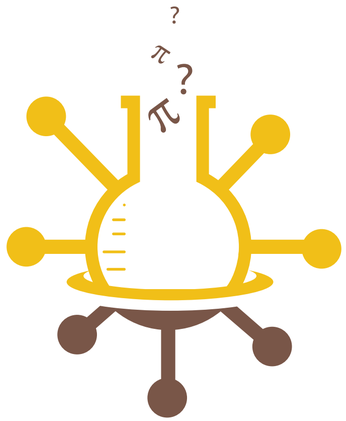
Consensus probabilistic predictions of the timing, efficacy, and safety of a SARS-COV-2 vaccine by experts and trained forecasters



Computational UncertaintyLab

LEHIGH UNIVERSITY

tom mcandrew

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Timeline of project and goal

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Timeline

The pandemic began in late December 2019

Cases were reported in the US in February including the first US death

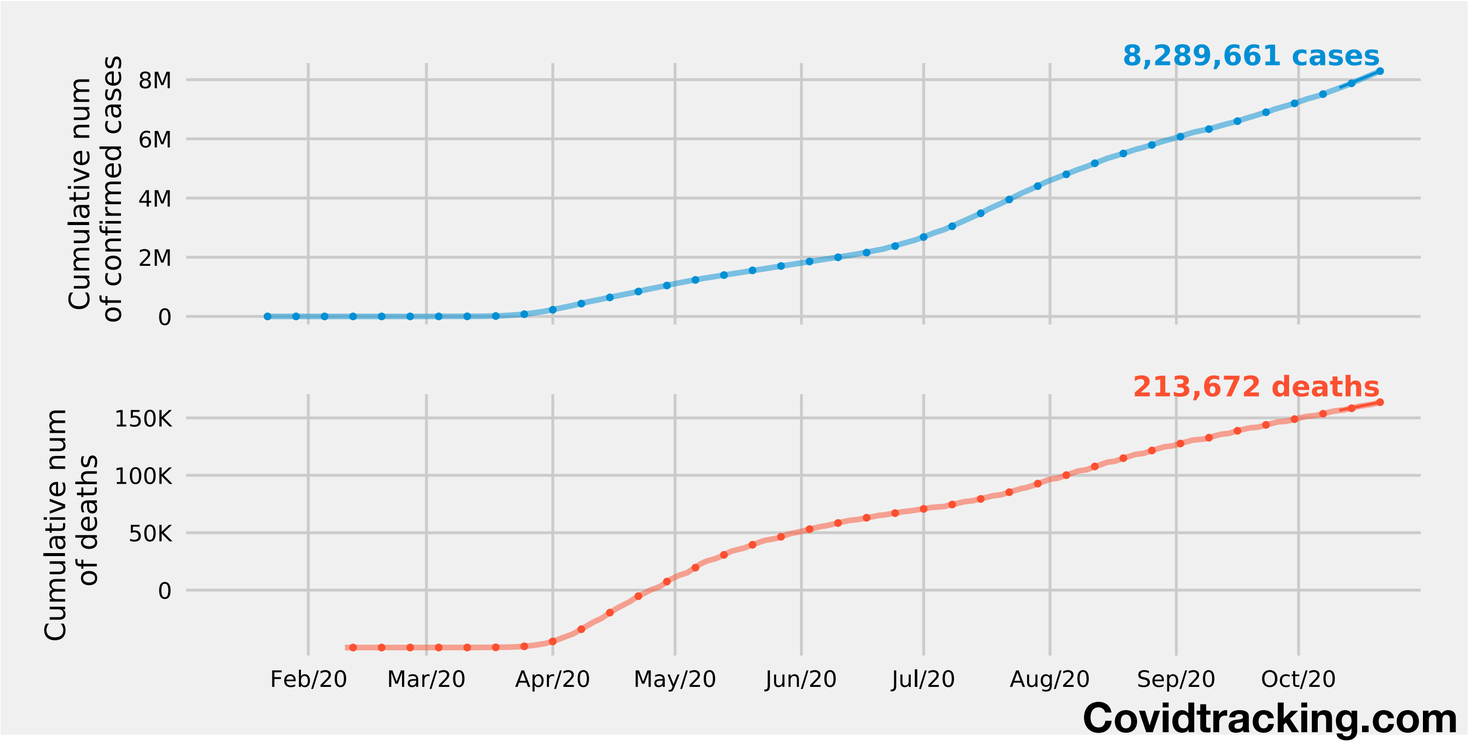
May 15: Remarks by WH on Vaccine Development

Jun 30: Our first summary of predictions from experts and trained forecasters

Jul. 27: Moderna launches P3 Trial under Operation Warp speed

Aug 18: Oxford & Astrazeneca P3 Trial design is posted to clinicaltrials.gov

Sept 13: Pew research poll finds 49% of americans would not volunteer for inoculation



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SEPTEMBER 17, 2020

U.S. Public Now Divided Over Whether To Get COVID-19 Vaccine

Concerns about the safety and effectiveness of possible vaccine, pace of approval process

BY ALEC TYSON, COURTNEY JOHNSON AND CARY FUNK

About half of U.S. adults (51%) now say they would definitely or probably get a vaccine to prevent COVID-19 if it were available today; nearly as many (49%) say they definitely or probably *would not* get vaccinated at this time.

Science & technology

Oct 21st 2020 edition ›

Controlling the pandemic

Should covid be left to spread among the young and healthy?

Two petitions by scientists clash on the matter

The Great Barrington plan, then, is a high-risk, high-reward proposition. The John Snow one, by contrast, would minimise covid deaths in the short term, but lives lost in the long-term, because of lockdowns and other disruptions, might end up being more numerous.

With luck, this whole debate will be rendered irrelevant by the invention of a vaccine or the development of suitable drugs to treat covid. The results of several efficacy trials of vaccines, and tests on promising pharmaceuticals, are expected in the coming weeks. If covid-19 is less deadly and some herd immunity comes from a vaccine, the paths charted by the two petitions will, eventually, come together.

