NAM Leadership Consortium

Collaboration for a Value & Science-Driven Health System

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

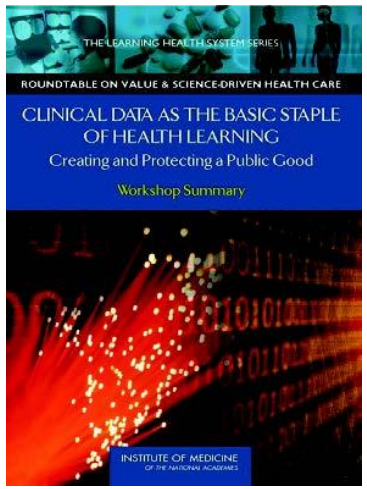
Michael McGinnis
National Academy of Medicine

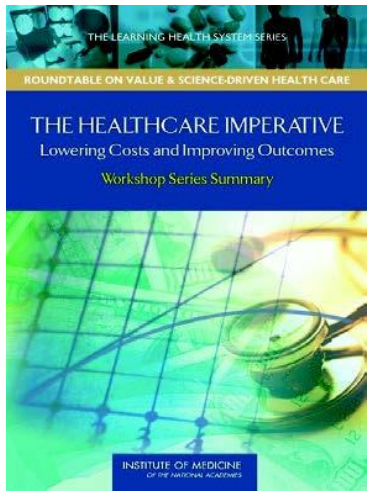
Learning Health System

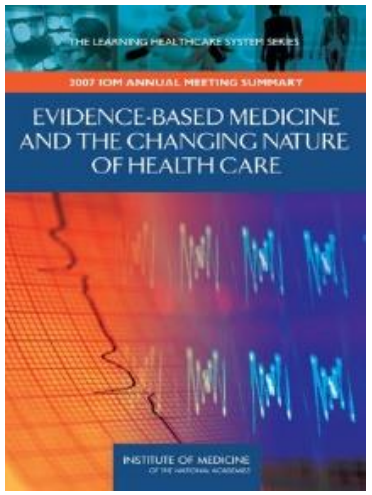
"A learning health care system is one in which **science**, **informatics**, **incentives**, and **culture** are aligned for continuous improvement, innovation, and equity, with best practices seamlessly embedded in the care process, patients and families active participants in all elements, and new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

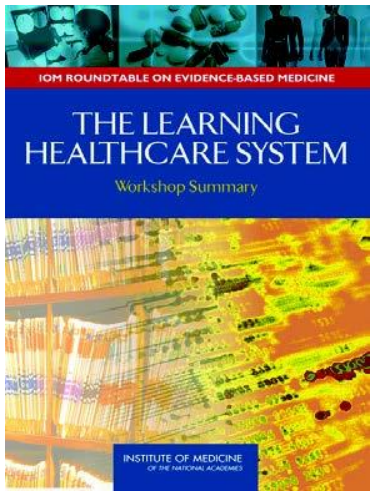
NAM Leadership Consortium Charter, 2006

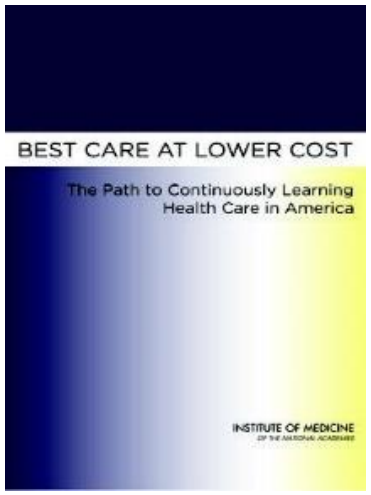
Learning Health System Series











Vision • Research • Evidence • Effectiveness • Trials • IT Platform • Data Quality & Use • Health Costs • Value • Complexity • Best Care • Patients • Systems • Measures • Leadership

THE LEARNING HEALTH SYSTEM SERIES

Anchor Principles

...for health system performance

Quality Chasm

- ✓ Patient-centered
- ✓ Safe
- ✓ Effective
- ✓ Equitable
- ✓ Efficient
- ✓ Timely

Learning Health System

- ✓ Personal
- ✓ Safe
- ✓ Effective
- ✓ Equitable
- ✓ Efficient
- ✓ Accessible
- ✓ Transparent
- ✓ Adaptive
- ✓ Secure

NAM Leadership Consortium
Collaboration for a Value & Science-Driven Health System

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

Agenda

Welcome 10:00 – 10:15 AM

Michael McGinnis, National Academy of Medicine
Rich Platt, Harvard University
Rick Kuntz, Medtronic

Strategic Framing 10:15 – 10:30 AM

Michael McGinnis, National Academy of Medicine
Collaborative Co-chairs

COVID-19 Pandemic: Tracking and Tracing 10:30 – 11:00 AM

Ashish Jha, Harvard T.H. Chan School of Public Health

COVID-19 Pandemic: Clinical Presentation 11:00 – 11:30 AM

Howard Zucker, Health Commissioner, State of New York

COVID-19 Pandemic: Treatment 11:30 – 12:00 PM

Carlos del Rio, Emory University School of Medicine

Agenda

Break	12:00 – 12:15 PM
COVID-19 Pandemic: Mobilizing Evidence and the General Public	12:15 – 12:45 PM

Dietram A. Scheufele, University of Wisconsin-Madison

FDA Evidence Accelerator	12:45 – 1:15 PM

Amy Abernethy, Food and Drug Administration

Reflection From Speakers	1:15 – 1:30 PM
Summary of Next Steps and Closing Remarks	1:30 – 1:45 PM

