

**WHO Strategic Advisory Group of Experts (SAGE) on Immunization
Working Group on COVID-19 Vaccines:
Prioritized Infectious Disease and Economic Modelling Questions**

Request for Information

- As part of its scoping of the landscape of modelling groups and initiatives related to COVID-19 vaccines, we invite modellers and economists to provide information about their work on COVID-19 vaccination that addresses prioritized modelling questions to contribute to informing deliberations around policy recommendations from the WHO SAGE on Immunization.
- Groups are encouraged to share early stage and interim results for any of the questions as part of the ongoing process of evidence review, gap identification, and refinement of priority questions and scenarios.
- We particularly encourage models that have been fit to available epidemiological and/or economic data or validated through comparison with these data. Model review and future invitations to participate in presentations to the Working Group will be based on assessment of model performance and minimum standards as described in this document.
- Brief summaries of any completed work or work planned or underway for any question may be sent via email to the WHO SAGE Secretariat at: vaccineresearch@who.int.
- Initial responses are requested as soon as possible and no later than **4th September 2020** for consideration in initial reviews and deliberations. This will be an ongoing process of consultation with the modelling community and we will also be seeking input at later dates.

I. Background

- The Terms of Reference for the SAGE Working Group on COVID-19 Vaccines include:
 - Provide guidance for the development of prediction models to determine the optimal age groups and target populations for vaccine introduction and guide vaccine introduction for optimal impact, and contribute to updates of target product profiles of vaccines for outbreak and for endemic use;
- Recognizing the evolving landscape of evidence on SARS-CoV-2, COVID-19, and vaccine candidates, the Working Group has developed an initial set of prioritized modelling questions with the intent to help focus efforts in the modelling community towards results that would be useful in informing SAGE deliberations about any eventual specific vaccine candidates.
- The Working Group does not anticipate that all questions would necessarily be addressed by the same model or modelling group, as different modelling approaches may be needed for different questions. Modelling addressing any of the questions can contribute to the Working Group's deliberations.
- The prioritization of modelling questions reflects the Working Group's current understanding of:
 - the epidemiology of SARS-CoV-2 and COVID-19, the vaccine landscape, and possible vaccine supply and uptake scenarios;
 - the groups that have been proposed for possible prioritization for vaccination according to different public health objectives (e.g., reducing morbidity and mortality; reducing transmission; protecting essential services; minimizing economic and societal disruption);
 - the available models and data elements at this time (i.e., which questions may be most tractable to address first).
- The prioritization of questions or of analysis features does not imply any value judgment about how different public health objectives should be weighted, or any recommendation about which groups should be prioritized for vaccination under any given scenario.
- The scenarios provided are hypothetical and intended to facilitate (i) comparison across models, and (ii) exploration of the sensitivity of model results to different assumptions about key parameters. The scenarios are not intended as an endorsement of any particular vaccine or vaccination strategy, but rather to inform the Working Group and SAGE about the potential ranges of outcomes depending on scenario assumptions.
- None of the elements of this document – including questions, scenarios, key data, and analysis features – are official WHO or SAGE recommendations, nor do they have any legal or policy status.
- Given the rapidly evolving evidence base and dynamic policy and supply environment, the prioritized questions, scenarios, key data elements, and analysis features may be updated as new evidence and needs emerge.

II. Modelling Questions

Note: See “III. Initial Scenarios and Essential Data” for assumptions about vaccine characteristics, coverage, supply, analytic horizon, and target population definitions. See “IV. Analysis Features” for additional measures and analysis extensions of interest. Modelling groups are requested to consider sections III and IV in addressing the questions.

Health and epidemiological impacts

1. What would be the impact of vaccinating each of the following target groups on SARS-CoV-2 infections, COVID-19 deaths, and COVID-19 years of life lost, for vaccines given during 2020-21 when vaccination is added to counterfactual scenarios of: (i) no interventions, or (ii) continued implementation of non-pharmaceutical interventions (NPIs)?
 - a. older adults (50+, 65+ or 75+ years)
 - b. younger adults (18-49 years)
 - c. school-age children (5-17 years)
 - d. those at high risk of severe disease because of their underlying health conditions (e.g., cardiovascular disease, kidney disease; *see section III*)
 - e. key workers (e.g., workers in health and social care, teachers; *see section III*)
 - f. groups at high risk of infection (e.g., dense urban slums/informal settlements; *see section III*)
2. What are the optimal vaccination strategies in terms of target groups under different possible supply scenarios for COVID-19 vaccine during 2020-21 to achieve the maximum reduction in SARS-CoV-2 infections, COVID-19 deaths or years of life lost?
3. How would health impacts be distributed across country income groups (high, middle, low) and within countries across household wealth quintiles for the different vaccination targeting approaches described in Questions 1-2? (*Note: distribution of impacts across other social groups is also of interest; see section IV.*)

