

# Life in the Time of COVID-19

Adrian Hernandez, MD

Susanna Naggie, MD

Eric Perakslis, PhD

# Disclosure

- This is a rapidly moving area and what we say in the *next hour* may not be true for the *following hour*.

# 3 Key Questions



What can we do as a community to address COVID-19?



What should we do with the ongoing research that millions of people are participating in currently?



How can we learn from this crisis to be better the next time (e.g. learning health system)?

# Agenda

- Current Status of COVID-19
- Impact on Current Trials and Approach
- COVID-19 Key Questions
  - Acute
  - Long-term
- Current Considerations & Potential Solutions

# Current Status of COVID-19

Susanna Naggie, MD

# Perspective

Provider in San Francisco

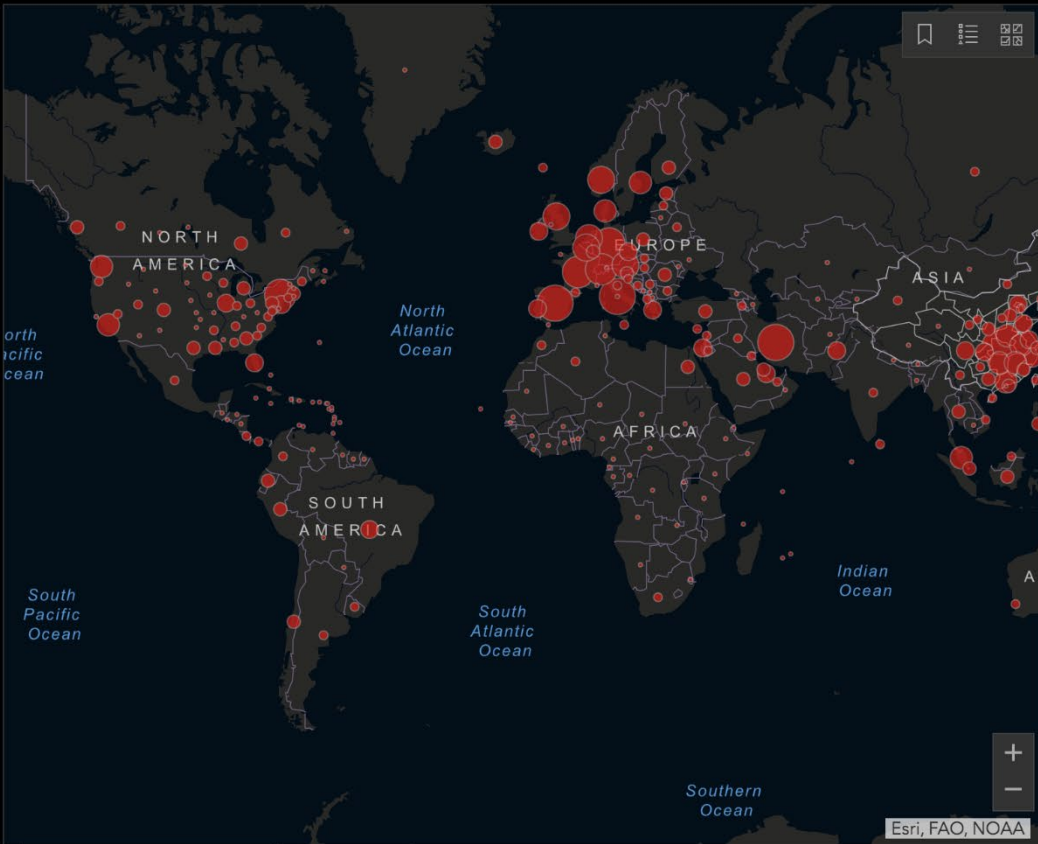
*“What made perfect sense an hour ago now seems completely ludicrous.... Things are moving so fast I am finding the need to have more agile approaches to things, and not getting to wed to any decisions we make because new information in the next hour could make them irrelevant.”*



Total Confirmed  
**245,484**

- Confirmed Cases by Country/Region/Sovereignty
- 81,250 China
  - 41,035 Italy
  - 18,407 Iran
  - 18,077 Spain
  - 16,290 Germany
  - 14,250 US
  - 10,891 France
  - 8,652 Korea, South
  - 4,164 Switzerland
  - 2,717 United Kingdom
  - 2,468 Netherlands
  - 2,013 Austria
  - 1,795 Belgium
  - 1,781 Norway
  - 1,439 Sweden

Country/Region/Sover...  
Last Updated at (M/D/YYYY)  
**3/20/2020, 6:13:39 AM**



Cumulative Confirmed Cases Active Cases

**163** countries/regions

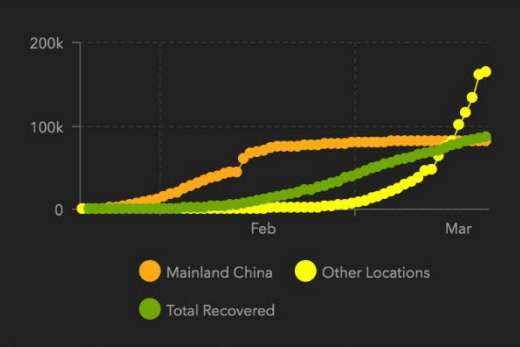
Lancet Inf Dis Article: [Here](#). Mobile Version: [Here](#). Visualization: JHU CSSE. Automation Support: [Esri Living Atlas team](#) and [JHU APL](#). Contact [US](#). [FAQ](#).  
Data sources: [WHO](#), [CDC](#), [ECDC](#), [NHC](#), [DXY](#), [1point3acres](#), [Worldmeters.info](#), [BNO](#), state and national government health department, and local media reports. Read more in this [blog](#).  
Downloadable database: [GitHub](#); [Here](#). Feature layer: [Here](#).