Michael McGinnis, National Academy of Medicine
Collaborative Co-chairs

Adjourn	1:45 PM

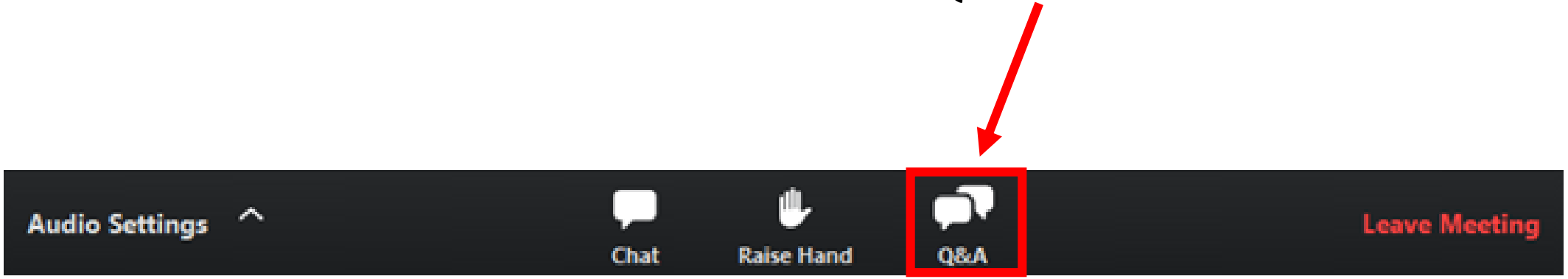
Zoom Instructions

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

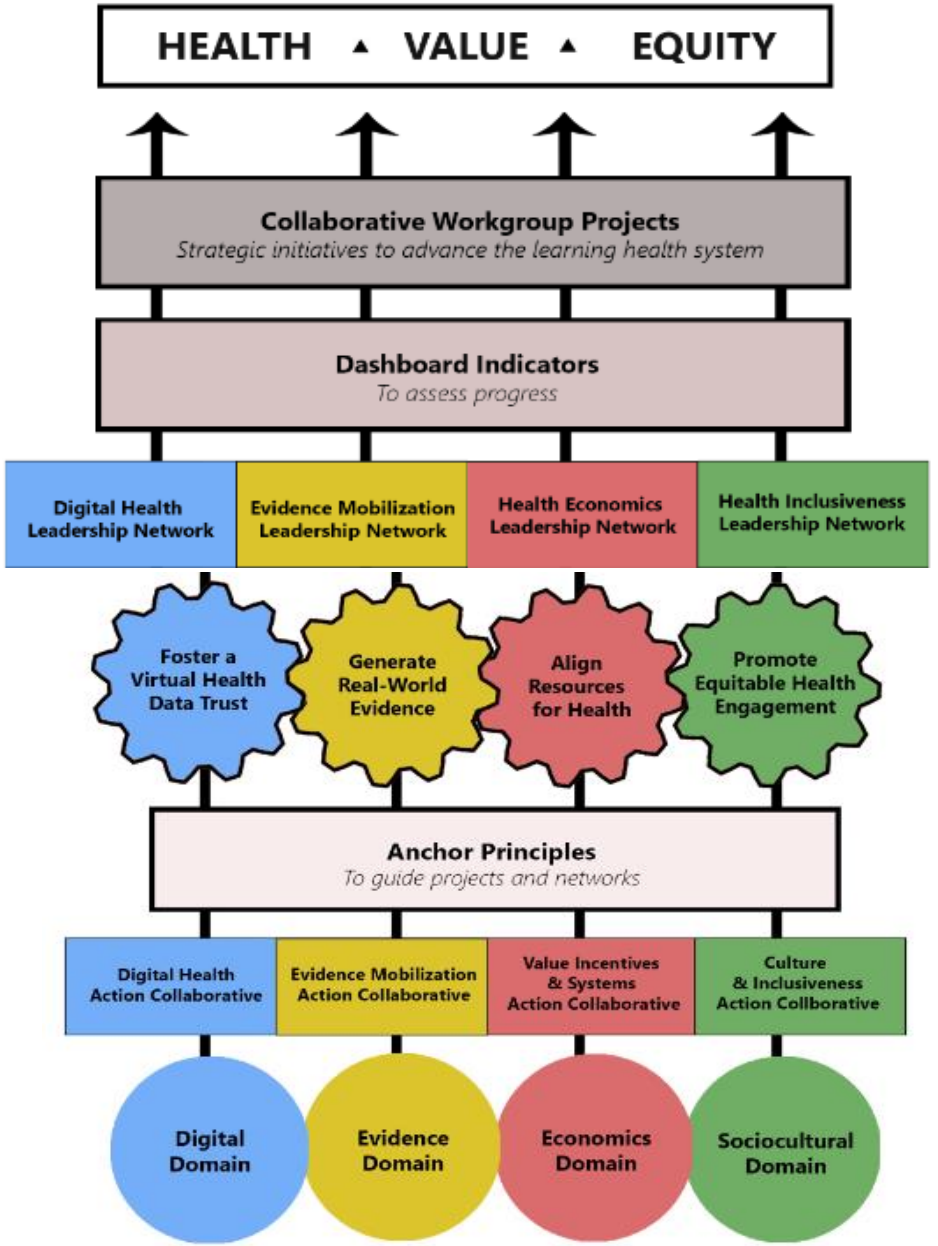


NAM Leadership Consortium

Collaboration for a Value & Science-Driven Health System

Strategic Framing

NATIONAL ACADEMY OF MEDICINE


HEALTH ▲ VALUE ▲ EQUITY
Collaborative Workgroup Projects
Strategic initiatives to advance the learning health system
Dashboard Indicators
To assess progress
Digital Health Leadership Network
Evidence Mobilization Leadership Network
Health Economics Leadership Network
Health Inclusiveness Leadership Network
Foster a Virtual Health Data Trust
Generate Real-World Evidence
Align Resources for Health
Promote Equitable Health Engagement
Anchor Principles
To guide projects and networks
Digital Health Action Collaborative
Evidence Mobilization Action Collaborative
Value Incentives & Systems Action Collaborative
Culture & Inclusiveness Action Collborative
Digital Domain
Evidence Domain
Economics Domain
Sociocultural Domain

Evidence Mobilization

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:

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

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

NAM Leadership Consortium

Collaboration for a Value & Science-Driven Health System

Evidence Generation During the COVID-19 Pandemic: Tracking and Tracing

NATIONAL ACADEMY OF MEDICINE

Ashish Jha
Harvard T.H. Chan
School of Public Health

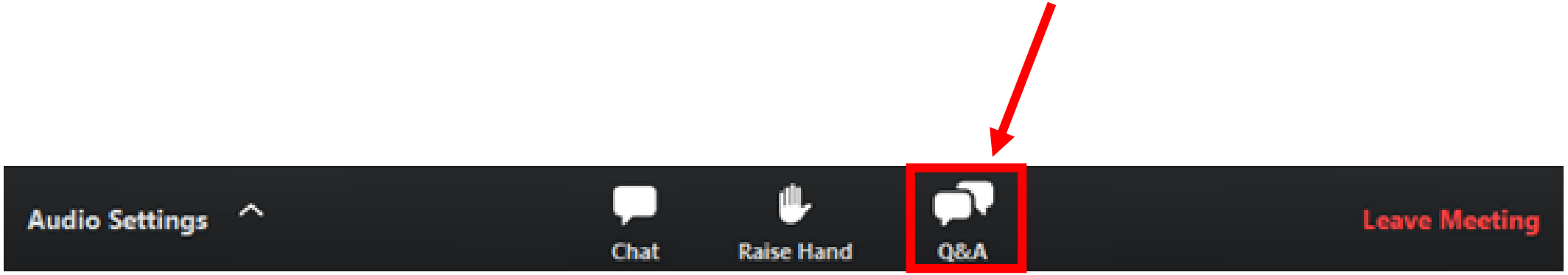
Question & Answer

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



NAM Leadership Consortium

Collaboration for a Value & Science-Driven Health System

Evidence Generation During the COVID-19 Pandemic: Clinical Presentation

NATIONAL ACADEMY OF MEDICINE

Howard Zucker
Health Commissioner
State of New York

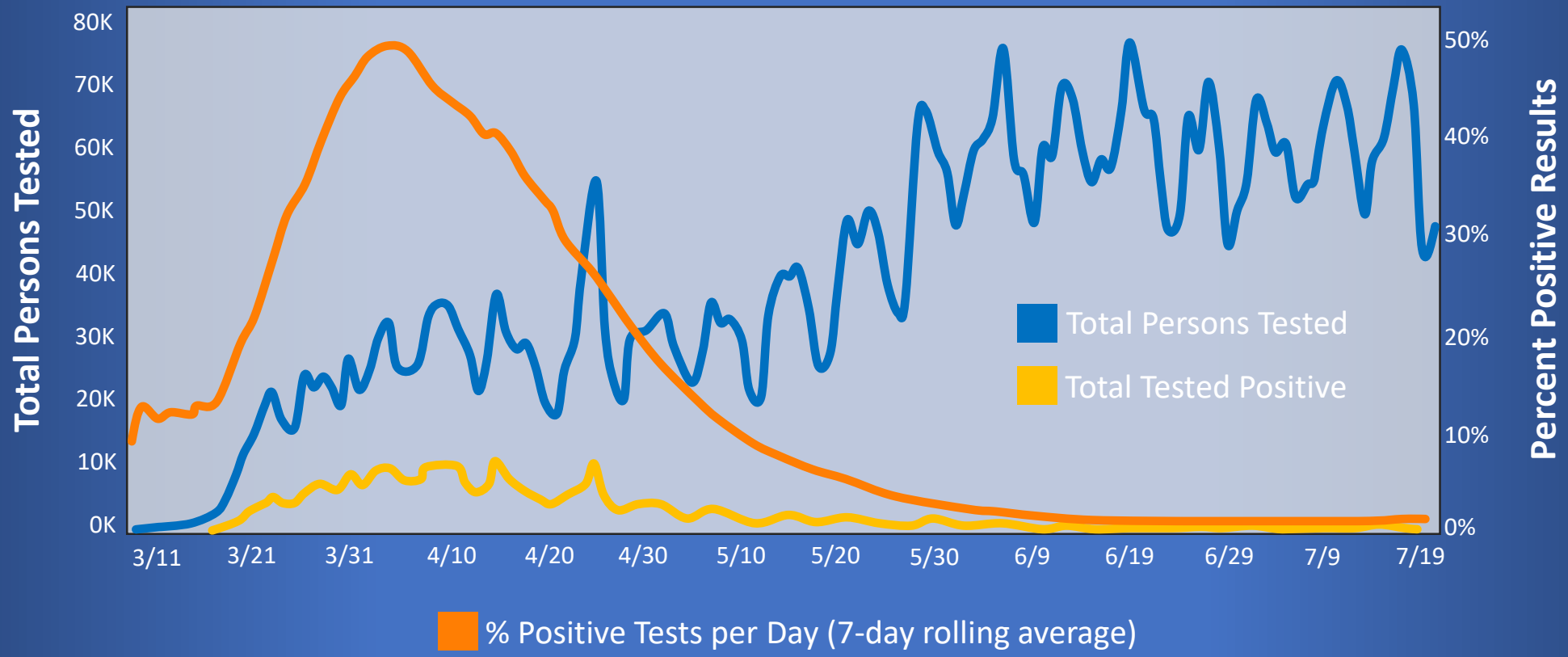
New York State's Pandemic Response:
Identifying Documenting, and Communicating Novel Presentation of COVID-19

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

National Academy of Medicine Leadership Consortium • July 28, 2020

NEW YORK STATE | Department of Health

How did we get down from the mountain?



NEW YORK STATE | Department of Health

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*

NEW YORK STATE | Department of Health

Guidance & Polices Sources

Before First Case

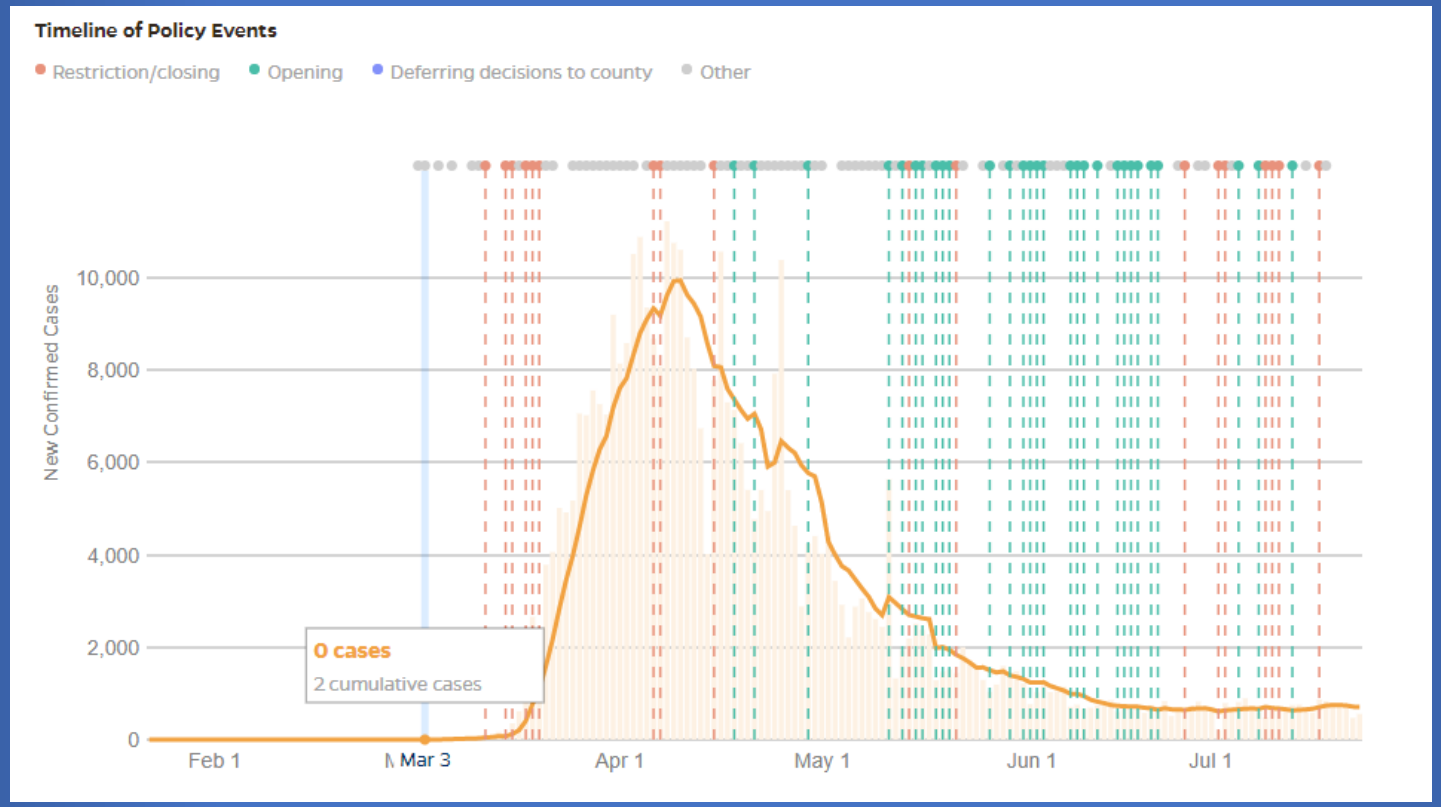
- Clinical data from China
- Epidemiologic data from WHO-China Joint Mission
- CDC case definitions & testing/isolation/quarantine guidance

Outbreak Phase

- NYS data collection
- CDC Epi-Aid
- CDC case definitions & testing/isolation/quarantine guidance
- Academic studies

NEW YORK STATE | Department of Health

NYS Case Counts and State Policy Directives



Source: https://coronavirus.jhu.edu/data/state-timeline/new-confirmed-cases/new-york/1