Economic and social impacts

4. What would be the impact on protecting essential services (e.g., health and social care, education) of the different vaccination targeting approaches described in Questions 1-2?
5. At what level of vaccine efficacy and vaccination coverage for which target groups could those NPIs that are most economically and societally disruptive (e.g., lockdowns, travel restrictions) be discontinued?
6. What would be the impacts in terms of economic welfare (e.g., as measured by GDP growth) and economic security (e.g., as measured by number of people living in poverty) of different vaccination targeting approaches (e.g., those in Questions 1-2) across country income groups (high, middle, low)?
7. From the societal perspective, what would be the cost-effectiveness per averted SARS-CoV-2 infection, COVID-19 death, and COVID-19 year of life lost for the vaccination targeting approaches described in Questions 1-2?
8. In monetary terms, what is the full public health and societal value of vaccination with a COVID-19 vaccine?

III. Initial Scenarios and Essential Data

Note: Initial scenarios are hypothetical and exploratory. Additional scenarios may be identified and requested as evidence and needs evolve.

Summary of scenario dimensions

Counterfactual scenario	Vaccine characteristics scenario	Coverage scenario	Supply scenario	Analytic horizon
I. No intervention	A. Efficacy vs. disease and infection*, all ages	1. High (80%)	a. COVAX	i. Short term (end-2021)
II. Continued NPIs	B. Efficacy vs. disease, all ages	2. Mid (50%)	b. COVAX + direct	ii. Medium term (end-2022)
	C. Efficacy vs. disease, younger ages only	3. Low (20%)	c. COVAX + direct (shared)	iii. Long term (end-2030)

*Vaccine protects against becoming infected and therefore being infectious to others (see "Vaccine characteristics" below).

Counterfactuals

- Vaccination scenarios should be implemented for each counterfactual (i.e., counterfactual vs. counterfactual + vaccination):
 - No intervention*: Assume no NPIs are in place and pandemic runs its course. This captures the value of vaccines that allow a return to 'normal' with no NPIs in place.
 - Continued NPIs*: Assume that there is continued implementation of NPIs that keep the effective reproduction number at its level prior to the introduction of the vaccine, potentially allowing for seasonal and herd immunity effects.
- As different approaches to modelling the effects of NPIs have been adopted, and as NPI implementation and effectiveness varies across countries, modelling groups should describe their methods and data sources for modelling NPI effects or justify their choice of a particular reproduction number(s) if NPIs are not explicitly modelled. Analyses that model the effects of different combinations of NPIs for different vaccination scenarios and epidemiological and country settings are desirable; see *IV. Analysis Features*.

Vaccine characteristics

- Scenario parameter values provided below with desired sensitivity analysis ranges in parentheses. For example, a 2-dose schedule would be the base case with sensitivity analysis of how results would change if a 1-dose schedule was administered.

Scenario	Schedule	Efficacy against COVID-19 (%)	Efficacy against SARS-CoV2 infection* (%)	Relative efficacy in 65+ age-group	Mean duration of immunity (years)
A. Efficacy vs. disease and infection, all ages	2 doses (1 dose)	70 (10-90)	70 (0-90)	1.0 (0.5-1.0)	1 (0.5-lifelong)
B. Efficacy vs. disease only all ages	2 doses (1 dose)	70 (10-90)	0	1.0 (0.5-1.0)	1 (0.5-lifelong)
C. Efficacy vs. disease only, younger ages only	2 doses (1 dose)	70 (10-90)	0	0.3 (0-0.5)	1 (0.5-lifelong)

*Protection against infection and therefore infectiousness to others. Vaccines may protect against COVID-19 disease but not against becoming infected and potentially being infectious to others. Explicit modelling of differential infectiousness of breakthrough infections among vaccinated individuals is desirable; see *IV. Analysis Features*.

