IDSA 2025 Guidelines on the Use of Vaccines for the Prevention of Seasonal COVID-19, Influenza, and RSV Infections in Immunocompromised Patients

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Figure 1. Approach and implications to rating the quality of evidence and strength of recommendations using GRADE methodology (unrestricted use of figure granted by the U.S. GRADE Network)

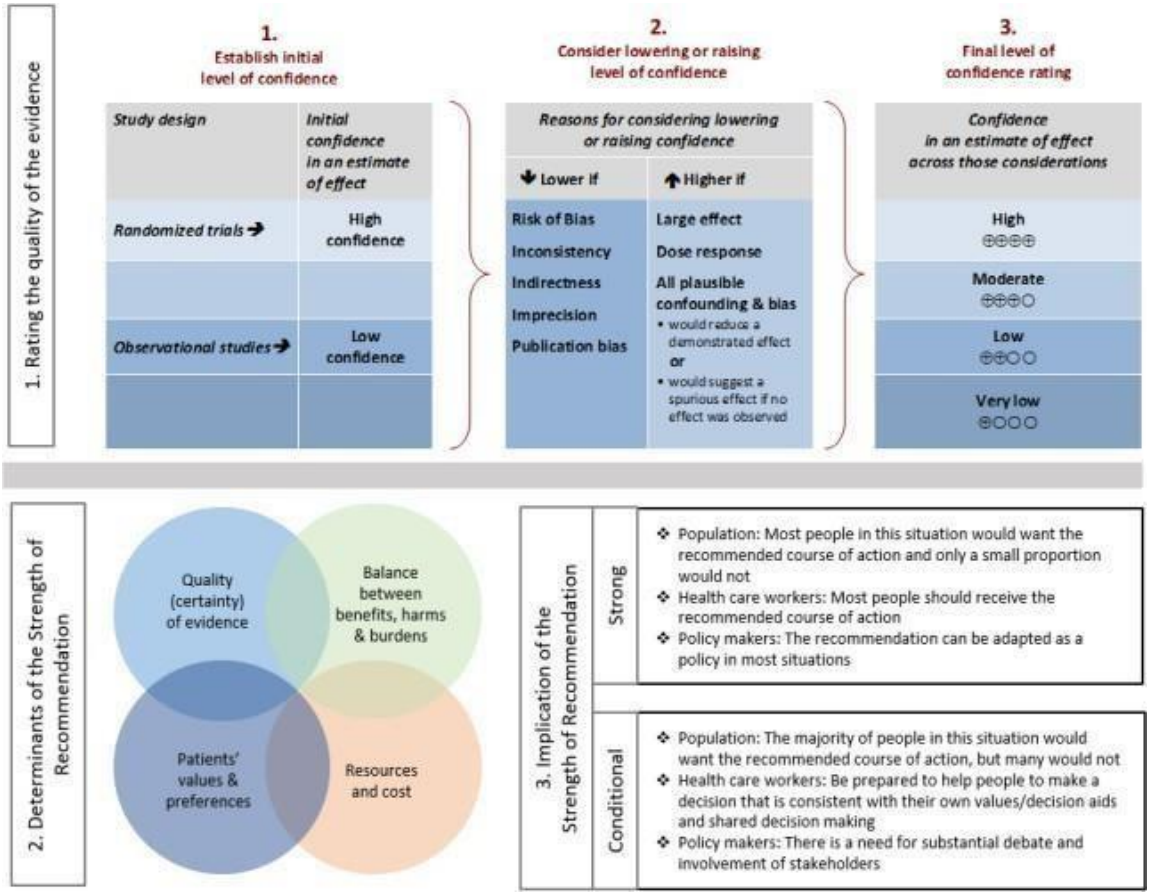

Table 1. COVID-19 Vaccination Guidance by Immunocompromised Population[2-8]

Group	Suggested timing of 2025-2026 COVID-19 vaccine*, **
Solid organ transplant	• At least 2 weeks pre-SOT; or ≥3 months post-SOT
Hematologic malignancy	• Optimal timing includes ≥2 weeks before starting treatment and ≥ 3 months after last infusion o For B-cell depletion, consider ≥3-6 months after last infusion • If optimal timing not feasible, administer during treatment (blunted immune response likely)
HCT/CAR-T	• Optimal timing includes ≥3 months after transplant or CAR-T treatment o For B-cell depletion, consider ≥3-6 months after last infusion • If optimal timing not feasible, administer during treatment (blunted immune response likely)
Solid tumor chemotherapy	• At least 2 weeks before starting therapy; during/after is acceptable
Primary Immuno-deficiency	• Align with IVIG/SCIG or clinic access
Autoimmune immunosuppression	• Optimal timing includes ≥2 weeks before starting treatment and ≥ 3 months after last infusion o For B-cell depletion, consider ≥3-6 months after last infusion • If optimal timing not feasible, administer during treatment (blunted immune response likely)
HIV	• Align with preventive routine care

