Evidence Mobilization Action Collaborative

Webinar
July 28, 2020 | 10:00 AM – 1:45 PM EST

Share your thoughts!

@theNAMedicine

NATIONAL ACADEMY OF MEDICINE
Welcome & Introduction

Michael McGinnis
National Academy of Medicine
Learning Health System

"A learning health care system is one in which science, informatics, incentives, and culture are aligned for continuous improvement, innovation, and equity, with best practices seamlessly embedded in the care process, patients and families active participants in all elements, and new knowledge captured as an integral by-product of the care experience."

NAM Leadership Consortium Charter, 2006
Learning Health System Series
# Anchor Principles

...for health system performance

<table>
<thead>
<tr>
<th>Quality Chasm</th>
<th>Learning Health System</th>
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<tr>
<td>✓ Patient-centered</td>
<td>✓ Personal</td>
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<td>✓ Effective</td>
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<td>✓ Secure</td>
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COVID-19 Sector Impact Assessments

1. Patients, families, and consumers
2. Clinicians and professional societies
3. Care delivery organizations
4. Digital health
5. State and local public health
6. Health payers
7. Health product manufacturers and innovators
8. Health and biomedical research
9. Quality, safety, and standards
Evidence Mobilization
Action Collaborative Chairs

Rick Kuntz
Medtronic

Rich Platt
Harvard University
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:00 – 10:15 AM</td>
<td>Welcome</td>
<td>Michael McGinnis, National Academy of Medicine, Rich Platt, Harvard University, Rick Kuntz, Medtronic</td>
</tr>
<tr>
<td>10:15 – 10:30 AM</td>
<td>Strategic Framing</td>
<td>Michael McGinnis, National Academy of Medicine, Collaborative Co-chairs</td>
</tr>
<tr>
<td>10:30 – 11:00 AM</td>
<td>COVID-19 Pandemic: Tracking and Tracing</td>
<td>Ashish Jha, Harvard T.H. Chan School of Public Health</td>
</tr>
<tr>
<td>11:30 – 12:00 PM</td>
<td>COVID-19 Pandemic: Treatment</td>
<td>Carlos del Rio, Emory University School of Medicine</td>
</tr>
<tr>
<td>Time</td>
<td>Event</td>
<td>Speaker/Details</td>
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<tr>
<td>12:00–12:15 PM</td>
<td>Break</td>
<td></td>
</tr>
<tr>
<td>12:45–1:15 PM</td>
<td>FDA Evidence Accelerator</td>
<td>Amy Abernethy, Food and Drug Administration</td>
</tr>
<tr>
<td>1:15–1:30 PM</td>
<td>Reflection From Speakers</td>
<td></td>
</tr>
<tr>
<td>1:30–1:45 PM</td>
<td>Summary of Next Steps and Closing Remarks</td>
<td>Michael McGinnis, National Academy of Medicine</td>
</tr>
<tr>
<td>1:45 PM</td>
<td>Adjourn</td>
<td></td>
</tr>
</tbody>
</table>
Zoom Instructions

Panelists

• Always keep your line muted unless you are called on to speak
• If possible, turn on video while speaking to the group. To enable video click the ‘start video’ option at the bottom left of your screen

Attendees - Q & A

• Please type in questions into the Q&A located at the bottom of the screen on your zoom interface
• Question format:
  • Your name and organization
  • To whom
  • Question
Strategic Framing
Anchor principles for stewards of evidence generation and use

Organizations and individuals developing, interpreting, and applying evidence in a learning health system are responsible for assuring that the activities are:

<table>
<thead>
<tr>
<th>Principle</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Personal</strong></td>
<td>Services assessed and delivered are tailored to circumstances and individual goals.</td>
</tr>
<tr>
<td><strong>Safe</strong></td>
<td>Health services and research contain safeguards against unintended harm.</td>
</tr>
<tr>
<td><strong>Effective</strong></td>
<td>Services delivered are supported by, and contribute to, best available evidence.</td>
</tr>
<tr>
<td><strong>Equitable</strong></td>
<td>Evidence is generated and applied using objective standards to eliminate bias.</td>
</tr>
<tr>
<td><strong>Efficient</strong></td>
<td>Evidence is provided in content, form, and manner appropriate to need.</td>
</tr>
<tr>
<td><strong>Accessible</strong></td>
<td>Relevant evidence is available at the point of service.</td>
</tr>
<tr>
<td><strong>Transparent</strong></td>
<td>Evidence is transparent as to source, strength, and applicability.</td>
</tr>
<tr>
<td><strong>Adaptive</strong></td>
<td>Evidence protocols are continuously assessed for, and responsive to, new information.</td>
</tr>
<tr>
<td><strong>Secure</strong></td>
<td>Personal health data are securely tracked, reported, and stored.</td>
</tr>
</tbody>
</table>
Candidate dashboard indicators