NEW YORK STATE | Department of Health

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 | Department of Health

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

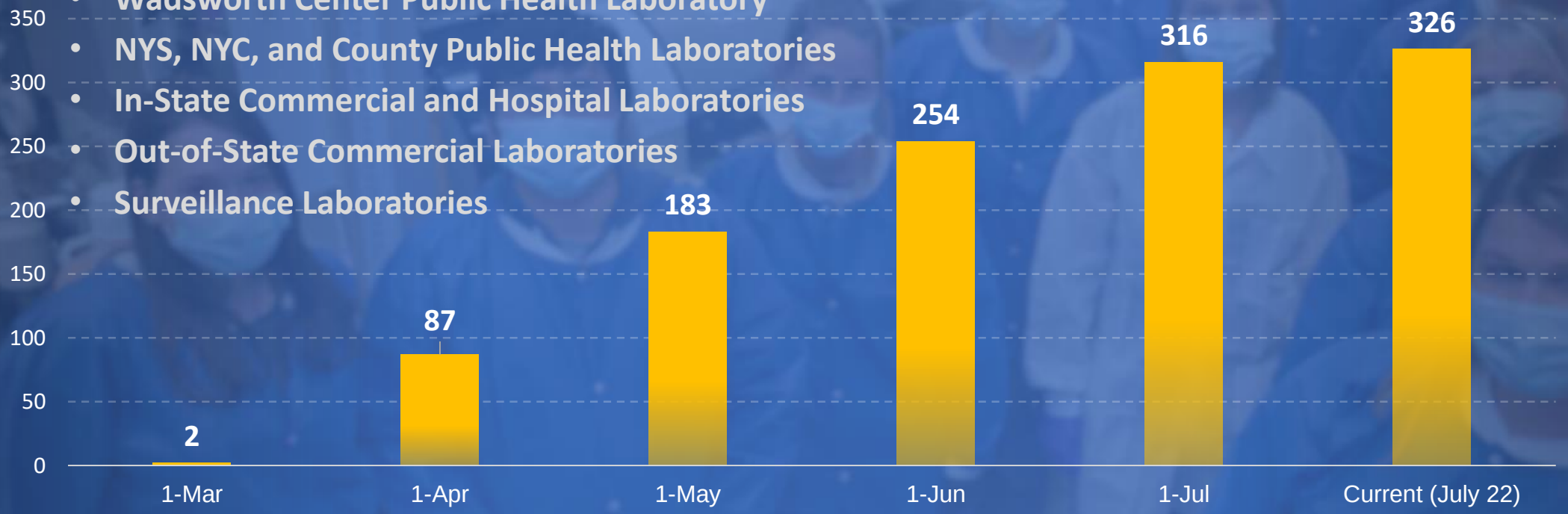
Wadsworth Center Laboratory

- 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.

NEW YORK STATE | Department of Health

Increasing NYS Laboratory Testing Capacity

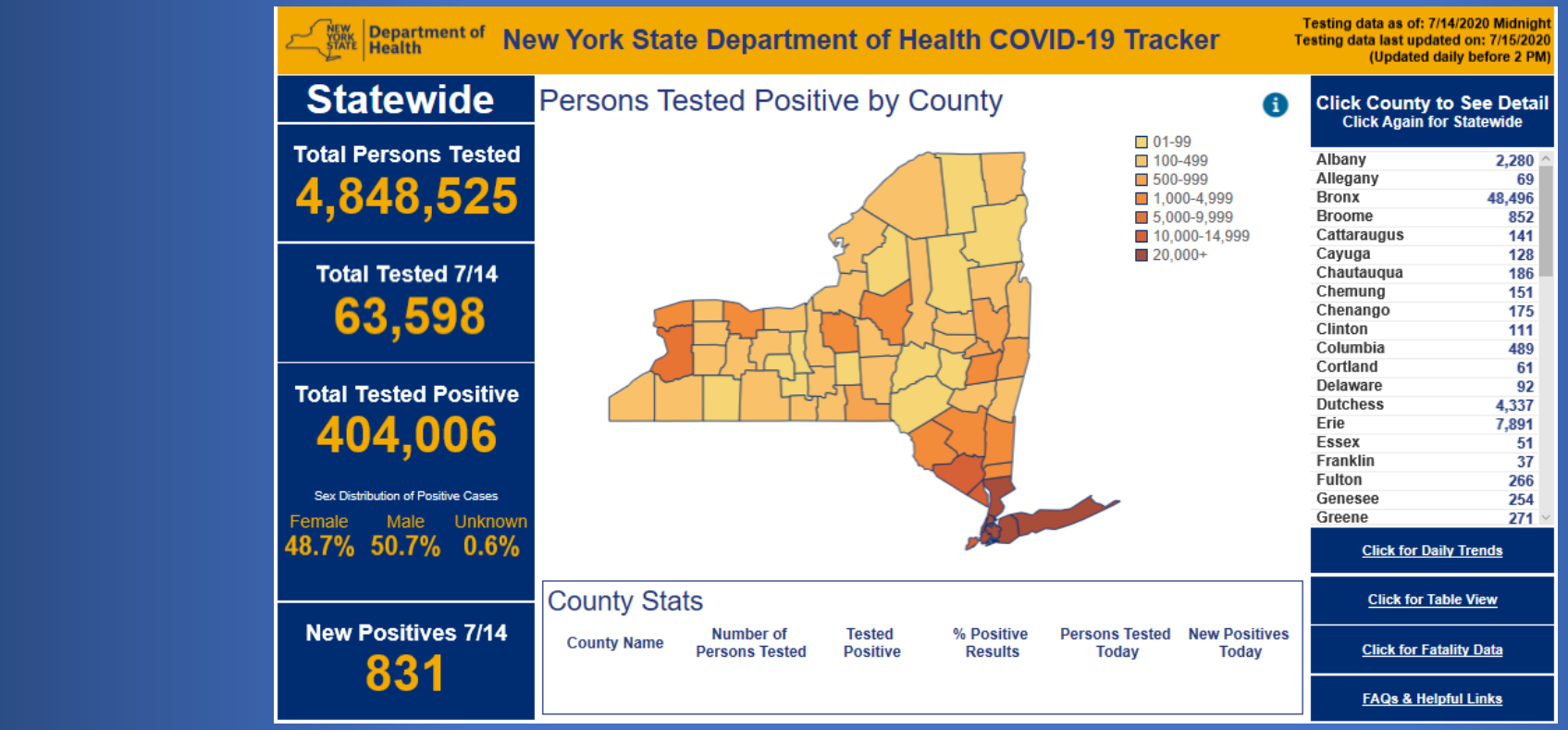
- Wadsworth Center Public Health Laboratory
- NYS, NYC, and County Public Health Laboratories
- In-State Commercial and Hospital Laboratories
- Out-of-State Commercial Laboratories
- Surveillance Laboratories