*Defer during acute transplant rejection treatment or severe/acute illness
**Use shared-decision making for early windows based on levels of community virus circulation

Table 2. GRADE Evidence Profile: Should COVID-19 vaccination vs. no vaccination be used in immunocompromised patients (adults and children)?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	COVID19 vaccination	no vaccination	Relative (95% CI)	Absolute (95% CI)		
COVID-19 associated hospitalization												
1 [9]	non-randomised studies (cohort)	serious[a,b]	not serious	not serious	not serious	none	474/236490 (0.2%)	711/236490 (0.3%)	**VE 46%** (39.0 - 52.0) **HR 0.54** (0.48 to 0.61	**138 fewer per 100,000** (from 156 fewer to 117 fewer)	⨁⨁⨁◯ Moderate[a,b]	CRITICAL
								1.0%[c]		**459 fewer per 100,000** (from 519 fewer to 389 fewer)		
COVID-19 associated hospitalization												
4 [11-13, 15]	non-randomised studies (test-negative case contro	serious[a,b]	not serious	not serious	not serious	none	3,569 cases 29,909 controls		**VE 37%** (29-44) **OR 0.63** (0.56 to 0.71)	-	⨁⨁⨁◯ Moderate[a,b]	CRITICAL
							-	1.0%[c]		**368 fewer per 100,000** (from 438		

	l)									fewer to 288 fewer)		

Critical illness

1 [14]	non-randomised studies (test-negative case control)	serious[a]	not serious	not serious	not serious	none	627 cases 30,977 controls		**VE 40%** (26-51) **OR 0.60** (0.49 to 0.74)	- **40 fewer per 100,000** (from 51 fewer to 26 fewer)	⊕⊕⊕◯ Moderate[a]	CRITICAL
							-	0.1%				

COVID-19 related mortality

1 [10]	non-randomised studies (cohort)	serious[a]	not serious	not serious	serious[d]	none	27/6,575 (0.4%)	339/27,501 (1.2%)	**VE 61%** (36-77) **HR 0.39** (0.23 to 0.64)	**750 fewer per 100,000** (from 948 fewer to 442 fewer)	⊕⊕◯◯ Low[a,d]	CRITICAL

Prevention of long COVID-19

0							No studies were identified for the selected search period evaluating vaccine effects on post COVID conditions / long COVID in the immunocompromised population.			-		

Medically-attended visits (hospitals admissions, ED visits, UC visits, office visits, telemedicine visits)

1 [9]	non-randomised studie	serious[a,b]	not serious	not serious	not serious	none	4583/236490 (1.9%)	4685/236490 (2.0%)	**VE: 21%** (18-24)	**413 fewer per 100,0**	⊕⊕⊕◯ Moderate[a,b]	CRITICAL

	s (cohort)								**HR 0.79** (0.76 to 0.82)	**00** (from 472 fewer to 354 fewer)		

Medically-attended visits (ED/UC visits)

1 [11]	non-randomised studies (test-negative case control)	serious[a]	not serious	not serious	not serious	none	3236 cases 18,526 controls		**VE: 34%** (22-45) **OR 0.66** (0.55 to 0.78)	-	⊕⊕⊕◯ Moderate[a]	CRITICAL
							-	2.0%		**671 fewer per 100,000** (from 890 fewer to 433 fewer)		

Medically-attended visits (outpatient visits)

1 [11]	non-randomised studies (test-negative case control)	serious[a]	not serious	not serious	not serious	none	977 cases 7,148 controls		**VE: 40%** (19-55) **OR 0.60** (0.45 to 0.81)	-	⊕⊕⊕◯ Moderate[a]	CRITICAL
							-	2.0%		**790 fewer per 100,000** (from 1,090 fewer to 374 fewer)		

Serious adverse events

1 [16]	non-randomised studies (case series)	very serious[e]	not serious	not serious	not serious	none	In an analysis of 583,541 people identified as immunocompromised in the United Kingdom, 52 adverse events were analyzed. No significant increase was associated with the first two	⊕⊕◯◯ Low[e]	CRITICAL

							COVID vaccine injections. After the third dose, an increased risk in a small number of conditions was observed; however, due to a large number of evaluated conditions, multiple testing, and low event rates, a spurious association cannot be ruled out (Bonferroni-corrected p value was not significant at the 1% level (corrected p=0.22 [16].		