• % of standardized **national guidelines** supported by high quality evidence

• % of health **care delivered and reimbursed** which is supported by high quality evidence

• % of **individuals endorsing** protected use of their personal health data for evidence generation, using an understandable, uniform consent vehicle
Evidence Generation During the COVID-19 Pandemic: Tracking and Tracing
Ashish Jha
Harvard T.H. Chan
School of Public Health
Question & Answer

Panelists

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Evidence Generation During the COVID-19 Pandemic: Clinical Presentation
Howard Zucker
Health Commissioner
State of New York
New York State’s Pandemic Response: Identifying Documenting, and Communicating Novel Presentation of COVID-19

Howard Zucker, M.D., J.D.
Commissioner of Health, New York State

National Academy of Medicine Leadership Consortium • July 28, 2020
How did we get down from the mountain?

% Positive Tests per Day (7-day rolling average)
Channels for COVID-19 Evidence Generation in NYS

- **Guidance & Policy:** 124+ provider documents released
- **Diagnostics:** Identifying those who have COVID-19
- **Serology:** Identifying those who had COVID-19
- **Contract Tracing:** Finding/isolating those who might have COVID-19
- **Therapeutics:** Treatments for novel presentations of COVID-19
- **Data Communication:** COVID-19 Tracker & Early Warning Dashboard
Guidance & Polices Sources

Before First Case
- Clinical data from China
- Epidemiologic data from WHO-China Joint Mission
- CDC case definitions & testing/isolation/quarantine guidance

Outbreak Phase
- NYS data collection
- CDC Epi-Aid
- CDC case definitions & testing/isolation/quarantine guidance
- Academic studies
NYS Case Counts and State Policy Directives

Source: https://coronavirus.jhu.edu/data/state-timeline/new-confirmed-cases/new-york/1
New York State COVID-19 Testing

February 29, 2020

- 2 FDA EUA molecular assays, including test from Wadsworth Center

July 21, 2020

- 117 molecular diagnostic assays (4 POC)
- 2 antigen-based diagnostic assays
- 31 serology assays
New York State COVID-19 Testing Operations

Mobile Testing Sites
- Set up **40 drive-through & walk-in sites** statewide to collect specimen samples from individuals
- Each drive-through site staffed by several state, county, and local agencies
- State partnered with Department using our Incident Command System and organizational structure

Wadsworth Center Laboratory
- Performed **2,000+ diagnostic & 2,000+ serologic (antibody)** tests per day.
- Over **70+ laboratory personnel** were engaged from other parts of the Lab to provide adequate coverage for round-the-clock operations.
Increasing NYS Laboratory Testing Capacity

Clinical Laboratories (CLIA) Reporting PCR Diagnostic and Serology Results for NYS Specimens

- Wadsworth Center Public Health Laboratory
- NYS, NYC, and County Public Health Laboratories
- In-State Commercial and Hospital Laboratories
- Out-of-State Commercial Laboratories
- Surveillance Laboratories
# Antibody Testing

## Department of Health Serology Initiative Wadsworth DBS Sample

<table>
<thead>
<tr>
<th>Population Tested</th>
<th>Region</th>
<th>Number Tested</th>
<th>Percent Reactive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grocery Store Sample (April)</td>
<td>Statewide</td>
<td>15,340</td>
<td>12.4%</td>
</tr>
<tr>
<td>Grocery Store Sample #2 (June)</td>
<td>Statewide</td>
<td>12,368</td>
<td>10.4%</td>
</tr>
<tr>
<td>Grocery Store Workers</td>
<td>Statewide</td>
<td>1,784</td>
<td>11.6%</td>
</tr>
<tr>
<td>Food Service Workers</td>
<td>Statewide</td>
<td>1,919</td>
<td>10.6%</td>
</tr>
<tr>
<td>Healthcare Workers</td>
<td>NYC/Metro</td>
<td>7,838</td>
<td>15.3%</td>
</tr>
<tr>
<td>First Responders</td>
<td>NYC/Metro</td>
<td>1,997</td>
<td>14%</td>
</tr>
<tr>
<td>Essential State Employees</td>
<td>Statewide</td>
<td>7,024</td>
<td>6.8%</td>
</tr>
<tr>
<td>New York State Police</td>
<td>Statewide</td>
<td>2,369</td>
<td>2.7%</td>
</tr>
</tbody>
</table>
New York State’s “Contact Tracing Playbook”

Replicable program developed with partners:

- Bloomberg Philanthropies
- Johns Hopkins Bloomberg School of Public Health
- Resolve to Save Lives
Convalescent Serology & Hydroxychloroquine Studies