Our goal is to support public health strategies and decision making with probabilistic predictions from subject matter experts and trained generalist forecasters from Metaculus

Past work has shown probabilistic forecasts better communicate risk

Subject matter experts provide access to information computational models may not

Trained forecasters complement experts who may have an extensive background studying vaccines but

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Our pool of forecasters

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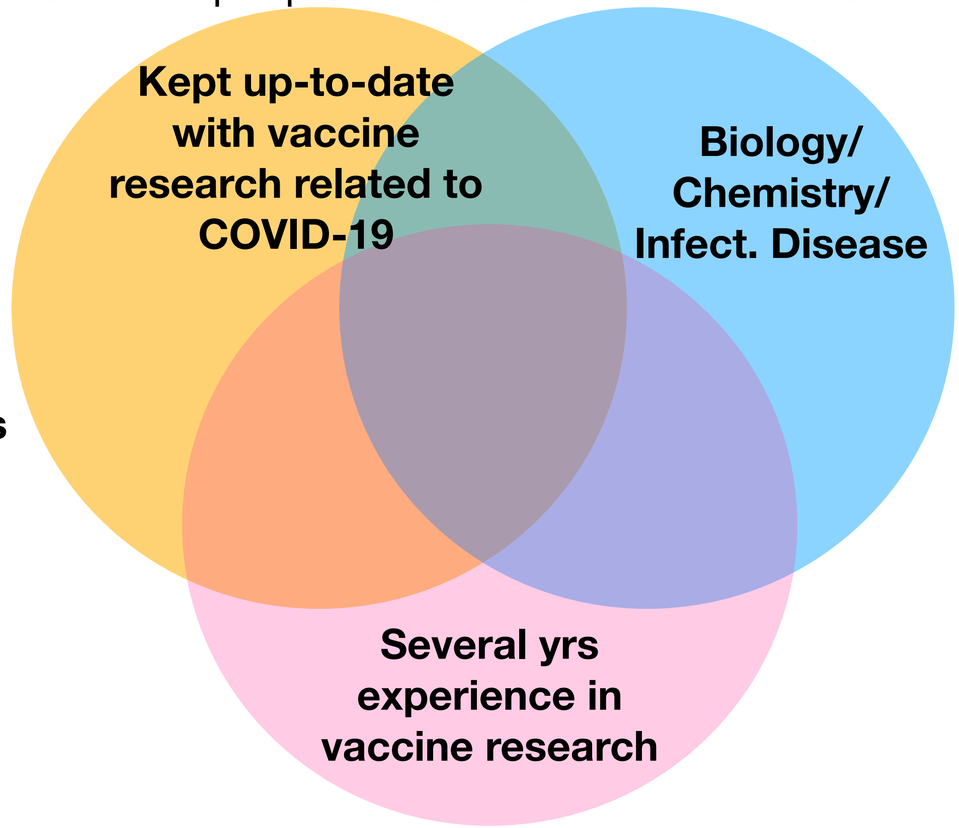
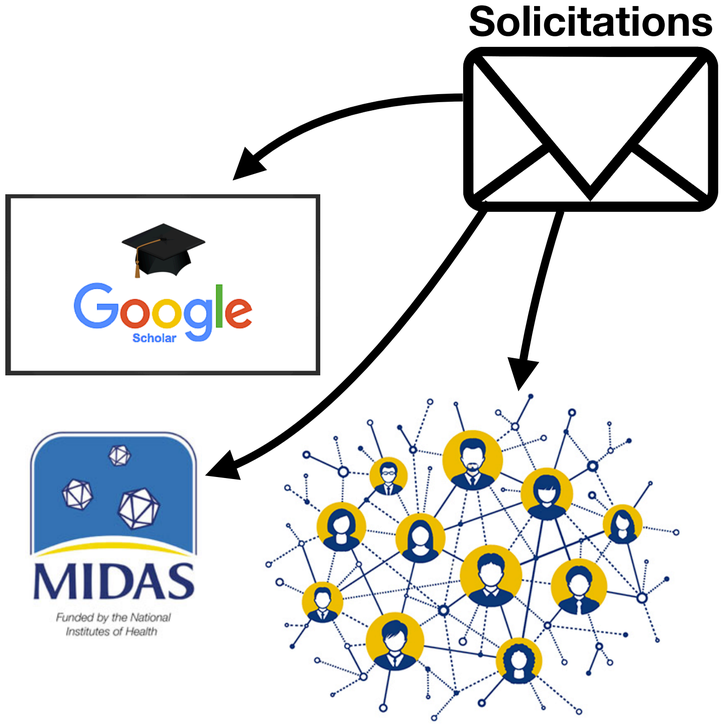
How we defined an expert

We are soliciting experts in molecular and cellular biology, microbiology, virology, biochemistry, and infectious disease. We ask that participants have several years of experience in vaccine, antiviral, or biological research related to infectious agents and kept up-to-date with vaccine and antiviral research specifically focused on the novel coronavirus.

