Annexes to the interim recommendations for use of the Novavax NVX-CoV2373 vaccine against COVID-19

Grading of evidence –
Evidence to recommendations tables

20 December 2021

World Health Organization

Background

These are the annexes to the Interim recommendations for use of the Novavax NVX-CoV2373 vaccine against COVID-19 Trade names are Nuvaxovid and COVOVAX.

Annexes 1–6 contain tables that summarize the grading of recommendations, assessment, development and evaluations (GRADE) of Novavax NVX-CoV2373 vaccine. Annexes 7–9 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 30 November 2021).

Contents

Annex 1. GRADE table: Efficacy of NVX-CoV2373 vaccine in adults

Population:	Adults (aged 18–64 years)
Intervention:	Two doses of NVX-CoV2373 vaccine
Comparison:	Placebo/active control
Outcome:	COVID-19 (PCR-confirmed)

What is the efficacy of two doses of NVX-CoV2373 vaccine compared with placebo/active control in preventing PCR-confirmed COVID-19 in adults (18–64 years)?

			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		3/ RCT*(1-3)*	4
	Factors decreasing confidence	Limitation in study design[a]	Not serious[b]	0
		Inconsistency	Not serious	0
		Indirectness	Not serious	0
		Imprecision	Not serious	0
		Publication bias	Not serious	0
	Factors increasingconfidence	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 that of the estimate of the effect on the health outcome (level 4).**
	Conclusion			We are very confident that 2 doses of NVX-CoV2373 vaccine are efficacious in preventing PCR-confirmed COVID-19 in adults (18–64 years).

[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] Data on long-term protection emerging from the ongoing phase 3 clinical trial remain limited, as trial data have so far been reported only for a follow-up of approximately 3 months. This was considered as not constituting a limitation that would lead to downgrading of the evidence. SAGE will continue to review any emerging data and adjust its quality assessment as required.

Annex 2. GRADE table: Safety of NVX-CoV2373 vaccine in adults

Population:	Adults (aged 18–64 years)
Intervention:	Two doses of NVX-CoV2373 vaccine
Comparison:	Placebo/active control
Outcome:	Serious adverse events following immunization

What is the risk of serious adverse events following NVX-CoV2373 vaccination compared with placebo/active control in adults (18–64 years)?

			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		5/ RCT *(1-5)*	4
	Factors decreasing confidence	Limitation in study design[a]	Serious[b]	-1
		Inconsistency	Not serious	0
		Indirectness	Not serious	0
		Imprecision	Not serious	0
		Publication bias	Not serious	0
	Factors increasingconfidence	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 that of the estimate of the effect on the health outcome (level 3).**
	Conclusion			We are moderately confident that the risk of serious adverse events following 1 or 2 doses of NVX-CoV2373 vaccine in adults (18–64 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.

[b] Downgraded for the following limitations: The trial was not adequately powered to detect rare adverse events. These may emerge only when large populations have been vaccinated.

Annex 3. GRADE table: Efficacy of NVX-CoV2373 vaccine in older adults

Population:	Older adults (aged ≥65 years)
Intervention:	Two doses of NVX-CoV2373 vaccine
Comparison:	Placebo/active control
Outcome:	COVID-19 (PCR-confirmed)

What is the efficacy of two doses of NVX-CoV2373 vaccine compared with placebo/active control in preventing PCR-confirmed COVID-19 in older adults (≥65 years)?

			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		1/ RCT*(1-3)*	4
	Factors decreasing confidence	Limitation in study design[a]	Not serious	0
		Inconsistency	Not serious	0
		Indirectness	Not serious	0
		Imprecision	Serious[b]	-1
		Publication bias	Not serious	0
	Factors increasingconfidence	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 that of the estimate of the effect on the health outcome (level 4).**
	Conclusion			We are moderately confident that 2 doses of NVX-CoV2373 vaccine are efficacious in preventing PCR-confirmed COVID-19 in older adults (≥65 years).

[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] Of the trial participants in the UK trial, approximately 28% (vaccine arm: n=1953) were 65 years of age or older. Overall vaccine efficacy against symptomatic disease was 88.9% (95% CI, 12.8 to 98.6). While supportive evidence (immunogenicity data in this age group) suggest that the vaccine elicits an immune response comparable to older adults, the evidence was downgraded for imprecision due to large confidence intervals and the limited sample size. Data on long-term protection emerging from the phase 3 clinical trial remain limited, as trial data have so far been reported only for a follow-up of a median of 3 months after dose 2. This was considered as not constituting a limitation that would lead to downgrading of the evidence. SAGE will continue to review any emerging data and adjust its quality assessment as required.

Annex 4. GRADE table: Safety of NVX-CoV2373 vaccine in older adults

Population:	Older adults (aged ⩾65 years)
Intervention:	One or two doses of NVX-CoV2373 vaccine
Comparison:	Placebo/active control
Outcome:	Serious adverse events following immunization

What is the risk of serious adverse events following NVX-CoV2373 vaccination compared with placebo/active control in older adults (≥65 years)?

			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		4/ RCT *(1-4)*	4
	Factors decreasing confidence	Limitation in study design[a]	Serious[b]	-1
		Inconsistency	Not serious	0
		Indirectness	Not serious	0
		Imprecision	Not serious	0
		Publication bias	Not serious	0
	Factors increasingconfidence	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 that of the estimate of the effect on the health outcome (level 3).**
	Conclusion			We are moderately confident that the risk of serious adverse events following 1 or 2 doses of NVX-CoV2373 vaccine in older adults (≥65 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.

[b] Downgraded for the following limitations: The trials were not adequately powered to detect rare adverse events. These may emerge only when large populations have been vaccinated.

Annex 5. GRADE table: Efficacy of NVX-CoV2373 vaccine in individuals with underlying conditions

Population:	Individuals with comorbidities or health states that increase risk for severe COVID-19
Intervention:	Two doses of NVX-CoV2373 vaccine
Comparison:	Placebo/active control
Outcome:	COVID-19 (PCR-confirmed)

What is the efficacy of two doses of NVX-CoV2373 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		1/ RCT*(1-3)*	4
	Factors decreasing confidence	Limitation in study design[a]	Not serious	0
		Inconsistency	Not serious	0
		Indirectness	Serious[b]	-1
		Imprecision	Not serious[c]	0
		Publication bias	Not serious	0
	Factors increasingconfidence	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 that of the estimate of the effect on the health outcome (level 3).**
	Conclusion			We are moderately confident that 2 doses of NVX-CoV2373 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. No data were obtained on vaccination of pregnant or breastfeeding women, or persons who were immunocompromised.