March 20: *Gautret et al.* study posted on pre-print server MedRxiv

March 23: Began planning for an observational study

Evaluated hospitalized patients admitted March 15-28

Follow-up through April 27 for outcomes

May 11: Published online in *JAMA*
Multisystem Inflammatory Syndrome in Children Associated with COVID-19 (MIS-C)

- End of April, reports out of UK and Europe
- May 6th NYSDOH Health Advisory
- Reportable to NYSDOH
- Evaluated hospitalized patients reported as potential MIS-C cases to NYSDOH retrospective to March 1 and through May 10, 2020
- Published in *New England Journal of Medicine* on June 29, 2020
Department of Health Early-Warning Dashboard
STOPPING THE SPREAD

New York is leading the way by:

• Sharing best practices with cities around the United States,
• Stopping the spread through diagnostic testing and contact tracing,
• Urging residents to wear masks, practice frequent handwashing, and maintain social distancing.
Question & Answer

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Evidence Generation During the COVID-19 Pandemic: Treatment
Carlos del Rio
Emory University
School of Medicine
COVID-19 Treatment

CARLOS DEL RIO, MD
EMORY UNIVERSITY SCHOOL OF MEDICINE
FOREIGN SECRETARY, NATIONAL ACADEMY OF MEDICINE

CarlosdelRio7
COVID-19 Spectrum

<table>
<thead>
<tr>
<th>Stage</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic/presymptomatic infection</td>
<td>Positive test for SARS-CoV-2 but no symptoms</td>
</tr>
<tr>
<td>Mild illness</td>
<td>Varied symptoms (e.g., fever, cough, sore throat, taste/smell disturbance) but no shortness of breath or abnormal imaging</td>
</tr>
<tr>
<td>Moderate illness</td>
<td>SpO₂ ≥ 94% &amp; lower respiratory disease (clinical or imaging findings)</td>
</tr>
<tr>
<td>Severe illness</td>
<td>SpO₂ &lt; 94%, PaO₂/FiO₂ &lt; 300, respiratory rate &gt; 30/min, or lung infiltrates &gt; 50%</td>
</tr>
<tr>
<td>Critical illness</td>
<td>Respiratory failure, shock, and/or multiorgan dysfunction</td>
</tr>
</tbody>
</table>

Coronavirus [COVID-19]: the severity of diagnosed cases in China

Described are 44,415 confirmed cases of COVID-19 nationwide in China. Included are confirmed cases in the early period of the outbreak of the disease up to February 11, 2020.

2.3% of all cases died
1,023 of the 44,415 infected people, for which the breakdown is shown on the right, died. The case fatality rate is therefore 2.3%.

5% Critical cases
Critical cases include patients who suffered respiratory failure, septic shock, and/or multiple organ dysfunction/failure.

14% Severe cases
Severe cases include patients suffer from shortness of breath, respiratory frequency ≥ 30/minute, blood oxygen saturation ≤ 93%, PsO2/FIO2 ratio < 300, and/or lung infiltrates > 50% within 24–48 hours.

81% Mild cases
Mild cases include all patients without pneumonia or cases of mild pneumonia.


OurWorldInData.org – Research and data to make progress against the world’s largest problems. Licensed under CC-BY by Hannah Ritchie and Max Roser
Goals of Treatment Across the COVID-19 Spectrum

**Phase:**
- **Before exposure**
- **After exposure**
- **During illness**
- **After illness**

**Goal:**
- **Prevent infection:** Pre-exposure prophylaxis
- **Prevent acquisition/disease:** Post-exposure prophylaxis
- **Treat disease to prevent progression/complications/death:** Early treatment may prevent transmission
- **Hasten recovery/clearance of infection**

**Disease Pathogenesis:**
- **Viral replication**
- **Inflammation**

**Potential intervention:**
- **Antivirals**
- **Boost immune responses**
- **Decrease inflammation**

Adapted from slide by Dr. Arthur Kim, MGH
- **Viral entry**: ACE2 and TMPRSS2: camostat
- **Membrane fusion and endocytosis**: hydroxychloroquine (HCQ)
- **Viral protease**: lopinavir/ritonavir
- **RNA-dependent RNA polymerase**: remdesivir, favipiravir
## Treatment: Some Suggested Options

<table>
<thead>
<tr>
<th>Antivirals</th>
<th>Immunosuppressants</th>
</tr>
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<tbody>
<tr>
<td>Remdesivir</td>
<td>Nelfinavir</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>Penciclovir</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>Mefloquine</td>
</tr>
<tr>
<td>Lopinavir/ritonavir</td>
<td>Oseltamivir</td>
</tr>
<tr>
<td>Darunavir/cobicistat</td>
<td></td>
</tr>
<tr>
<td>Ribavirin</td>
<td><strong>Immunomodulators</strong></td>
</tr>
<tr>
<td>Nitazoxanide</td>
<td>◦ Corticosteroids</td>
</tr>
<tr>
<td>Niclosamide</td>
<td>◦ Tocilizumab</td>
</tr>
<tr>
<td>Favipiravir</td>
<td>◦ INF-alpha (inhaled)</td>
</tr>
<tr>
<td>Convalescent serum</td>
<td>◦ IVIG</td>
</tr>
<tr>
<td>Monoclonal antibody</td>
<td>◦ Baricitinib</td>
</tr>
<tr>
<td></td>
<td>◦ Interferon lambda</td>
</tr>
</tbody>
</table>

