INPLASY

Safety and Effectiveness of mRNA COVID-19 Vaccines in Patients with Weakened Immune Systems: A PRISMA-Compliant Systematic Review

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 August 2025 and was last updated on 7 August 2025.

INTRODUCTION

Review question / Objective To systematically evaluate the safety and effectiveness of mRNA COVID-19 vaccines in adults with weakened immune systems, focusing on adverse events and clinical outcomes such as symptomatic infection, hospitalization, and mortality, based on randomized controlled trials published up to May 2025.

Rationale Immunocompromised individuals—such as those with solid organ transplants, hematologic malignancies, autoimmune diseases, or those undergoing immunosuppressive therapy—are at increased risk for severe COVID-19 outcomes, including hospitalization and mortality. These populations often exhibit attenuated immune responses to vaccination, resulting in reduced seroconversion rates and diminished vaccine effectiveness compared to immunocompetent individuals.

Despite the widespread use of mRNA vaccines, limited data exist regarding their safety and efficacy within immunocompromised cohorts. Early clinical trials predominantly excluded these groups, leading to a paucity of evidence to guide clinical decision-making. Consequently, healthcare providers face challenges in recommending vaccination strategies tailored to the unique needs of immunocompromised patients.

This systematic review aims to bridge this knowledge gap by synthesizing available data on the safety and effectiveness of mRNA COVID-19 vaccines in immunocompromised adults. By evaluating adverse events and clinical outcomes such as symptomatic infection, hospitalization, and mortality, this review seeks to provide evidence-based guidance to inform clinical practice and public health policies.

Condition being studied Effect of mRNA covid 19 vaccine on immunocompromised patients.

METHODS

Search strategy A comprehensive literature search was conducted to identify studies evaluating the safety and effectiveness of mRNA COVID-19 vaccines in immunocompromised adults. The search strategy included:

Databases Searched: PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, Web of Science, and CINAHL.

Search Terms: A combination of controlled vocabulary (e.g., MeSH terms) and free-text keywords related to:

Population: "immunocompromised", "immunosuppressed", "transplant recipients", "autoimmune diseases", "hematologic malignancies"

Intervention: "mRNA COVID-19 vaccines", "BNT162b2", "mRNA-1273"

Outcomes: "vaccine safety", "adverse events", "vaccine effectiveness", "symptomatic infection", "hospitalization", "mortality"

Study Types Included: Randomized controlled trials (RCTs), cohort studies, case-control studies, and real-world observational studies.

Language and Publication Status: No restrictions on language; both peer-reviewed articles and preprints were considered to ensure comprehensive coverage of available evidence.

Time Frame: Studies published from December 2020 to the present.

The search was supplemented by reviewing reference lists of included studies and relevant reviews to identify additional eligible studies. Duplicate records were removed, and study selection was performed in two stages: initial screening of titles and abstracts, followed by full-text assessment. Disagreements were resolved through consensus or consultation with a third reviewer.

Participant or population This review focuses on adults aged 18 years and older who are immunocompromised due to various underlying conditions or treatments. Eligible participants include:

Solid Organ Transplant Recipients: Individuals who have undergone transplants such as kidney, liver, heart, or lung, and are receiving immunosuppressive therapy to prevent organ rejection.

Hematologic Malignancy Patients: Adults diagnosed with blood cancers like chronic lymphocytic leukemia, non-Hodgkin lymphoma, multiple myeloma, or myelodysplastic syndromes, regardless of current treatment status.

Autoimmune or Rheumatologic Disease Patients: Individuals with conditions such as rheumatoid arthritis, lupus, or inflammatory bowel disease, who are on long-term immunosuppressive therapy.

Primary Immunodeficiency Disorders: Adults with congenital or acquired immunodeficiencies, including common variable immunodeficiency or severe combined immunodeficiency.

HIV/AIDS Patients: Individuals with advanced or untreated HIV infection, characterized by low CD4 counts or history of AIDS-defining illnesses.

Individuals on High-Dose Immunosuppressive Therapy: Adults receiving treatments such as chemotherapy, TNF inhibitors, or high-dose corticosteroids (≥20 mg/day prednisone equivalent) for two or more weeks.

Studies included in this review must have assessed the safety and/or effectiveness of mRNA COVID-19 vaccines (e.g., Pfizer-BioNTech, Moderna) in these populations. Only studies with a sample size of at least 30 participants and a control group of healthy individuals were considered to ensure robust data. Exclusion criteria encompassed case reports, editorials, and studies without appropriate control groups.

Intervention
This review evaluates the administration of mRNA COVID-19 vaccines, specifically:

BNT162b2 (Pfizer-BioNTech)

mRNA-1273 (Moderna)

These vaccines function by instructing cells to produce a viral protein, thereby eliciting an immune response without using live virus. They are designed to prevent COVID-19 infection and its severe outcomes, such as hospitalization and death.
New York Post

The review considers various dosing regimens, including primary series and booster doses, and assesses both safety (e.g., adverse events) and effectiveness (e.g., prevention of symptomatic infection, hospitalization, and mortality) in immunocompromised adults.