Vaccination uptake and coverage

1. *High uptake*: 80% coverage of the target group. Follow “greatest benefit” prioritization within target group up to the supply constraint; if supply is insufficient to cover 80% of target population, prioritization in order of “greatest benefit” (e.g., highest impact age range, highest risk comorbidity, highest exposure to infection) within the target population up to the supply constraint.
 2. *Mid-range uptake*: 50% coverage of the target group. Follow “greatest benefit” prioritization within target group up to the supply constraint.
 3. *Low uptake*: 20% coverage of the target group. Follow “greatest benefit” prioritization within target group up to the supply constraint.
- For Question 1, it is anticipated that vaccination coverage scenarios would be implemented individually for each target group (e.g., 80%/50%/20% coverage in children vs. 0% coverage in other age groups). For Question 2, it is anticipated that analyses would consider different coverage levels across combinations of target groups.
 - Vaccination uptake and coverage assumptions are intended to serve as proxy measures of the intersection of other critical underlying variables related to: (i) programmatic feasibility of vaccination delivery (e.g., available delivery platforms, cold chain requirements, human resource requirements, feasibility of identifying/accessing the target population), and (ii) vaccine acceptance and demand (e.g., knowledge, attitudes, perceptions, values, norms, intentions, behaviours of potential vaccine recipients, caregivers, and providers). Analyses specifically exploring the effect of these supply and demand variables on coverage are desirable; see *IV. Analysis Features*.

Supply

- All supply scenarios are hypothetical and exploratory. Analyses exploring the sensitivity of results to different supply scenarios (e.g., earlier vs. later) are encouraged. Supply scenarios may also consider buffer stock (e.g., 5%) and wastage rates (e.g., 15%).

Supply scenario	Total by end-2021	Incremental availability by end of quarter* (millions of doses)					Distribution across countries (LIC: low-income, LMIC: lower-middle-income, UMIC: upper-middle-income, HIC: high-income)
		2020	2021				
		Q4	Q1	Q2	Q3	Q4	
a. COVAX Facility	2 B doses	100	100	400	600	800	<ul style="list-style-type: none">• Assume 90 LICs + LMICs, and 76 UMICs + HICs participating• 3% of total population initial allocation target among participating countries• Additional supply tranches allocated as available based on countries' share of phase I cumulative allocation target of 20% of total population among participating countries
b. COVAX + direct country procurement	4.25 B doses	400	400	800	1200	1450	<ul style="list-style-type: none">• COVAX scenario assumptions +• Self-procuring HICs: 1.15B doses• Self-procuring MICs: 1.10B doses
c. COVAX + direct country procurement (shared)	4.25 B doses	400	400	800	1200	1450	<ul style="list-style-type: none">• COVAX + direct scenario +• Self-procuring HICs allocate excess doses to MICs and LICs (e.g., through COVAX Facility) after achieving their coverage scenario target for target groups (for target groups with unmet coverage targets in MICs/LICs)

*Assume that dose availability in each quarter is equally distributed over the 3 months of that quarter.

Analytic horizon

- Defined as the timeframe over which benefits from vaccination during 2020-21 are counted (e.g., years of life saved).
 - i) short-term (from Q4 2020 to end-2021);
 - ii) medium-term (from Q4 2020 to end-2022);
 - iii) long-term (from Q4 2020 to end-2030).

Vaccine and vaccination delivery costs

- Economic evaluations should explore a range of potential vaccine prices across country income groups (high, middle, low) and report assumptions used.
- Economic evaluations should describe their assumptions about the delivery modality used (e.g., facility-based, outreach, campaign) and data sources used for delivery cost estimates, with consideration for how the context of COVID-19 affects delivery costs.

Prevalence of comorbidities by age

- Ideally, use estimates published in Clark, A., et al. (2020). "Global, regional, and national estimates of the population at increased risk of severe COVID-19 due to underlying health conditions in 2020: a modelling study." The Lancet Global Health.

Key worker groups

- Examples of possible groups below without any order of priority. Note that these show some overlap with groups at high risk of infection but modelled separately as rationale for prioritization for vaccination is different.
- Analyses should specify definitions and data sources used.
- In the absence of detailed data, when considering vaccine supply constraints, analyses may make the simplifying assumption that workers in health and social care are 3% of the total population and other essential workers are up to an additional 5% of the total population.
 - Workers in health care
 - Workers in care homes and other social care
 - Teachers, childcare providers
 - Emergency response and public safety personnel
 - Sanitation, including sewage and garbage removal
 - Utility workers (e.g., water, electricity, gas, communications)
 - Public works and infrastructure maintenance/repair workers
 - Transportation workers
 - Food and agriculture workers
 - Retail workers for provision of food and essential goods (e.g., pharmacies, medical supplies, fuel)
 - Critical banking/financial services workers for processing and maintaining access to currency and payments
 - Mortuary services
 - Critical manufacturing of essential goods (e.g., medical equipment, supplies)