Total Deaths  
**10,031**

- 3,405 deaths Italy
- 3,133 deaths Hubei China
- 1,284 deaths Iran
- 833 deaths Spain
- 371 deaths France France
- 137 deaths United Kingdom United Kingdom
- 94 deaths Korea, South
- 76 deaths Netherlands Netherlands

Total Recovered  
**86,035**

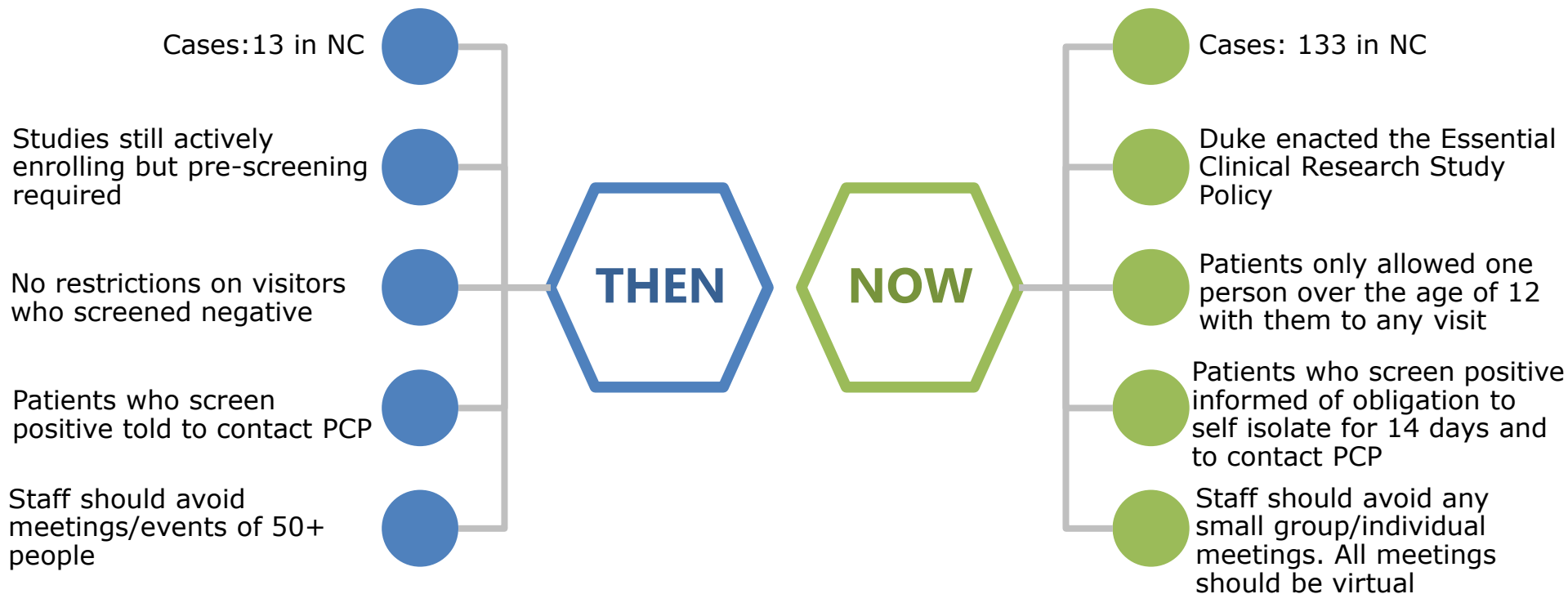
- 58,382 recovered Hubei China
- 5,979 recovered Iran
- 4,440 recovered Italy
- 1,540 recovered Korea, South
- 1,323 recovered Guangdong China
- 1,250 recovered Henan China
- 1,219 recovered Zhejiang China
- 1,107 recovered Spain



