

The background of the slide is a photograph of a brick building with many windows, partially obscured by trees. In the foreground, there is a large sculpture of an alligator standing on a globe, which is mounted on a brick pedestal. There are also some benches and bushes in the foreground. The entire image has a blue tint and some faint, glowing geometric patterns overlaid on it.

**UF**

# COVID-19: vaccines & therapeutics

Data Science Zoomposium

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# VACCINES



## COVID-19 vaccine platforms

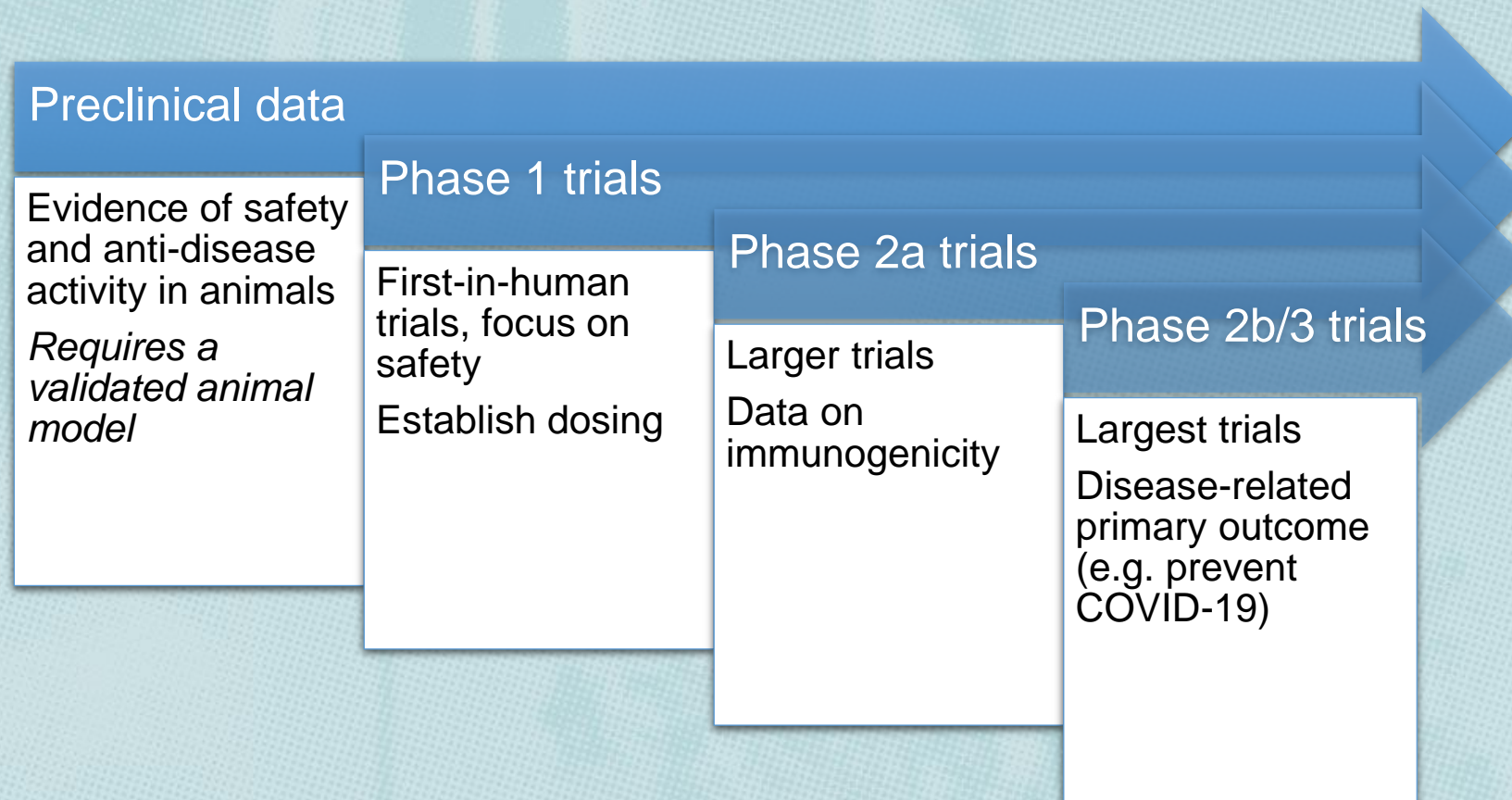
Over 50 vaccine candidates currently in development, utilizing a range of vaccine platforms