[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] Trial excluded pregnant and breastfeeding women and persons who were severly immunocompromised. This was considered as constituting a limitation that leads to downgrading of the evidence.

[c] Underlying comorbidities included HIV, BMI ≥30 kg/m2, chronic respiratory, cardiac, renal, neurologic, hepatic as well as immunocompromising conditions . The clinical trial 2019 nCoV-501, a Phase 2a/b in South Africa, included 244 medically stable HIV-positive participants ≥ 18 to ≤ 64 years of age though vaccine efficacy could not be assessed in this population group due to small sample size. This was considered as not constituting a limitation that would lead to downgrading of the evidence. SAGE will continue to review any emerging data and adjust the quality assessment as required.

Annex 6. GRADE table: Safety of NVX-CoV2373 vaccine in individuals with underlying conditions

Population:	Individuals with comorbidities or health states that increase risk for severe COVID-19
Intervention:	One or two doses of NVX-CoV2373 vaccine
Comparison:	Placebo/active control
Outcome:	Serious adverse events following immunization

What is the risk of serious adverse events following NVX-CoV2373 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		3/ RCT *(1-3)*	4
	Factors decreasing confidence	Limitation in study design[a]	Serious[b]	-1
		Inconsistency	Not serious	0
		Indirectness	Serious[c]	-1
		Imprecision	Not serious	0
		Publication bias	Not serious	0
	Factors increasingconfidence	Large effect	Not applicable	0
		Dose–response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**2**
Summary of Findings	**Statement on quality of evidence**			**Evidence supports a low level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 2).**
	Conclusion			We have low confidence in the quality of evidence that the overall 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 NVX-CoV2373 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] Downgraded for the following limitations: the trial was not adequately powered to detect rare adverse events. These may emerge only when large populations have been vaccinated.

[c] Underlying comorbidities included HIV, BMI ≥30 kg/m2, chronic respiratory, cardiac, renal, neurologic, hepatic as well as immunocompromising conditions. The clinical trial 2019 nCoV-501, a Phase 2a/b in South Africa, included 244 medically stable HIV-positive participants ≥ 18 to ≤ 64 years of age. Trial excluded pregnant and breastfeeding women and persons who were severely immunocompromised. This was considered as constituting a limitation that leads to downgrading of the evidence.

Annex 7. SAGE evidence-to-recommendation framework NVX-CoV2373 vaccine use in adults

Question:	Should NVX-CoV2373 vaccine be administered to adults to prevent COVID-19?
Population:	Adults (aged 18–64 years)
Intervention:	Two doses of NVX-CoV2373 vaccine
Comparison(s):	Active control/placebo
Outcome:	COVID-19 (PCR-confirmed)

Background:

On 31 December 2019, WHO was alerted to several cases of pneumonia of unknown origin in Wuhan City, Hubei Province, China. The cause was found to be a novel coronavirus, SARS-CoV-2. The disease caused by this novel virus has been named COVID-19. The outbreak of COVID-19 was declared a public health emergency of international concern in January 2020. The disease has since spread, with an enormous impact on the health and well-being of individuals and populations worldwide. It has further caused major disruptions to various sectors of society and the economy across the globe.

Vaccines are a critical tool in combating the COVID-19 pandemic. In the rapidly evolving field of COVID-19 vaccines, WHO has issued to date interim recommendations on the use of a number of COVID-19 vaccines *(6)*. .

	CRITERIA	JUDGEMENTS				RESEARCH EVIDENCE	ADDITIONAL INFORMATION
PROBLEM	Is the problem a public health priority?	*No* ☐	*Uncertain* ☐	*Yes* ☒	*Varies by setting* ☐	The cumulative number of COVID-19 cases globally has surpassed 270 791 973, with more than 5 318 216 deaths. Cases have been found in 190 different countries or territories throughout the world (status 16 December 2021). There has been collateral damage to other public health programmes.	The COVID-19 situation is evolving rapidly; the most recent epidemiological situation can be found on the following website: https://covid19.who.int/table
BENEFITS & HARMS OF THE OPTIONS	Benefits of the intervention Are the desirable anticipated effects large?	*No* ☐	*Uncertain* ☐	*Yes* ☒	*Varies* ☐	Across seronegative individuals 18 to 64 years of age enrolled in a Phase 3 clinical trial in the UK, vaccine vaccine efficacy was 90% (95%CI: 80-95%) for PCR-confirmed mild, moderate, or severe COVID-19 with onset from 7 days after second vaccination*(2)*. In the US and Mexico, vaccine efficacy in those aged 18-64 years was 92% (95%CI: 84-95)*(3)*. High vaccine efficacy in this subpopulation was confirmed in a Phase 2a/b trial *(1)*.	

	Harms of the intervention Are the undesirable anticipated effects small?	*No* ☐	*Uncertain* ☐	*Yes* ☒	*Varies* ☐			Most unsolicited adverse events were mild or moderate in severity. Severe adverse events and serious adverse eventse (SAEs) were reported infrequently and at similar frequencies between the 2 treatment groups *(1-3)*.	
	Balance between benefits and harms	*Favours intervention* ☒	*Favours comparison* ☐	*Favours both* ☐	*Favours neither* ☐	Unclear ☐		Efficacy data suggest benefit in those aged 18–59 years. Overall, the vaccine is well tolerated. Balancing benefits and harms of COVID-19 disease and vaccination with NVX-CoV2373, the benefit of the intervention is larger than the potential harms.	
	What is the overall quality of this evidence for the critical outcomes?	**Effectiveness of the intervention** *No included studies* ☐	*Very low* ☐	*Low* ☐	*Moderate* ☐	*High* ☒		Please see the related GRADE tables.	
		Safety of the intervention *No included studies* ☐	*Very low* ☐	*Low* ☐	*Moderate* ☒	*High* ☐			
VALUES & PREFERENCES	How certain is the relative importance of the desirable and undesirable outcomes?	*Important uncertainty or variability* ☐	*Possibly important uncertainty or variability* ☒	*Probably no important uncertainty or variability* ☐	*No important uncertainty or variability* ☐	*No known undesirable outcomes* ☐		Available scientific evidence on the relative importance of the intervention, as well as the relative weights that the target population attributes to the desirable (i.e. protection conferred by the vaccine) and the undesirable outcomes (i.e. the currently reported safety signals), varies. Different population groups may have different opinions regarding the weights assigned to desirable and undesirable outcomes.	
	Values and preferences of the target population:	*No*	*Probably No*	*Uncertain*	*Probably Yes*	*Yes*	*Varies*	Available scientific evidence suggests that the target population assigns more weight to the desirable effects than to the undesirable effects related to COVID-19	