Actual Logarithmic Daily Cases

# COVID-19 THEN AND NOW

## How things change in a ~ 2 weeks





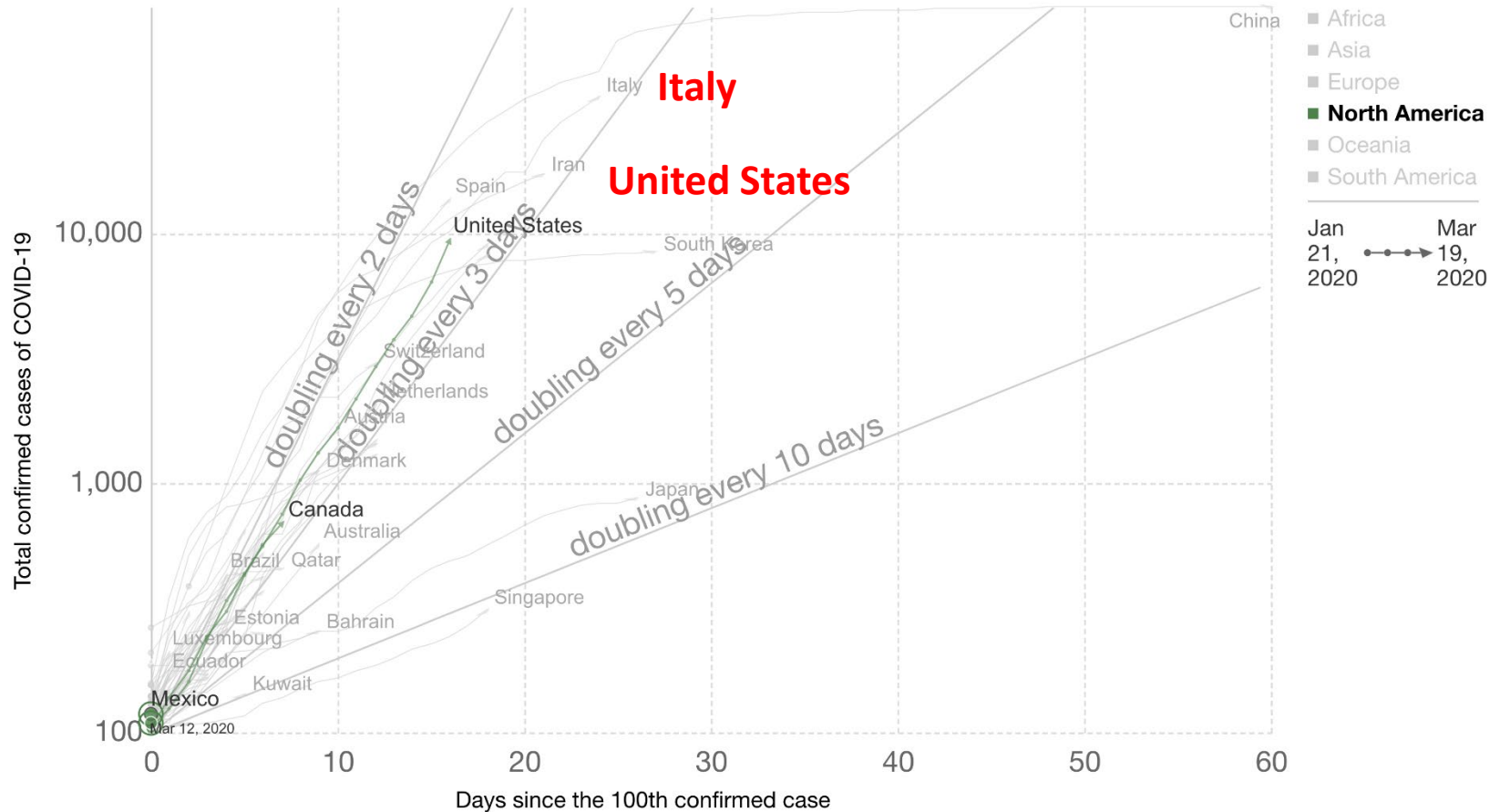
# Doubling Time Matters...

## Total confirmed cases of COVID-19

The starting point for each country is the day that country had reached 100 confirmed cases.

This allows us to compare the trajectory of confirmed cases between countries.

The number of confirmed cases is lower than the number of total cases. The main reason for this is limited testing.