*Open Forum Infectious Diseases, ofaa105, [https://doi.org/10.1093/ofid/ofaa105](https://doi.org/10.1093/ofid/ofaa105)*
Case of HCQ: From single arm studies and observational cohorts...

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial


Clinical efficacy of hydroxychloroquine in patients with COVID-19 pneumonia who require oxygen: observational comparative study using routine care data


Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19

Joshua Geleris, M.D., Yifei Sun, Ph.D., Jonathan Platt, Ph.D., Jason Zucker, M.D., Matthew Baldwin, M.D., George Hripcsak, M.D., Angelena Labella, M.D., Daniel K. Merson, M.D., Christine Kubiri, P.H.A., R. Graham Barr, M.D., Dr. P.H., Magdalena E. Sobieszczyk, M.D., M.P.H., and Nei W. Schluger, M.D.
HCQ: To randomized controlled trials...

Post-exposure prophylaxis

Hospitalized patients

Limitation: only 2-3% confirmed dx
The Case of Remdesivir (RDV)

- Nucleotide prodrug: inhibits viral RNA polymerase: chain terminator
  - Developed in 2009 by Gilead for Hep C treatment → didn’t work


- RCT in 2018 in DRC comparing remdesivir with Zmapp and other 2 monoclonal Ab → lower mortality with 2 monoclonal Ab compared to remdesivir and Zmapp

- Inhibits viral replication in cell cultures: SARS CoV, MERS-CoV, SARS CoV2 → human trials for COVID-19
Remdesivir Clinical Trials

Seven ongoing registered clinical trials world-wide

- **Gilead Moderate COVID-19** (NCT04292730) (SIMPLE)
  - Phase 3, Open label, Randomized. Enrollment = 1600
  - 3 arms: (1) RDV 5 days, (2) RDV 10 days, (3) Standard of Care

- **Gilead Severe COVID-19** (NCT04292899) (SIMPLE)
  - Phase 3, Open label, Randomized. E = 1600
  - 2 arms: (1) RDV 5 days, (2) RDV 10 days

- **NIAID Adaptive Trial** (NCT04280705) (ACTT)
  - Phase 2, Blinded, Randomized. Enrollment = 800
  - 2 arms: (1) RDV 10 days, (2) Placebo (adaptive)

- **NIAID Combination Trial** (NCT04401579) (ACTT-II)
  - Phase 2, Blinded, Randomized. Estimated enrollment = 1032
  - 2 arms: (1) RDV 10 days + Baricitinib, (2) RDV 10 days + placebo (adaptive)


*The New England Journal of Medicine*

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**Baseline ordinal score**

<table>
<thead>
<tr>
<th>Score Description</th>
<th>Count</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 (not receiving oxygen)</td>
<td>127</td>
<td>1.38 (0.94–2.03)</td>
</tr>
<tr>
<td>5 (receiving oxygen)</td>
<td>421</td>
<td>1.47 (1.17–1.84)</td>
</tr>
<tr>
<td>6 (receiving high-flow oxygen or noninvasive mechanical ventilation)</td>
<td>197</td>
<td>1.20 (0.79–1.83)</td>
</tr>
<tr>
<td>7 (receiving mechanical ventilation or ECMO)</td>
<td>272</td>
<td>0.95 (0.64–1.40)</td>
</tr>
</tbody>
</table>

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**Graphs**

- Overall Survival
- Patients Not Receiving Oxygen
- Patients Receiving Oxygen
- Patients Receiving High-flow Oxygen or Noninvasive Mechanical Ventilation

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**DOI:** 10.1056/NEJMoa2007764

This article was published on May 22, 2020, at NEJM.org.
Passive Antibody Therapy

- Passive transfer of neutralizing Ab: eg convalescent plasma (CP), monoclonal antibodies (mAb)
- CP used to treat other viral infections, eg Argentine hemorrhagic fever
- Case series show radiographic improvement, reduction of viral shedding
- Open label randomized trial suggested benefit of CP in severe disease (treatment given late in disease course)
- Risks: transfusion reactions (rare), antibody dependent enhancement
- Ongoing prophylactic and therapeutic trials of CP, mAb