Exacerbations of immunocompromising or autoimmune conditions

3 [17-19]	non-randomised studies	very serious[f]	not serious	serious[g]	serious[h]	none	In studies of 736 people identified as immunocompromised, evaluated conditions included multiple sclerosis, advanced cancer, and inflammatory bowel disease. Overall, exacerbations of immunocompromising or autoimmune conditions were not increased due to vaccination; however, one study with MRI imaging results in patients with multiple sclerosis, showed an increase in brain lesions; though no description was provided how this affected the patients clinically [19].	⊕◯◯◯ Very low[f,g,h]	IMPORTANT

CI: confidence interval; **HR:** hazard ratio; **OR:** odds ratio

Explanations

a. Applying ROBINS-I tool, residual, unknown confounders could not be ruled out

b. Some identified confounders were unlikely to have materially inflated the vaccine effectiveness; rather point in the opposite direction to potentially strengthen our inference of vaccine effectiveness. Not rated down further.

c. To further illustrate population impact by providing absolute risk differences, an additional baseline risk for hospitalization of 1% was set; estimated using COVID-net (Taylor CA, Patel K, Pham H, et al. COVID-19-Associated Hospitalizations Among U.S. Adults Aged ≥18 Years - COVID-NET, 12 States, October 2023-April 2024. MMWR Morb Mortal Wkly Rep **2024**; 73(39): 869-75) cumulative incidence rate (88% of hospitalized patients were not vaccinated), multiplied by RR of 2.75 to account for immunocompromised conditions (Chapman A, Berenbaum F, Curigliano G, Pliakas T, Sheikh A, Abduljawad S. Risk of Severe Outcomes From COVID-19 in Immunocompromised People During the Omicron Era: A Systematic Review and Meta-Analysis. Clin Ther **2025**; 47(9): 770-87).

d. Due to low number of events, fragility in the estimate may be present

e. Applying ROBINS-I tool, bias was present for confounding and measurement of outcomes

f. Applying ROBINS-I tool, bias was present in several domains including confounding, selection of participants, and measurement of outcomes

g. Increase in imaging detected brain lesions of uncertain clinical relevance

h. Due to low number of events

Table 3. Influenza Vaccination Guidance by Immunocompromised Population[1-10]

Group	Suggested timing of 2025-2026 Influenza vaccine*, **
Solid organ transplant	• At least 2 weeks pre-SOT; or ≥1 months post-SOT, may give earlier if influenza season has started
Hematologic malignancy	• Optimal timing includes ≥2 weeks before starting treatment and ≥ 3 months after last infusion o For B-cell depletion, consider ≥3-6 months after last infusion • If optimal timing not feasible based on influenza season, earlier administration reasonable (blunted immune response possible)
HCT/CAR-T	• Optimal timing includes ≥3 months after transplant or CAR-T treatment o For B-cell depletion, consider ≥3-6 months after last infusion • If optimal timing not feasible based on influenza season, administer earlier (blunted immune response possible)
Solid tumor chemotherapy	• Optimally at least 2 weeks before starting therapy; during/after is acceptable
Primary Immuno-deficiency	• Align with IVIG/SCIG or clinic access
Autoimmune immunosuppression	• Optimal timing includes ≥2 weeks before starting treatment and ≥ 3 months after last infusion o For B-cell depletion, consider ≥3-6 months after last infusion • If optimal timing not feasible based on timing of influenza season, earlier administration reasonable (blunted immune response possible)
HIV	• Align with preventive routine care

*Defer during most intense periods of acute transplant rejection treatment or severe/acute illness
** Since influenza vaccine is recommended annually, timing of vaccination is of particular concern. While response may be blunted if administered prior to the recommended interval, during the fall and winter months optimal timing of influenza vaccine in relation to immunosuppression will depend on local circulation of influenza virus.