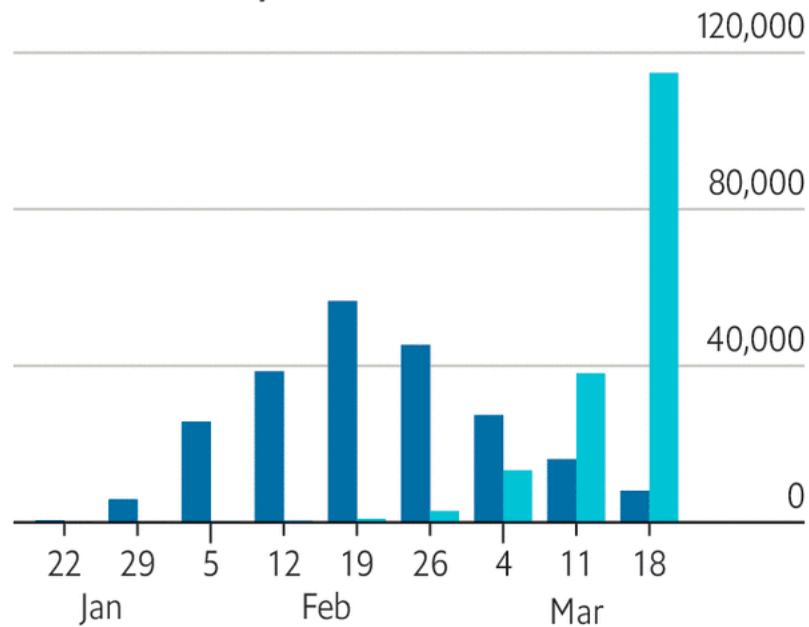


# Surge & Consequences

## The coronavirus crisis

2020

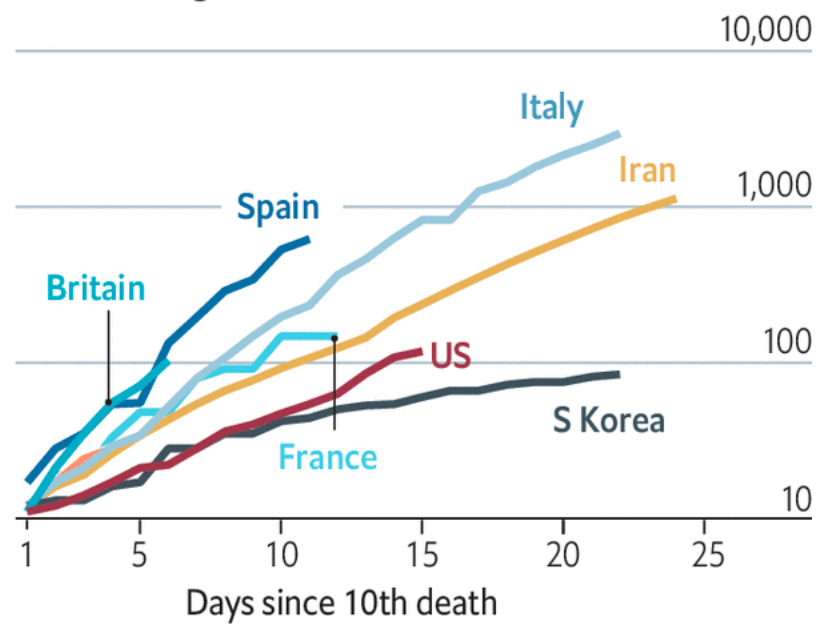
Active cases\*, by week



Sources: Johns Hopkins CSSE; NHS

The Economist

Deaths†, log scale



\*Confirmed cases minus recovered and dead †To March 18th 2020

# Why we need rapid answers?

## Case fatality rates: COVID-19 vs. US Seasonal Flu

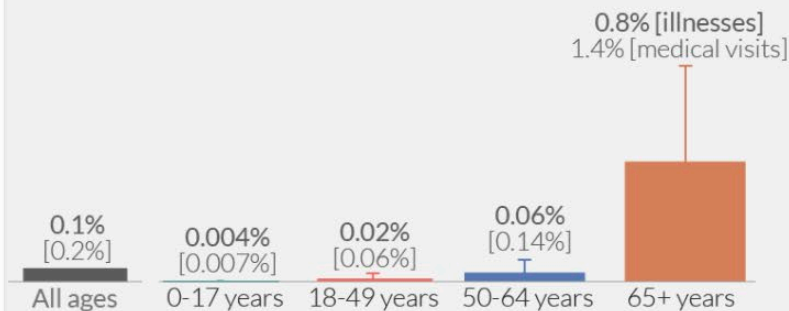
Our World  
in Data

Case fatality rate (CFR) is specific to a location and time. It is calculated by dividing the total number of deaths from a disease by the number of confirmed cases.

### Seasonal Flu

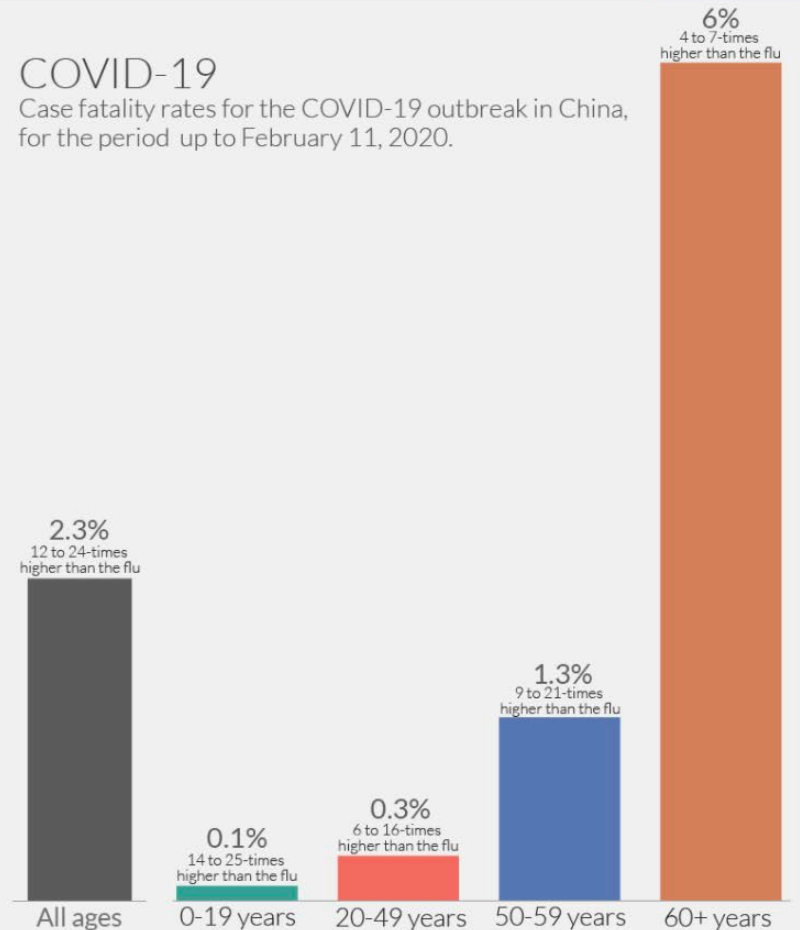
Case fatality rates for the influenza season 2018-19 in the USA.

Symptomatic cases are calculated based on models which aim to account for underreporting – figures based on medical visits are therefore also shown in square brackets, which may be a closer comparison to COVID-19 case fatality rates.



### COVID-19

Case fatality rates for the COVID-19 outbreak in China, for the period up to February 11, 2020.



Data: Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. *Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020.* China CDC Weekly.  
US Influenza data is sourced from the US Centers for Disease Control and Prevention (CDC).

OurWorldinData.org – Research and data to make progress against the world's largest problems.