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

NEW YORK STATE | Department of Health

Department of Health COVID-19 Tracker



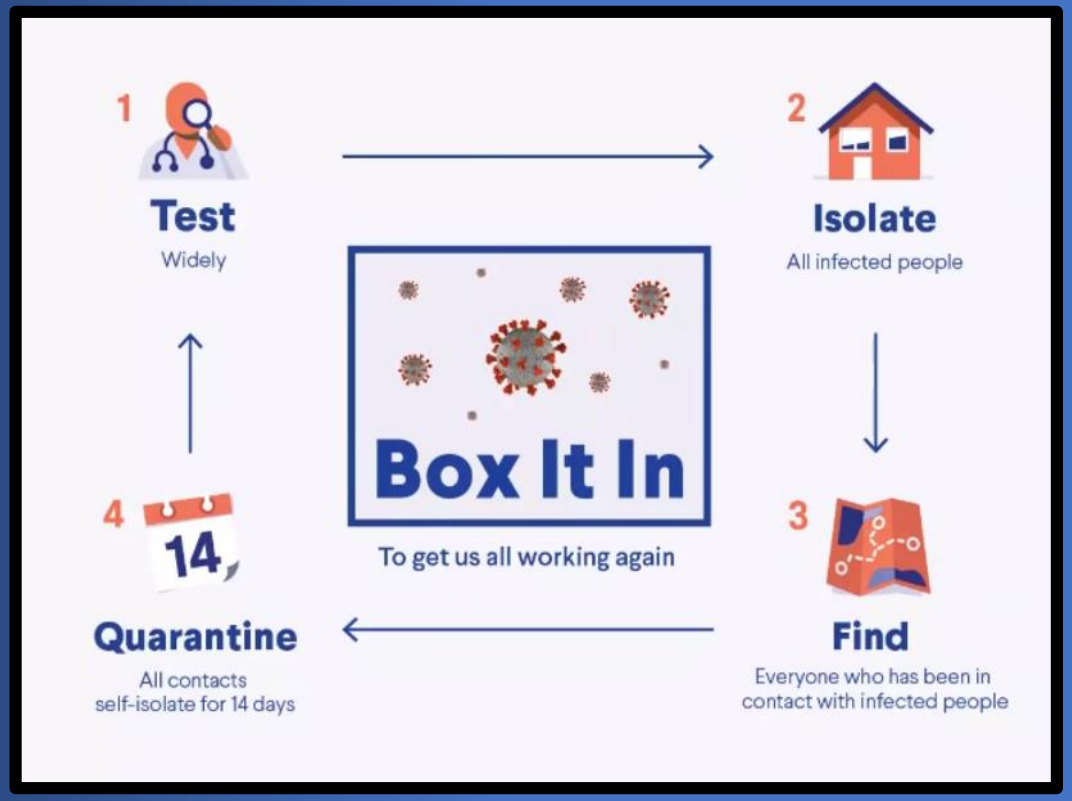
NEW YORK STATE | Department of Health

Antibody Testing

Department of Health Serology Initiative Wadsworth DBS Sample			
Population Tested	**Region**	**Number Tested**	**Percent Reactive**
Grocery Store Sample (April)	Statewide	15,340	12.4%
Grocery Store Sample #2 (June)	Statewide	12,368	10.4%
Grocery Store Workers	Statewide	1,784	11.6%
Food Service Workers	Statewide	1,919	10.6%
Healthcare Workers	NYC/Metro	7,838	15.3%
First Responders	NYC/Metro	1,997	14%
Essential State Employees	Statewide	7,024	6.8%
New York State Police	Statewide	2,369	2.7%

NEW YORK STATE | Department of Health

New York State's "Contact Tracing Playbook"

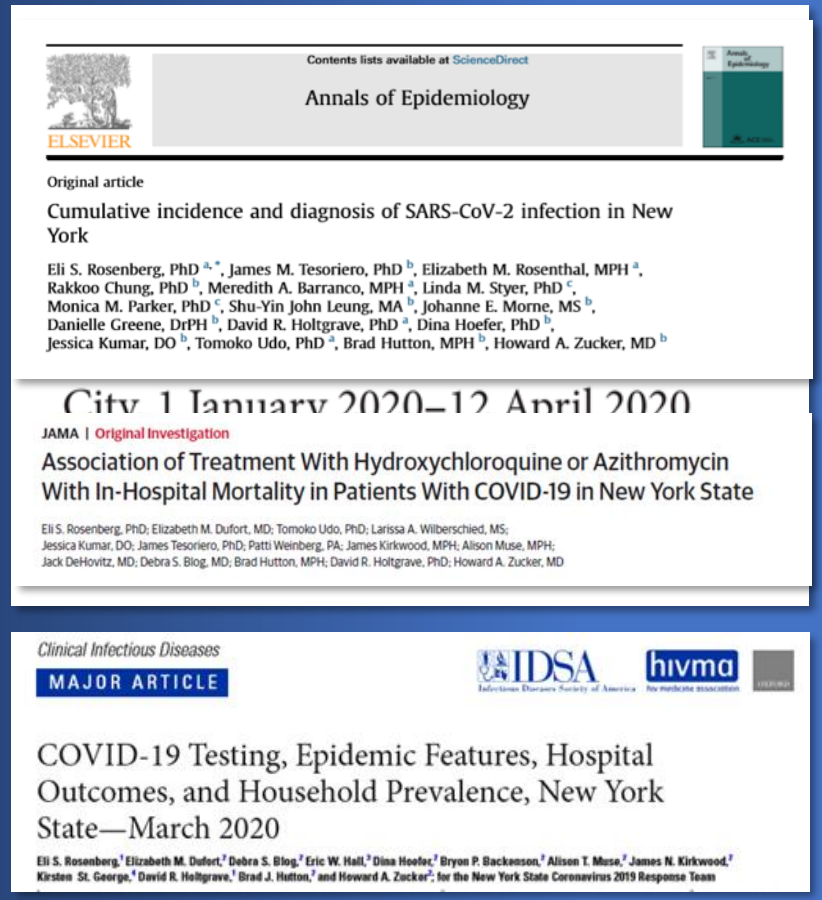


Replicable program developed with partners:

- **Bloomberg Philanthropies**
- **Johns Hopkins Bloomberg School of Public Health**
- **Resolve to Save Lives**

NEW YORK STATE | Department of Health

Convalescent Serology & Hydroxychloroquine Studies



Contents lists available at ScienceDirect

Annals of Epidemiology

ELSEVIER

Original article

Cumulative incidence and diagnosis of SARS-CoV-2 infection in New York

Eli S. Rosenberg, PhD [a,*], James M. Tesoriero, PhD [b], Elizabeth M. Rosenthal, MPH [a], Rakkoo Chung, PhD [b], Meredith A. Barranco, MPH [a], Linda M. Styer, PhD [c], Monica M. Parker, PhD [c], Shu-Yin John Leung, MA [b], Johanne E. Morne, MS [b], Danielle Greene, DrPH [b], David R. Holtgrave, PhD [a], Dina Hoefer, PhD [b], Jessica Kumar, DO [b], Tomoko Udo, PhD [a], Brad Hutton, MPH [b], Howard A. Zucker, MD [b]

City, 1 January 2020–12 April 2020

JAMA | Original Investigation

Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State

Eli S. Rosenberg, PhD; Elizabeth M. Dufort, MD; Tomoko Udo, PhD; Larissa A. Wilberschied, MS; Jessica Kumar, DO; James Tesoriero, PhD; Patti Weinberg, PA; James Kirkwood, MPH; Alison Muse, MPH; Jack DeHovitz, MD; Debra S. Blog, MD; Brad Hutton, MPH; David R. Holtgrave, PhD; Howard A. Zucker, MD

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA

hivma

COVID-19 Testing, Epidemic Features, Hospital Outcomes, and Household Prevalence, New York State—March 2020

Eli S. Rosenberg,[1] Elizabeth M. Dufort,[2] Debra S. Blog,[2] Eric W. Hall,[3] Dina Hoefer,[2] Bryon P. Backenson,[2] Alison T. Muse,[2] James N. Kirkwood,[2] Kirsten St. George,[4] David R. Holtgrave,[1] Brad J. Hutton,[2] and Howard A. Zucker[2]; for the New York State Coronavirus 2019 Response Team