	Are the desirable effects large relative to undesirable effects?	☐	☐	☐	☒	☐	☐	vaccination. This may vary by (sub)population.	
RESOURCE USE	Are the resources required small?	*No*	*Uncertain*	*Yes*	*Varies*			NVX-CoV2373 can be distributed and stored using existing cold chain infrastructure (at 2–8 °C), and does not require ultra-cold chain capacity. Prices for NVX-CoV2373 are expected to be within the range of other COVID-19 vaccines with WHO EUL, with potential differential pricing by procurement mechanism (e.g., COVAX AMC vs. direct country procurement vs. private market) *(7, 8)*. Nevertheless, considerable resources will be needed to ensure the implementation of a COVID-19 vaccination programme, especially given: (i) that COVID-19 vaccination is likely to be prioritized for populations (e.g. health-care workers, older adults) without pre-existing robust immunization programmes in many settings; and (ii) the urgency of vaccination roll-out worldwide, which may necessitate additional surge resources to accelerate implementation with adequate infection prevention and control procedures in the context of COVID-19. Resources required include, but are not restricted to, human resources, vaccine costs, logistics, planning and coordination, training, social mobilization and communications, and immunization safety surveillance.	An estimated US$ 15.9 billion is needed for the vaccines pillar (COVAX) of the Access to COVID-19 Tools Accelerator (ACT-A) for 2020–21, when the initiative aims to deliver 2 billion doses. This does not include all delivery costs in all countries participating in COVAX, bilateral procurement deals, or research and development investments outside of COVAX *(9)*. The World Bank has approved a financing window of up to US$ 12 billion to support low- and middle-income countries in purchasing and distributing vaccine *(10)*.
		☒	☐	☐	☐				
	Cost–effectiveness	*No*	*Uncertain*	*Yes*	*Varies*			Formal global cost–effectiveness analyses have not been conducted, but the emerging evidence indicates that the benefits, including the impact on recovery of the global economy, are likely to outweigh the costs of COVID-19 vaccination in general at global level. No formal cost–effectiveness analyses of NVX-CoV2373 compared to other vaccines have been conducted. The NVX-CoV2373 vaccine is expected to be less costly than some other COVID-19 vaccines (see previous sub-criterion).	The global economy is estimated to be losing US$ 375 billion per month due to the coronavirus pandemic. G20 countries have invested approximately US$ 10 trillion in domestic economic stimulus to mitigate the economic consequences of reduced business activity and unemployment due to the pandemic. Initial estimates suggest that
		☐	☐	☐	☒				

								The ability to use NVX-CoV2373 in existing cold chain infrastructure in all country settings may enable higher population-level coverage. Cost–effectiveness analyses should be conducted at country level; cost–effectiveness of COVID-19 vaccination may vary by country depending on COVID-19 burden, comparator interventions assessed, analysis perspective, and local cost–effectiveness thresholds used.	COVID-19 vaccination will provide substantial economic value in terms of averted morbidity and mortality costs and averted GDP losses *(9, 11-17)*.
EQUITY	What would be the impact on health inequities?	*Increased*	*Uncertain*	*Reduced*		*Varies*		Equity and ethical considerations are critical. SAGE has produced a Values Framework *(18)*, which offers guidance on the fair allocation of COVID-19 vaccines based on 6 core ethical principles that should guide distribution. If distributed fairly, COVID-19 vaccines may have considerable impact on reducing health inequities.	Vaccine nationalism is seen as a threat to reducing health inequity, in particular as high-income countries have arranged bilateral contracts with manufacturers. This has led to the establishment of the Access to COVID-19 Tools (ACT) Accelerator and within this, the COVAX facility, which aims to ensure equitable access to vaccines for its participating Member States *(19)*.
		☐	☐	☒		☐			
ACCEPTABILITY	Which option is acceptable to key stakeholders (e.g. ministries of health, immunization managers)?	*Intervention*	*Comparison*	*Both*	*Neither*	*Unclear*		No scientific evidence is available. As vaccination is an important tool to combat COVID-19, it is assumed that key stakeholders, in particular ministries of health and immunization managers, are strongly in favour of it.	190 economies are participating in COVAX suggesting a very high acceptability of COVID-19 vaccination in general.
		☒	☐	☐	☐	☐			
	Which option is acceptable to target group?	*Intervention*	*Comparison*	*Both*	*Neither*	*Unclear*		COVID-19 vaccine acceptability, in general, varies between (sub-) population groups and may be correlated with the perceived risk posed	

		☒	☐	☐	☐	☐	by the vaccine versus the perceived risk posed by the disease. In a global survey (19 countries) of acceptance rates in the general population of any COVID-19 vaccine product, 71.5% of participants reported that they would be very or somewhat likely to take a COVID-19 vaccine. Acceptance rates ranged from almost 55% to 87% *(20)*. Polls have been launched (periodically), assessing vaccine acceptance in selected countries. These polls confirm overall, not product-specific, vaccine acceptance, with variations across countries *(21, 22)*.	
FEASIBILITY	Is the intervention feasible to implement?	*No* ☐	*Probably* No ☐	*Uncertain* ☐	*Probably* Yes ☐	*Yes* ☒	*Varies* ☐	NVX-CoV2373 vaccine is assumed to be easily implementable in settings, including low- and middle-income countries, with existing vaccine logistics and delivery infrastructure. Storage and distribution requirements of the NVX-CoV2373 vaccine are the same as those of many other vaccines currently in use globally. Therefore existing vaccine cold chain capacity, available in almost all countries worldwide could be leveraged for vaccine distribution. Administration of the vaccine to novel target groups currently not reached by national immunization programmes may pose a challenge in certain settings.	

