COVID-19 Vaccine and Therapeutics Expert Predictions

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SURVEY TIME PERIOD, DEFINITION OF EXPERTS, AND LOGISTICS

From June 15$^{\text{th}}$ 2020 to June 25$^{\text{th}}$ 2020, predictions were made for **6** questions related to vaccine and therapeutic solutions to COVID-19. Two groups of experts were asked to participate: (i) subject matter experts (SMEs) and (ii) trained forecasters (TFs). SMEs were defined as those in the fields of molecular and cellular biology, microbiology, virology, biochemistry, and infectious disease, who have several years of experience in vaccine, antiviral, or biological research related to infectious agents, and are up-to-date with 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 17 experts (8 subject matter experts and 9 trained forecasters) participated and submitted 154 predictions for aggregation into a consensus distribution.

During the survey period, experts could submit multiple predictions for the same question and collaborate via a comment section underneath each question. To minimize starting-point bias or groupthink, the consensus distribution for each question was hidden from experts from June 15$^{\text{th}}$ to June 20$^{\text{th}}$. On June 21$^{\text{th}}$ the consensus distribution was revealed and experts could view the ongoing consensus distribution until the close of the survey on June 25$^{\text{th}}$. We hypothesize predictions were revised by experts as they received new external information on vaccines and therapeutics or because of the differences between the expert's prediction and the ongoing consensus distribution prediction.

Below is a textual summary of the consensus predictions, an estimate of the consensus probability mass (density) function and cumulative mass (density) for each of the six questions, brief details on how the consensus was formed, a record of questions and their resolution criteria, and a list of subject matter experts and trained forecasters.

SUMMARY OF PREDICTIONS

1. The expert median prediction that a SARS-CoV-2 vaccine candidate will demonstrate $\geq 70\%$ efficacy is September 2021 (80% CI: December 2020, June 2023 or later), or experts assigned 0.50 probability to dates before Sept. 2021 and 0.50 probability to dates after Sept. 2021.

2. Experts assigned a median of June 2021 (80% CI: November 2020, June 2023 or later) to when a SARS-CoV-2 vaccine candidate be approved for use in the United States or European Union.

3. Experts median prediction that the first SARS-CoV-2 vaccine to be approved in the US or EU and administered to more than 100K people is November 2021 (80% CI: January 2021, June 2023 or later).

4. Experts assigned a median prediction of March 2021 (80% CI: September 2020, June 2023) that a COVID-19 therapeutic or therapeutics cocktail will show a statistically significant survival benefit in a $N > 200$ RCT.

5. Experts assigned a median prediction of 55% (80% CI: 7.5%, 84%) to the efficacy of the Phase I/II trial testing the Oxford/AstraZeneca ChAdOx1 nCoV-19 vaccine candidate .

6. Experts assigned a median 17 (80% CI: 9, 25) to the number of SARS-CoV-2 vaccine candidates that will be in human trials as of 1 August 2020

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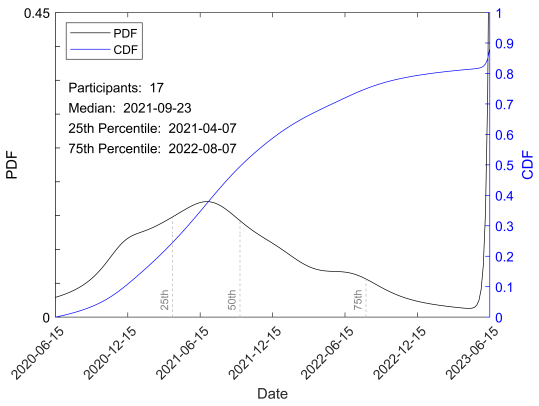
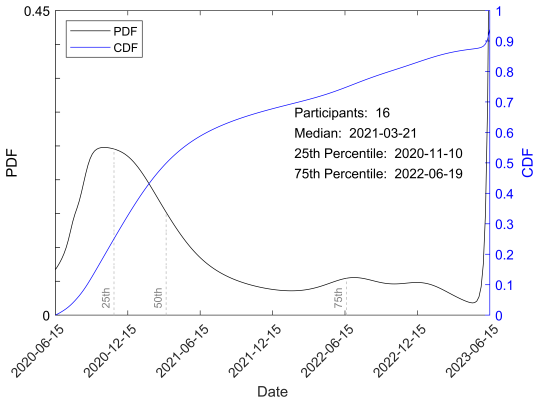
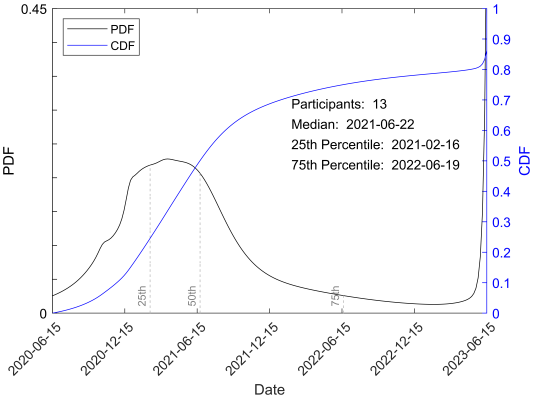