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**

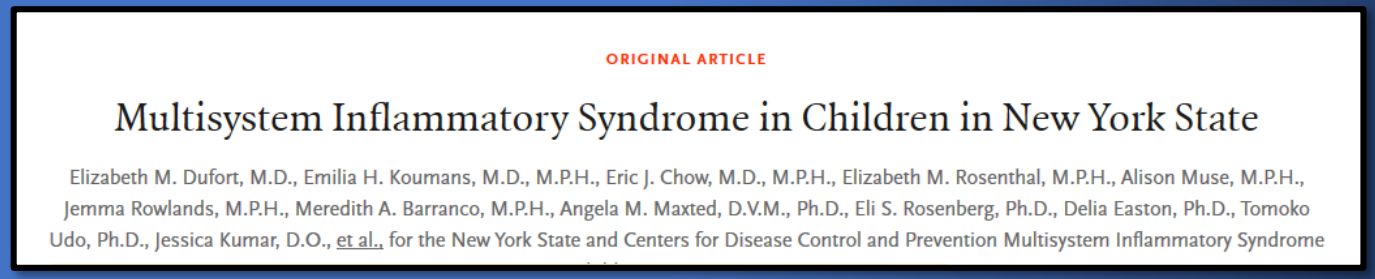
Follow-up through **April 27** for outcomes

May 11: Published online in ***JAMA***

NEW YORK STATE | Department of Health

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



ORIGINAL ARTICLE

Multisystem Inflammatory Syndrome in Children in New York State

Elizabeth M. Dufort, M.D., Emilia H. Koumans, M.D., M.P.H., Eric J. Chow, M.D., M.P.H., Elizabeth M. Rosenthal, M.P.H., Alison Muse, M.P.H., Jemma Rowlands, M.P.H., Meredith A. Barranco, M.P.H., Angela M. Maxted, D.V.M., Ph.D., Eli S. Rosenberg, Ph.D., Delia Easton, Ph.D., Tomoko Udo, Ph.D., Jessica Kumar, D.O., et al., for the New York State and Centers for Disease Control and Prevention Multisystem Inflammatory Syndrome

- 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

NEW YORK STATE | Department of Health

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.**

NEW YORK STATE | Department of Health

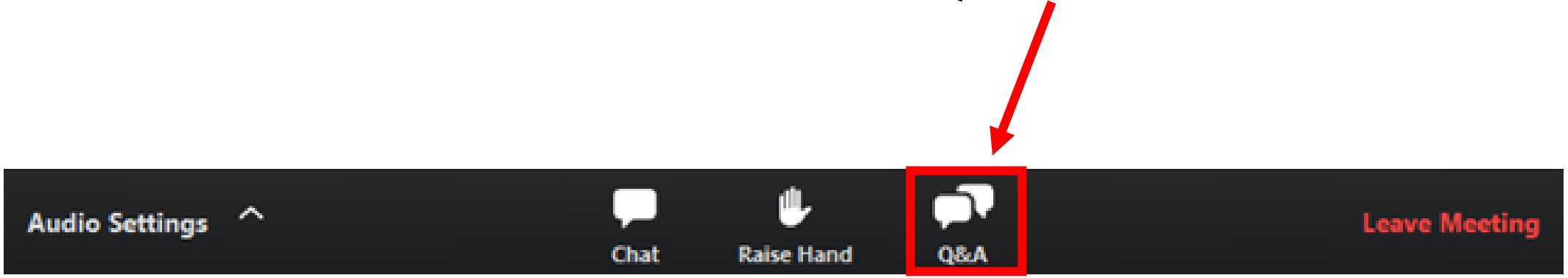
Question & Answer

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



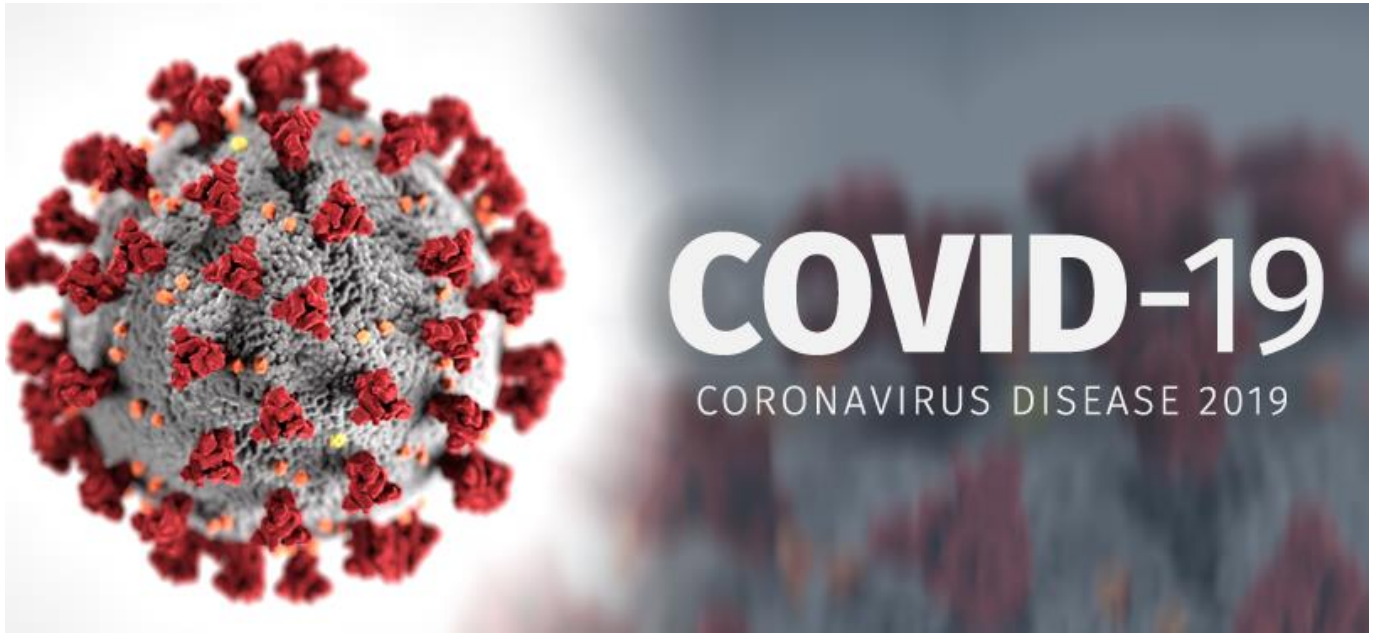
NAM Leadership Consortium

Collaboration for a Value & Science-Driven Health System

Evidence Generation During the COVID-19 Pandemic: Treatment

NATIONAL ACADEMY OF MEDICINE

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

Stage	Characteristics
Asymptomatic/ presymptomatic infection	▪ Positive test for SARS-CoV-2 but no symptoms
Mild illness	▪ Varied symptoms (eg, fever, cough, sore throat, taste/smell disturbance) but no shortness of breath or abnormal imaging
Moderate illness	▪ $SpO_2 \geq 94\%$ & lower respiratory disease (clinical or imaging findings)
Severe illness	▪ $SpO_2 < 94\%$, $PaO_2/FiO_2 < 300$, respiratory rate >30/min, or lung infiltrates > 50%
Critical illness	▪ Respiratory failure, shock, and/or multiorgan dysfunction

NIH COVID-19 Treatment Guidelines. Last updated June 11, 2020. www.covid19treatmentguidelines.nih.gov.