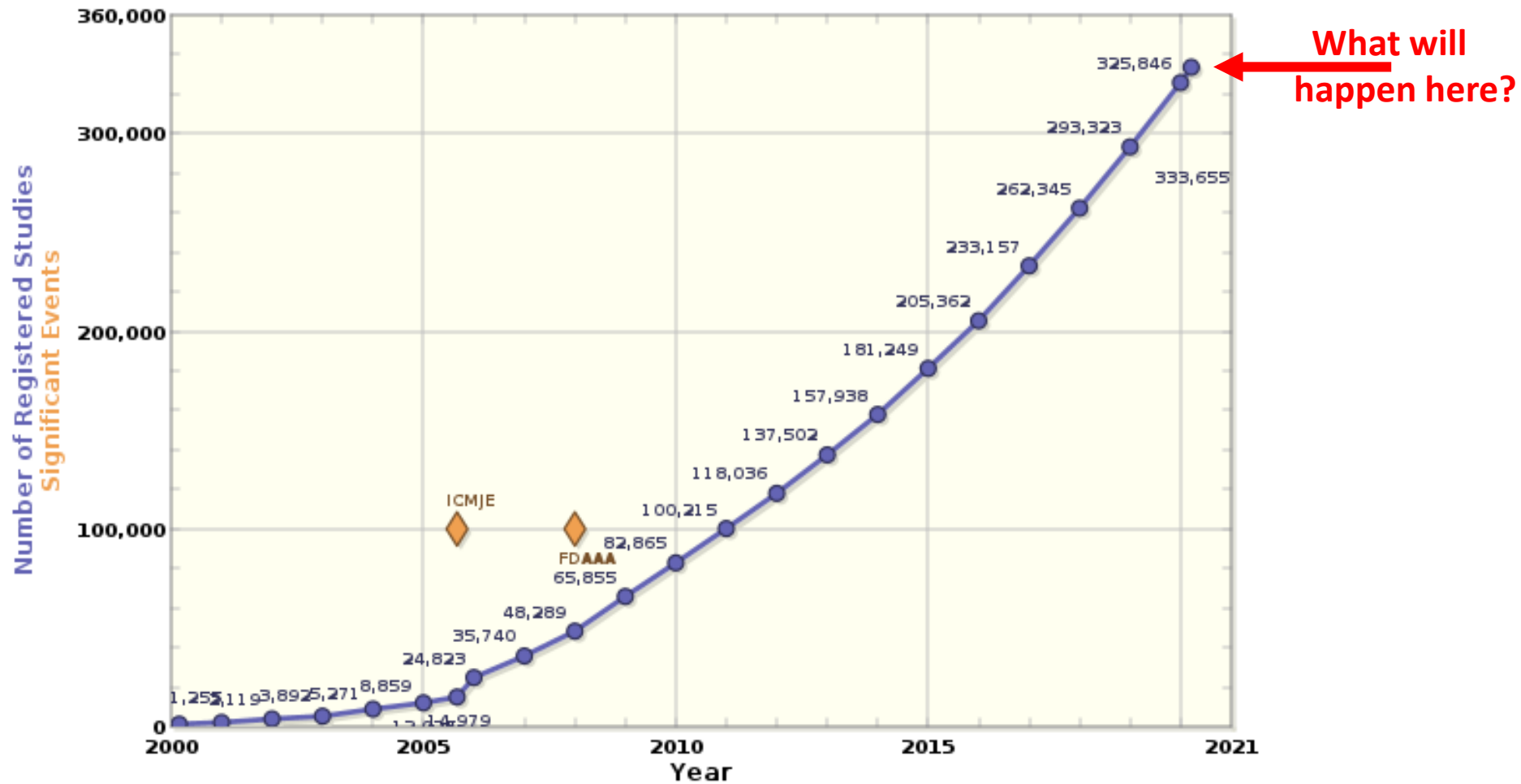
Licensed under CC-BY by the authors Hannah Ritchie and Max Roser.

# Impact on Current Trials and Approach

Adrian Hernandez, MD

# Number of Clinical Trials

Number of Registered Studies Over Time  
and Some Significant Events (as of March 18, 2020)

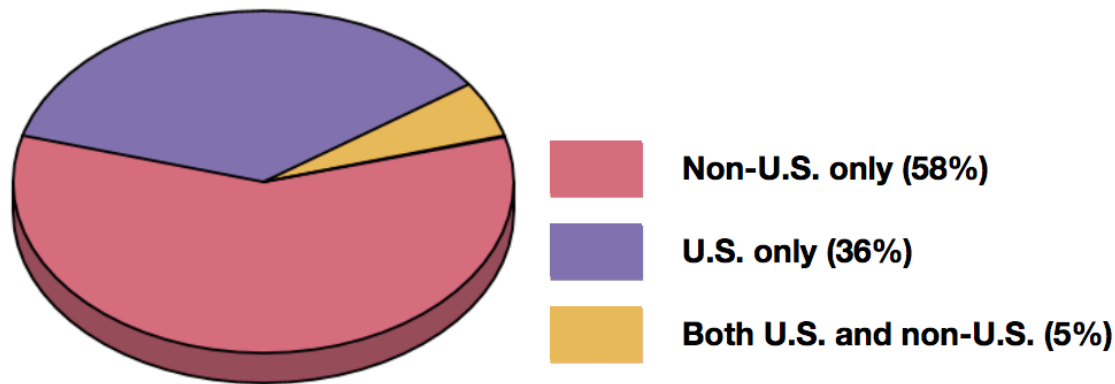


Source: <https://ClinicalTrials.gov>

# Total Number of Trials

## Percentage of Recruiting Studies by Location (as of March 18, 2020)

Total of 53,079 recruiting studies



<b>Location</b>	<b>Number of Recruiting Studies and Percentage of Total (as of March 18, 2020)</b>
Non-U.S. only	31,048 (58%)
U.S. only	19,118 (36%)
Both U.S. and non-U.S.	2,782 (5%)
Not provided	131 (0%)
Total	53,079 (100%)

# Some issues...

- Should you keep enrolling?
- Should you keep follow-up?
- How should you modify protocols **rapidly**?
- What happens with data adversely effected by COVID19 disruptions?

