Annexes to the recommendations for use of the Pfizer–BioNTech vaccine BNT162b2 against COVID-19

Grading of evidence –

Evidence to recommendation tables

First issued 14 January 2021
(included in the background document)

Updated 15 June 2021

Updated 19 November 2021

Updated 21 January 2022

World Health Organization

Background

These are the annexes to the Interim recommendations for use of the Pfizer–BioNTech vaccine BNT162b2vaccine.

Annexes 1–8 contain tables that summarize the grading of recommendations, assessment, development and evaluations (GRADE). Annexes 9–12 contain the SAGE evidence-to-recommendation framework tables (ETR tables). The ETR tables are based on the DECIDE Work Package 5: Strategies for communicating evidence to inform decisions about health system and public health interventions. Evidence to a recommendation (for use by a guideline panel) (www.decide-collaboration.eu/, accessed 5 November 2021).

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Annex 1. GRADE table: Efficacy of BNT162b2 vaccine in adults

Population:	Adults (aged 16–55 years)			
Intervention:	Two doses of BNT162b2 vaccine			
Comparison:	Placebo/active control			
Outcome:	COVID-19 (PCR-confirmed)			
What is the efficacy of two doses of BNT162b2 vaccine compared with placebo/active control in preventing PCR-confirmed COVID-19 in adults (aged 16–55 years)?				
			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating[a]		1/ RCT *(1, 2)*	4
	Factors decreasing confidence	Limitation in study design[b]	Not serious	0
		Inconsistency	Not serious	0
		Indirectness	Not serious	0
		Imprecision	Not serious	0
		Publication bias	Not serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose–response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**4**
Summary of Findings	**Statement on quality of evidence**			**Evidence supports a high level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 4).**
	Conclusion			We are very confident that 2 doses of BNT162b2 vaccine are efficacious in preventing PCR-confirmed COVID-19 in adults (aged 16–55 years) up to approx. 2 months following immunization.

[a] High vaccine effectiveness of BNT162b2 has been confirmed in post-introduction observational studies.

[b] For the risk-of-bias assessments using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), please see: www.covid-nma.com/vaccines.

Annex 2. GRADE table: Safety of BNT162b2 vaccine in adults

Population:	Adults (aged 16–55 years)
Intervention:	Two doses of BNT162b2 vaccine
Comparison:	Placebo/active control
Outcome:	Serious adverse events following immunization

What is the risk of serious adverse events following BNT162b2 vaccination compared with placebo/active control in adults (aged 16–55 years)?

			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		2/ RCT *(1-3)*[a]	4
	Factors decreasing confidence	Limitation in study design[b]	Not serious	0
		Inconsistency	Not serious	0
		Indirectness	Not serious	0
		Imprecision	Not serious	0
		Publication bias	Not serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose–response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**4**
Summary of Findings	**Statement on quality of evidence**			**Evidence supports a high level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 4).**
	Conclusion			We are confident that the risk of serious adverse events following 1 or 2 doses of BNT162b2 vaccine in adults (aged 16–55 years) is low. A very rare, but significantly elevated risk of myocarditis/pericarditis has been reported after mRNA COVID-19 vaccine use. These cases occurred more often in younger men (16-24 years of age) and after the second dose of the vaccine, typically within few days after vaccination.

[a] Post-licensure data have identified a very rare but increased risk of myocarditis and pericarditis, mainly in male individuals who received COVID-19 mRNA vaccines.

[b] For the risk-of-bias assessments using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), please see: www.covid-nma.com/vaccines.

Annex 3. GRADE table: Efficacy of BNT162b2 vaccine in older adults

Population:	Older adults (aged >55 years)
Intervention:	Two doses of BNT162b2 vaccine
Comparison:	Placebo/active control
Outcome:	COVID-19 (PCR-confirmed)

What is the efficacy of two doses of BNT162b2 vaccine compared with placebo/active control in preventing PCR-confirmed COVID-19 in older adults (aged >55 years)?

			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating[a]		*1/ RCT (1, 2)*	4
	Factors decreasing confidence	Limitation in study design[b]	Not serious	0
		Inconsistency	Not serious	0
		Indirectness	Not serious	0
		Imprecision	Not serious	0
		Publication bias	Not serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose–response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**4**
Summary of Findings	**Statement on quality of evidence**			**Evidence supports a high level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 4).**
	Conclusion			We are confident that 2 doses of BNT162b2 vaccine are efficacious in preventing PCR-confirmed COVID-19 in older adults (aged >55 years) up to approx. 2 months following immunization.

[a] High vaccine effectiveness of BNT162b2 has been confirmed in post-introduction observational studies.

[b] For the risk-of-bias assessments using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), please see: www.covid-nma.com/vaccines.

Annex 4. GRADE table: Safety of BNT162b2 vaccine in older adults

Population:	Older adults (aged >55 years)
Intervention:	Two doses of BNT162b2 vaccine
Comparison:	Placebo/active control
Outcome:	Serious adverse events following immunization

What is the risk of serious adverse events following BNT162b2 vaccination compared with placebo/active control in older adults (aged >55 years)?