Experts need to meet 3 conditions





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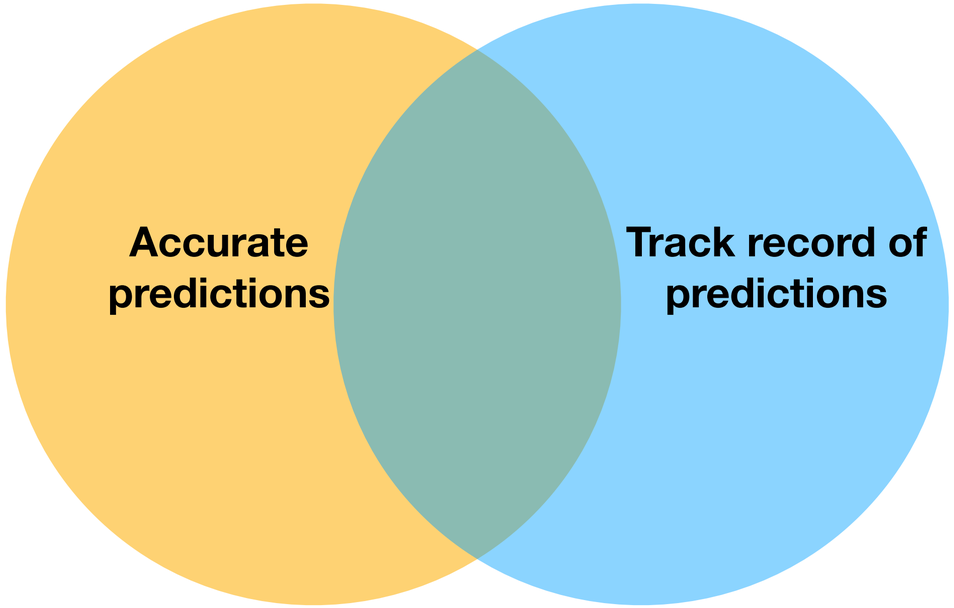
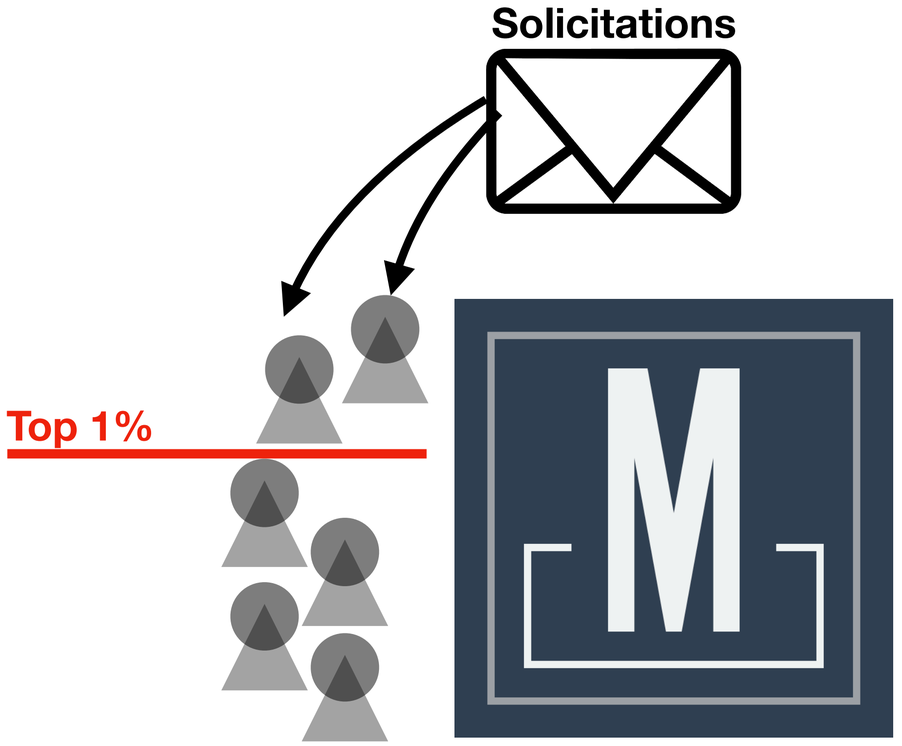
How we defined a trained forecaster

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 **Metaculus** forecasting platform.

Forecasters need to meet 2 conditions





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Our pool of forecasters

Prediction period	**2020-06-14 to 2020-06-25**	**2020-07-15 to 2020-07-26**	**2020-08-19 to 2020-08-29**	**2020-09-21 to 2020-10-03**
Number of forecasters	17	15	11	12
Experts	8	7	5	3
Trained forecasters	9	8	6	9

An almost even distribution of experts and trained forecasters

Consistent number of forecasters over four months

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Number of predictions

Prediction period	**2020-06-14 to 2020-06-25**	**2020-07-15 to 2020-07-26**	**2020-08-19 to 2020-08-29**	**2020-09-21 to 2020-10-03**
Number of predictions made	161	148	153	75
Experts	77	72	47	17
Trained forecasters	84	76	106	58

Experts and trained forecasters made frequent revisions to their predictive distributions

The number of revisions over all four surveys was consistent

Even distribution of predictions from experts and trained forecasters

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Number of comments

Prediction period	**2020-06-14 to 2020-06-25**	**2020-07-15 to 2020-07-26**	**2020-08-19 to 2020-08-29**	**2020-09-21 to 2020-10-03**
Total number of comments made	26	11	14	5
Experts	12	3	2	2
Trained forecasters	14	8	12	3

Small number of comments compared to predictions

Besides the first survey, trained forecasters make more comments than experts

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Questions we asked

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We asked 26 questions and will focus on

Efficacy

Timing

Safety

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We asked 26 questions and will focus on

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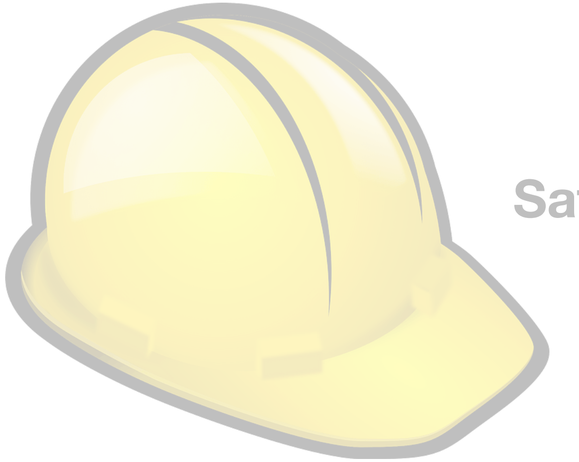

Safety

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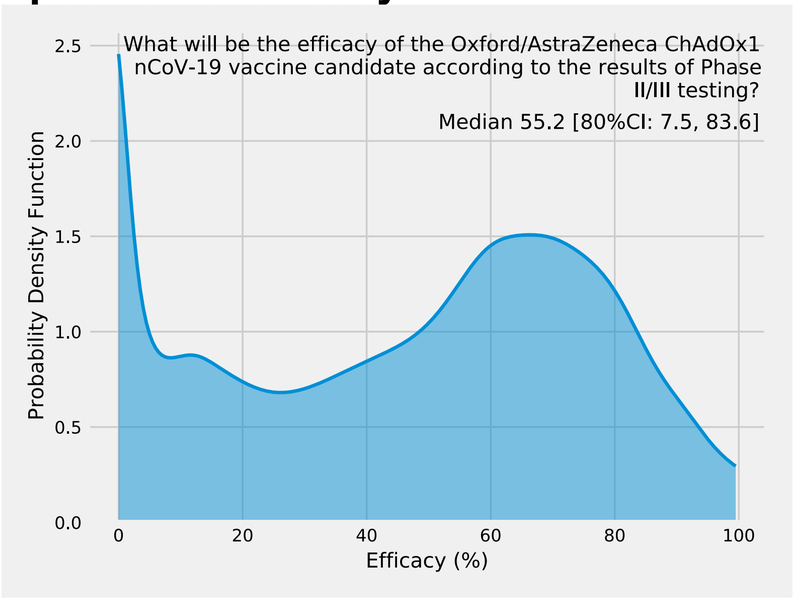
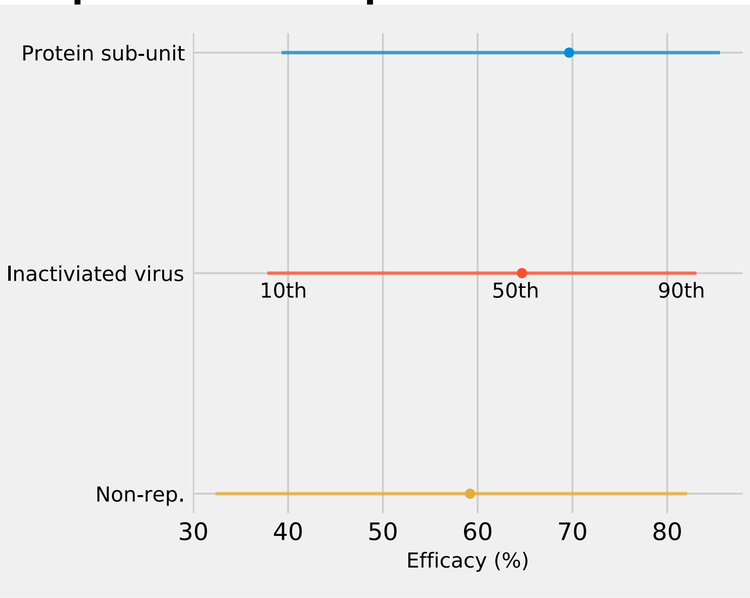
Efficacy