# NEW FDA guidance

For all trials that are impacted by the COVID-19 pandemic:

- Sponsors should describe in appropriate sections of the clinical study report (or in a separate study-specific document):
  - 1. Contingency measures implemented to manage study conduct during disruption of the study as a result of COVID-19 control measures.
  - 2. A listing of all participants affected by the COVID-19 related study disruption by unique subject number identifier and by investigational site, and a description of how the individual's participation was altered.
  - 3. Analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., trial participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the study.

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-pandemic>



# Benefits and Risks

- Providing access for patients to protocols when alternatives don't exist
- Limiting risk
  - To potential participants
  - To research staff
  - Propagating community exposure

# An Approach:



*Tier 1 (Essential)* – High Potential Direct Benefit to Research Participants

*Tier 2 (Essential)*- Moderate Potential Direct Benefit to Research Participants

*Tier 3 (Non-essential)*- Primarily observational, behavioral studies without potential direct benefit

# An Approach:

## Study Classification

***Tier 1 (Essential)*** – High Potential Direct Benefit to Research Participants

***Tier 2 (Essential)***- Moderate Potential Direct Benefit to Research Participants

***Tier 3 (Non-essential)***- Primarily observational, behavioral studies without potential direct benefit

## Actions

- Enrollment allowed
- Convert to virtual visits as much as possible
  
- Suspend enrollment
- Convert to virtual visits as much as possible with likely all visits virtual/tele
  
- Suspend enrollment
- Convert all visits to virtual/tele

# A time for new research models...

## Direct to Participant

## A couple of case examples

- Personalized
- Streamlined
- Valuable
- Safer...?

2019/2020 Influenza/RSV Program #1	2019/2020 Influenza Program #2
4 month 1-arm observational study of influenza and RSV	10 month 1-arm observational study of influenza and complications  Part 11 compliant
<ul style="list-style-type: none"><li>• Daily 1-click (short survey) and follow up symptom surveys</li><li>• Activity trackers</li><li>• Self swab diagnostics kit</li><li>• Real-time diagnostics test kit</li></ul>	<ul style="list-style-type: none"><li>• Daily 1-click (short survey) and follow up symptom surveys</li><li>• Activity trackers</li><li>• Follow-on on complications survey</li><li>• Self swab diagnostics kit</li></ul>
<ul style="list-style-type: none"><li>• <b>Speed and Scale: 100% enrollment hit: 5,200 individuals in 8 weeks</b></li></ul>	<ul style="list-style-type: none"><li>• <b>Speed and Scale: 100% enrollment hit: 10,000 individuals in 7 weeks</b></li></ul>
<ul style="list-style-type: none"><li>• 86% wearable data compliance</li><li>• 87% daily survey completion</li></ul>	<ul style="list-style-type: none"><li>• 89% Fitbit daily wear</li><li>• 88% daily survey completion</li></ul>

[www.evidation.com](http://www.evidation.com)

[bpatricklake@evidation.com](mailto:bpatricklake@evidation.com)

# COVID-19 Key Questions

## Acute

## Long-term

# Acute Questions

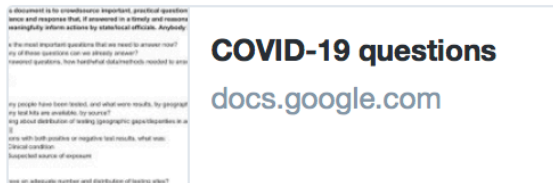
## 2-3 weeks, 2-3 months



**Aaron McKethan**

@A\_McKethan

Researchers want to help w COVID, which as @Farzad\_MD posted this morning, starts with defining good Qs. Since issues are common, let's ce and edit a list of the most important Qs every jurisdiction needs to answer. Please edit & post comments [docs.google.com/document/d/14R...](https://docs.google.com/document/d/14R.../14R...)

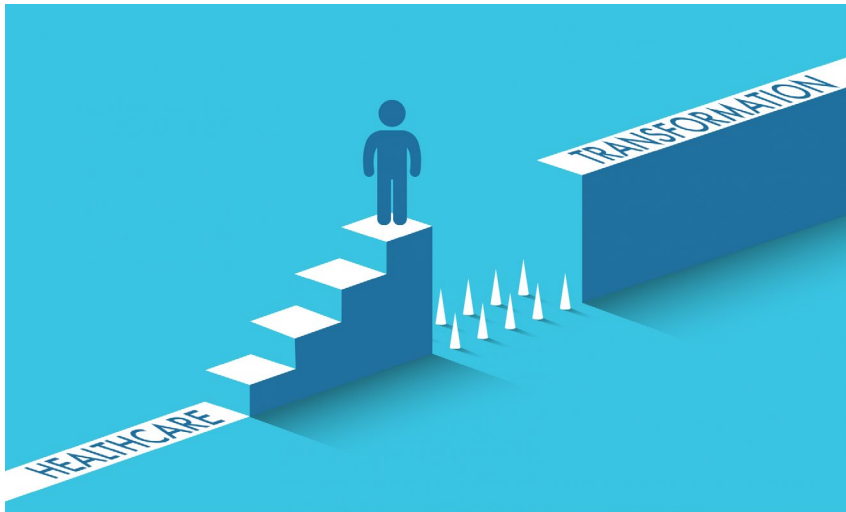


- Surveillance
- Predicted medical demand
- Current and predicted hospital demand
- Point of Care Diagnostics
- Co-morbidities, other drugs
  - ACE/ARB
  - NSAIDs
- Interventions
  - Treatment
  - Prophylaxis
  - High risk
  - Vulnerable populations
  - Pregnancy