			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		2/ RCT *(1-3)*	4
	Factors decreasing confidence	Limitation in study design[a]	Not serious	0
		Inconsistency	Not serious	0
		Indirectness	Not serious	0
		Imprecision	Not serious	0
		Publication bias	Not serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose–response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**4**
Summary of Findings	**Statement on quality of evidence**			**Evidence supports a high level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 4).**
	Conclusion			We are confident that the risk of serious adverse events following 1 or 2 doses of BNT162b2 vaccine in older adults (aged >55 years) is low.

[a] For the risk-of-bias assessments using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), please see: www.covid-nma.com/vaccines.

Annex 5. GRADE table: Efficacy of BNT162b2 vaccine in individuals with underlying conditions

Population:	Individuals with comorbidities or health states that increase risk for severe COVID-19
Intervention:	Two doses of BNT162b2 vaccine
Comparison:	Placebo/active control
Outcome:	COVID-19 (PCR-confirmed)

What is the efficacy of two doses of BNT162b2 vaccine compared with placebo/active control in preventing PCR-confirmed COVID-19 in individuals with comorbidities or health states that increase risk for severe COVID-19?

			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating[a]		1/ RCT *(1, 2, 4)* [b]	4
	Factors decreasing confidence	Limitation in study design[c]	Not serious	0
		Inconsistency	Not serious	0
		Indirectness	Not serious[d]	0
		Imprecision	Serious[e]	-1
		Publication bias	Not serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose–response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**3**
	Statement on quality of evidence			**Evidence supports a moderate level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 3).**
Summary of Findings	**Conclusion**			We are moderately confident that 2 doses of BNT162b2 vaccine are efficacious in preventing PCR-confirmed COVID-19 in individuals with comorbidities or health states that increase risk for severe COVID-19 as included in the clinical trial up to approx. 2 months following immunization. Data suggests that individuals with moderately to severely compromised immune systems, such people living with organ or stem cell transplants, blood cancer, certain autoimmune disease and treatment with specific immunosuppressive medications, may not mount the same level of immunity following a regular 2-dose vaccination schedule compared to people who are not immunocompromised.

[a] High vaccine effectiveness of BNT162b2 has been confirmed in post-introduction observational studies.

[b] Observational data has been generated on vaccine effectiveness in specific subpopulations.

[c] For the risk-of-bias assessments using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), please see: www.covid-nma.com/vaccines.

[d] The phase 3 trial excluded pregnant and breastfeeding women, and persons who were immunocompromised. Around 46% of the trial population were either obese or affected by comorbidities. Additional studies in pregnant and lactating women with regard to the COVID-19 mRNA vaccines (BNT162b2 or mRNA-1273) were conducted and data generated demonstrating immunogenicity in these populations.

[e] Missing effect estimates in certain subpopulations and data in immunocompromised individuals were considered as limitations that led to downgrading of the evidence.

Annex 6. GRADE table: Safety of BNT162b2 vaccine in individuals with underlying conditions

Population:	Individuals with comorbidities or health states that increase risk for severe COVID-19
Intervention:	Two doses of BNT162b2 vaccine
Comparison:	Placebo/active control
Outcome:	Serious adverse events following immunization

What is the risk of serious adverse events following BNT162b2 vaccination compared with placebo/active control in individuals with comorbidities or health states that increase risk for severe COVID-19?

			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		1/ RCT *(1, 2, 5)*	4
	Factors decreasing confidence	Limitation in study design[a]	Not serious	0
		Inconsistency	Not serious	0
		Indirectness	Not serious[b]	0
		Imprecision	Serious[c]	-1
		Publication bias	Not serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose–response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**3**
Summary of Findings	**Statement on quality of evidence**			**Evidence supports a moderate level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 3).**
	Conclusion			We are moderately confident that the risk of serious adverse events in individuals with comorbidities or health states that increase risk for severe COVID-19 following 1 or 2 doses of BNT162b2 vaccine is low.

[a] For the risk-of-bias assessments using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), please see: www.covid-nma.com/vaccines.

[b] The phase 3 trial excluded pregnant and breastfeeding women, and persons who were immunocompromised. Around 46% of the trial population were either obese or affected by comorbidities. Additional studies in pregnant and lactating women with regard to the COVID-19 mRNA vaccines (BNT162b2 or mRNA-1273) were conducted and data generated demonstrating a good safety profile in these populations.

[c] Missing safety data in certain subpopulations and data in immunocompromised individuals were considered as limitations that led to downgrading of the evidence.

Annex 7. GRADE table: Efficacy of BNT162b2 vaccine in children (12–15 years)

Population:	Children (aged 12–15 years)
Intervention:	Two doses of BNT162b2 vaccine
Comparison:	Placebo/active control
Outcome:	COVID-19 (PCR-confirmed)

What is the efficacy of two doses of BNT162b2 vaccine compared with placebo/active control in preventing PCR-confirmed COVID-19 in children (aged 12–15 years)?

			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating[a]		1/ RCT *(6-8)*	4
	Factors decreasing confidence	Limitation in study design[b]	Not serious	0
		Inconsistency	Not serious	0
		Indirectness	Not serious	0
		Imprecision	Not serious	0
		Publication bias	Not serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose–response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**4**
Summary of Findings	**Statement on quality of evidence**			**Evidence supports a high level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 4).**
	Conclusion			We are confident that 2 doses of BNT162b2 vaccine are efficacious in preventing PCR-confirmed COVID-19 in children (aged 12–15 years) up to approx. 2 months following immunization.