State of the pandemic

16th April 2020

cmetcalf@princeton.edu
Cases numbers driven by introductions and physical distancing

- New York
- New Jersey
- Illinois
- Texas
- Florida
Cases numbers driven by introductions and physical distancing

An emerging role for immunity
Cases numbers driven by introductions and physical distancing

An emerging role for immunity

Novel variants
Cases numbers driven by introductions and physical distancing

An emerging role for immunity

Novel variants

Vaccines
What do we know about the variants?

ACE2 expression falls

Binds ACE2, enters cells
What do we know about the variants?

- Binds ACE2, enters cells
- Starts to replicate
- Worse symptoms associated with replicating lower in the lungs
What do we know about the variants?

starts to replicate

Binds ACE2, enters cells

cleared by immunity

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What do we know about the variants?

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!immunity also drives many of the symptoms
What do we know about the variants?

New phenotypes from new variants
- increased **avidity** for ACE2
- increased **transmissibility**
- increased capacity to **overcome** natural or vaccinal immunity
- increased **virulence**

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B.1.1.7

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immunity also drives many of the symptoms

cleared by immunity
What do we know about the variants?

**New phenotypes from new variants**
- increased **avidity** for ACE2
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- increased **virulence**

**B.1.351**

- Binds ACE2, enters cells
- starts to replicate
- cleared by immunity
- worse symptoms associated with replicating lower in the lungs

Immunity also drives many of the symptoms.
What do we know about the variants?

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P1

*immunity also drives many of the symptoms
What do we know about the variants?

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Why the sudden surge in variants at the end of 2020?
What do we know about the vaccines?

• That we have **so many**, that they have shown such **high efficacy** in trials (and so far **effectiveness** in populations seems high), these are all extraordinary triumphs.

Authorised and recommended in the USA:
Pfizer-BioNTech
Moderna
Johnson & Johnson / Janssen

Others:
Astra-Zeneca
Cansino
Sinovac
Sinopharm
Novavax
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• Most trials had symptoms as the focal endpoint, not severe disease or prospects for transmission but accumulating evidence is generally positive.

Data from Israel

Rossman et al. Medarxiv
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- Critical questions remain about the duration of protection, can it be boosted, will it respond to mixing and matching of vaccine platforms, how will it hold in the face of variants?
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• What is the optimal **boosting interval**?
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• Can we identify in vitro surrogates of vaccine efficacy and protection? Increasingly important! Trials are going to become harder and harder to do.
What do we know about the vaccines?

- Can we identify *in vitro* surrogates of vaccine efficacy and protection? Increasingly important! Trials are going to become harder and harder to do.
“Africa will need about 1.5 billion doses of vaccine. (Its population is 1.2 billion, and most vaccine candidates require two doses.) The cost of the vaccine and of building systems and structures required for delivery is estimated at between $7 billion and $10 billion, according to Africa CDC. For comparison, the 2020 US PEPFAR budget was $6.9 billion.”

John N. Nkengasong (director of Africa CDC), Nicaise Ndemb (senior science adviser at Africa CDC), Akhona Tshangela (programme manager for mortality surveillance at Africa CDC), Tajudeen Raji (head of the division of public-health institutes and research at Africa CDC).
Getting Vaccines

Gavi is co-leading COVAX, the vaccines pillar of the Access to COVID-19 Tools (ACT) Accelerator. This involves coordinating the COVAX Facility, a global risk-sharing mechanism for pooled procurement and equitable distribution of COVID-19 vaccines.

https://www.gavi.org/covax-vaccine-roll-out

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Getting Vaccines

The African Vaccine Acquisition Task Team has also secured 250 million additional doses from Pfizer, AstraZeneca, and Johnson & Johnson.

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Last week, Johnson & Johnson pledged 400 million doses to the AU
Immune escape variants

• Vaccination that results in intermediate immunity might favour selection for immune escape variants

• There seems to be reasonable amounts of cross-protection among variants, i.e., immunity developed to escape variants seems likely to protect against other strains.

• The characteristics of secondary infections, or infection after vaccination are still very poorly known but are likely to govern the years to come.
Reporting of cases, and even of deaths may be extremely low, yielding a very incomplete picture of the state of the pandemic in much of the world.
The future

Hesitancy, equity, waning and evolution
The future

Hesitancy, equity, waning and evolution

How to mitigate? How to manage vaccine adverse events responses?
The future

Hesitancy, equity, waning and evolution

How to mitigate? How to manage vaccine adverse events responses?

How to manage global access to vaccine doses?
The future

Hesitancy, equity, waning and evolution

- How to mitigate? How to manage vaccine adverse events responses?
- How to manage global access to vaccine doses?
- How long does immunity last? What is the nature of secondary infections?
The future

Hesitancy, equity, waning and evolution

How to mitigate? How to manage vaccine adverse events responses?
How to manage global access to vaccine doses?
How long does immunity last? What is the nature of secondary infections?
Rate and context of emergence of variants? Vaccine update needs?
References

Future SARS-CoV-2 landscape of immunity:
https://science.sciencemag.org/content/early/2020/09/18/science.abd7343

An Immune Observatory to meet a time of pandemics
https://elifesciences.org/articles/58989

SARS-CoV-2 in SubSaharan Africa
https://www.nature.com/articles/s41591-021-01234-8

Mortality registration and detection of SARS-CoV-2 in Madagascar:

Thank you

C. Jessica E. Metcalf
cmetcalf@princeton.edu
@CJEMetcalf