- <https://docs.google.com/document/d/14RFaKgRnf7CiczplpEaCpMX3 - AuVG7FwEBE9Lq9SQ/edit>

# Longer Term Questions

## 6-12 months and beyond



- Prevention
  - Vaccine
- Pandemic response system
- Healthcare transformation
- Healthcare disparities
- Post-COVID-19 management
  - Mental health
  - Recovery

# Regulatory Considerations

## Advancing Treatments to Save Lives and Reduce the Risk of COVID-19

March 19, 2020

### Duke-Margolis Paper Details Strategies to Treat COVID-19

Scott Gottlieb and Mark McClellan Co-Author

**Durham, NC**— Efficiently launching medical products to combat the current and Drug Administration's (FDA) work with manufacturers that have high potential and prophylactics, stated former FDA Commissioners Scott Gottlieb, MD and the Duke-Margolis Center for Health Policy.

The co-authors call for FDA to establish two task forces: one focused rapid development of effective therapeutics and prophylaxis. In addition nationwide COVID-19 surveillance partnership to support these efforts and

"We need these drugs and testing tools to help patients now. We also need

## Key Areas:

- Point of care diagnostics
- Therapeutics and Prophylaxis
- Surveillance

[https://healthpolicy.duke.edu/sites/default/files/atoms/files/covid-19\\_tx\\_working\\_paper.pdf](https://healthpolicy.duke.edu/sites/default/files/atoms/files/covid-19_tx_working_paper.pdf)

FDA NEWS RELEASE

## Coronavirus (COVID-19) Update: FDA Continues to Facilitate Development of Treatments

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**For Immediate Release:** March 19, 2020

The U.S. Food and Drug Administration continues to play a critical role in the multifaceted all-of-government response to the COVID-19 pandemic, which includes, among other things, facilitating medical countermeasures to treat and prevent the disease, and surveilling the medical product and food supply chains for potential shortages or disruptions and helping to mitigate such impacts, as necessary.

As part of those efforts, President Trump has directed the FDA to continue its work with the public and private sector to ensure the availability of potentially safe and effective life-



# Current Considerations & Potential Solutions


Eric Perakslis, PhD

## Essential Considerations

- Continuity – Airway (connectivity), Breathing (capability), Circulation (productivity of systems and processes)
- Care – best and safest care environment and outcomes
- Research – assurance of clin ops, supply chain, data and sample integrity etc

# Digital Tools can Ensure Ethical Practices

 **BMC** Part of Springer Nature

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**Conflict and Health**

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Review | [Open Access](#) | [Published: 14 May 2018](#)

## Using digital health to enable ethical health research in conflict and other humanitarian settings

[Eric D. Perakslis](#) 

[Conflict and Health](#) **12**, Article number: 23 (2018) | [Cite this article](#)

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**Rule #1: Do not drop standards or obligations**

# Priority Outbreak Informatics Use cases

## What is contact tracing?

Contact tracing can stop an Ebola outbreak in its tracks



U.S. Department of Health and Human Services  
Centers for Disease Control and Prevention

**Contact tracing** is finding everyone who comes in direct contact with a sick Ebola patient. Contacts are watched for signs of illness for 21 days from the last day they came in contact with the Ebola patient. If the contact develops a fever or other Ebola symptoms, they are immediately isolated, tested, provided care, and the cycle starts again—all of the new patient's contacts are found and watched for 21 days. **Even one missed contact can keep the outbreak going.**

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## 3 Lessons from Contact Tracing During the Ebola Outbreak

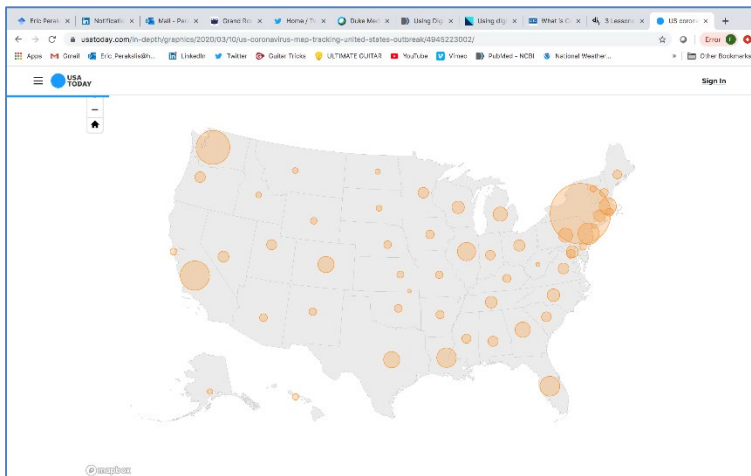
March 7, 2016

# Enabling and Enhancing Telehealth

## Real-time Telehealth Geospatial Dashboard **During Sessions**

Opportunity to use data from telehealth consults to provide a real-time geo-spatial map of telehealth consults and the resulting/associated covid-19 testing results.