Abraham J, Nature Reviews Immunology, 2020; Shen et al, JAMA 2020; Li JAMA 2020
- Controversy regarding use of steroids in viral pneumonia, acute respiratory distress syndrome
- Given hyperinflammatory state in COVID-19, steroids evaluated as potential intervention
  = Open label, randomized trial among hospitalized patients in the UK: 2104 received dex, 4321 usual care

<table>
<thead>
<tr>
<th></th>
<th>Dex</th>
<th>Usual Care</th>
<th>RR mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>No oxygen required</td>
<td>85/501 (17%)</td>
<td>137/1034 (13%)</td>
<td>1.22 (0.86 – 1.75)</td>
</tr>
<tr>
<td>Oxygen only</td>
<td>275/1279 (21.5%)</td>
<td>650/2604 (25%)</td>
<td>0.8 (0.67 – 0.96)</td>
</tr>
<tr>
<td>Ventilation/ECMO</td>
<td>94/324 (29%)</td>
<td>278/683 (40.7%)</td>
<td>0.65 (0.45 – 0.88)</td>
</tr>
<tr>
<td>All participants</td>
<td>454/2104 (21.6%)</td>
<td>1065/4321 (24.6%)</td>
<td>0.83 (0.74-0.92) p=0.0007</td>
</tr>
</tbody>
</table>

Conclusion: Dexamethasone associated with decreased mortality among those on supplemental oxygen or on mechanical ventilation/ECMO. No benefit in those not requiring oxygen.
- Infection with SARS-CoV-2 associated with an inflammatory and pro-thrombotic state

- Thromboembolic disease reported in people with COVID-19, particularly in those with critical illness

- Hospitalized patients should receive venous thromboembolism prophylaxis

- Ongoing and upcoming trials of anticoagulation in COVID-19

NIH Covid-19 Treatment Guidelines; Bikdeli B et al JACC 2020
Effective treatment of severe COVID-19 patients with tocilizumab

Xiaoling Xu\textsuperscript{a,1,2}, Mingfeng Han\textsuperscript{b,1}, Tiantian Li\textsuperscript{a}, Wei Sun\textsuperscript{b}, Dongsheng Wang\textsuperscript{a}, Binqing Fu\textsuperscript{c,d}, Yonggang Zhou\textsuperscript{c,d}, Xiaohu Zheng\textsuperscript{c,d}, Yun Yang\textsuperscript{e}, Xiuyong Li\textsuperscript{f}, Xiaohua Zhang\textsuperscript{b}, Aijun Pan\textsuperscript{e}, and Haiming Wei\textsuperscript{c,d,2}

In patients with coronavirus disease 2019, a large number of T lymphocytes and mononuclear macrophages are activated, producing cytokines such as interleukin-6 (IL-6), which bind to the IL-6 receptor on the target cells, causing the cytokine storm and severe inflammatory responses in lungs and other tissues and organs. Tocilizumab, as a recombinant humanized anti-human IL-6 receptor monodonal antibody, can bind to the IL-6 receptor with high affinity, thus preventing IL-6 itself from binding to its receptor, rendering it incapable of immune damage to target cells, and alleviating the inflammatory responses.
Goals of Treatment Across the COVID-19 Infection Spectrum

<table>
<thead>
<tr>
<th>Phase:</th>
<th>Before exposure</th>
<th>After exposure</th>
<th>During illness</th>
<th>After illness</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Incubation</td>
<td>Mild disease</td>
<td>Moderate disease</td>
<td>Severe disease</td>
</tr>
<tr>
<td>Goal:</td>
<td>Prevent infection: Pre-exposure prophylaxis</td>
<td>Prevent acquisition/disease: Post-exposure prophylaxis</td>
<td>Treat disease to prevent transmission/progression/complications/death</td>
<td>Hasten recovery/clearance of infection</td>
</tr>
<tr>
<td>Disease Pathogenesis:</td>
<td>Viral replication</td>
<td>Inflammation</td>
<td>Remdesivir</td>
<td>Dexamethasone</td>
</tr>
<tr>
<td>Potential intervention:</td>
<td>Antivirals</td>
<td>Boost immune responses</td>
<td>Decrease inflammation</td>
<td>-</td>
</tr>
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</table>

Adapted from slide by Dr. Arthur Kim, MGH
EIDD-2801

Orally available broad-spectrum antiviral ribonucleoside analog.

Effective in cell lines and primary human airway epithelial cultures against multiple coronaviruses including SARS-CoV-2.

Drug developed by DRIVE, a non-for-profit biotechnology company owned by Emory University.

Licensed by Ridgeback

Phase 1 (NCT04392219) has begun.

Merck & Co announced plans to acquire Ridgeback to develop and commercialize it.
Writing COVID-19 Guidelines in a Maelstrom

Coronavirus Disease 2019 (COVID-19) Treatment Guidelines

Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19

Published by IDSA. 4/11/2020

COVID-19 Guideline, Part 2: Infection Prevention
COVID-19 Guideline, Part 3: Diagnostics

Final Thoughts

COVID-19 treatment requires multidimensional approach, with an understanding of the host, the stage/severity of disease, and intervention.