Headline: The Efficacy of a SARS-COV-2 vaccine predicted by experts and trained forecasters can focus on a specific trial, compare different vaccine platforms, and compare different federal authorizations.

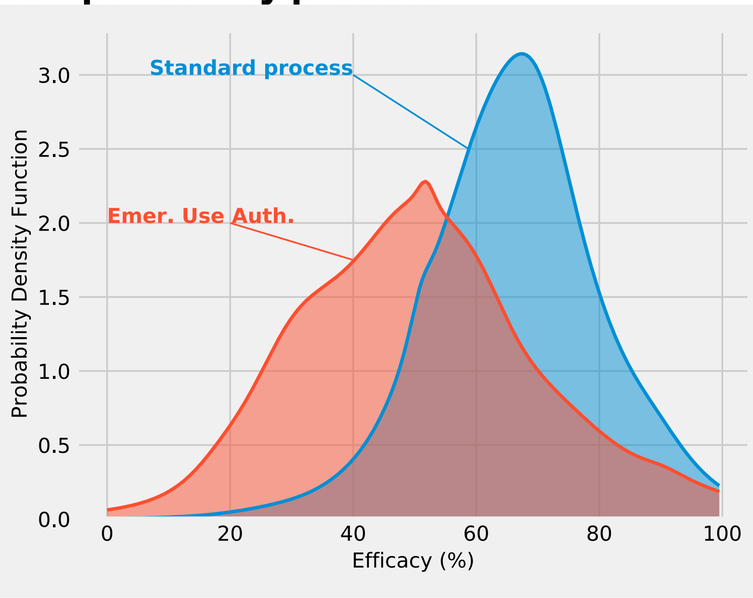
Specific trial efficacy



Comparison across platforms



Comparison by process



Forecaster commentary:

The bigger question here is “how long will the effectiveness last”.

I think very low efficacies are possible here.

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We asked 26 questions and will focus on

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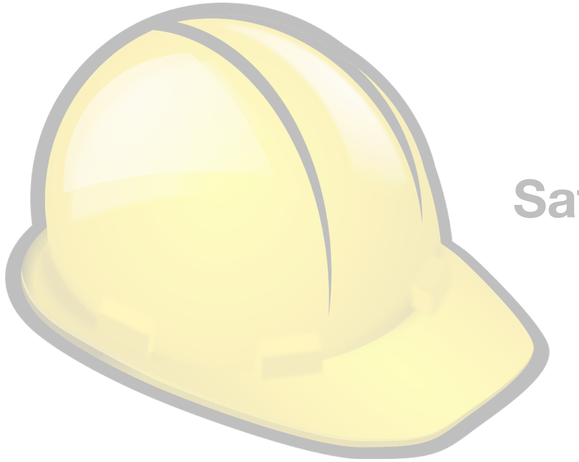
Timing



Safety

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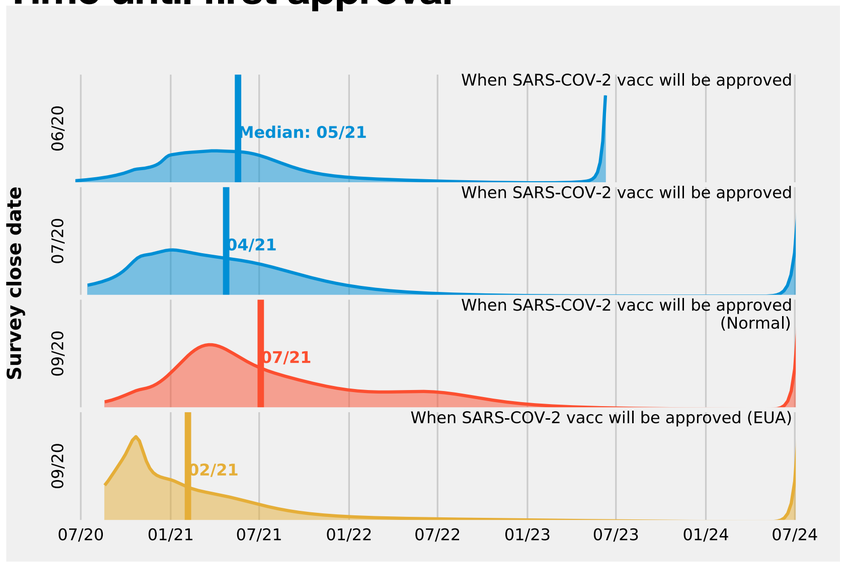
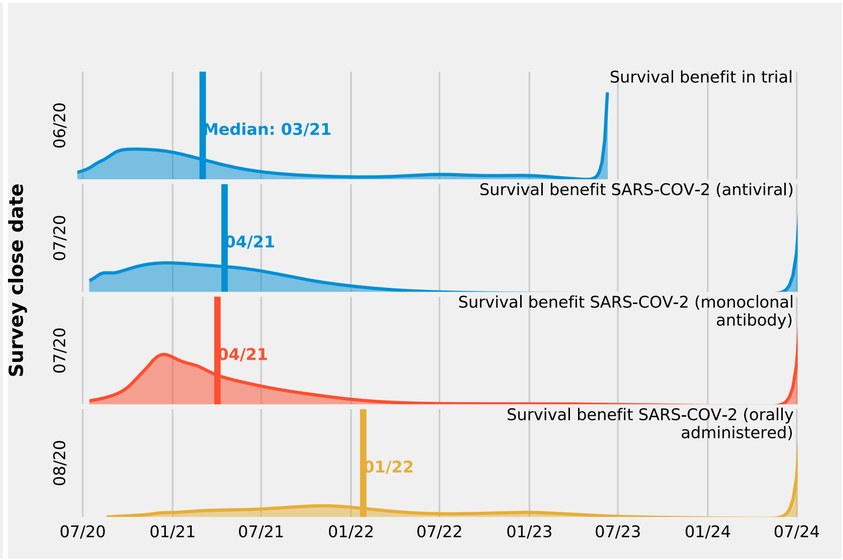
Timing