BALANCE OF CONSEQUENCES	Undesirable consequences *clearly outweigh* desirable consequences in most settings ☐	Undesirable consequences *probably outweigh* desirable consequences in most settings ☐	The balance between desirable and undesirable consequences *is closely balanced or uncertain* ☐	Desirable consequences *probably outweigh* undesirable consequences in most settings ☐	Desirable consequences *clearly outweigh* undesirable consequences in most settings ☒
TYPE OF RECOMMENDATION	We recommend the intervention	We suggest considering recommendation of the intervention	We recommend the comparison	We recommend against the intervention and the comparison	

	☐	☐ Only in the context of rigorous research ☒ Only with targeted monitoring and evaluation ☐ Only in specific contexts or specific (sub)populations	☐	☐
RECOMMENDATION (TEXT)	Please see the interim recommendations.			
IMPLEMENTATION CONSIDERATIONS	Please see the interim recommendations.			
MONITORING, EVALUATION AND RESEARCH PRIORITIES	Please see the interim recommendations.			

Annex 8. SAGE evidence-to-recommendation framework: NVX-CoV2373 vaccinevaccine use in older adults

Question:	Should NVX-CoV2373 vaccine be administered to older adults to prevent COVID-19?
Population:	Older adults (aged ≥65 years)
Intervention:	Two doses of NVX-CoV2373 vaccine
Comparison(s):	Active control/placebo
Outcome:	COVID-19 (PCR-confirmed)

Background:

On 31 December 2019, WHO was alerted to several cases of pneumonia of unknown origin in Wuhan City, Hubei Province, China. The cause was found to be a novel coronavirus, SARS-CoV-2. The disease caused by this novel virus has been named COVID-19. The outbreak of COVID-19 was declared a public health emergency of international concern in January 2020. The disease has since spread with an enormous impact on the health and well-being of individuals and populations worldwide. It has further caused major disruptions to various sectors of society and the economy across the globe.

Vaccines are a critical tool in combating the COVID-19 pandemic. In the rapidly evolving field of COVID-19 vaccines, WHO has issued to date interim recommendations on the use of a number of COVID-19 vaccines *(6)*.

	CRITERIA	JUDGEMENTS				RESEARCH EVIDENCE	ADDITIONAL INFORMATION
PROBLEM	Is the problem a public health priority?	*No* ☐	*Uncertain* ☐	*Yes* ☒	*Varies by setting* ☐	The cumulative number of COVID-19 cases globally has surpassed 270 791 973, with more than 5 318 216 deaths. Cases have been found in 190 different countries or territories throughout the world (status 16 December 2021). There has been collateral damage to other public health programmes.	The COVID-19 situation is evolving rapidly; the most recent epidemiological situation can be found on the following website: https://covid19.who.int/table
BENEFITS &		*No*	*Uncertain*	*Yes*	*Varies*	Across seronegative individuals ≥65 to 84 years of age enrolled in a Phase 3 clinical trial in the UK *(2)*, vaccine	

	Benefits of the intervention Are the desirable anticipated effects large?	☐	☒	☐		☐	vaccine efficacy was 89% (95%CI: 20-100%) for PCR-confirmed mild, moderate, or severe COVID-19 with onset from 7 days after second vaccination.	
	Harms of the intervention Are the undesirable anticipated effects small?	*No* ☐	*Uncertain* ☐	*Yes* ☒		*Varies* ☐	Most unsolicited adverse events were mild or moderate in severity. Severe adverse events and serious adverse eventse (SAEs) were reported infrequently and at similar frequencies between the 2 treatment groups, with slightly higher incidence rate (6.74 vs. 3.28) among participants in the older age vaccine recipients (⩾ 65 years of age) vs the younger vaccine recipients (18-64 years) *(1-3)*.	
	Balance between benefits and harms	*Favours intervention* ☒	*Favours comparison* ☐	*Favours both* ☐	*Favours neither* ☐	Unclear ☐	Evidence on efficacy data suggest significant benefit of the intervention and safety data suggest limited harms.	
	What is the overall quality of this evidence for the critical outcomes?	**Effectiveness of the intervention** *No included studies* ☐	*Very low* ☐	*Low* ☐	*Moderate* ☒	*High* ☐	Please see the related GRADE tables.	
		Safety of the intervention *No included studies* ☐	*Very low* ☐	*Low* ☐	*Moderate* ☒	*High* ☐		
VALUES & PREFERENCES	How certain is the relative importance of the desirable and undesirable outcomes?	*Important uncertainty or variability* ☐	*Possibly important uncertainty or variability* ☒	*Probably no important uncertainty or variability* ☐	*No important uncertainty or variability* ☐	*No known undesirable outcomes* ☐	The majority of severe disease occurs in older individuals. Available scientific evidence suggests that the target population probably considers the desirable effects (i.e. the potential protection conferred by the vaccine), more important than the undesirable effects (i.e. the currently reported safety signals related to COVID-19 vaccination).	

										Different population groups may have different opinions regarding the weights assigned to desirable and undesirable outcomes.	
	Values and preferences of the target population: Are the desirable effects large relative to undesirable effects?	*No* ☐	*Probably No* ☐	*Uncertain* ☐	*Probably Yes* ☒	*Yes* ☐	*Varies* ☐			Available scientific evidence suggests that the target population probably assigns more weight to the desirable effects than the undesirable effects related to COVID-19 vaccination. With the most recent data on vaccine efficacy in older adults, the uncertainty around the importance of the desirable effects of the intervention will likely be reduced.	
RESOURCE USE	Are the resources required small?	*No* ☐		*Uncertain* ☐	*Yes* ☒		*Varies* ☐			NVX-CoV2373 can be distributed and stored using existing cold chain infrastructure (at 2–8 °C), and does not require ultra-cold chain capacity Prices for NVX-CoV2373 are expected to be within the range of other COVID-19 vaccines with WHO EUL, with potential differential pricing by procurement mechanism (e.g., COVAX AMC vs. direct country procurement vs. private market) *(7, 8)*. Nevertheless, considerable resources will be needed to ensure the implementation of a COVID-19 vaccination programme, especially given: (i) that COVID-19 vaccination is likely to be prioritized for populations (e.g. health-care workers, older adults) without pre-existing robust immunization programmes in many settings, and (ii) the urgency of vaccination roll-out worldwide, which may necessitate additional surge resources to accelerate implementation with adequate infection prevention and control procedures in the context of COVID-19. Resources required include, but are not restricted to, human resources, vaccine costs, logistics, planning and coordination, training, social mobilization and communications, and immunization safety surveillance.	An estimated US$ 15.9 billion is needed for the vaccines pillar (COVAX) of the Access to COVID-19 Tools Accelerator (ACT-A) for 2020–21, when the initiative aims to deliver 2 billion doses. This does not include all delivery costs in all countries participating in COVAX, bilateral procurement deals, or research and development investments outside of COVAX *(9)*. The World Bank has approved a financing window of up to US$ 12 billion to support low- and middle-income countries in purchasing and distributing vaccine *(10)*.
		No		*Uncertain*	*Yes*		*Varies*			Formal global cost–effectiveness analyses have not been conducted, but	The global economy is estimated to be losing

