.[148] The World Health Organisation (WHO) states that there is currently insufficient data on this issue, and further studies are needed to recommend vaccination in this population.[149] In general, it seems that Covid-19 vaccines with Emergency Use Authorisation (EUA), including Pfizer/BioNTech, and Moderna vaccines, are prioritised in eligible pregnant mothers, such as women older than 35 years, healthcare personnel, those with multiple gestation, cancer, chronic hypertension, chronic kidney disease, chronic obstructive pulmonary disease, cardiac diseases, immunodeficiency, autoimmune diseases, obesity, sickle cell disease, smoking, and diabetes mellitus.[150]

Vaccinated pregnant mothers can pass the IgG antibodies produced to their offspring, with one case study reporting vertical transmission.[151] It was also shown that the transplacental transfer of vaccine-induced antibodies to the newborn is more likely if the mother is vaccinated in the third trimester.[152] Similar passive transfer of IgA or IgG antibodies has not yet been observed in breastfed infants.[153,154] The Academy of Breastfeeding Medicine has stated that breastfeeding should not be ceased for individuals vaccinated against Covid-19.[155] If vaccinated, it seems that pregnant and lactating women achieve comparable antibody levels to other individuals of their age.[135] Therefore, after delivery, it is essential to follow up with vaccinated mothers and their newborns to investigate possible maternal and foetal complications related to the vaccine.[156] The Joint Committee on Vaccination and Immunisation (JCVI) stated that individuals trying to conceive could also be vaccinated if they meet the eligibility criteria. These women can get pregnant even before the second dose of the vaccine.[157]

16 | ELDERLY

Since the beginning of the Covid-19 pandemic, the elderly have been the most affected by the social distancing measures applied to prevent virus transmission. Government measures have caused isolation and loneliness, which have led to physical inactivity and depression in these individuals.[158] Nevertheless, older individuals (i.e., >65 years old) have a high risk of Covid-19-related hospitalisation, ICU admission, and mortality due to comorbidities, poor nutrition, depressed immunity, and lower organ function.[159,160] Moreover, the elderly are at higher risk of getting severe Covid-19 and are less likely to have an excellent response to vaccines. Moreover, some people reside in nursing homes, which puts them at increased risk of acquiring communicable infections, such as Covid-19.[161] Therefore, prevention of SARS-CoV-2 infection seems to be the most desirable approach in these patients. There is substantial concern that these people would not achieve favourable protective immunity post-vaccination, considering this population's relatively weak antibody response.[162] However, despite the lower efficacy of the Covid-19 vaccine in the elderly, the vaccines are still effective against preventing mortality. Therefore, vaccination is strongly recommended for this age group,[163] and all currently approved Covid-19 vaccines are safe and effective in the geriatric population.

17 | CHILDREN

Until the evolution of the most recent SARS-CoV-2 variants, it was believed that children did not become afflicted with Covid-19, or at least not in its most severe forms. Thus, paediatric vaccination did not seem to be necessary.[164] Nonetheless, reports of more severe forms of the disease and increases in the hospitalisation of children due to the alpha (B.1.1.7) and delta (B.1.617.2) variants prompt the discussion of including them in the Covid-19 vaccination program and developing a suitable vaccine for this subsection of the population.[165,166] Moreover, vaccinating children can decrease infection transmission to others, meaning producing herd immunity in the community. They can also be a tool to prevent postinfectious conditions, such as Kawasaki-like and toxic shock syndrome-like diseases, commonly referred to as multisystem inflammatory syndrome in children (MIS-C),[167] occurring 2–4 weeks after SARS-CoV-2

infection.[168] However, if proved to be safe and effective, there are still significant challenges to persuade hesitant parents to accept the vaccination of their children.