Headline: Experts and trained forecasters can quantify when a SARS-COV-2 vaccine will be approved, when a trial will show a survival benefit, and the time until 100M doses are produced. This information is valuable for two different audiences. The public can benefit from estimates of the time until first approval and when a survival benefit will be confirmed to taking a vaccine. Time until 100M doses stratified by the type of vaccine platform can be useful information for vaccine developers. Experts/Trained forecasters can communicate risk to a broad audience.

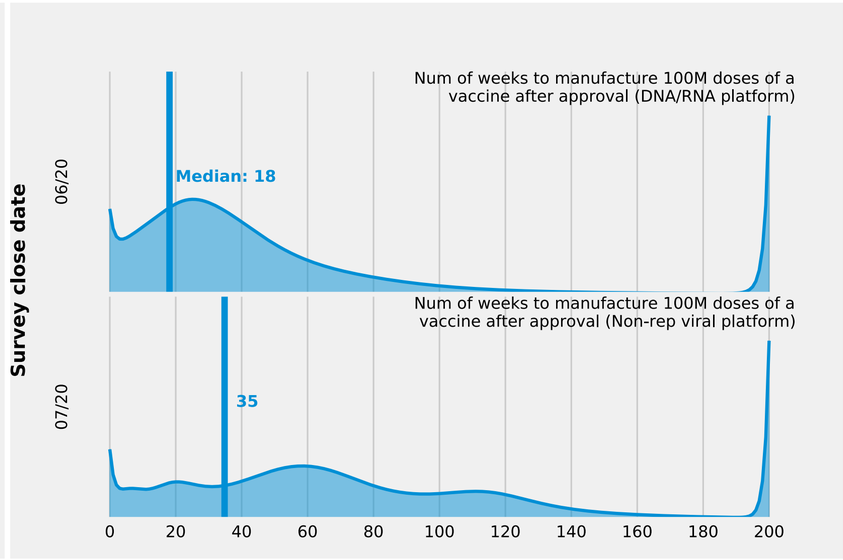
Time until first approval



Time until survival benefit



Time until 100M doses



Forecaster commentary:

IIUC, Moderna's vaccine is based on a replicating vector, CanSino's is not.

Documenting my thoughts. […]

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We asked 26 questions and will focus on

Efficacy

Timing

Safety

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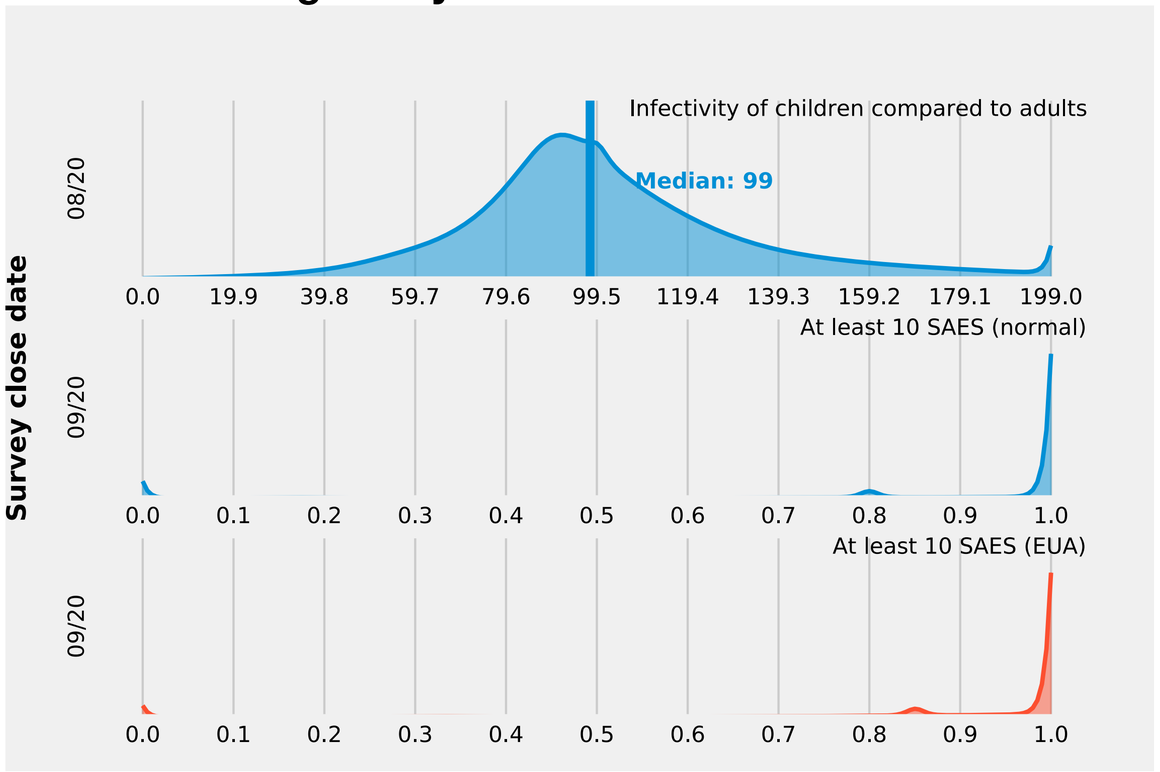
Safety

Headline: Experts/Trained forecasters can communicate short-term risks immediately relevant to the public and longer-term risks relevant to pharmaceutical companies and public health officials.