**Table: Summary of general attributes**

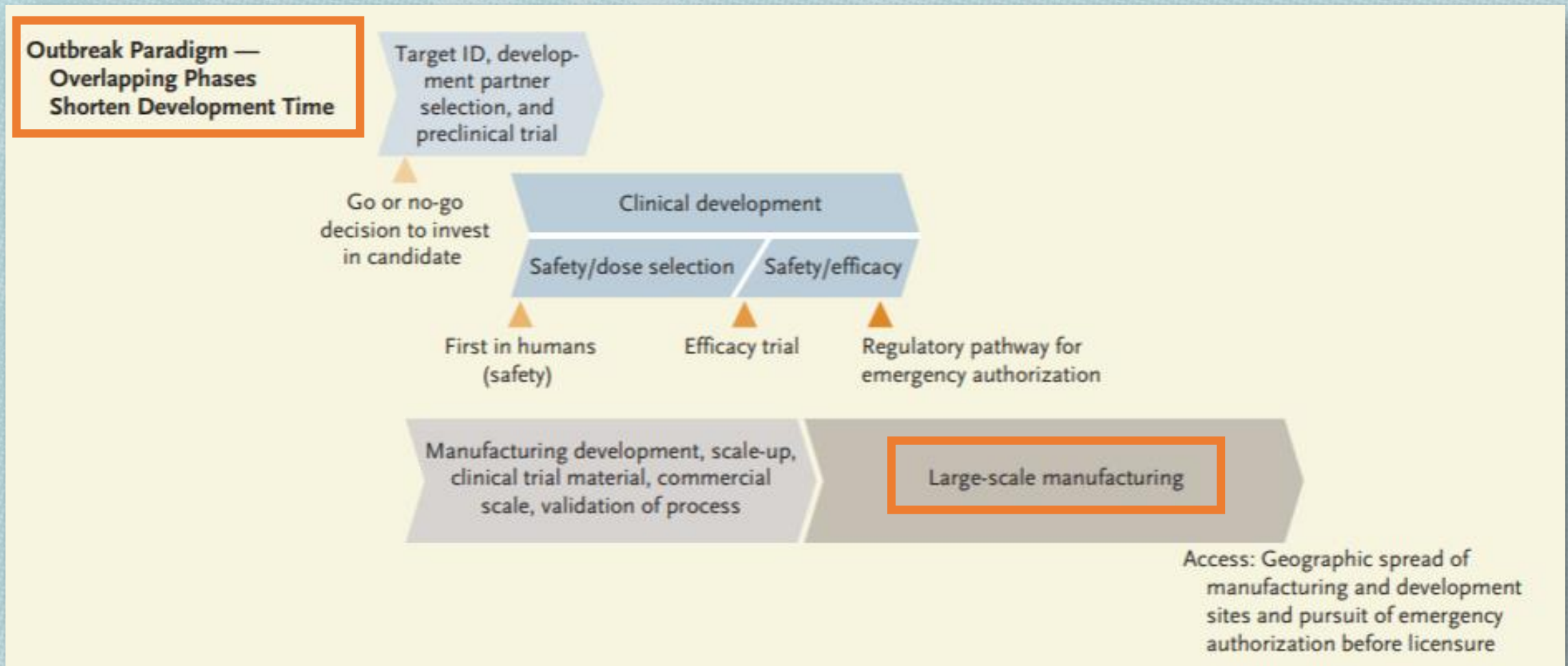
	Single dose	Licensed platform	Fast to develop
RNA			✓✓
DNA			✓✓
Non replicating vector	✓		✓
Inactivated		✓	✓
Live attenuated	✓	✓	
Replicating viral vector	✓	✓	✓
Protein subunit		✓	✓



## Typical regulatory pathway for vaccines



## Accelerated regulatory pathway for vaccines





## COVID-19 vaccine landscape (March 26, 2020)

### 2 candidate vaccines in clinical evaluation

Platform	Type of candidate vaccine	Developer	Coronavirus target	Current stage of clinical evaluation/regulatory status- Coronavirus candidate	Same platform for non-Coronavirus candidates
Non-Replicating Viral Vector	Adenovirus Type 5 Vector	CanSino Biological Inc. and Beijing Institute of Biotechnology	COVID-19	Phase 1 <a href="#">ChiCTR2000030906</a>	Ebola
RNA	LNP-encapsulated mRNA	Moderna/NIAID	COVID-19	Phase 1 <a href="#">NCT04283461</a>	multiple candidates

### 52 candidate vaccines in preclinical evaluation



## What to look out for with vaccines?

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- ❑ **Pay close attention to potential enhanced disease**
- ❑ **Enrollment may be strategically targeted**
  - Health-care workers, elder-care workers
- ❑ **Event-based monitoring**
  - Duration of the trial will depend on smart placement of the study sites



## Vaccine study site enrollment

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- ☐ Case-based surveillance
- ☐ Serosurveys!
- ☐ Spatially resolved models to integrate the two



