COVID-19 Evidence Accelerator Collaborative

Lab Meeting # 37

Thursday, July 15th, 2021, 3 - 4:00 pm ET

Call Summary

Overview of Lab Meeting 37

The focus of Lab Meeting 37 was on the modeling of infection rates and vaccinations. We heard two presentations discussing various approaches to isolating the effect of vaccinations on infection rates and how modeling can be developed and employed to forecast the trajectory of the pandemic. First, Dr. Carson Chow of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) at the National Institutes of Health (NIH), introduced modeling of infection rates and how vaccines, among other factors, influence these predictions. Next, Dr. Christopher Murray of the Institute of Health Metrics and Evaluation (IHME) presented on the various iterations and applications for modeling COVID data such as for predicting cross-variant vaccine effectiveness, long-term coverage of vaccines, and zip-code level vaccine hesitancy.

Vaccines & the Effect on SARS-CoV2 Infection

Carson Chow, NIH/NIDDK

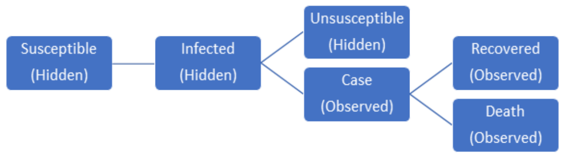
How well are vaccines working to quell COVID-19?

- Cases are declining in some places, rising in others
- How much of the decline in infection is attributable to vaccination rates and how much is attributable to herd immunity/other factors?
- Answers hinge on how many people are infected (including those not reported), i.e., the Case Ascertainment Ratio (CARt)

SIR Model – Simplistic way of thinking about infection that can be used to help model rates of infection/cases, susceptible population (S), infected (I), recovered (R), death (D)

- The SIR model can effectively capture the biology of the virus.
- However, what it cannot do is to capture the spatial heterogeneity of the pandemic including biology of the virus and who interacts with whom. It is not that the infected will inevitably interact with susceptible but that how they interact can vary from place to place.
- The model assumes homogeneous interaction but there can and will be social network effects where some pockets interact more than others.

SICR Model -- Considers "hidden" variables



Rate of change of infection

Susceptible fraction

$$\frac{dI}{dt} = \beta \frac{S}{N} I - \sigma_C I - \sigma_U I$$

Rate of infection/interaction

- If everything remained constant (e.g., social distancing measures/adherence, biology of the virus) the herd immunity threshold can be determined by dI/di = 0, but this is not the case and therefore determining herd immunity threshold is not a perfect math
- Vaccines reduce the rate of infection (R_t) by reducing S (susceptible individuals, but nonidentifiable)

Predicted Measures

- R_t = time dependent reproduction number
- CAR_t = total cases / total infected
- IR_t = total infection / population
- IFR_t = total deaths / total infected

Bayesian Inference – helps mitigate overfitting when there are too many parameters

- Compute posteriors for time dependent parameters (for various models)
- Priors on Rt, CARt, smoothness, etc.
- Model comparison: fit vs. Complexity

Observations

- Using these tools, the impact vaccines have on rate of infection can be observed.
- In states with more vaccinations, there are fewer infections.
- Vaccinations are contributing to the decline in infections.

Discussion

- Need more standardized definitions for what it means to be recovered, died from infection, etc.
    - When data is uniform you can be more confident in observations.
- Not clear who is getting tested and who is getting the vaccine. Most states only reporting test numbers, not who gets these tests.
    - Would be helpful to know who is getting tested – is it the same people getting tested repeatedly or different people.
    - Would be helpful to also know who are vaccinated – susceptible people, or those who were previously infected and were recovered/no longer susceptible.

<u>COVID-19 Estimation</u>

Christopher Murray, Institute of Health Metrics & Evaluation (IHME), University of Washington

IHME Model Development Throughout COVID

- IHME has been modeling COVID cases since the first months of the pandemic
- Have gone through a series of different approaches to modeling to reflect different outcomes of the pandemic
    - March-April 2020 – curvefit, statistical death-based model, focused on predicting the peak post-implementation of social distancing measures
    - May 2020 – curvefit-SEIR Hybrid
    - June-December 2021 – Used spline on past deaths / the infection-fatality rate to get infections. Fit SEIR model where R effective predicted by key covariates including mobility, mask use, testing per capita, pneumonia seasonality.
    - January 2021 – map cases, hospitalizations and deaths into daily infections using infection detection rate, infection-hospitalization rate, and the infection fatality rate.
    - February 2021 – revised model to account for spread of Alpha variant
    - March 2021 – revised model to account for cross-variant immunity between ancestral and escape variants and their spread
- Early on, tried to address the problem of knowing what daily infections to be able to fit the model to this