Table 4. GRADE Evidence Profile: Should Influenza vaccination vs. no vaccination be used in immunocompromised patients (adults and children)?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Influenza vaccination	no vaccination	Relative (95% CI)	Absolute (95% CI)		
Influenza-associated hospitalization (Immunocompromised adults)												
1[1]	non-randomised studies	serious[a]	not serious	not serious	not serious[b]	none	212 cases 1,639 controls		**VE: 32%** (7-50%) **OR 0.68** (0.50 to 0.93)	-	⨁⨁⨁◯ Moderate[a,b]	CRITICAL
							-	2.0%[c]		**631 fewer per 100,000** (from 990 fewer to 137 fewer)		
Influenza-associated hospitalization (Overall adults ≥65 yrs; test negative case-control studies)												
10[1,2,3,4,5,6,7,8,9,10]	non-randomised studies	serious[a]	not serious[d]	not serious	not serious	none	18,148 cases 138,698 controls		**VE: 42%** (36-47%) **OR 0.58** (0.53 to 0.64)	-	⨁⨁⨁◯ Moderate[a,d]	CRITICAL
							-	0.5%		**209 fewer per 100,000** (from 234 fewer to 179 fewer)		
All-cause mortality (Overall adults ≥60 years)												
1[11]	non-rando	serious[a]	not serious	serious[e]	serious[f]	none	68/7,372	1,765/59,172	**VE: 53%**	**1,570**	⨁◯◯◯	CRITICAL

	mised studies						(0.9%)	(3.0%)	(41-63%) **HR 0.47** (0.37 to 0.59)	**fewer per 100,000** (from 1,869 fewer to 1,212 fewer)	Very low[a,e,f]	
Severe Disease (ICU admission; in overall adults >18 years)												
1[10]	non-randomised studies	serious[a]	not serious	serious[e]	not serious	none	824 cases 12,644 controls -	20.0%	**VE: 41%** (31-50%) **OR 0.59** (0.50 to 0.69)	- **71 fewer per 1,000** (from 89 fewer to 53 fewer)	⊕⊕◯◯ Low[a,e]	CRITICAL
Guillain Barre Syndrome (in overall adults ≥65 years)												
2[12,13]	non-randomised studies	serious[a]	not serious	not serious	not serious	none	163/31,234,097 (0.0005%)	186/31,234,097 (0.0005%)	**IRR 0.96** (0.73 to 1.27)	**0 more per 1,000,000** (from 2 fewer to 2 more)	⊕⊕⊕◯ Moderate[a]	CRITICAL
Severe adverse events (in overall adults/older adults)												
2[12, 14]	non-randomised studie	serious[a]	not serious	not serious	serious[g]	none	An SCCS including people on Medicare found no increased risk of ischemic or hemorrhagic stroke following				⊕⊕◯◯ Low[a,g]	CRITICAL

	s						various influenza vaccines overall but identified a statistically significant increased risk of a composite of ischemic stroke or TIA occurring 22-42 days after influenza vaccination (i.e. Medicare Advantage population, IRR 1.10, 95% CI, 1.02 to 1.17). [Lloyd 2025]. However, this translates into approximately 1 additional endpoint in 10,000 vaccinated Medicare Advantage enrollees. In addition, a Canadian cohort study found influenza vaccine within 30 days was associated with reduced risk of stroke (aHR 0.66, 95% CI, 0.65 to 0.68) [Tanaka 2024]		
Exacerbation of immunocompromising or autoimmune condition									
1[15,16,17]	non-randomised studies	very serious[h]	not serious	not serious	not serious	none	A study evaluating safety of vaccination in 450 kidney transplant recipients found no significant difference between vaccinated and no-vaccinated groups in changes of eGFR, Serum creatinine (sCr) and occurrence of clinically significant proteinuria. None amongst the vaccinated group experienced leucopenia, neutropenia, or thrombocytopenia after vaccination. One study evaluating multiple sclerosis showed no increased risk of flares (OR 0.9, 95% CI 0.88 to 1.09). Conversely, another study showed no increased risk of flu vaccine and excess inflammatory bowel disease flares (aIRR 0.68, 95% CI 0.46 to 1.02).	⊕⊕◯◯ Low[h]	IMPORTANT

Explanations

a. Possibility of unknown and potential residual confounding warrants rating down in ROBINS-I. Although some studies were rated as higher risk of bias, sensitivity analysis by the VIP SR comparing low risk of bias studies to higher risk of bias studies did not show an effect difference strengthening our assessment of moderate certainty evidence.
b. Given a large body of indirect evidence of VE in older, presumable immunocompetent adults (42% 95% CI 36-47%), the panel decided to not rate down for imprecision
c. CDC estimates an influenza hospitalization rate of around 600/100,000 for the elderly (O'Halloran A, Habeck JW, Gilmer M, et al. Influenza-Associated Hospitalizations During a High Severity Season — Influenza Hospitalization Surveillance Network, United States, 2024–25 Influenza Season. MMWR Morb Mortal Wkly Rep 2025;74:529–537. DOI: http://dx.doi.org/10.15585/mmwr.mm7434a1.). Correcting for influenza vaccine status (rate: 32%) and increased risk due to immunocompromised conditions (RR: 4.4 (PMID: 33252189)), the displayed rate facilitates visualizing the population effects of the flu vaccination.
d. Although statistically significant heterogeneity was observed (I squared of 81%), 9 out of 10 studies revealed a clinically meaningful vaccination effectiveness - not rated down
e. Indirect evidence of VE in overall adult population
f. Given the relative low number of deaths in the cases, fragility of the estimate could not be ruled out
g. Some outcomes with few events
h. Potential unknown and residual confounding