Preventive measures, such as face masks, hand hygiene, and social distancing, are less applicable in pediatrics than adults since adults adhere more strictly to the health protocols.[169] Therefore, the need for a vaccine for children seems to be increasingly important. Several factors should be considered in considering vaccine responses in children, including congenital or developmental disorders, nutritional status, and maturational changes.[103] However, immunocompromised children are also likely to show lower antibody response to Covid-19 vaccines.[103] Presently, no children younger than 12 years old have been enrolled in Covid-19 vaccination trials since it was believed that only older children were at risk of developing severe SARS-CoV-2 infection, and therefore, the vaccine trials could be extended to younger children at a later date.[170] The FDA has approved Covid-19 vaccines for those older than 12 years, but the age limit can perhaps be lowered again after further research.[171]

18 | ALLERGIC DISEASES

In the period December 14–23, 2020, almost 1.9 million doses of Pfizer/BioNTech Covid-19 vaccine were administered in the US, among which 21 cases of anaphylaxis were reported to the CDC, corresponding to an estimated rate of 11.1 cases per million.[172] Allergic reactions to vaccines and medications can be caused by two primary mechanisms: IgE-mediated and IgE-independent pathways.[173,174] These reactions are mainly triggered by non-active vaccine ingredients, such as formaldehyde, thimerosal, egg protein, and gelatin, rather than the active vaccine ingredients.[175] Other ingredients commonly used in vaccines to improve their solubility in water are polyethylene glycol (PEG) and polysorbate.[175] PEG is used in the Pfizer/BioNTech and Moderna mRNA vaccines to enhance the stability of the mRNA-containing lipid nanoparticles,[175,176] while polysorbate 80 is used in the Oxford/AstraZeneca and Johnson & Johnson adenoviral vector vaccines.[177] These substances can trigger IgE formation in the body, causing mast cell degranulation. Thus, skin testing for PEG and polysorbate could be an option to prevent such catastrophic events following vaccination against Covid-19.[178]

The IgE-independent pathway is another proposed mechanism behind vaccine-related allergic reactions.[174] In these cases, activating complement elements, including C3a, C4a, and C5a, would trigger these inflammatory responses.[174] Hence, measuring serum tryptase and complement system elements may help diagnose vaccine-induced reactions following Covid-19 vaccination.[177] This vividly highlights the importance of taking a detailed history of previous severe allergic reactions to an injectable medication, vaccine, or other allergens, mainly PEG- and polysorbate-containing agents, to help prevent these types of adverse events.[175] Nevertheless, CDC recommends vaccinating individuals with a prior history of allergic reactions unless a positive skin test is present. In such cases, vaccination is contraindicated under the EUA.[177]

19 | CONCLUSION

This article has highlighted that several high-risk population groups should be at the top of the priority list for receiving a vaccination. It was also demonstrated that significant research gaps in this topic require many more studies to determine whether these populations should receive Covid-19 vaccines.

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CONFLICT OF INTEREST

Terence T. Sio reports that he provides strategic and scientific recommendations as a member of the Advisory Board and speaker for Novocure, Inc. and also as a member of the Advisory Board to Galera Therapeutics, which are not in any way associated with the content or disease site as presented in this manuscript. All other authors have no relevant financial interests to be declared.

AUTHOR CONTRIBUTIONS

- Zeinab Mohseni Afshar: Data collection and writing the manuscript. Arefeh Babazadeh: Data collection and writing the manuscript. Alireza Janbakhsh: Data collection and helped with manuscript writing. Feizollah Mansouri: Data collection and helped with manuscript writing. Terence T. Sio: Contributed substantial revisions to the manuscript's content. Mark J. M. Sullman: Contributed substantial revisions to the manuscript's content. Kristin Carson-Chahhoud: Helped with manuscript writing and contributed substantial revisions to the manuscript's content. Rezvan Hosseinzadeh: Data collection and helped with manuscript writing. Mohammad Barary: Data collection, helped with manuscript writing, and contributed substantial revisions to the manuscript's content. Soheil Ebrahimpour: Design of the research study and supervision.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Zeinab Mohseni Afshar https://orcid.org/0000-0002-1085-374X
Arefeh Babazadeh https://orcid.org/0000-0002-1362-7203
Alireza Janbakhsh https://orcid.org/0000-0001-6339-4666
Feizollah Mansouri https://orcid.org/0000-0002-2099-5362
Terence T. Sio https://orcid.org/0000-0003-4210-5479
Mark J. M. Sullman https://orcid.org/0000-0001-7920-6818
Kristin Carson-Chahhoud https://orcid.org/0000-0001-9966-9289
Rezvan Hosseinzadeh https://orcid.org/0000-0001-9399-3854
Mohammad Barary https://orcid.org/0000-0001-8733-9370
Soheil Ebrahimpour https://orcid.org/0000-0003-3204-0448

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