

COVID-19 Vaccines and Therapeutics Expert Predictions

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EXPERT CONSENSUS SUGGESTS A SARS-COV-2 VACCINE THAT IS AT LEAST 50% EFFECTIVE WILL BE APPROVED IN THE FIRST HALF OF 2021

This month, we solicited predictions about the efficacy, timeline, and production of a SARS-COV-2 vaccine, and the proportion of secondary infections children generate compared to adults. Predictions for this forecasting session were solicited before news emerged that the FDA is willing to fast-track vaccine approval, with the possibility of this occurring before the completion of Phase 3 trials [1].

Experts expect that a vaccine that meets the FDA's minimum efficacy threshold of 50% efficacy [2] will be approved for use in early-to-mid 2021.

Experts median prediction of when a vaccine will be approved through the normal approval mechanism was July 2021 (80% CI: Dec. 2020 - March 2023) and the consensus median prediction of the approved vaccine's efficacy was 66.0% (80% CI: 48.5% - 83.5%). Experts predicted a median of Feb. 2021 (80% CI: Sep. 2020 - July 2024) for the approval of a vaccine through an emergency procedure with a predicted median efficacy of 49.5% (80% CI: 26.0% - 76.0%). A vaccine never approved by an emergency procedure was assigned a 0.059 probability by experts.

Expert predict a median ratio of the number of secondary infections generated by children compared to adults of 0.98 (80% CI: 0.66 - 1.56). It appears experts are uncertain about the relative rates of infection children generate compared to adults.

With respect to vaccine manufacturing, we asked experts to predict the number of weeks after approval that 100 million doses of a (i) DNA/RNA vaccine and a (ii) non-replicating viral vector vaccine would be produced.

The expert consensus predicted a median of 18.7 weeks (80% CI: 4.7, 103.0) after approval for a DNA/RNA vaccine, and a median of 36.0 weeks (80% CI: 9.8 - 102.5) for the first 100 million doses of an approved non-replicating viral vector vaccine.

Experts also predicted that an orally administered SARS-CoV-2 antiviral with a survival benefit—a gold standard treatment option—is unlikely to be available soon. The expert median prediction was March 2022 (80% CI: February 2021 - July 2024)). However, the 80% confidence interval shows there is considerable uncertainty on this matter.

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FORECASTING SESSION DURATION, DEFINITION OF EXPERTS, AND LOGISTICS

From August 19th 2020 to August 29th 2020, predictions were made for 7 questions related to vaccine and therapeutic solutions to COVID-19, as well as 1 question related to the infectivity of children relative to adults when schools are open. Two groups of experts were asked to participate: (i) subject matter experts (SMEs) and (ii) trained forecasters (TFs). SMEs were defined as infectious disease experts, in particular those in the fields of molecular and cellular biology, microbiology, virology, biochemistry, or epidemiology. They have several years of experience in infectious disease research, and are apprised of developments regarding vaccine/antiviral research specifically focused on the novel coronavirus. TFs were defined as the top 1% out of a total pool of approximately 13,000 forecasters according to a Metaculus point system with track records spanning several years on the [Metaculus](#) forecasting platform.

A total of 11 experts (5 subject matter experts and 6 trained forecasters) participated and submitted 153 predictions for aggregation into a consensus distribution.

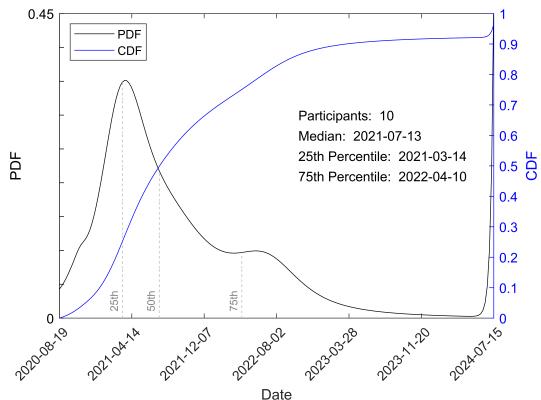
During the entire forecasting session, experts could submit multiple predictions for the same question and collaborate via a comment section underneath each question. Experts shared 16 comments with one another across all questions.