Communicating safety



Forecaster commentary:

Given that such a vaccine will be distributed widely, I would expect that even very rare and expected SAEs will occur >10 times, so this seems very very likely.

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Reporting and communication

Open source, public access, GitHub link

https://github.com/computationalUncertaintyLab/vaccinceAndTherapeuticsCrowd

COVID-19 Vaccine and Therapeutics Expert Predictions

We aim to build an expert consensus prediction on developments related to SARS-CoV-2 vaccines and COVID-19 therapeutics. Each survey asks a small group of subject matter experts and trained forecasters to make predictions starting on the 15th and closing on the 25th of every month. Results will be compiled and on this repository on the 1st of the subsequent month.

Description of project

Expert definitions

Subject matter experts 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.

How we defined an expert

Trained Forecasters 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.

Survey Number	Date Issued	Date Closed	Summary
01	2020-06-15	2020-06-30	Summary 01
02	2020-07-15	2020-07-30	Summary 02
03	2020-08-15	2020-08-30	Summary 03

Links to summary reports

Contact information

- Daniel Sluder - daniel@metaculus.com
- Tamay Besiroglu - tamay@metaculus.com
- Juan Cambeiro - juan@metaculus.com
- tom mcandrew - mcandrew@lehigh.edu

Contact information

master · 1 branch · 0 tags · Go to file · Add file · Code

tomcm39 updates 1af137a 7 days ago 25 commits

consensusPredictionData	updates	7 days ago
figs	updates	7 days ago
helperfunctions	updates	7 days ago
summaryReports	Report 3 up	last month
supportData	added meta data to support folder	4 months ago
README.md	Update README.md	last month
numberOfUniqueForecasters.py	updates	7 days ago
plotDistributionByQID.py	added code to make density plots	9 days ago
tableOfPredictorStats.py	updates	7 days ago

Code to reproduce/explore predictions

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Reporting and communication

Introduction and predictions in context

COVID-19 Vaccines and Therapeutics Expert Predictions

Juan Cambeiro,[1,*] Tamay Besiroglu,[1,2] Dan Sluder,[1] and Thomas McAndrew[3,†]

[1] *Metaculus*

[2] *Faculty of Economics, University of Cambridge, Cambridge, United Kingdom*

[3] *College of Health, Lehigh University, Bethlehem, Pennsylvania, United States of America*

(Dated: September 22, 2020)

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

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 5.9% 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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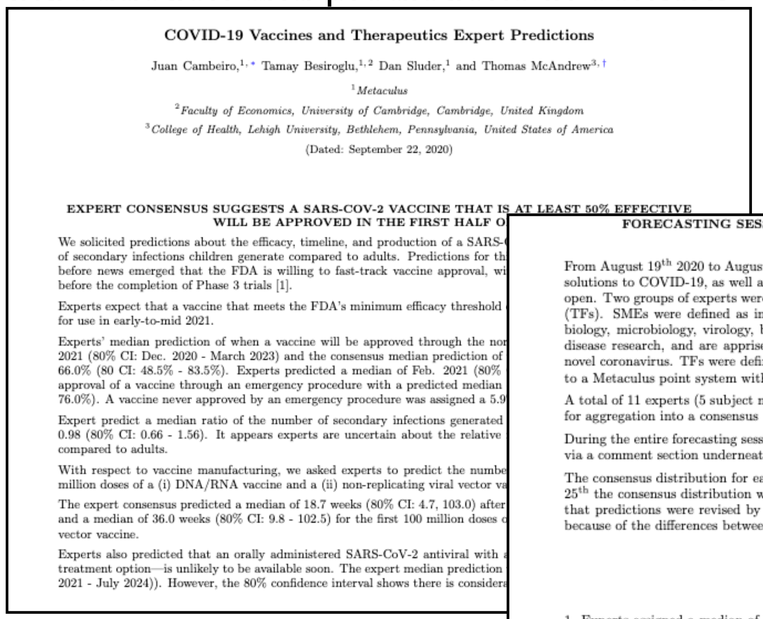
Reporting and communication

Introduction and predictions in context



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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%.

Summary of predictions from consensus

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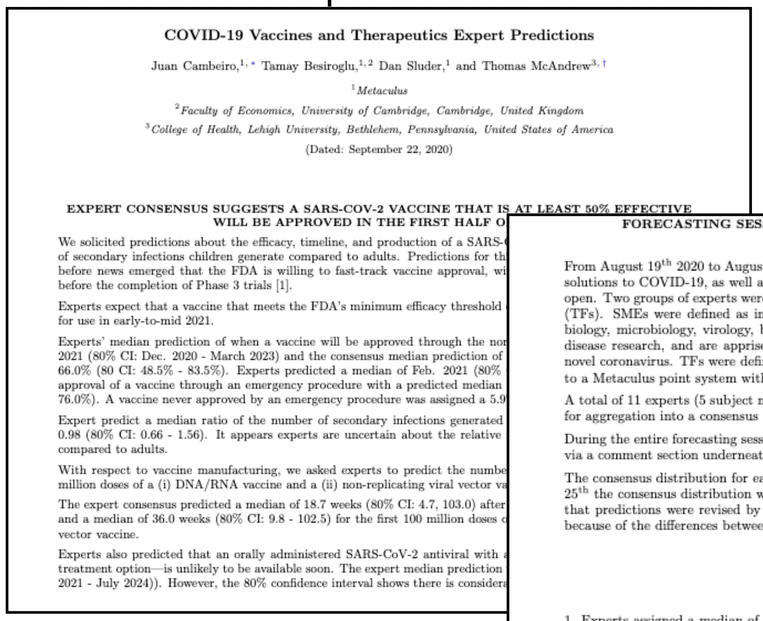
Reporting and communication