	Cost–effectiveness	☐	☐	☐	☒		the emerging evidence indicates that the benefits, including the impact on recovery of the global economy, are likely to outweigh the cost of COVID-19 vaccination in general at global level. No formal cost–effectiveness analyses of NVX-CoV2373 vaccine compared to other vaccines have been conducted. The NVX-CoV2373 vaccine is expected to be less costly than many other COVID-19 vaccines (see previous sub-criterion). The ability to use NVX-CoV2373 vaccine in existing cold chain infrastructure in all country settings may enable higher population-level coverage. Cost–effectiveness analyses should be conducted at country level; cost–effectiveness of COVID-19 vaccination may vary by country depending on COVID-19 burden, comparator interventions assessed, analysis perspective, and local cost–effectiveness thresholds used.	US$ 375 billion per month due to the coronavirus pandemic. G20 countries have invested approximately US$ 10 trillion in domestic economic stimulus to mitigate the economic consequences of reduced business activity and unemployment due to the pandemic. Initial estimates suggest that COVID-19 vaccination will provide substantial economic value in terms of averted morbidity and mortality costs and averted GDP losses *(9, 11-17)*.
EQUITY	What would be the impact on health inequities?	*Increased* ☐	*Uncertain* ☐	*Reduced* ☒	*Varies* ☐		Equity and ethical considerations are critical. SAGE has produced a Values Framework *(18)*, which offers guidance on the fair allocation of COVID-19 vaccines based on 6 core ethical principles that should guide distribution. If distributed fairly, COVID-19 vaccines may have considerable impact on reducing health inequities.	Vaccine nationalism is seen as a threat to reducing health inequity, in particular as high-income countries have arranged bilateral contracts with manufacturers. This has led to the establishment of the Access to COVID-19 Tools (ACT) Accelerator and within this, the COVAX facility, which aims to ensure equitable access to vaccines for its participating Member States *(19)*.
ACCEPTABILITY	Which option is acceptable to key stakeholders	*Intervention*	*Comparison*	*Both*	*Neither*	*Unclear*	No scientific evidence is available. As vaccination is an important tool to combat COVID-19, it is assumed that key stakeholders, in particular ministries of health and immunization managers	A total of 190 economies are participating in COVAX which suggests a very high acceptability of COVID-19 vaccination in general,

	(e.g. ministries of health, immunization managers)?	☒	☐	☐	☐	☐	are strongly in favour of COVID-19 vaccination.	although not the NVX-CoV2373 vaccine in particular.
	Which option is acceptable to target group?	*Intervention* ☒	*Comparison* ☐	*Both* ☐	*Neither* ☐	*Unclear* ☐	COVID-19 vaccine acceptability in general varies between (sub-) population groups and may be correlated with the perceived risk posed by the vaccine versus the perceived risk posed by the disease. In a global survey (19 countries) of acceptance rates in the general population of any COVID-19 vaccine product, 71.5% of participants reported that they would be very, or somewhat, likely to take a COVID-19 vaccine. Acceptance rates ranged from almost 55% to 87% *(20)*. Polls have been launched, (periodically) assessing vaccine acceptance in selected countries. These polls confirm overall, not product-specific, vaccine acceptance, with variations across countries *(21, 22)*.	
FEASIBILITY	Is the intervention feasible to implement?	*No* ☐	*Probably* No ☐	*Uncertain* ☐	*Probably* Yes ☐	*Yes* ☒	*Varies* ☐	NVX-CoV2373 vaccine is assumed to be easily implementable in settings, including low- and middle-income countries, with existing vaccine logistics and delivery infrastructure. Storage and distribution requirements of the NVX-CoV2373 vaccine are the same as those of many other vaccines currently in use globally. Therefore existing vaccine cold chain capacity, available in almost all countries worldwide could be leveraged for vaccine distribution. Administration of the vaccine to novel target groups currently not reached by national immunization programmes may pose a challenge in certain settings.	

BALANCE OF CONSEQUENCES	Undesirable consequences *clearly outweigh* desirable consequences in most settings ☐	Undesirable consequences *probably outweigh* desirable consequences in most settings ☐	The balance between desirable and undesirable consequences *is closely balanced or uncertain* ☐	Desirable consequences *probably outweigh* undesirable consequences in most settings ☐	Desirable consequences *clearly outweigh* undesirable consequences in most settings ☒
TYPE OF RECOMMENDATION	We recommend the intervention ☐	We suggest considering recommendation of the intervention ☐ Only in the context of rigorous research ☒ Only with targeted monitoring and evaluation ☐ Only in specific contexts or specific (sub)populations	We recommend the comparison ☐	We recommend against the intervention and the comparison ☐	
RECOMMENDATION (TEXT)	Please see the interim recommendations.				
IMPLEMENTATION CONSIDERATIONS	Please see the interim recommendations.				
MONITORING, EVALUATION AND RESEARCH PRIORITIES	Please see the interim recommendations.				