The consensus distribution for each question was hidden from experts from August 19th to August 24th. On August 25th the consensus distribution was revealed until the end of the forecasting session on August 29th. We hypothesize that predictions were revised by experts as they received new external information on vaccines and therapeutics or because of the differences between the predictions of the experts and the ongoing consensus predictions.

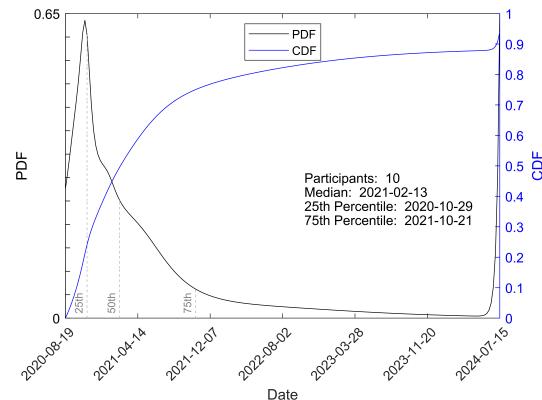
SUMMARY OF PREDICTIONS

1. Experts assigned a median of July 2021 (80% CI: December 2020, March 2023) to when a SARS-CoV-2 vaccine candidate will be approved for use in the US or EU through a normal approval process. A probability of 3.4% was assigned to a date of July 2024 or later.
2. Experts assigned a median of February 2021 (80% CI: September 2020, July 2024) to when a SARS-CoV-2 vaccine candidate will be approved for use in the US or EU through an emergency approval process. A probability of 5.9% was assigned to a date of July 2024 or later.
3. Experts assigned a median prediction of 66.0% (80% CI: 48.5%, 83.5%) for the efficacy of the first US- or EU-approved SARS-CoV-2 vaccine candidate approved through a normal approval process.
4. Experts assigned a median prediction of 49.5% (80% CI: 26.0%, 76.0%) for the efficacy of the first US- or EU-approved SARS-CoV-2 vaccine candidate approved through an emergency approval process.
5. Experts predicted a median of 18.7 (80% CI: 4.7, 103.0) as the number of weeks after approval that the first 100 million doses of the first US- or EU- approved SARS-CoV-2 vaccine candidate based on a DNA or RNA platform will be manufactured. A probability of 5.4% was assigned to more than 104 weeks (about 2 years).
6. Experts predicted a median of 36.0 (80% CI: 9.8, 102.5) as the number of weeks after approval that the first 100 million doses of the first US- or EU- approved SARS-CoV-2 vaccine candidate based on a non-replicating viral vector platform will be manufactured. A probability of 4.8% was assigned to more than 104 weeks (about 2 years).
7. Experts assigned a median of March 2022 (80% CI: February 2021, July 2024) to when an orally administered SARS-CoV-2 antiviral show a statistically significant survival benefit for the treatment group in an n > 200 RCT. A probability of 9.1% was assigned to a date of July 2024 or later.
8. Experts assigned a median of 98.0% (80% CI: 66.0%, 156.0%) to the SARS-CoV-2 infectivity of children relative to adults when schools are open. A probability of 3.4% was assigned to a relative infectivity of children greater than 200%.