1. Data, such as IP addresses, already exists within these systems
2. Privacy preserved via tokenization technologies
3. Could be done to the address, city-block or census block level (the last two most likely to be privacy-preserving)
4. Primary use cases are triage and risk determination
5. The value and utility would be greatly enhanced if executed in conjunction with the standardized, lightweight collection form



# A Standardized Lightweight Case Collection Form

Collect questions - lots of tests done, still lots of unknowns, don't know about community spread, how to gain epidemiological value - creating the 5 questions - all states should have visibility. Generate and propose it. Great precedent from WHO during EVD outbreak in West Africa.

## 1. What are the most common questions?

- ILI symptomology
- Contact information
- Background medical history (vulnerability)
- Testing information
- ...

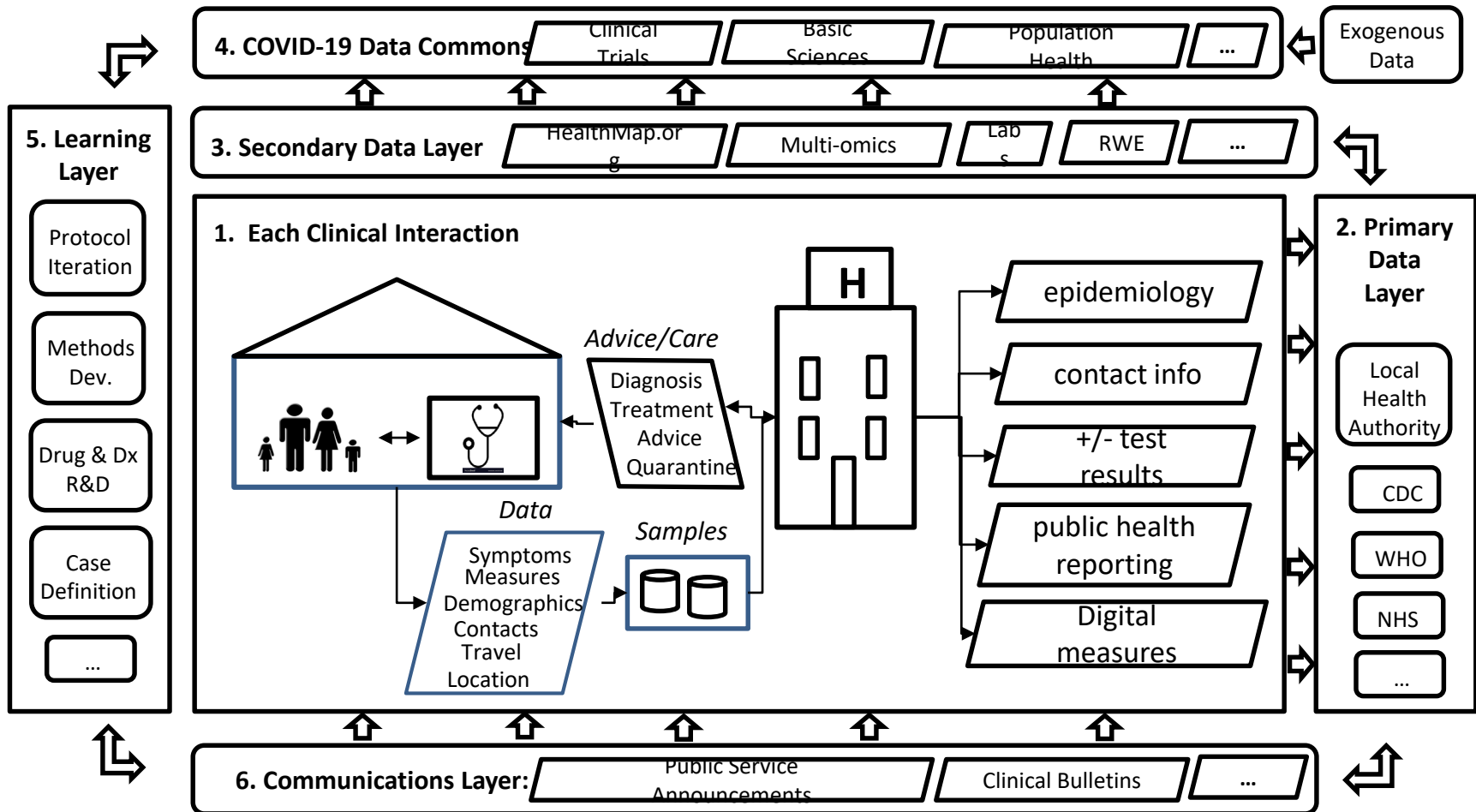
## 2. How to standardize collection and dissemination?

- Mobile app
- National Registry
- Single protocol under change control @ CDC
- Online training

# Other Outbreak Informatics Use cases

1. Did any pts. go to the ED with fever, cough, etc.? Un-filter ADT feeds, include Medicare feeds, **aggregate and push**
2. Syndromic surveillance – have the ER registration data – are the huge increases covid-related? Is there an increase in Influenza-like-illnesses (ILI) visits? Negative flu testing? Smart Search?
3. How to acquire certain specific data – supply chain. Verily search?

# A Telehealth-based Outbreak Learning Health Unit





# Discussion



What can we do as a community to address COVID-19?



What should we do with the ongoing research that millions of people are participating in currently?



How can we learn from this crisis to be better the next time (e.g. learning health system)?