Introduction and predictions in context



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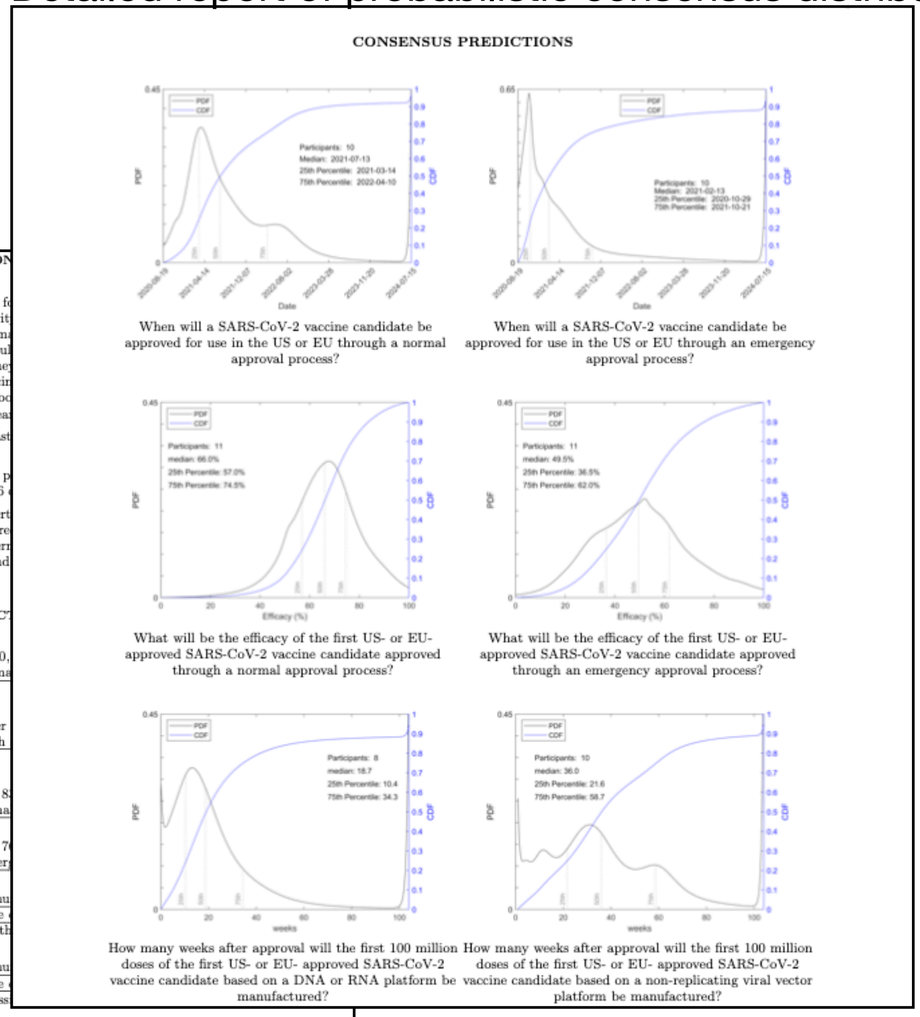
Summary of predictions from consensus

Detailed report of probabilistic consensus distributions



CONSENSUS PREDICTIONS

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

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

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

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

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?

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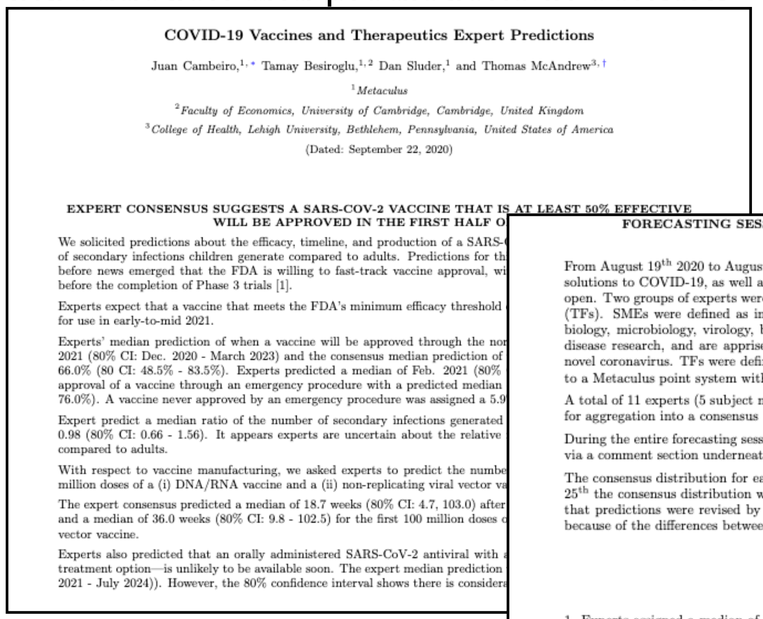
Reporting and communication

Introduction and predictions in context



COVID-19 Vaccines and Therapeutics Expert Predictions

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(Dated: September 22, 2020)

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

We solicited predictions about the efficacy, timeline, and production of a SARS-C of secondary infections children generate compared to adults. Predictions for th before news emerged that the FDA is willing to fast-track vaccine approval, wi before the completion of Phase 3 trials [1].

Experts expect that a vaccine that meets the FDA's minimum efficacy threshold for use in early-to-mid 2021.

Experts' median prediction of when a vaccine will be approved through the nor 2021 (80% CI: Dec. 2020 - March 2023) and the consensus median prediction of 66.0% (80 CI: 48.5% - 83.5%). Experts predicted a median of Feb. 2021 (80% approval of a vaccine through an emergency procedure with a predicted median 76.0%). A vaccine never approved by an emergency procedure was assigned a 5.9