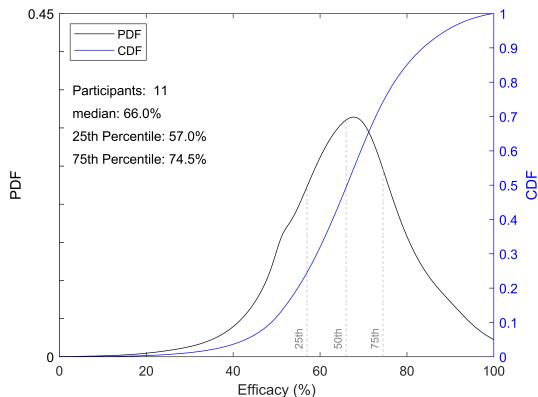
CONSENSUS PREDICTIONS



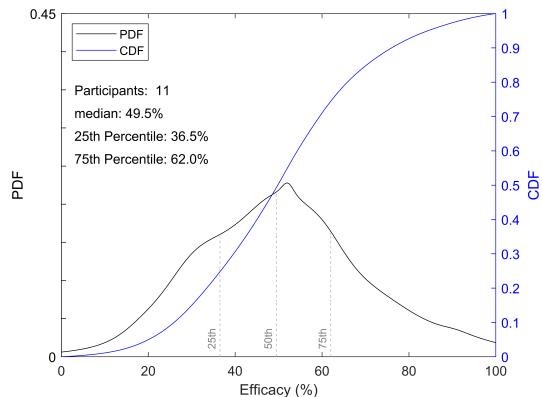
When will a SARS-CoV-2 vaccine candidate be approved for use in the US or EU through a normal approval process?



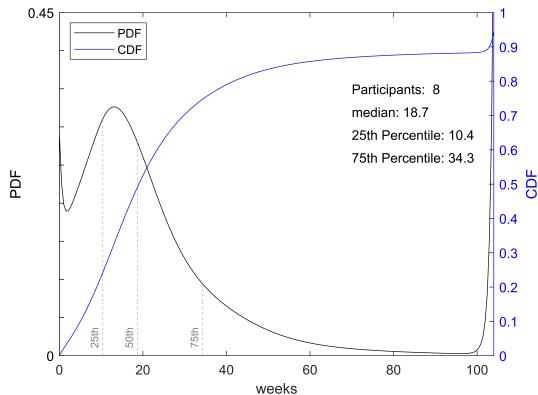
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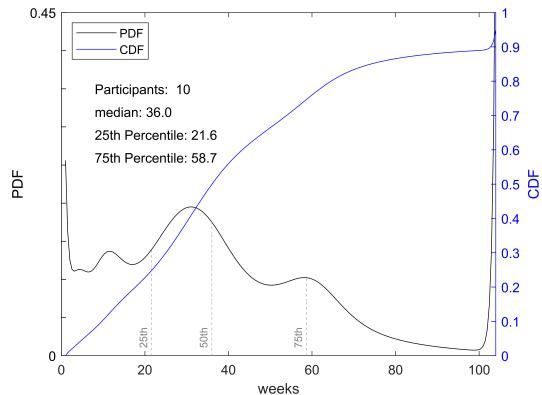
What will be the efficacy of the first US- or EU-approved SARS-CoV-2 vaccine candidate approved through a normal approval process?



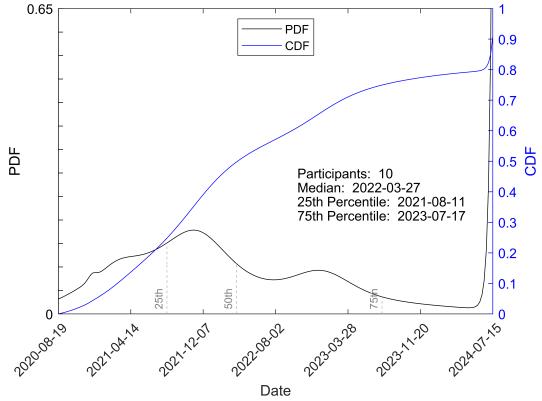
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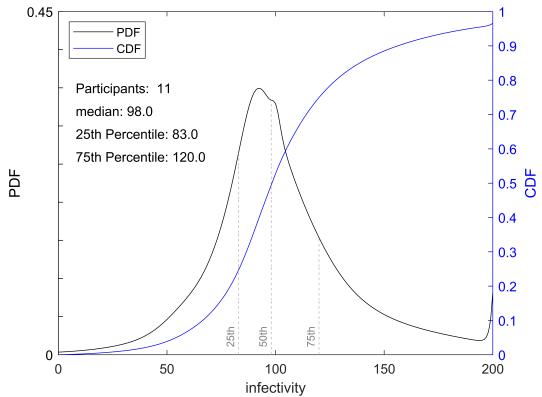
How many weeks after approval will the first 100 million doses of the first US- or EU- approved SARS-CoV-2 vaccine candidate based on a DNA or RNA platform be manufactured?