Emerging New Variants

- Started out with a standard SEIR model based on non-escape variants
- Now more complex because of
    - Need to account for vaccination status & whether it gave immunity against infection and/or against severe disease/death
    - Also needs to account for the various escape variants

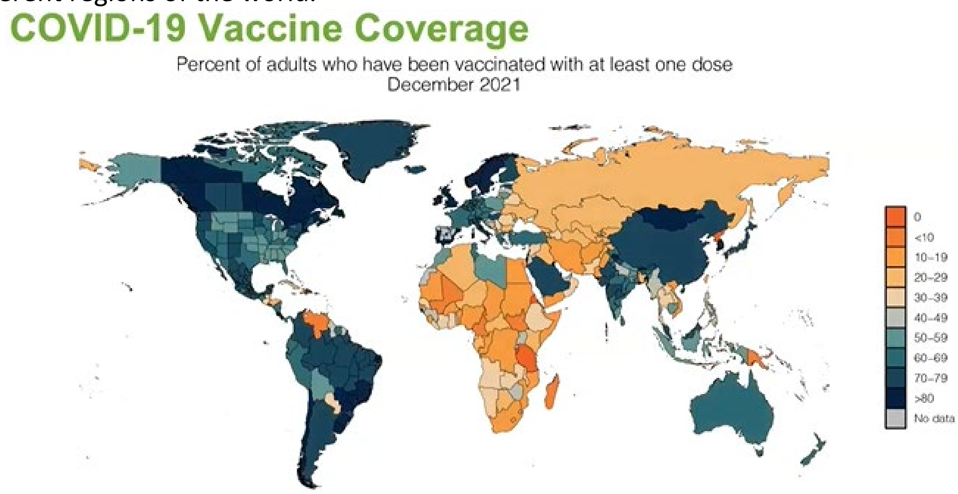
Weekly Production

1. Curation of case, hospitalization, death and seroprevalence data.
2. Input data and modeling exercises: vaccine scale-up, variant spread, mask use, mobility, social distancing measures.
3. Product weekly forecasts for all countries or locations with more than 5 cumulative COVID-19 deaths.
4. Public release of forecasts 4-months into future.
5. Public release of detailed policy briefs outlining input data, key drivers such as mobility, mask use, variant spread and vaccination scale-up
6. Models run to the end of 2022

Vaccination

- **Supply --** Combine data on manufacturer production capacity by quarter and purchasing agreements with manufacturers to determine supply by vaccine, geographic location, and time. Supplement production/purchasing data with data from country-specific reports.
- **Delivery**
    - **Initial Approach –** Exponential scale up over 60 days to a maximum delivery rate, model based on the maximum delivery rate of 3 million doses/day during seasonal flu. Adjusted/scaled for other locations based on healthcare access and quality index.
    - **Revised Approach –** More data helps fit the model better. Cascading spline model of locations with minimal supply constraints, calibrate scale-up curve to observed delivery, empirical dosing period.

- **Demand –** Proportion reporting they would or probably receive a COVID-19 vaccine used to determine the fraction of adults are likely to want to be vaccinated. Demand limit based on 10% dropout.
- Models project by the end of 2021 there will be large disparities in vaccine coverage across different regions of the world.



Determining the Impact of Vaccines in the Model

- Vaccine effectiveness -- use a ratio of vaccine effectiveness specific to different strains as an adjustment for clinical trial reported efficacies for each vaccine.
- Neutralizing antibody response as a predictor of cross variant immunity and vaccine efficacy
  - Neutralizing antibody response is a good predictor of vaccine efficacy and can be used to determine vaccine effectiveness against new/emerging variants
  - Limited evidence on cross-variant immunity and vaccine efficacy against variants of concern (VOCs)
  - Systematically analyze studies of neutralizing antibody response to predict cross variant immunity and efficacy against VOCs

Vaccine Hesitancy

- Working on a model to estimate vaccine hesitancy at the zip-code level
- Occupational analyses to target various occupational groups to inform vaccine outreach strategies.

Forecasts

- Expect numbers of infections to slowly increase through mid-fall.
- Longer range forecasts predict larger surge in the winter. Size of the surge will depend on how many have been naturally infected, vaccination, and other behavioral attributes.
- Winter surge will likely start later because of higher rates of immunity, predicted to peak in March.
- Vaccines more protective against deaths.

Discussion

- Seasonality and surges – statistical evidence of seasonality's impact on spread and most corona viruses are seasonal.
  - Summer 2020 in Brazil – B.1 appears, summer surge very much related to new variant, also related to the government and behavioral response.

- December 2020 surge in Europe
- IHME's model predicted US's winter surge when other models did not because it accounts for seasonality.