Groups at high risk of infection

- Examples of possible groups below without any order of priority. Note that these show some overlap with key worker groups but modelled separately as rationale for prioritization for vaccination is different.
- Analyses should specify definitions and data sources used.
- In the absence of detailed data, when considering vaccine supply constraints, analyses may make the simplifying assumption that workers in health and social care are 3% of

the total population and other essential workers are up to an additional 5% of the total population.

- Workers in health care
- Workers in care homes and other social care
- Emergency response and public safety personnel
- Those living in dense urban slums or informal settlements
- Refugees, internally displaced persons

Provision of essential services

- Examples of possible outcomes below without any order of priority. Analyses should specify definitions and data sources used.
 - Healthcare system capacity (as measured by hospital beds, ventilators, high-flow oxygen, Intensive Care Unit (ICU) beds in settings where applicable) is not exceeded due to COVID-19 caseload.
 - Proportion of students able to access primary and secondary education (may be operationalized through different measures, e.g., as inverse of proportion of learners affected by country-wide school closures as measured by UNESCO).

IV. Analysis Features

Essential:

Feature	Questions for which most relevant
• Differences in COVID-19 severity by age	Q1-2
• Different vaccine profiles	All
• Separate analyses for high-, middle- and low-income countries or country groups	All
• Uncertainty and sensitivity analysis to model parameters	All
• Counterfactual analysis	All

Desirable:

(in no particular order)

Feature
• Indirect (herd) effects of vaccination (including consideration of acquired immunity and its variation across countries) and age-dependent transmission risk
• Differences in COVID-19 severity by comorbidities, ideally stratified by age
• Additional health, social, and economic outcome measures, e.g., <ul style="list-style-type: none"> ○ COVID-19 cases, hospitalisations, cases with long-term sequelae, years lived with disability, DALYs, SEYLL; ○ SARS-CoV-2 infection averted per dose; COVID-19 death averted per dose; COVID-19 YLL averted per dose; ○ Excess deaths and years of life lost due to the COVID-19 pandemic generally; ○ In GNI, poverty gap, GNI per capita, income inequality, employment
• Potential reduction in infectiousness of breakthrough infections among vaccinated individuals
• Potential differences in vaccine efficacy against mild or severe/fatal COVID-19 disease

<ul style="list-style-type: none"> • Risk/benefit analysis for vaccines with hypothetical risks of adverse outcomes (e.g., vaccine-associated enhanced disease) at different frequencies
<ul style="list-style-type: none"> • Health system capacity (ventilators, ICU beds) and available therapies and non-vaccine pharmaceutical interventions (e.g., therapeutics, monoclonal antibodies) that may affect the infection fatality rate (IFR)
<ul style="list-style-type: none"> • Distribution of impacts across social groups (e.g., gender, rural/urban, race/ethnicity)
<ul style="list-style-type: none"> • Impact of vaccinating seropositives, and potential impact of pre-vaccination serological testing and exclusion of seropositives from vaccination
<ul style="list-style-type: none"> • Impact of inclusion/exclusion of pregnant women from groups eligible for vaccination
<ul style="list-style-type: none"> • Effect on coverage, cost, and cost-effectiveness of different programmatic delivery assumptions (e.g., delivery platforms such as facility-based, outreach, campaign; cold chain availability; human resource requirements) and how this may vary among countries
<ul style="list-style-type: none"> • Effect on coverage of different vaccine acceptance and demand assumptions and how this may vary among countries
<ul style="list-style-type: none"> • Scenarios exploring impacts of combinations of different COVID-19 vaccines with different characteristics
<ul style="list-style-type: none"> • Effects of different combinations of NPIs for different vaccination scenarios and epidemiological and country settings
<ul style="list-style-type: none"> • Cost-effectiveness analyses conducted from other perspectives (e.g., health system, government)
<ul style="list-style-type: none"> • Sensitivity analysis of results to potential viral mutation and antigenic change
<ul style="list-style-type: none"> • Detailed analysis of exemplar country(ies) that have good epidemiologic data
<ul style="list-style-type: none"> • Implementation of models or model results in interactive software that can be used in countries by decision makers to explore scenarios