How many weeks after approval will the first 100 million doses of the first US- or EU- approved SARS-CoV-2 vaccine candidate based on a non-replicating viral vector platform be manufactured?



When will an orally administered SARS-CoV-2 antiviral show a statistically significant survival benefit for the treatment group in an $n > 200$ RCT?



What will be the SARS-CoV-2 infectivity of children relative to adults when schools are open?

DETAILS ON EXPERT CONSENSUS DISTRIBUTIONS

The consensus distributions reported above include only the most recent predictions from each expert. The experts were allowed to update their predictions as many times as they wished. The consensus prediction assigned a probability to a value x of

$$f(x) = \frac{1}{E} \sum_{i=1}^E f_i(x)$$

where f is the consensus probability distribution, $f_i(x)$ is the most recent probability expert i assigned to the value x , and E is the number of experts .

RECORD OF QUESTIONS, QUESTION TYPE, AND RESOLUTION CRITERIA

- When will a SARS-CoV-2 vaccine candidate be approved for use in the US or EU through a normal approval process?
 - Available prediction range: [19 August 2020, 15 July 2024], where the upper bound was left open allowing experts to assign weight to a resolution of > 15 July 2024.
 - Resolution Criteria: Resolution will be determined by the date of the first FDA press release or EMA press release on the normal approval of a SARS-CoV-2 vaccine candidate. US approval is defined as the date a vaccine candidate is licensed by the FDA as stated in a relevant press

release. EU approval is defined as the date an EMA-recommended vaccine candidate is granted approval by the EC via marketing authorization as stated in a relevant press release. Note that this must occur through the normal regulatory approval mechanisms. Approval under any other emergency procedures, such as under a FDA Emergency Use Authorization or EMA emergency Conditional Approval, would not count for positive resolution. A vaccine that was previously approved on an emergency basis and then approved via the normal regulatory mechanisms would count upon the second approval.

2. When will a SARS-CoV-2 vaccine candidate be approved for use in the US or EU through an emergency approval process?

- Available prediction range: [19 August 2020, 15 July 2024], where the upper bound was left open allowing experts to assign weight to a resolution of > 15 July 2024.
- Resolution Criteria: Resolution will be determined by the date of the first FDA press release or EMA press release on the emergency approval of a SARS-CoV-2 vaccine candidate. US approval is defined as the date a vaccine candidate is licensed through an Emergency Use Authorization by the FDA as stated in a relevant press release. EU approval is defined as the date an EMA-recommended vaccine candidate is granted Conditional Approval by the EC as stated in a relevant press release.

3. What will be the efficacy of the first US- or EU- approved SARS-CoV-2 vaccine candidate approved through a normal approval process?

- Available prediction range: Between 0% and 100%, inclusive.
- Resolution Criteria: Resolves as the median estimate of the absolute vaccine efficacy of the first US- or EU- SARS-CoV-2 vaccine approved through a normal approval process, $[(ARU - ARV)/(ARU)] \times 100$, where ARU is the disease attack rate in the unvaccinated group and ARV is the disease attack rate in the vaccinated group.

4. What will be the efficacy of the first US- or EU- approved SARS-CoV-2 vaccine candidate approved through an emergency approval process?