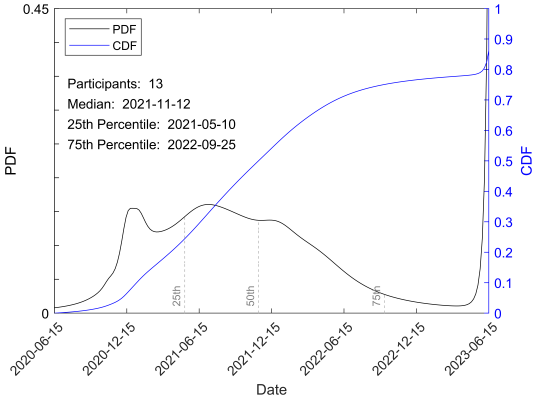
When will a SARS-CoV-2 vaccine candidate demonstrate $\geq 70\%$ efficacy?



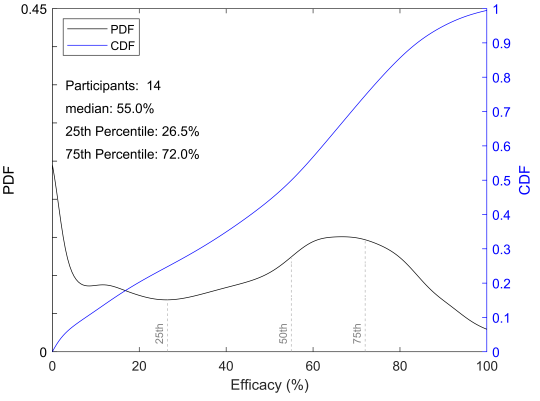
When will a COVID-19 therapeutic or therapeutics cocktail show a statistically significant survival benefit for the treatment group in a $N > 200$ RCT?



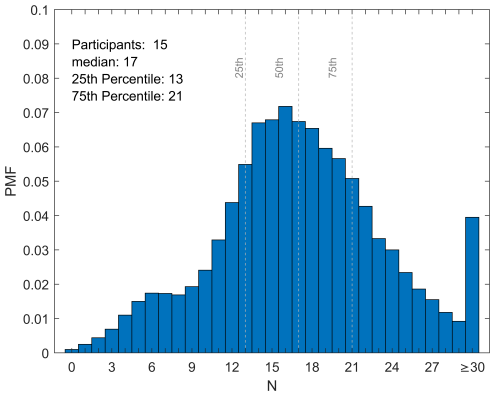
When will a SARS-CoV-2 vaccine candidate be approved for use in the US or EU?



When will the first SARS-CoV-2 vaccine to be approved in the US or EU be administered to >100k people?



What will be the efficacy of the Oxford/AstraZeneca ChAdOx1 nCoV-19 vaccine candidate according to the results of Phase II/III testing?



How many SARS-CoV-2 vaccine candidates will be in human trials as of 1 August 2020?

DETAILS ON EXPERT CONSENSUS DISTRIBUTIONS

Though experts were allowed to update their predictions as many times as they wished, the consensus distributions reported above include only the most recent predictions from each expert. 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

1. When will a SARS-CoV-2 vaccine candidate demonstrate $\geq 70\%$ efficacy?

    - Available prediction range: [15 June 2020, 15 June 2023], where the upper bound was left open allowing experts to assign weight to a resolution of $>$ 15 June 2023.
    - Resolution Criteria: Resolves as the date when the first peer-reviewed research article of a Phase III RCT publishes a median estimate of the absolute vaccine efficacy (AVE) of at least 70%. The lower confidence limit of AVE can be smaller than 70%. If the median is not presented, then we will compare the mean estimate to a threshold of 70%. As stated in the WHO's target profile, the reduction in disease attack rate should be "consistent in the elderly" — for our purposes, this means the point estimate is $\geq 50\%$ for those 65 years or older. AVE is defined as $\frac{ARU-ARV}{ARU} \times 100$, where ARU is the disease attack rate in the unvaccinated group and ARV is the disease attack rate in the vaccinated group. The disease attack rate is the proportion of virologically confirmed (PCR positive) symptomatic cases of COVID-19.