Annex 9. SAGE evidence-to-recommendation framework: NVX-CoV2373 vaccine use in individuals with comorbidities

Question:	Should NVX-CoV2373 vaccine be administered to individuals with comorbidities[a] or health states that increase risk for severe COVID-19 to prevent COVID-19?
Population:	Individuals with comorbidities or health states that increase risk for severe COVID-19
Intervention:	Two doses of NVX-CoV2373 vaccine
Comparison(s):	Active control/placebo
Outcome:	COVID-19 (PCR-confirmed)

Background:

On 31 December 2019, WHO was alerted to several cases of pneumonia of unknown origin in Wuhan City, Hubei Province, China. The cause was found to be a novel coronavirus, SARS-CoV-2. The disease caused by this novel virus has been named COVID-19. The outbreak of COVID-19 was declared a public health emergency of international concern in January 2020. The disease has since spread, with an enormous impact on the health and well-being of individuals and populations worldwide. It has further caused major disruptions to various sectors of society and the economy across the globe.

Vaccines are a critical tool in combating the COVID-19 pandemic. In the rapidly evolving field of COVID-19 vaccines, WHO has issued to date interim recommendations on the use of a number of COVID-19 vaccines *(6)*.

	CRITERIA	JUDGEMENTS				RESEARCH EVIDENCE	ADDITIONAL INFORMATION
PROBLEM	Is the problem a public health priority?	*No*	*Uncertain*	*Yes*	*Varies by setting*	The cumulative number of COVID-19 cases globally has surpassed 270 791 973, with more than 5 318 216 deaths. Cases have been found in 190 different countries or territories throughout the world (status 16 December 2021). There has been collateral damage to other public health programmes. Individuals with certain comorbidities are particularly affected by COVID-19 and bear a higher risk of severe COVID-19 outcomes and death. Identified risk factors include comorbidities such as hypertension, chronic cardiac disease, non-asthmatic chronic pulmonary disease, chronic kidney disease, liver	The COVID-19 situation is evolving rapidly; the most recent epidemiological situation can be found on the following website: https://covid19.who.int/table
		☐	☐	☒	☐		

[a] These conditions included chronic respiratory, cardiac, renal, neurologic, hepatic, and immunocompromising conditions as well as obesity (BMI ⩾30 kg/m2)

						disease, and obesity (particularly a body mass index (BMI) >40). People with multiple comorbidities are at a higher risk of COVID-19-related adverse outcomes *(23)*. Although the relative risk may be high for some conditions, the absolute risk for younger adults with comorbidities is typically lower than for healthy older adults (aged >75 years).	
BENEFITS & HARMS OF THE OPTIONS	Benefits of the intervention Are the desirable anticipated effects large?	*No* ☐	*Uncertain* ☐	*Yes* ☒	*Varies* ☐	Across seronegative individuals with underlying comorbidities[a] enrolled in a Phase 3 clinical trial in the UK, vaccine vaccine efficacy was 91% (95%CI: 70-97%) for PCR-confirmed mild, moderate, or severe COVID-19 with onset from 7 days after second vaccination *(2)*. High vaccine efficacy in this subpopulation was confirmed in the Phase 3 clinical trial in the US and Mexico *(3)*. In persons living with HIV, the Phase 2a/b trial (1) did not demonstrate efficacy against mild, moderate, or severe COVID-19 in this population (wide confidence interval (VE -35% [95% CI: -237–46]) reflecting the small sample size). No data are available on vaccine efficacy in pregnant women after NVX-Co2373 vaccination.	.
	Harms of the intervention Are the undesirable anticipated effects small?	*No* ☐	*Uncertain* ☐	*Yes* ☒	*Varies* ☐	The the Phase 2a/b trial evaluated the safety of NVX-CoV2373 in 244 medically stable HIV-positive participants 18 to ⩽ 64 years of age (122 in each treatment group). Across the safety assessments, the safety profile of NVX-CoV2373 in HIV-positive participants was similar to that seen in HIV-negative participants (1). In the pooled analysis of safety data across the clinical trials including approx. 30000 vaccine recipients, only few pregnancy events were recorded. Therefore, available data on vaccination of pregnant women with NVX-Co2373 vaccine are insufficient to assess	A Good Laboratory Practice developmental and reproductive toxicity study in rats indicates no adverse findings of NVX-Co2373 on fertility, pregnancy/lactation, or development of the embryo/fetus and offspring through post-natal Day 21. The Matrix-MTM adjuvant has not been used in any other licensed vaccine.

[a] Comorbid participants were those who had at least 1 of the comorbid conditions reported as a medical history or had a screening BMI > 30 kg/m2.

							vaccine safety in pregnancy. Further studies in pregnant women are planned .	
	Balance between benefits and harms	*Favours intervention* ☒	*Favours comparison* ☐	*Favours both* ☐	*Favours neither* ☐	Unclear ☐	Efficacy data suggest benefit in those individuals with comorbidities or health states that increase risk for severe COVID-19 for which there are data. Balancing benefits and harms of COVID-19 disease and vaccination with NVX-CoV2373, the benefit of the intervention is larger than the potential harms.	
	What is the overall quality of this evidence for the critical outcomes?	**Effectiveness of the intervention** *No included studies* ☐	*Very low* ☐	*Low* ☐	*Moderate* ☒	*High* ☐	Please see the related GRADE tables.	
		Safety of the intervention *No included studies* ☐	*Very low* ☐	*Low* ☒	*Moderate* ☐	*High* ☐		
VALUES & PREFERENCES	How certain is the relative importance of the desirable and undesirable outcomes?	*Important uncertainty or variability* ☐	*Possibly important uncertainty or variability* ☐	*Probably no important uncertainty or variability* ☒	*No important uncertainty or variability* ☐	*No known undesirable outcomes* ☐	There is possibly important uncertainty related to the target population weighing of desirable and undesirable effects (i.e. the protection conferred by the vaccine weighed against the currently reported safety signals) related to COVID-19 vaccination. Different population groups may have different opinions regarding the relative weights attributed to desirable and undesirable outcomes.	
	Values and preferences of the target population: Are the desirable effects large relative to undesirable effects?	*No* ☐	*Probably No* ☐	*Uncertain* ☐	*Probably Yes* ☒	*Yes* ☐	*Varies* ☐	Available scientific evidence suggests that the target population probably attached more weight to the desirable effects than the undesirable effects related to COVID-19 vaccination.