- Available prediction range: Between 0% and 100%, inclusive.
- Resolution Criteria: Resolves as the median estimate of the absolute vaccine efficacy of the first US- or EU- SARS-CoV-2 vaccine approved through an emergency approval process, $[(ARU - ARV)/(ARU)] \times 100$, where ARU is the disease attack rate in the unvaccinated group and ARV is the disease attack rate in the vaccinated group.

5. How many weeks after approval will the first 100 million doses of the first US- or EU- approved SARS-CoV-2 vaccine candidate based on a DNA or RNA platform be manufactured?

- Available prediction range: [0 weeks, 104 weeks], where the upper bound was left open allowing experts to assign weight to a resolution of > 104 weeks.
- Resolution Criteria: Resolves as the date when the first credible article is published that presents the claim that at least 100 million doses of the first US- or EU- approved SARS-CoV-2 vaccine candidate based on a DNA or RNA platform have been manufactured. Approval can occur through either an emergency approval or normal approval process to count. If the vaccine candidate is a two-dose vaccine, then 100 million doses of each of the two dosage types must be manufactured (200 million total).

6. How many weeks after approval will the first 100 million doses of the first US- or EU- approved SARS-CoV-2 vaccine candidate based on a non-replicating viral vector platform be manufactured?

- Available prediction range: [0 weeks, 104 weeks], where the upper bound was left open allowing experts to assign weight to a resolution of > 104 weeks.
- Resolution Criteria: Resolves as the date when the first credible article is published that presents the claim that at least 100 million doses of the first US- or EU- approved SARS-CoV-2 vaccine candidate based on a non-replicating viral vector platform have been manufactured. Approval can occur through either an emergency approval or normal approval process to count. If the vaccine candidate is a two-dose vaccine, then 100 million doses of each of the two dosage types must be manufactured (200 million total).

7. When will an orally administered SARS-CoV-2 antiviral show a statistically significant survival benefit for the treatment group in an $n > 200$ RCT?

- Available prediction range: [19 August 2020, 15 July 2024], where the upper bound was left open allowing experts to assign weight to a resolution of > 15 July 2024.
- Resolution Criteria: resolves as the date when the first peer-reviewed research article of an orally administered SARS-CoV-2 antiviral to enroll more than 200 patients publishes a statistically significant survival benefit for the treatment group. For our purposes, "statistically significant" means that the upper bound of the 95% confidence interval of the hazard ratio for death between treated and control patients is less than 1.0. Moreover, the results would have to be statistically significant for the entire treatment group when compared to the control group in order to resolve positively.

8. What will be the SARS-CoV-2 infectivity of children relative to adults when schools are open?

- Available prediction range: [0%, 200%], where the upper bound was left open allowing experts to assign weight to a resolution of $> 200\%$.
- Resolution Criteria: Resolves as the numeric value of the infectivity of children relative to adults in the first peer-reviewed research article in which there are $n > 1000$ COVID-19 positive cases and $n > 500$ households that are considered. We define relative infectivity as "the ratio of the probabilities per unit time that these individuals generate infection, when making contact with individuals who have identical susceptibilities." The population being studied must be in an area where schools are open — for our purposes, this is defined as $> 50\%$ of classroom instruction being done in-person.

PARTICIPATING EXPERTS

Subject-matter experts	
Name	Affiliation
Ulrich Strych	Baylor College of Medicine
R. Kiplin Guy	University of Kentucky College of Pharmacy
Robert Schooley	University of California San Diego
David J. Margraf	University of Minnesota
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Cory Schillinger	
Jack Chen	
Eli Lifland	
Linchuan Zhang	

[1] Financial Times. Fda head says he is willing to fast-track covid-19 vaccine. <https://www.ft.com/content/f8ecf7b5-f8d2-4726-ba3f-233b8497b91a>. (Accessed on 09/15/2020).

[2] U.S. Food and Drug Administration. Coronavirus (covid-19) update. <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-takes-action-help-facilitate-timely-development-safe-effective> (Accessed on 09/15/2020).