2. When will a SARS-CoV-2 vaccine candidate be approved for use in the United States or European Union?

    - Available prediction range: [15 June 2020, 15 June 2023], where the upper bound was left open allowing experts to assign weight to a resolution of $>$ 15 June 2023.
    - Resolution Criteria: Resolution will be determined by the date of the first U.S. Food and Drug Administration (FDA) press release or European Medicines Agency (EMA) press release on the approval of a SARS-CoV-2 vaccine candidate. U.S. 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 European Commission (EC) via marketing authorization as stated in a relevant press release. Approval under any other emergency procedures, such as under a FDA Emergency Use Authorization or EMA emergency procedure authorization, would not count for positive resolution.

3. When will the first SARS-CoV-2 vaccine to be approved in the US or EU be administered to $> 100K$ people?

    - Available prediction range: [15 June 2020, 15 June 2023], where the upper bound was left open allowing experts to assign weight to a resolution of $>$ 15 June 2023.
    - Resolution Criteria: Resolves as the publication date of the first credible source that states at least 100,000 people were administered with the first SARS-CoV-2 vaccine approved by the US or EU. Only after regular approval will vaccinated people count towards the 100,000 figure. If the vaccine is a multiple-dose regimen, all doses must be administered to count toward the 100,000 figure. The vaccine can be administered to people outside the US or EU so long as it is administered after approval in the US or EU. To avert the possibility of any approvals later being revoked, approval must occur under the regular FDA or EU mechanisms — any approval under emergency procedures will not be considered.

4. When will a COVID-19 therapeutic or therapeutics cocktail show a statistically significant survival benefit for the treatment group in a $N > 200$ RCT?

    - Available prediction range: [15 June 2020, 15 June 2023], where the upper bound was left open allowing experts to assign weight to a resolution of $>$ 15 June 2023.
    - Resolution Criteria: Resolves as the date when the first peer-reviewed research article of a COVID-19 therapeutic or therapeutics cocktail to enroll more than 200 patients publishes a statistically significant survival benefit for the treatment group. For the purpose of this question, "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. The groups should include subsamples of participants who: require ventilation, need oxygen support, and do not require respiratory support (do not necessitate ventilation or oxygen). If the hazard ratio is not reported, an alternative measure of survival benefit that is statistically significant at a 5% significance level will be considered.

5. What will be the efficacy of the Oxford/AstraZeneca ChAdOx1 nCoV-19 vaccine candidate according to the results of Phase II/III testing?

    - Available prediction range: Between 0% and 100% inclusive.
    - Resolution Criteria: Resolves as the median estimate of the AVE of ChAdOx1 nCoV-19. Such a finding should be presented in a peer-reviewed research article authored and/or supported by Oxford/AstraZeneca. If no median is provided, the question will resolve as the mean AVE.

6. How many SARS-CoV-2 vaccine candidates will be in human trials as of 1 August 2020?

    - Available prediction range: Between 0 and 30, where the upper bound was left open allowing experts to assign weight to a resolution of $>$ 30.
    - Resolution Criteria: Resolves to the number of vaccines in active clinical evaluation according to the version of the WHO's Draft landscape of COVID-19 candidate vaccines that is most recent as of 1 August 2020 (including 1 August).

PARTICIPATING EXPERTS

Subject-matter experts

Name	Affiliation
Andrew Azman	Johns Hopkins University
Rebecca Dutch	University of Kentucky College of Medicine
R. Kiplin Guy	University of Kentucky College of Pharmacy
Nelson Lee	University of Alberta, Canada
David J. Margraf	University of Minnesota
Jeff Morgan	Catholic University of America
Frank Romanell	University of Kentucky College of Pharmacy
Ulrich Strych	Baylor College of Medicine

Top Forecasters

Name	Affiliation
Shahar Avin	Centre for the Study of Existential Risk, University of Cambridge
Anthony Boyles	
Damon Cham	
Jack Chen	
Sylvain Chevalier	
James Clough	
Eli Lifland	
David Manheim	University of Haifa's Health and Risk Communication Research Center
Cory Schillinger	