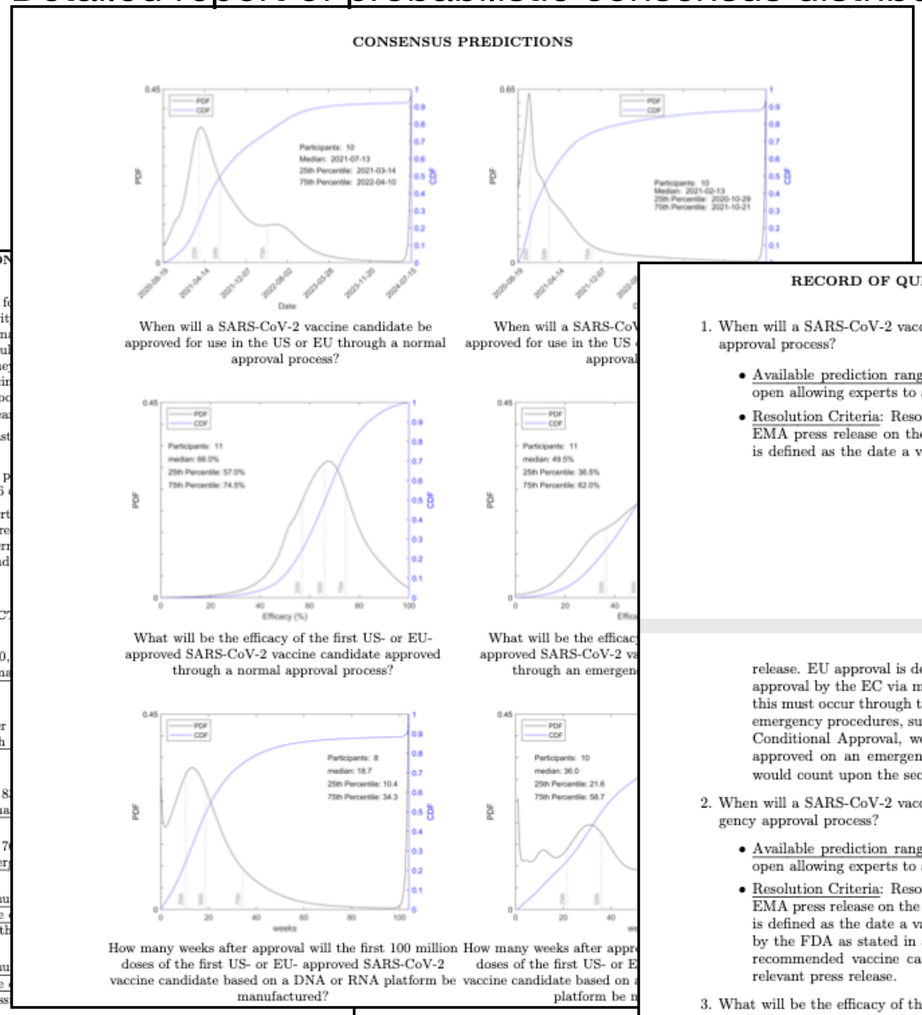
Expert predict a median ratio of the number of secondary infections generated 0.98 (80% CI: 0.66 - 1.56). It appears experts are uncertain about the relative compared to adults.

With respect to vaccine manufacturing, we asked experts to predict the numbe million doses of a (i) DNA/RNA vaccine and a (ii) non-replicating viral vector va

The expert consensus predicted a median of 18.7 weeks (80% CI: 4.7, 103.0) after and a median of 36.0 weeks (80% CI: 9.8 - 102.5) for the first 100 million doses o vector vaccine.

Experts also predicted that an orally administered SARS-CoV-2 antiviral with treatment option—is unlikely to be available soon. The expert median prediction 2021 - July 2024)). However, the 80% confidence interval shows there is considera

Detailed report of probabilistic consensus distributions



CONSENSUS PREDICTIONS

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

When will a SARS-CoV approved for use in the US approval

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

What will be the efficac approved SARS-CoV-2 va through an emergen

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 appr doses of the first US- or E vaccine candidate based on platform be

Line list of questions, possible answers, and resolution

RECORD OF QUESTIONS, QUESTION TYPE, AND RESOLUTION CRITERIA

1. 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, $[(\text{ARU} - \text{ARV})/(\text{ARU})] \times 100$, 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, $[(\text{ARU} - \text{ARV})/(\text{ARU})] \times 100$, where ARU is the disease attack rate in the unvaccinated group and ARV

FORECASTING SESSION DURATION, DEFINITION

From August 19th 2020 to August 29th 2020, predictions were made fo solutions to COVID-19, as well as 1 question related to the infectivit open. Two groups of experts were asked to participate: (i) subject ma (TFs). SMEs were defined as infectious disease experts, in particul biology, microbiology, virology, biochemistry, or epidemiology. The disease research, and are apprised of developments regarding vaccin novel coronavirus. TFs were defined as the top 1% out of a total poo to a Metaculus point system with track records spanning several yea

A total of 11 experts (5 subject matter experts and 6 trained forecast for aggregation into a consensus distribution.

During the entire forecasting session, experts could submit multiple p via a comment section underneath each question. Experts shared 16

The consensus distribution for each question was hidden from expert 25th the consensus distribution was revealed until the end of the fore that predictions were revised by experts as they received new extern because of the differences between the predictions of the experts and

SUMMARY OF PREDIC

1. Experts assigned a median of July 2021 (80% CI: December 2020, candidate will be approved for use in the US or EU through a norma assigned to a date of July 2024 or later.

2. Experts assigned a median of February 2021 (80% CI: September vaccine candidate will be approved for use in the US or EU through 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%, 8 approved SARS-CoV-2 vaccine candidate approved through a norma

4. Experts assigned a median prediction of 49.5% (80% CI: 26.0%, 7 approved SARS-CoV-2 vaccine candidate approved through an emer

5. Experts predicted a median of 18.7 (80% CI: 4.7, 103.0) as the nu million doses of the first US- or EU- approved SARS-CoV-2 vaccine will be manufactured. A probability of 5.4% was assigned to more th

6. Experts predicted a median of 36.0 (80% CI: 9.8, 102.5) as the nu million doses of the first US- or EU- approved SARS-CoV-2 vaccine vector platform will be manufactured. A probability of 4.8% was ass

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%.

Summary of predictions from consensus

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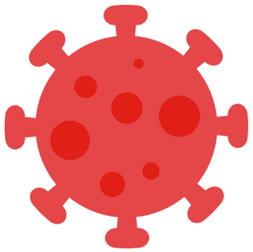
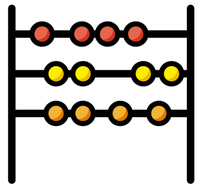
and

can provide probabilistic predictions of the efficacy, timing, and safety of a vaccine to

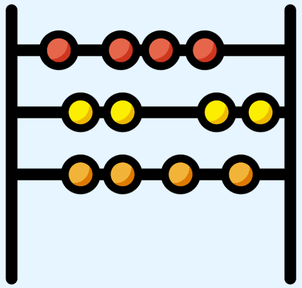


. Predictions are fast and flexible, and can target several audiences such as the public, public health officials, and companies developing vaccines. Human judgment can complement



Unlike computational models, Humans can access unstructured data, rely on intuition and experience, and present a rationale alongside their prediction.

Future



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G1: Forecast outbreak

G2: Optimal interventions

G3: Open source tools

MIDAS

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Thank you

Collaborators

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https://github.com/computationalUncertaintyLab/vaccinceAndTherapeuticsCrowd

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