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*R<sub>0</sub> for Zika by season  
& location per the  
GLEAM model*

Zhang et al. 2017 PNAS

<https://doi.org/10.1073/pnas.1620161114>

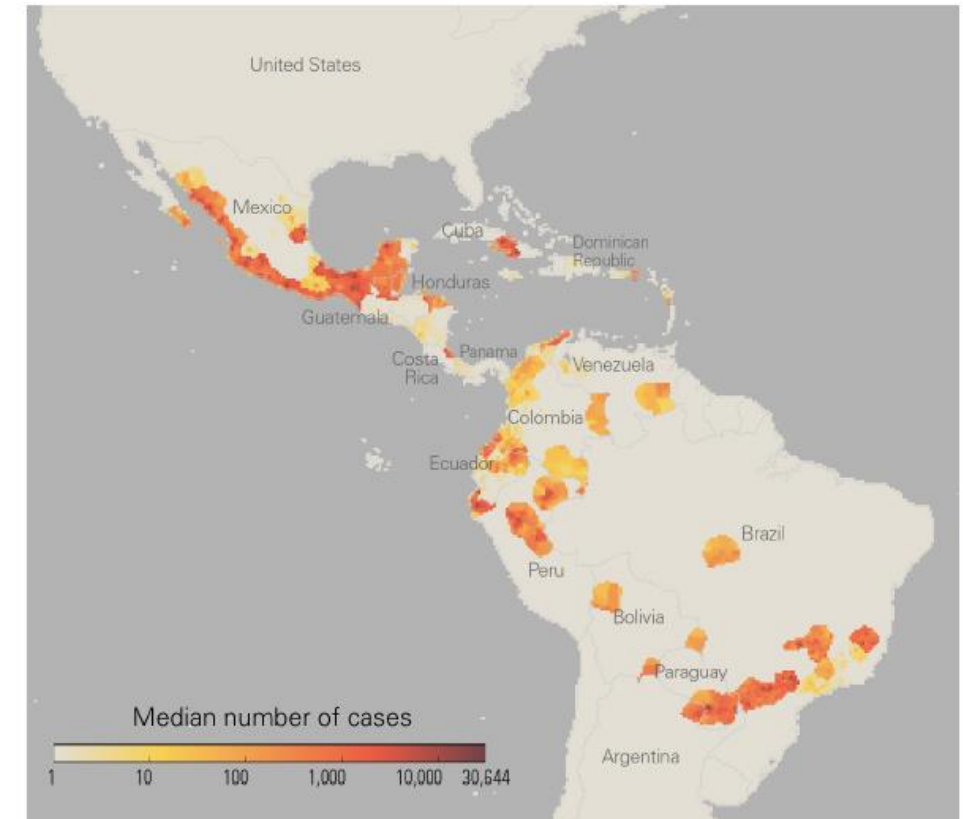
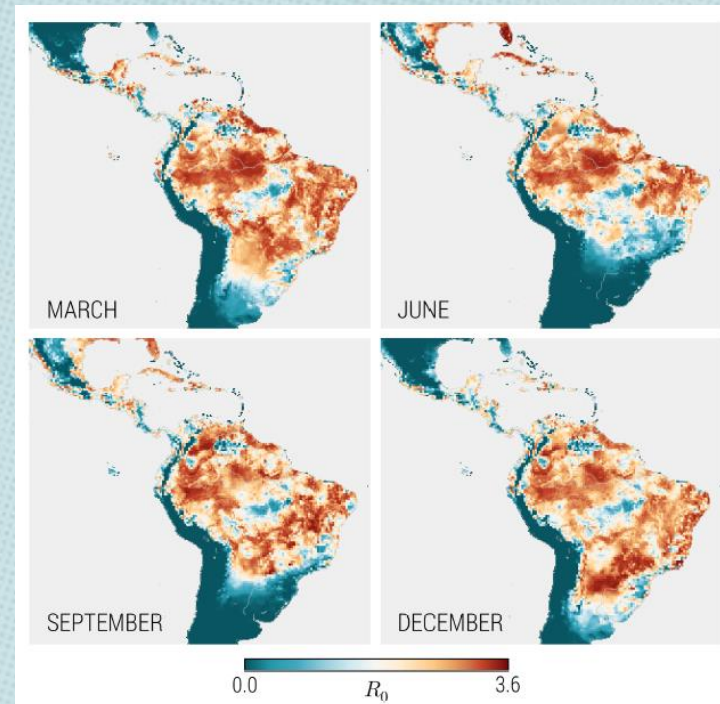


Figure 2. Median number of symptomatic cases for the affected areas in the Americas during the period January 2017 through December 2017, when we consider an infection rate of at least 10% during that period.

