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

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	COVID19 vaccination	no vaccination	Relative (95% CI)	Absolute (95% CI)		
COVID19 associated hospitalization												
2[9,20]	non-randomised studies (cohort studies)	serious [a,b]	not serious	not serious	not serious	none	786/388698 (0.2%)	1357/388603 (0.3%) 1.0%[c]	**VE 48% (43-53)** Note: HR 0.52 (0.47 to 0.57)	167 fewer per 100,000 (from 185 fewer to 150 fewer) 479 fewer per 100,000 (from 529 fewer to 429 fewer)	⊕⊕⊕◯ Moderate [a,b]	CRITICAL
COVID19 associated hospitalization (test-negative case control)												
6[11, 12, 13, 15, 21, 22]	non-randomised studies (case-control studies)	serious [a,b]	not serious	not serious	not serious	none	4240 cases 32248 controls -	1.0%[c]	**VE 36% (28-42)** Note: OR 0.64 (0.58 to 0.72)	- 358 fewer per 100,000 (from 418 fewer to 278 fewer)	⊕⊕⊕◯ Moderate [a,b]	CRITICAL
Critical illness												
1[14]						none	627 cases 30977 controls			-		CRITICAL
	non-randomised studies (case-control studies)	serious [a]	not serious	not serious	not serious		-	0.1%	**VE 40% (26-51)** Note: OR 0.60 (0.49 to 0.74)	40 fewer per 100,000 (from 51 fewer to 26 fewer)	⊕⊕⊕◯ Moderate [a]	
COVID19 related mortality												
1[10]	non-randomised studies (cohort studies)	serious [a]	not serious	not serious	serious [d]	none	27/6575 (0.4%)	339/27501 (1.2%)	**VE 61% (36-77)** Note: 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 vaccince 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 studies (cohort studies)	serious [a,b]	not serious	not serious	not serious	none	4583/236490 (1.9%)	4685/236490 (2.0%)	**VE: 21% (18-24)** Note: HR 0.79 (0.76 to 0.82)	413 fewer per 100,000 (from 472 fewer to 354 fewer)	⊕⊕⊕◯ Moderate [a,b]	CRITICAL
Medically-attended visits (ED/UC visits)												
1[11]						none	3236 cases 18526 controls			-		CRITICAL
	non-randomised studies (case-control studies)	serious [a]	not serious	not serious	not serious		-	2.0%	**VE: 34% (22-45)** Note: OR 0.66 (0.55 to 0.78)	671 fewer per 100,000 (from 890 fewer to 433 fewer)	⊕⊕⊕◯ Moderate [a]	
Medically-attended visits (outpatient visits)												
1[11]	non-randomised studies (case-control studies)	serious [a]	not serious	not serious	not serious	none	977 cases 7148 controls -	2.0%	**VE: 40% (19-55)** Note: OR 0.60 (0.45 to 0.81)	- 790 fewer per 100,000 (from 1,090 fewer to 374 fewer)	⊕⊕⊕◯ Moderate [a]	CRITICAL
Medically-attended visits (hospital, ED, outpatient, or physician encounters)												
1[20]	non-randomised studies (cohort studies)	serious [a]	not serious	not serious	not serious	none	4123/152208 (2.7%)	4242/152113 (2.8%)	**VE: 24% (20-27)** Note: HR 0.76 (0.73 to 0.80)	662 fewer per 100,000 (from 745 fewer to 551 fewer)	⊕⊕⊕◯ Moderate [a]	CRITICAL
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 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				⊕⊕◯◯ Low [e]	CRITICAL
							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, 18, 19]	non-randomised studies (cohort 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 et al. MMWR | October 3, 2024 | Vol. 73 | No. 39) cumulative incidence rate (88% of hospitalized patients were not vaccinated), multiplied by RR of 2.75 to account for immunocompromised conditions (Chapman et al PMID: 40850887)

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, classification of intervention, and measurement of outcomes

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

h. Due to low number of events