RESOURCE USE	Are the resources required small?	*No* ☐	*Uncertain* ☐	*Yes* ☒	*Varies* ☐	NVX-CoV2373 can be distributed and stored using existing cold chain infrastructure (at 2–8 °C), and does not require ultra-cold chain capacity. Prices for NVX-CoV2373 are expected to be within the range of other COVID-19 vaccines with WHO EUL, with potential differential pricing by procurement mechanism (e.g., COVAX AMC vs. direct country procurement vs. private market) *(7, 8)*. Nevertheless, considerable resources will be needed to ensure the implementation of a COVID-19 vaccination programme, especially given: (i) that COVID-19 vaccination is likely to be prioritized for populations (e.g. health-care workers, older adults) without pre-existing robust immunization programmes in many settings; and (ii) the urgency of vaccination roll-out worldwide, which may necessitate additional surge resources to accelerate implementation with adequate infection prevention and control procedures in the context of COVID-19. Resources required include, but are not restricted to, human resources, vaccine costs, logistics, planning and coordination, training, social mobilization and communications, and immunization safety surveillance.	An estimated US$ 15.9 billion is needed for the vaccines pillar (COVAX) of the Access to COVID-19 Tools Accelerator (ACT-A) for 2020–21, when the initiative aims to deliver 2 billion doses. This does not include all delivery costs in all countries participating in COVAX, bilateral procurement deals, or research and development investments outside of COVAX *(9)*. The World Bank has approved a financing window of up to US$ 12 billion to support low- and middle-income countries in purchasing and distributing vaccine *(10)*.
	Cost–effectiveness	*No* ☐	*Uncertain* ☐	*Yes* ☐	*Varies* ☒	Formal global cost–effectiveness analyses have not been conducted, but the emerging evidence indicates that the benefits, including the impact on recovery of the global economy, are likely to outweigh the cost of COVID-19 vaccination in general at global level. No formal cost–effectiveness analyses of NVX-CoV2373 vaccine compared to other vaccines have been conducted. The NVX-CoV2373 vaccine is expected to be less costly than many other COVID-19 vaccines (see previous sub-criterion). The ability to use NVX-CoV2373 in existing cold chain infrastructure in all country settings may enable higher population-level coverage.	The global economy is estimated to be losing US$ 375 billion per month due to the coronavirus pandemic. G20 countries have invested approximately US$ 10 trillion in domestic economic stimulus to mitigate the economic consequences of reduced business activity and unemployment due to the pandemic. Initial estimates suggest that COVID-19 vaccination will provide substantial economic value in terms of averted morbidity and

							Cost–effectiveness analyses should be conducted at country level; cost–effectiveness of COVID-19 vaccination may vary by country depending on COVID-19 burden, comparator interventions assessed, analysis perspective, and local cost–effectiveness thresholds used.	mortality costs and averted GDP losses *(9, 11-17)*.
EQUITY	What would be the impact on health inequities?	*Increased* ☐	*Uncertain* ☐	*Reduced* ☒	*Varies* ☐		Equity and ethical considerations are critical. SAGE has produced a Values Framework *(18)*, which offers guidance on the fair allocation of COVID-19 vaccines based on 6 core ethical principles that should guide distribution. If distributed fairly, COVID-19 vaccines may have considerable impact on reducing health inequities.	Vaccine nationalism is seen as a threat to reducing health inequity, in particular as high-income countries have arranged bilateral contracts with manufacturers. This has led to the establishment of the Access to COVID-19 Tools (ACT) Accelerator and within this, the COVAX facility, which aims to ensure equitable access to vaccines for its participating Member States *(19)*.
ACCEPTABILITY	Which option is acceptable to key stakeholders (e.g. ministries of health, immunization managers)?	*Intervention* ☒	*Comparison* ☐	*Both* ☐	*Neither* ☐	*Unclear* ☐	No scientific evidence is available. As vaccination is an important tool to combat COVID-19, it is assumed that key stakeholders, in particular ministries of health and immunization managers are strongly in favour of COVID-19 vaccination.	The fact that 190 economies are participating in COVAX suggests a very high acceptability of COVID-19 vaccination in general, although not the NVX-CoV2373 vaccine in particular.
	Which option is acceptable to target group?	*Intervention*	*Comparison*	*Both*	*Neither*	*Unclear*	COVID-19 vaccine acceptability in general varies between (sub-) population groups and may be correlated with the perceived risk posed by the vaccine versus the perceived risk	

		☒	☐	☐	☐	☐	posed by the disease. In a global survey (19 countries) of acceptance rates in the general population of any COVID-19 vaccine product, 71.5% of participants reported that they would be very, or somewhat, likely to take a COVID-19 vaccine. Acceptance rates ranged from almost 55% to 87% *(20)*. Polls have been launched, (periodically) assessing vaccine acceptance in selected countries. These polls confirm overall, not product-specific, vaccine acceptance, with variations across countries *(21, 22)*.	
FEASIBILITY	Is the intervention feasible to implement?	*No* ☐	*Probably* No ☐	*Uncertain* ☐	*Probably* Yes ☐	*Yes* ☒	*Varies* ☐	NVX-CoV2373 vaccine is assumed to be easily implementable in settings, including low- and middle-income countries, with existing vaccine logistics and delivery infrastructure. Storage and distribution requirements of the NVX-CoV2373 vaccine are the same as those of many other vaccines currently in use globally. Therefore existing vaccine cold chain capacity, available in almost all countries worldwide could be leveraged for vaccine distribution. Administration of the vaccine to novel target groups currently not reached by national immunization programmes may pose a challenge in certain settings.	

BALANCE OF CONSEQUENCES	Undesirable consequences *clearly outweigh* desirable consequences in most settings ☐	Undesirable consequences *probably outweigh* desirable consequences in most settings ☐	The balance between desirable and undesirable consequences *is closely balanced or uncertain* ☐	Desirable consequences *probably outweigh* undesirable consequences in most settings ☒	Desirable consequences *clearly outweigh* undesirable consequences in most settings ☐

TYPE OF RECOMMENDATION	We recommend the intervention ☐	We suggest considering recommendation of the intervention ☐ Only in the context of rigorous research	We recommend the comparison ☐	We recommend against the intervention and the comparison ☐

		☒ Only with targeted monitoring and evaluation ☒ Only in specific contexts or specific (sub)populations		
RECOMMENDATION (TEXT)	Please see the interim recommendations.			
IMPLEMENTATION CONSIDERATIONS	Please see the interim recommendations.			
MONITORING, EVALUATION AND RESEARCH PRIORITIES	Please see the interim recommendations.			