Depending on host, stage and severity of disease, optimal intervention may differ: antiviral therapy, immunomodulator, combinations (antiviral + immunomodulator).

- **Lessons from HIV**
  - Pressure to deploy interventions must be tempered by importance of finding out if a treatment works: our guide must be the science.
  - Iterative process, building on advances until tipping point is achieved.
  - Critical to address disparities & inequities revealed by these “twin” pandemics.
Acknowledgement

Dr. Rajesh T. Gandhi
Dr. Stan Deresinski
Question & Answer

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@theNAMedicine
BREAK
Resume at 12:15 PM EST
Evidence Generation During the COVID-19 Pandemic: Mobilizing Evidence and the General Public
Dietram A. Scheufele
University of Wisconsin- Madison
UNDERSTANDING “INFODEMICS”

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Vilas Distinguished Achievement Professor

University of Wisconsin—Madison and
Morgridge Institute for Research

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A closer look at the COVID-19 “infodemic”
“Facts” are elusive during pandemics
When facts are what each of us wants them to be
The “accelerated” wickedness of COVID-19
UNDERSTANDING “INFODEMICS”


- A closer look at the COVID-19 “infodemic”
- “Facts” are elusive during pandemics
- When facts are what each of us wants them to be
- The “accelerated” wickedness of COVID-19
LITTLE SYSTEMATIC SOCIAL SCIENTIFIC EVIDENCE OF A UNIQUE COVID-19 “INFODEMIC”

- Is there really an “infodemic”?
- Is public trust in (COVID) science declining?
- Is mis/disinformation more prevalent or for COVID-19 than for other areas of science, politics, etc.?
- Does misinformation impact relevant behavioral outcomes, i.e., social distancing, wearing masks, vaccine hesitancy, etc.?

The scientific answer to many of these questions is either “no,” or “we do not know yet”

Intuitive informational interventions might not always be the best answer …
UNDERSTANDING “INFODEMICS”


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“[T]he lack of PPEs and masks for the health providers … led all of us … to say, “Right now we really need to save the masks for the people who need them most.” When it became clear that the infection could be spread by asymptomatic carriers … that made it very clear that we had to strongly recommend masks.”
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ABILITY OR MOTIVATION TO ENGAGED IN BIASED REASONING?


- Motivated reasoning
- (Dis)confirmation biases
- Biased assimilation
- Identity protection

- We believe misinformation because it fits our priors, even if a 3-second Google search could tell us otherwise …
Do you believe the number of Americans dying from COVID-19 is more, less, or about the same as the reported number?

Survey of 1,012 U.S. adults conducted May 1–4, 2020. Reported number in question was 61k deaths as of April 30, 2020.

<table>
<thead>
<tr>
<th></th>
<th>More</th>
<th>About the same</th>
<th>Less</th>
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</thead>
<tbody>
<tr>
<td>Total</td>
<td>44%</td>
<td>32%</td>
<td>23%</td>
</tr>
<tr>
<td>Democrats</td>
<td>63</td>
<td>29</td>
<td>7</td>
</tr>
<tr>
<td>Independents</td>
<td>45</td>
<td>31</td>
<td>24</td>
</tr>
<tr>
<td>Republicans</td>
<td>24</td>
<td>36</td>
<td>40</td>
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</tbody>
</table>
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… and certainly not one that works across controversies, stakeholders, or desired outcomes

But there are a few universal lessons

- Not repeating misinformation, even to debunk it
- Language that speaks to shared values rather than (what might unfairly be considered) tribal identities
- Making value propositions that address salient public concerns, scientific or not
- Acknowledging that we all hold views that are at odds with scientific evidence
- Presenting “best” evidence as “best available evidence right now” … acknowledging that it will (and should) change
- Our own biases as powerful tools for (behavior) change
THANK YOU

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National Science Foundation
U.S. Department of Agriculture
U.S. Department of Energy
Rita Allen Foundation
Office of the Vice Chancellor for Research and Graduate Education, University of Wisconsin–Madison
Question & Answer

Panelists
• Always keep your line muted unless you are called on to speak
• If possible, turn on video while speaking to the group. To enable video click the ‘start video’ option at the bottom left of your screen

Attendees - Q & A
• Please type in questions into the Q&A located at the bottom of the screen on your zoom interface
• Question format:
  • Your name and organization
  • To whom
  • Question
Amy Abernethy
Food and Drug Administration
Real-world Evidence Accelerator – Lessons Learned from COVID-19

Amy P. Abernethy, MD PhD
Principal Deputy Commissioner
Acting Chief Information Officer
U.S. Food and Drug Administration
WHY RWD?