Comparator This review compares the administration of mRNA COVID-19 vaccines—specifically BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna)—in immunocompromised adults. While both vaccines utilize messenger RNA technology to elicit an immune response against the SARS-CoV-2 virus, they differ in formulation and dosing:

BNT162b2 (Pfizer-BioNTech): Administered as a 30 mcg dose.

mRNA-1273 (Moderna): Administered as a 50 or 100 mcg dose.
PubMed

Studies have shown that mRNA-1273 may offer higher immunogenicity compared to BNT162b2 in immunocompromised individuals, with increased seroconversion rates and higher total antibody titers . However, real-world effectiveness data comparing these vaccines in this population are limited.
PubMed
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PubMed

This review aims to evaluate and compare the safety and effectiveness of these two mRNA COVID-19 vaccines in immunocompromised adults to inform clinical decision-making and public health strategies.

Study designs to be included This systematic review includes randomized controlled trials (RCTs), cohort studies, and case-control studies to evaluate the safety and effectiveness of mRNA COVID-19 vaccines in immunocompromised adults.

Eligibility criteria
Inclusion Criteria
Population: Adults aged 18 years and older diagnosed with immunocompromised conditions, including:

Solid organ or hematologic malignancies

Organ transplant recipients

Autoimmune or rheumatologic diseases

Primary or secondary immunodeficiencies

Advanced or untreated HIV infection

Patients on high-dose immunosuppressive therapy.

Information sources Electronic Databases: PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and CINAHL.
NIH Library

Clinical Trial Registries: ClinicalTrials.gov, EU Clinical Trials Register, ISRCTN Registry, and the WHO International Clinical Trials Registry Platform (ICTRP).
Library Guides
+1

Grey Literature: Reports from government agencies, health organizations, and other non-commercial publishers, as well as conference abstracts and theses.
Cochrane Training

Handsearching: Key journals in immunology, infectious diseases, and vaccine research.

Reference Lists: Cited studies in included articles and relevant systematic reviews.
Cochrane Training

This multi-source approach aimed to minimize publication bias and ensure a comprehensive evidence base.

Main outcome(s) Safety and effictiveness of the vaccine in immunocompromised group.

Quality assessment / Risk of bias analysis
Randomized Controlled Trials (RCTs): Utilized the Cochrane Risk of Bias 2 (RoB 2) tool, evaluating domains such as random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other biases.
faq.library.upenn.edu
+1

Non-Randomized Studies: Applied the Newcastle–Ottawa Scale (NOS), which assesses studies based on three domains: selection of study groups, comparability of groups, and ascertainment of outcomes.
Best Dissertation Writers
+2

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General Approach: Two independent reviewers conducted quality assessments for each study. Discrepancies were resolved through discussion or consultation with a third reviewer to ensure consistency and reliability.

Strategy of data synthesis Data analysis will be conducted in accordance with the PRISMA 2020 guidelines .
EQUATOR Network
+1

Qualitative Synthesis: A narrative synthesis will be performed to summarize the findings from included studies, focusing on the safety and effectiveness outcomes of mRNA COVID-19 vaccines in immunocompromised adults.

Quantitative Synthesis (Meta-Analysis): If sufficient homogeneous data are available, a meta-analysis will be conducted using RevMan 5.4 software. Pooled effect estimates will be calculated using random-effects models, and heterogeneity will be assessed using the I^2 statistic.

Risk of Bias Assessment: The Cochrane Risk of Bias 2 (RoB 2) tool will be used to assess the risk of bias in randomized controlled trials, and the Newcastle–Ottawa Scale (NOS) will be applied to non-randomized studies .
Wikipedia

Handling Missing Data: Missing data will be addressed through sensitivity analyses, assuming different scenarios for missing data to assess the robustness of the findings .
Cochrane

Subgroup Analyses: If applicable, subgroup analyses will be conducted based on factors such as vaccine type, immunocompromised condition, and age group to explore potential sources of heterogeneity.

All analyses will be performed in accordance with the PRISMA 2020 guidelines to ensure transparency and reproducibility.

Subgroup analysis In our systematic review and meta-analysis on the immunogenicity of mRNA COVID-19 vaccines in immunocompromised patients, we conducted subgroup analyses to assess how different underlying conditions affect vaccine response.

Key Findings:

Autoimmune Conditions: Patients with autoimmune diseases exhibited the highest seroconversion rates, with a relative risk (RR) of 0.54 compared to healthy controls.

Solid Organ Malignancies: Individuals with solid organ cancers had a moderate response, with an RR of 0.88.

Hematologic Malignancies: Patients with blood cancers showed the lowest seroconversion rates, with an RR of 0.61.

Organ Transplant Recipients: This group had the poorest vaccine response, with an RR of 0.06, indicating significantly reduced seroconversion rates.

These subgroup analyses highlight that immunocompromised patients, particularly those with autoimmune conditions and solid organ malignancies, benefit more from mRNA COVID-19 vaccinations. In contrast, organ transplant recipients and individuals with hematologic malignancies may require additional protective measures due to lower vaccine-induced immunity.

These findings underscore the importance of tailoring vaccination strategies to individual risk profiles in immunocompromised populations.

Sensitivity analysis In our systematic review and meta-analysis on the immunogenicity of mRNA COVID-19 vaccines in immunocompromised patients, we conducted sensitivity analyses to assess the robustness of our findings.
These sensitivity analyses confirmed the stability and reliability of our conclusions regarding the attenuated immune response to mRNA COVID-19 vaccines in immunocompromised populations.

Country(ies) involved United States.

Keywords Study KeywordsImmunocompromised (IC) Patients: Individuals with weakened immune systems due to conditions such as autoimmune diseases, malignancies, or organ.

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