• 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)?
• 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
"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."

Provider in San Francisco
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
- 4,146 Switzerland
- 2,717 United Kingdom
- 2,468 Netherlands
- 2,013 Austria
- 1,795 Belgium
- 1,781 Norway
- 1,439 Sweden

Total Deaths:
- 10,031
  - 3,405 deaths Italy
  - 3,133 deaths Hubei, China
  - 1,284 deaths Iran
  - 833 deaths Spain
  - 371 deaths France

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


https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6
COVID-19 THEN AND NOW

How things change in a ~ 2 weeks

Then:
- Cases: 13 in NC
- Studies still actively enrolling but pre-screening required
- No restrictions on visitors who screened negative
- Patients who screen positive told to contact PCP
- Staff should avoid meetings/events of 50+ people

Now:
- Cases: 133 in NC
- Duke enacted the Essential Clinical Research Study Policy
- Patients only allowed one person over the age of 12 with them to any visit
- Patients who screen positive informed of obligation to self isolate for 14 days and to contact PCP
- Staff should avoid any small group/individual meetings. All meetings should be virtual
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.

Source: European Centre for Disease Prevention and Control (ECDC)
Surge & Consequences

The coronavirus crisis
2020

Active cases*, by week

Deaths†, log scale

Sources: Johns Hopkins CSSE; NHS

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

The Economist
Why we need rapid answers?

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

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.


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
Total Number of Trials

Percentage of Recruiting Studies by Location (as of March 18, 2020)
Total of 53,079 recruiting studies

- Non-U.S. only (58%)
- U.S. only (36%)
- Both U.S. and non-U.S. (5%)

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

• 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**
- Personalized
- Streamlined
- Valuable
- Safer...?

### A couple of case examples

<table>
<thead>
<tr>
<th>2019/2020 Influenza/RSV Program #1</th>
<th>2019/2020 Influenza Program #2</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 month 1-arm observational study of influenza and RSV</td>
<td>10 month 1-arm observational study of influenza and complications</td>
</tr>
<tr>
<td>- Daily 1-click (short survey) and follow up symptom surveys</td>
<td>- Daily 1-click (short survey) and follow up symptom surveys</td>
</tr>
<tr>
<td>- Activity trackers</td>
<td>- Activity trackers</td>
</tr>
<tr>
<td>- Self swab diagnostics kit</td>
<td>- Follow-on on complications survey</td>
</tr>
<tr>
<td>- Real-time diagnostics test kit</td>
<td>- Self swab diagnostics kit</td>
</tr>
<tr>
<td>- <strong>Speed and Scale</strong>: 100% enrollment hit: 5,200 individuals in 8 weeks</td>
<td>- <strong>Speed and Scale</strong>: 100% enrollment hit: 10,000 individuals in 7 weeks</td>
</tr>
<tr>
<td>- 86% wearable data compliance</td>
<td>- 89% Fitbit daily wear</td>
</tr>
<tr>
<td>- 87% daily survey completion</td>
<td>- 88% daily survey completion</td>
</tr>
</tbody>
</table>

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

bpatriclake@evidation.com
COVID-19 Key Questions

Acute

Long-term
Acute Questions
2-3 weeks, 2-3 months

- 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/14RFaKgRnf7CicazplpEaCpMX3_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 COVID-19 pandemic is key, and the Food and Drug Administration's (FDA) work with manufacturers that have high priority diagnostics, therapeutics, and prophylactics, stated former FDA Commissioners Scott Gottlieb, MD and Mark McClellan, MD, of the Duke-Margolis Center for Health Policy.

The co-authors call for FDA to establish two task forces: one focused rapid development of diagnostics, and one focused on rapid development of effective therapeutics and prophylaxis. In addition, they call for the FDA to establish an immediate nationwide COVID-19 surveillance partnership to support these efforts and the speed of decision-making.

"We need these drugs and testing tools to help patients now. We also need to be nimble about the entire public health response," stated Co-Author Scott Gottlieb, MD of the Duke-Margolis Center for Health Policy. "We need to learn from this experience, to be better prepared for the next pandemic."

Key Areas:
- Point of care diagnostics
- Therapeutics and Prophylaxis
- Surveillance

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

Rule #1: Do not drop standards or obligations
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.

3 Lessons from Contact Tracing During the Ebola Outbreak

March 7, 2016
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
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
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

1. Each Clinical Interaction
   - Data: Symptoms, Measures, Demographics, Contacts, Travel, Location
   - Samples
   - Advice/Care: Diagnosis, Treatment, Advice, Quarantine

2. Primary Data Layer
   - Epidemiology
   - Contact info
   - +/- test results
   - Public health reporting
   - Digital measures

3. Secondary Data Layer
   - HealthMap.org
   - Multi-omics
   - Labs
   - RWE

4. COVID-19 Data Commons
   - Clinical Trials
   - Basic Sciences
   - Population Health

5. Learning Layer
   - Protocol Iteration
   - Methods Dev.
   - Drug & Dx R&D
   - Case Definition

6. Communications Layer:
   - Public Service Announcements
   - Clinical Bulletins

Exogenous Data

Local Health Authority
- CDC
- WHO
- NHS
- ...
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?

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