• Urgent need to rapidly understand the natural history of COVID-19
• Many critical clinical evidence needs but limited clinical trial resources (patients, time, competing tasks)
  – RWD evaluation of treatment patterns and impact provides understanding
  – RWD can help prioritize research questions to be answered with clinical trials
  – RWD can improve study design and support participant enrollment
  – Pragmatic and platform/adaptive study designs can improve efficiency and generalizability
• Near real-time performance of diagnostics authorized under EUA
• Near real-time vaccine performance of future potential vaccines
Real-World Data for COVID-19

Sits within a larger RWD Community
The RUF/FOCR* Evidence Accelerator

A community of data and analytic partners ready to urgently address questions about COVID-19

*Reagan-Udall Foundation (RUF) for the FDA /Friends of Cancer Research (FOCR)

Our Tools

- Prioritized research questions
- Common data elements and translation tables between common data models
- Common protocol for repeated analysis of priority research questions across multiple data partners (the “parallel analysis”)
- Meetings and forum for rapid cycle feedback and learning
- Individual Accelerator communities focused on specific topics (e.g., therapeutics, diagnostics)
The COVID-19 Evidence Accelerator is an initiative launched by the Reagan-Udall Foundation for the FDA, in collaboration with Friends of Cancer Research (Friends), to provide a unique venue for major data organizations, government and academic researchers, and health systems to gather and design quick-turnaround queries and share their results.

The Accelerator brings together the country’s leading experts in health data aggregation and analytics in a unified effort to share insights, compare results, and answer key questions about COVID-19 treatment and response as quickly as possible.

**Urgency and Action:** Since the beginning of the pandemic, data scientists around the country have been engaged in an intense effort to capture real-world data and rapidly display data analytics to help answer key questions related to the management of COVID-19 patients. These individual efforts are developing into valuable insights, by banding together we are collectively accelerating and maximizing the utility of this information. To do this effectively, a core set of common data elements have been developed that allow any willing data collection effort to embed these data elements into their on-going work in a uniform way to allow for rapid aggregation and analysis.

**Combining efforts will make the findings more robust and accelerate answers.**

Participants in the COVID-19 Evidence Accelerator helped develop an initial set of Key Questions and Core Data Elements that could be used in research using various real-world data sets.

- **Click here for Summary of Key Questions and Core Data Elements**

**Two Interactive Work Streams:**

1) **Accelerator Parallel Analyses:** Developing key research questions that multiple organizations and teams can address simultaneously.

Initial activities of this work stream include:

- (1) rapidly revising a list of core data elements;
- (2) identifying those critical to answering the primary question; and
- (2) establishing uniform collection parameters. It will be necessary to work collaboratively to determine how data elements are being extracted and how they are being defined in order to operationalize a platform that can not only answer questions now, but also inform how research activities could be conducted in the future.
Prioritized Research Questions

General questions / categories of questions:

- General epidemiology of COVID-19
- Predictors of patients at risk for development of severe COVID-19 disease
- Patterns of general outcomes for people with COVID-19 (e.g., death, time to disease resolution)
- Patterns of COVID-19 diagnostic testing and results
- Patterns of development of COVID-19 immunity across the US population
- Can real world data support the evaluation of the performance characteristics of COVID-19 diagnostics?
- Are there data that could help identify an evolving COVID-19 hot spot before molecular testing results become available?
- What medications are doctors prescribing for COVID-19 in the real world?
  - What treatments are being prescribed?
  - Which patients are most likely to get which treatments?
  - What medications are being used for pre- and post-exposure prophylaxis?
  - Which treatments are being prescribed in the context of clinical trials?
  - Treatment patterns for specific subpopulations (e.g., pregnant women, underlying COPD)
- Patterns of enrollment in COVID-19 clinical trials
- Can real world data provide initial understanding of safety and effectiveness of therapies used for COVID-19?
  - In particular: safety of hydroxychloroquine and chloroquine, with or without azithromycin
  - Predictors of treatment safety and effectiveness
  - Safety for specific subpopulations (e.g., pregnancy)
- Are there data that can inform risk and/or management of drug shortages (e.g., surge in demand, available drug supply)?
- Can data sources be used to help identify patients who can donate convalescent plasma?

*Reagan-Udall Foundation (RUF) for the FDA /Friends of Cancer Research (FOCR)
Parallel Analysis Projects

Developing key research questions that multiple organizations and teams can address simultaneously

Repeating analyses in parallel by collaborators using different analytical techniques and data sources will help strengthen findings and learnings

Initial activities of this work stream include:

1. Rapidly revising a list of core data elements critical to answering the primary question
2. Master protocol and common table shells
3. 5-10 research teams analyzing the question
COVID-19 Evidence Accelerator
Thursday, April 16, 2020, 3:00 – 4:30 pm ET

Call Summary

Background
Prior to the initiation of this call, 41 organizations were provided a list of draft core data elements and key questions to encourage additional feedback and characterization of key questions. Over 25 responses were collected through the course of three days and rapidly incorporated into a master document that reflects a comprehensive list of key questions across stakeholders and core data elements necessary to address them.