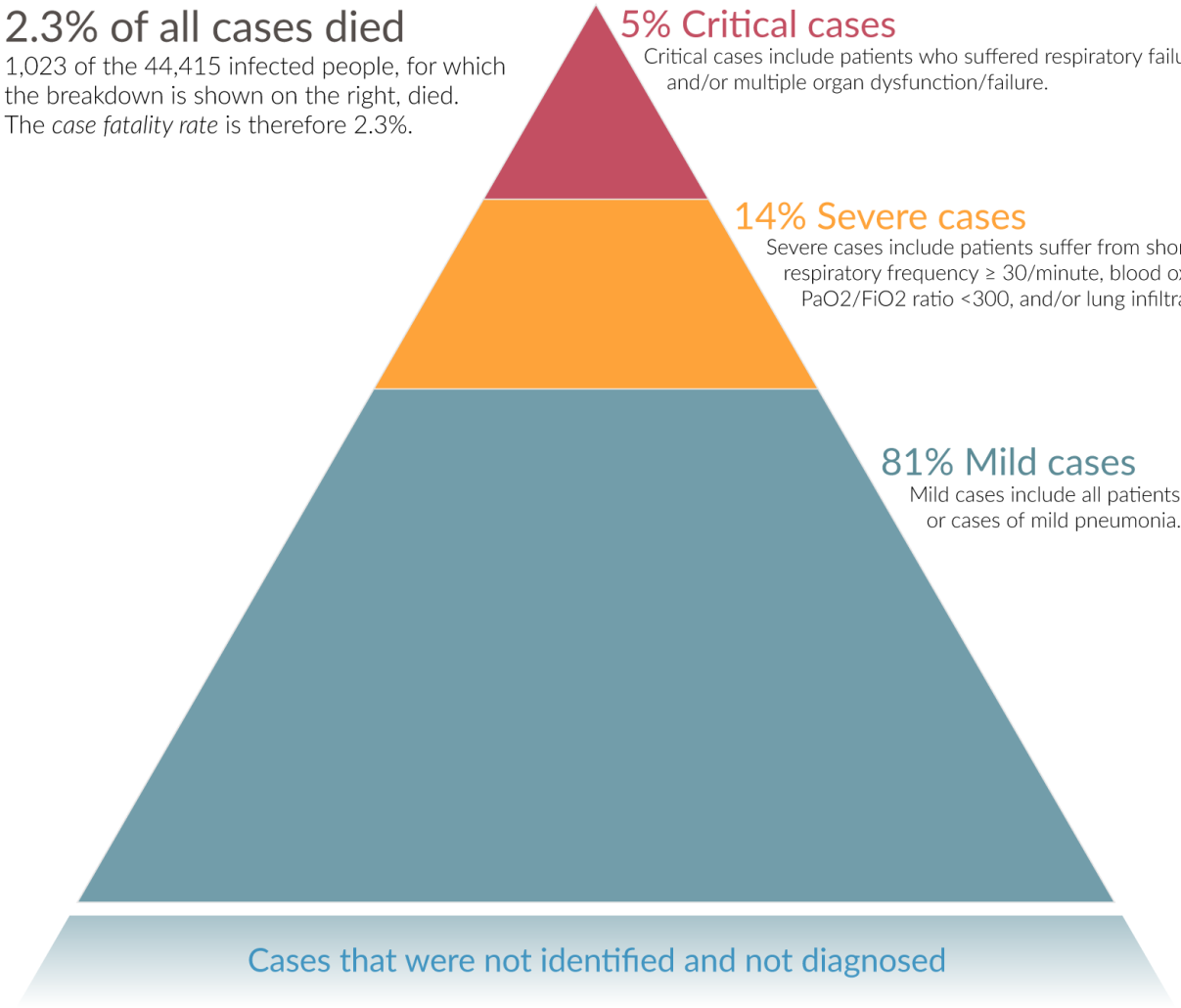
Coronavirus [COVID-19]: the severity of diagnosed cases in China

Descriptions of 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.

Our World in Data

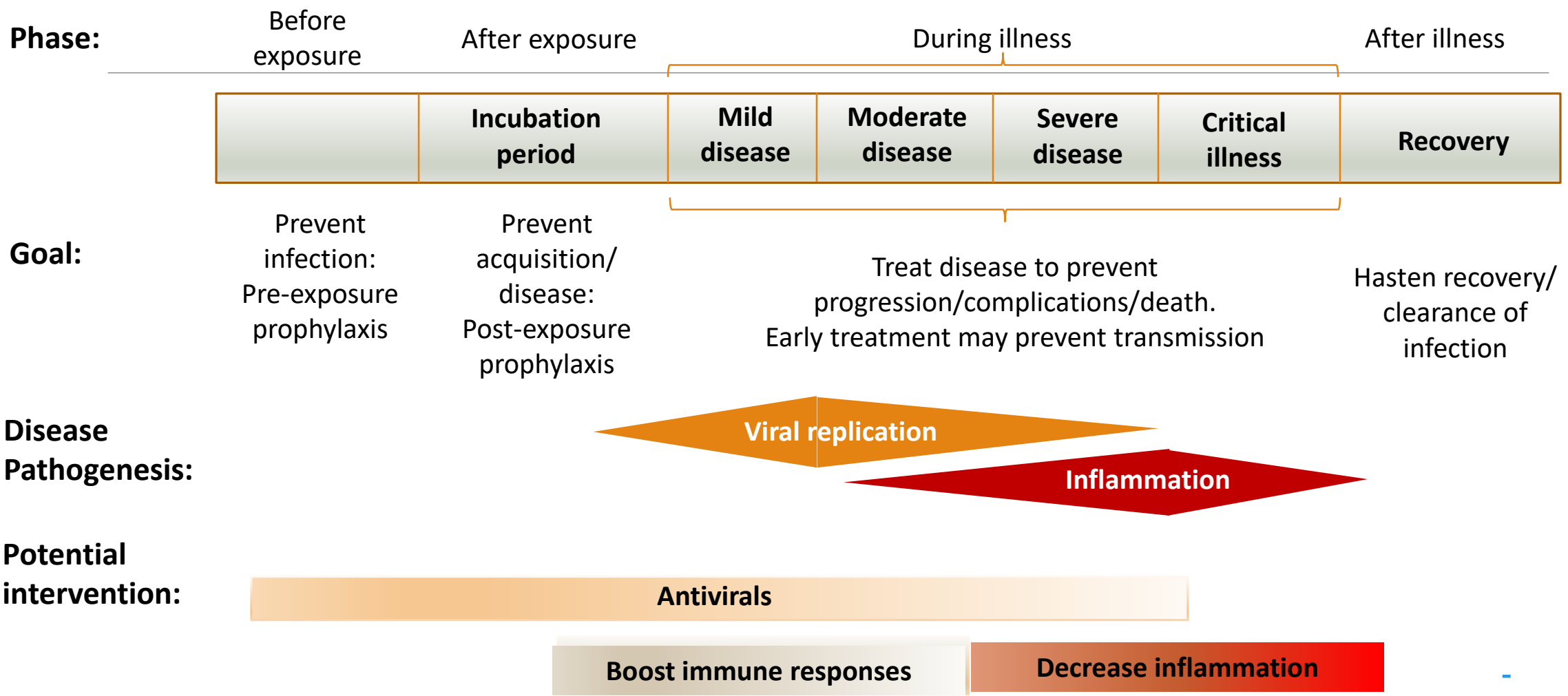
2.3% of all cases died

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%.