References

1. Shinde V, Bhikha S, Hoosain Z, Archary M, Bhorat Q, Fairlie L et al. Efficacy of NVX-CoV2373 Covid-19 Vaccine against the B.1.351 Variant. New England Journal of Medicine. 2021;384:1899-909. doi: 10.1056/NEJMoa2103055.
2. Heath PT, Galiza EP, Baxter DN, Boffito M, Browne D, Burns F et al. Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine. New England Journal of Medicine. 2021;385:1172-83. doi: 10.1056/NEJMoa2107659.
3. Dunkle LM, Kotloff KL, Gay CL, Áñez G, Adelglass JM, Barrat Hernández AQ et al. Efficacy and Safety of NVX-CoV2373 in Adults in the United States and Mexico. medRxiv. 2021:2021.10.05.21264567. doi: 10.1101/2021.10.05.21264567.
4. Formica N, Mallory R, Albert G, Robinson M, Plested JS, Cho I et al. Different dose regimens of a SARS-CoV-2 recombinant spike protein vaccine (NVX-CoV2373) in younger and older adults: A phase 2 randomized placebo-controlled trial. PLOS Medicine. 2021;18:e1003769. doi: 10.1371/journal.pmed.1003769.
5. Keech C, Albert G, Cho I, Robertson A, Reed P, Neal S et al. Phase 1-2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine. N Engl J Med. 2020. doi: 10.1056/NEJMoa2026920.
6. World Health Organization. COVID-19 vaccines technical documents. Geneva: World Health Organization; 2021 (www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials, accessed 17 June).
7. Wouters OJ, Shadlen KC, Salcher-Konrad M, Pollard AJ, Larson HJ, Teerawattananon Y et al. Challenges in ensuring global access to COVID-19 vaccines: production, affordability, allocation, and deployment. Lancet. 2021.
8. Gavi COVAX collaboration. (https://www.gavi.org/news/media-room/new-collaboration-makes-further-100-million-doses-covid-19-vaccine-available-low, accessed 15 December 2021).
9. ACT Accelerator: An economic investment case & financing requirements. (www.who.int/docs/default-source/coronaviruse/act-accelerator/economic-investment-case-final-v2.pdf?sfvrsn=91d67ff6_4&download=true, accessed 13 December 2020) 2020.
10. World Bank (2020) COVID-19 Strategic Preparedness and Response Program (SPRP) using the Multiphase Programmatic Approach (MPA) Project : Additional Financing (English).Washington, D.C. : World Bank Group. (http://documents.worldbank.org/curated/en/882781602861047266/World-COVID-19-Strategic-Preparedness-and-Response-Program-SPRP-using-the-Multiphase-Programmatic-Approach-MPA-Project-Additional-Financing, accessed 21 December 2020)2020.
11. Cutler DM, Summers LH. The COVID-19 Pandemic and the $16 Trillion Virus. JAMA. 2020;324:1495-6.
12. Sandmann F, Davies NG, CMMID COVID-19 Working Group, Vassall A, Edmunds JW, Jit M. (2020) The potential health and economic value of SARS-CoV-2 vaccination alongside physical distancing in the UK: transmission model-based future scenario analysis and economic evaluation; https://www.medrxiv.org/content/10.1101/2020.09.24.20200857v1. 2021.
13. Eurasia Group. 2020. Ending the COVID-19 Pandemic: The Need for a Global Approach. New York: Eurasia Group. (www.who.int/publications/m/item/ending-the-covid-19-pandemic-the-need-for-a-global-approach , accessed 13 December 2020)2020.
14. Hafner, Marco; Yerushalmi, Erez; Fays, Celment; Dufresne, Eliane; Van Stolk, Christian. 2020. COVID-19 and the cost of vaccine nationalism. Cambridge, UK: RAND Europe. (www.rand.org/t/RRA769-1 , accessed 13 December 2020)2020.
15. International Monetary Fund. 2020. World Economic Outlook: A Long and Difficult Ascent. Washington, DC: October 2020. (www.imf.org/en/Publications/WEO/Issues/2020/09/30/world-economic-outlook-october-2020#Full%20Report%20and%20Executive%20Summary , accessed 13 November 2020)2020.
16. Bartsch SM, O'Shea KJ, Ferguson MC, Bottazzi ME, Wedlock PT, Strych U et al. Vaccine Efficacy Needed for a COVID-19 Coronavirus Vaccine to Prevent or Stop an Epidemic as the Sole Intervention. AmJPrevMed. 2020;59:493-503.
17. Cakmakli C, Demiralp S, Kalemli-Ozcan, Yesiltas S, Yildirim M. (2021) The Economic Case for Global Vaccinations: An Epidemiological Model with International Production Networks. Paris: International Chamber of Commerce. (https://iccwbo.org/publication/the-economic-case-for-global-vaccinations/, accessed 1 February 2021)2021.
18. WHO. WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination, 14 September 2020. Geneva: World Health Organization; 2020 (https://www.who.int/publications/i/item/who-sage-values-framework-for-the-allocation-and-prioritization-of-covid-19-vaccination, accessed 28 May 2021).
19. ACT Accelarator and COVAX facility. www.who.int/initiatives/act-accelerator2020 (https://www.who.int/initiatives/act-accelerator.
20. Lazarus JV, Ratzan SC, Palayew A, Gostin LO, Larson HJ, Rabin K et al. A global survey of potential acceptance of a COVID-19 vaccine. NatMed. 2020.
21. YouGov COVID-19 Public Monitor. 2021 (https://yougov.co.uk/topics/international/articles-reports/2021/01/12/covid-19-willingness-be-vaccinated, accessed 22 April 2021).

22. Global Attitudes on COVID-19 vaccine. Ipsos survey. (www.ipsos.com/en/global-attitudes-covid-19-vaccine-december-2020 , accessed 22 April 2021) 2021.
23. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ. 2020;369:m1985. doi: 10.1136/bmj.m1985.

WHO reference number: WHO/2019-nCoV/vaccines/SAGE_recommendation/Novavax_NVX-CoV2373/annexes/2021.1