The responses provided to the initial core data elements and key questions have revealed several potential opportunities that could be implemented in different venues. In evaluating the feedback, the key question series below was identified as immediate and feasible and may be a prime candidate for multi-stakeholder collaboration:
The RUF/FOCR* Evidence Accelerator

Identifying unique populations, connecting the dots

Crowdsourcing the Question

How can RWE inform OCE’s efforts?

Tailored to Specific Topics

- Natural History of Cancer Patients with COVID-19
  - Rates and severity of COVID-19, Mortality
  - Therapeutic interventions
  - Coagulopathy, renal failure, cardiomyopathy, etc.
  - Long term sequelae

- Rates and Impact of Reduced Screening and Treatment
  - Delays in diagnosis, adjuvant treatment, impact on mortality

- Efficacy and Safety of Immunotherapy in COVID-19
  - Lung, melanoma, bladder, MSI, etc.

- Thrombosis/coagulopathy in select populations

- Natural History of Pediatric cancer patients with COVID-19
  - Incidence of Multi-organ Inflammatory Syndrome

- Diagnostic testing
  - Routine testing prior to initiation of therapy?

And the list goes on....

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Data or analytic EA partners participate in one or more groups

- Research questions generated within each accelerator
- Work groups cross boundaries of the different EAs

### RUF / FOCR* Evidence Accelerator Work Streams

<table>
<thead>
<tr>
<th>THERAPEUTICS EA</th>
<th>Weekly Lab Meeting</th>
<th>Weekly Parallel Analysis</th>
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<tbody>
<tr>
<td>DIAGNOSTICS EA</td>
<td>Weekly Lab Meeting</td>
<td>Weekly Parallel Analysis</td>
</tr>
<tr>
<td>TBD [VACCINES EA]</td>
<td>Weekly Lab Meeting</td>
<td>Weekly Parallel Analysis</td>
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*Reagan-Udall Foundation (RUF) for the FDA / Friends of Cancer Research (FOCR)
Real-World Data for COVID-19

Sits within a larger RWD Community

FDA
Real-World Data Approaches

Evidence Accelerator
RUF/FOCR managed workstream

Other Government
NIH, VA, PCORI, etc
Our Responsibility

The EA with RUF/FOCR provides a “safe space” for key players across the ecosystem to lead, scrutinize and “get this right”

• Data selection
• Protocol design
• Transparency
• Data provenance
• Data quality
• Analytical integrity
• Peer review
• Press interactions

*Ragan-Udall Foundation (RUF) for the FDA /Friends of Cancer Research (FOCR)
## DRAFT PRINCIPLES for the EA

<table>
<thead>
<tr>
<th>#</th>
<th>Principle</th>
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</thead>
<tbody>
<tr>
<td>01</td>
<td>Respect for <strong>patient privacy</strong></td>
</tr>
<tr>
<td>02</td>
<td><strong>Act fast</strong>, Traceability and provenance – understand data generation, processing, curation, and analytics</td>
</tr>
<tr>
<td>03</td>
<td><strong>Transparency</strong>, ruthless transparency</td>
</tr>
<tr>
<td>04</td>
<td><strong>Traceability and provenance</strong> – understand data generation, processing, curation, and analytics</td>
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<tr>
<td>05</td>
<td><strong>Sharing</strong> – show process, explore limitations, pitfalls, and celebration successes – bring work and learnings to the community</td>
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<tr>
<td>06</td>
<td><strong>Build trust</strong> – show processes. Show curation approaches. Show comparisons. Curation is expensive and takes time, many “eyes” along the way, yields trust, understanding, and confidence in the results</td>
</tr>
<tr>
<td>07</td>
<td>Embrace <strong>convergence and discordance</strong> to facilitate understanding</td>
</tr>
<tr>
<td>08</td>
<td>Learning is <strong>additive, and continuously integrated</strong> to improve knowledge and understanding</td>
</tr>
<tr>
<td>09</td>
<td><strong>Dissemination</strong> – responsible evidence generation (show what good looks like)</td>
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  - Your name and organization
  - To whom
  - Question
Reflections From Speakers
Evidence Mobilization Action Collaborative

For more information about the Evidence Mobilization Action Collaborative or to share opportunities to address and advance this work, please contact:

Noor Ahmed
National Academy of Medicine
MAhmed@nas.edu
Closing Remarks

Thank you for joining!

For more information about the National Academy of Medicine’s initiatives, please visit us at: nam.edu