Table 5. RSV Vaccination Guidance by Immunocompromised Population[1-5]

Group	Suggested timing of RSV vaccine*, **
Solid organ transplant	• At least 2 weeks pre-SOT; or ≥6 months post-SOT. Can be given as early as 1 month after transplant during RSV season
Hematologic malignancy	• Optimal timing includes ≥2 weeks before starting treatment and ≥ 6 months after last infusion o For B-cell depletion, consider ≥6 months after last infusion • If optimal timing not feasible, administer during treatment (blunted immune response likely)
HCT/CAR-T	• Optimal timing includes ≥6 months after transplant or CAR-T treatment o For B-cell depletion, consider ≥6 months after last infusion • If optimal timing not feasible, administer during treatment (blunted immune response likely)
Solid tumor chemotherapy	• At least 2 weeks before starting therapy; during/after is acceptable
Primary Immuno-deficiency	• Align with IVIG/SCIG or clinic access
Autoimmune immunosuppression	• Optimal timing includes ≥2 weeks before starting treatment and ≥ 3-6 months after last infusion o For B-cell depletion, consider ≥6 months after last infusion • If optimal timing not feasible, administer during treatment (blunted immune response likely)
HIV	• Align with preventive routine care

*Defer during acute transplant rejection treatment or severe/acute illness
**Use shared-decision making for early windows based on levels of community virus circulation

Table 6. GRADE Evidence Profile: Should RSV vaccination vs. no vaccination be used in immunocompromised patients (adults and children)?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	RSV vaccination	no vaccination	Relative (95% CI)	Absolute (95% CI)		
RSV-associated hospitalization (Immunocompromised adults)												
2[1,2]	non-randomised studies	serious[a]	not serious	not serious	not serious	none[b]	8,637 cases 137,156 controls		**VE: 70% (66-73)** **OR 0.30** (0.27 to 0.34)	-	⊕⊕⊕◯ Moderate[a,b]	CRITICAL
							-	1.0%		**698 fewer per 100,000** (from 728 fewer to 658 fewer)		
Critical illness (ICU admission or in-hospital death or both; in immunocompetent adults ≥60 yrs)												
1[1]	non-randomised studies	serious[a]	not serious	serious[c]	not serious	none	262 cases 26,669 controls		**VE: 81% (52–92)** **OR 0.19** (0.08 to 0.48)	-	⊕⊕◯◯ Low[a,c]	CRITICAL
							-	0.2%		**162 fewer per 100,000** (from 184 fewer to 104 fewer)		
Serious adverse events (SAEs; in overall adults ≥60 yrs)												
2[3,4,5]	randomised trials	not serious[d]	not serious	not serious	not serious	none	1,795/37,187 (4.8%)	1,732/36,845 (4.7%)	**RR 1.03** (0.97 to 1.09)	**1 more per 1,000** (from 1 fewer to 4 more)	⊕⊕⊕⊕ High[d]	CRITICAL
Gullian-Barre Syndrome (GBS; in overall adults ≥60 yrs)												

1[2]	non-randomised studies	serious[a]	not serious	not serious	not serious	none	102/4,746,518 (0.03%)	-	**IRR 2.1** (1.5 to 2.9)	**11.2 excess cases per 1,000,000 doses** (from 7.2 to 14.1 excess cases)	⊕⊕⊕◯ Moderate[a]	CRITICAL

Exacerbation of immunocompromising or autoimmune condition

0							No comparative evidence informing this outcome was identified.				-	IMPORTANT

CI: confidence interval; **OR:** odds ratio; **RR:** risk ratio; **IRR**: incidence rate ratio

Explanations

a. Rated down for unknown or possible residual confounding
b. Large effect. However, not rated up for concerns of possible residual confounding
c. Based on indirect evidence in immunocompetent adults
d. Loss to follow-up was similar in both groups - not rated down