*Unpublished modeling to guide  
Zika vaccine site selection*



# THERAPEUTICS



## COVID-19 candidate therapeutics (a partial list)

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- ❑ **Chloroquine, hydroxychloroquine**
  - Antimalarial, safe, widely available\*\*
- ❑ **Lopinavir/ritonavir**
  - Protease inhibitor licensed for HIV
  - Can be provided with interferon-beta
- ❑ **Remdesivir**
  - Unlicensed broad-spectrum antiviral
- ❑ **Favipiravir**
  - Antiviral licensed for influenza in Japan
- ❑ **Tocilizumab, sarilumab, etc.**
  - Antibodies licensed for arthritis
  - Could prevent an over-reactive inflammatory response in the lungs
- ❑ **Convalescent plasma**
  - Accepting donations now!
- ❑ **Manufactured antibodies**
  - In development



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Currently there are no licensed therapeutics available for the treatment of COVID-19!



## Tips on interpreting therapeutic study results

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- ❑ ***In vitro* activity does not often translate into clinical benefit**
- ❑ **Randomization is crucial**
  - Therapeutics are typically only MILDLY or MODERATELY effective
  - Expected outcomes (e.g. mortality) depend heavily upon the population studied
- ❑ **Pay attention to the sample size → Absence of evidence is not evidence of absence**
- ❑ **Similarly, pay attention to the trial population**
  - Antivirals are most effective when provided early in the course of illness



## Pre- and Post-Exposure Prophylaxis

### ❑ Pre-exposure prophylaxis

- Example: Healthcare workers

### ❑ Post-exposure prophylaxis

- Example: Household contacts

### ❑ Early treatment

- Example: Recent symptom onset

*Target enrollment for a post-exposure prophylaxis and early treatment trial (<http://www.trialcovid.com>)*

We are looking for participants who fit these criteria:

#### 1. Exposed and WITHOUT symptoms

- Closely exposed to a person with confirmed/test-proven COVID-19 disease within 4 days of enrolling, AND
- Live in the same household as this person or are a healthcare worker, OR

#### 2. WITH symptoms

- Currently diagnosed with confirmed/test-proven COVID-19 disease within 4 days of symptom onset, OR
- Are a household contact or healthcare worker with a confirmed/test-proven COVID-19 contact, and are currently within the first 4 days of experiencing compatible symptoms with pending/unavailable testing
- Not currently hospitalized



## GENERAL PRINCIPLES



# TRIALS, TRIALS, AND MORE TRIALS

NEWS • 15 FEBRUARY 2020

## More than 80 clinical trials launch to test coronavirus treatments

As HIV drugs, stem cells and traditional Chinese medicines vie for a chance to prove their worth, the World Health Organization attempts to bring order to the search.

Amy Maxmen

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Scientific Title		
Search here below...		
<input type="checkbox"/> A Clinical Multicenter Study On The Occurrence, Development And Prognosis Of 2019 Ncov Infection <input type="checkbox"/> A Clinical Research For The Changes Of Blood Cortisol Acth Level And Adrenal Morphology In Blood Cortisol To Guide The Application Of Individualized Hormone In Severe N... <input type="checkbox"/> A Clinical Study About The Diagnosis And Prognosis Of Novel Coronacirus Pneumonia (Covid-19) Based On Viral Genome, Host Genomic Sequencing, Relative Cytokines And ... <input type="checkbox"/> A Clinical Study For Effectiveness And Safety Evaluation For Recombinant Chimeric Covid-19 Epitope Dc Vaccine In The Treatment Of Novel Coronavirus Pneumonia		

<https://www.nature.com/articles/d41586-020-00444-3>

<https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus/en/>



## Our recommendations (out today!)

*The NEW ENGLAND JOURNAL of MEDICINE*

### SOUNDING BOARD

## Creating a Framework for Conducting Randomized Clinical Trials during Disease Outbreaks

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## Guiding principles for clinical trial design

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- ❑ **Avoid the publication of inconclusive results**
  - Inconclusive results occur when studies are underpowered
  - Inconclusive results can jeopardize our ability to ever establish efficacy
- ❑ **One big trial is better than many small trials**
  - Working together, we are best equipped to rapidly achieve answers
- ❑ **Have a plan in place at the start of the trial**
  - Plan to expand to different locations
  - Plan to extend protocol into subsequent outbreaks



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WHO launches global megatrial of the four most promising coronavirus treatments

By Kai Kupferschmidt, Jon Cohen | Mar. 22, 2020 , 3:28 PM

<https://www.sciencemag.org/news/2020/03/who-launches-global-megatrial-four-most-promising-coronavirus-treatments>



**THANK YOU!**

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This work is supported by  
NIH/NIAID R01-AI139761