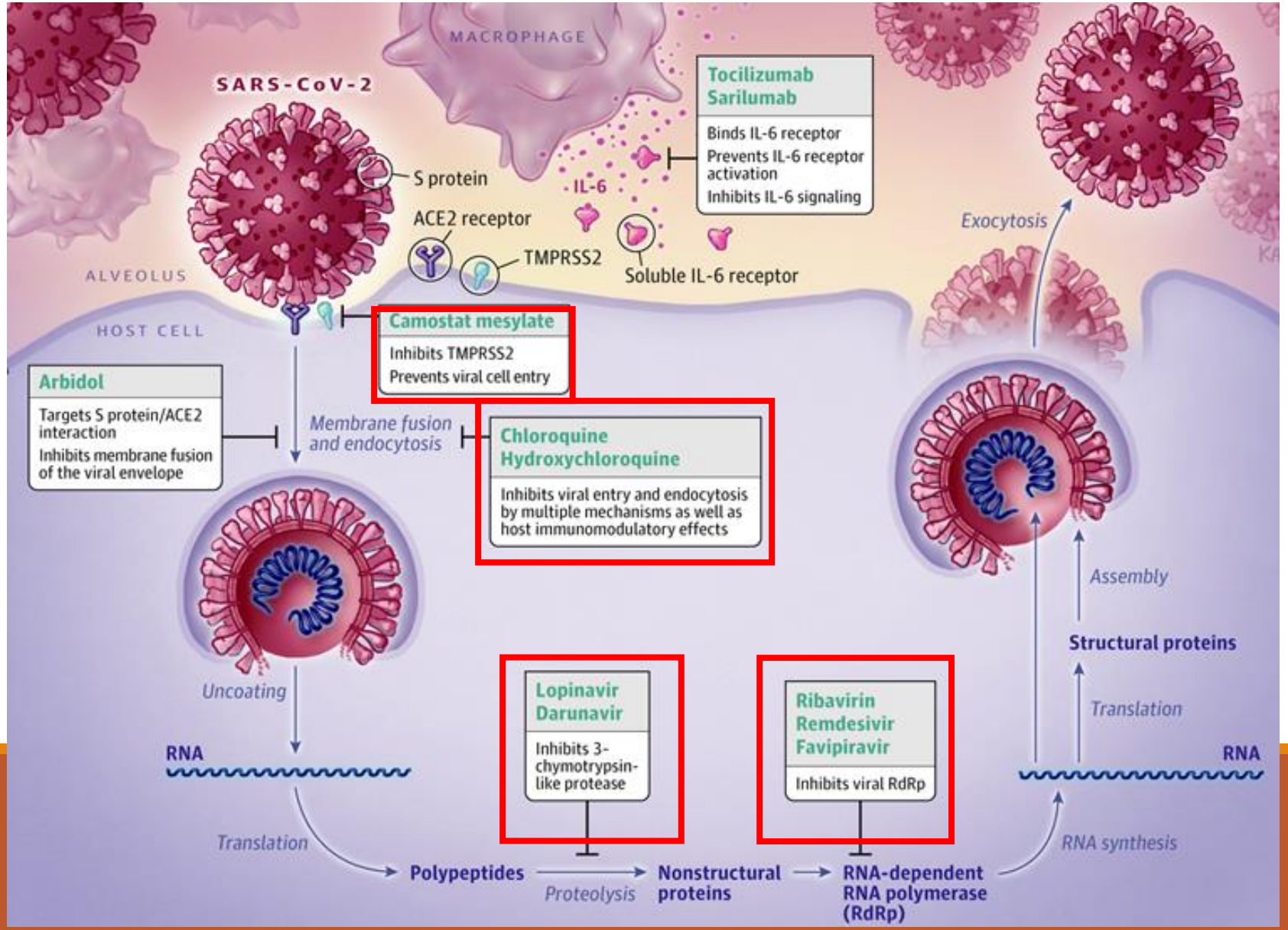


Data source: Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. *Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020.* China CDC Weekly. Case counts: 36,160 mild cases; 6,168 severe cases; 2,087 critical cases.

Goals of Treatment Across the **COVID-19 Spectrum**



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

Sanders et al JAMA 2020

Treatment: Some Suggested Options

Remdesivir

Chloroquine

Hydroxychloroquine

Lopinavir/ritonavir

Darunavir/cobicistat

Ribavirin

Nitazoxanide

Niclosamide

Favipiravir

Convalescent serum

Monoclonal antibody

Nelfinavir

Penciclovir

Mefloquine

Oseltamivir

Immunomodulators

- Corticosteroids
- Tocilizumab
- INF-alpha (inhalational)
- IVIG
- Baricitinib
- Interferon lambda

Open Forum Infectious Diseases, ofaa105, https://doi.org/10.1093/ofid/ofaa105

Case of HCQ: From single arm studies and observational cohorts …

International Journal of Antimicrobial Agents
Available online 20 March 2020, 105949
In Press, Journal Pre-proof

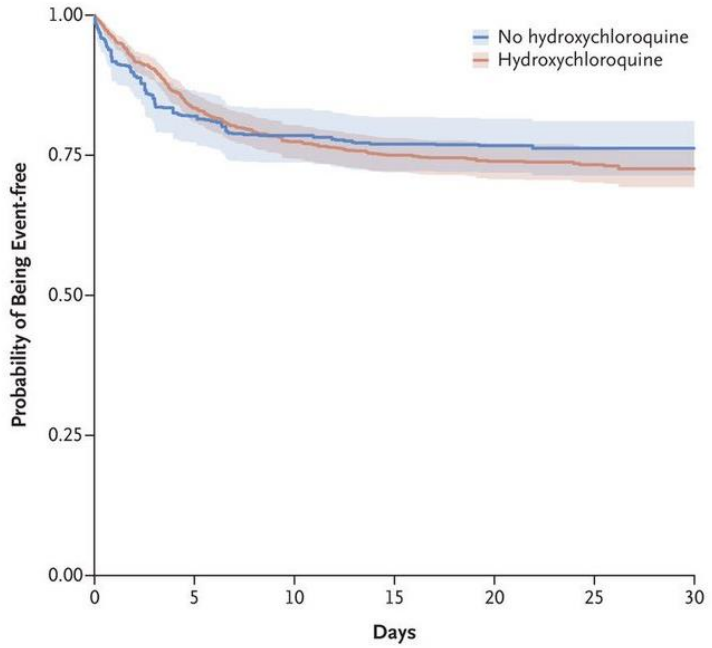
Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial

Philippe Gautret [a, b, $], Jean-Christophe Lagier [a, c, $], Philippe Parola [a, b], Van Thuan Hoang [a, b, d], Line Meddeb [a], Morgane Mailhe [a], Barbara Doudier [a], Johan Courjon [e, f, g], Valérie Giordanengo [h], Vera Esteves Vieira [a], Hervé Tissot Dupont [a, c], Stéphane Honoré [i, j], Philippe Colson [a, c], Eric Chabrière [a, c], Bernard La Scola [a, c], Jean-Marc Rolain [a, c], Philippe Brouqui [a, c], Didier Raoult [a, c]

ORIGINAL ARTICLE

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. Manson, M.D., Christine Kubin, Pharm.D., R. Graham Barr, M.D., Dr.P.H., Magdalena E. Sobieszczyk, M.D., M.P.H., and Neil W. Schluger, M.D.



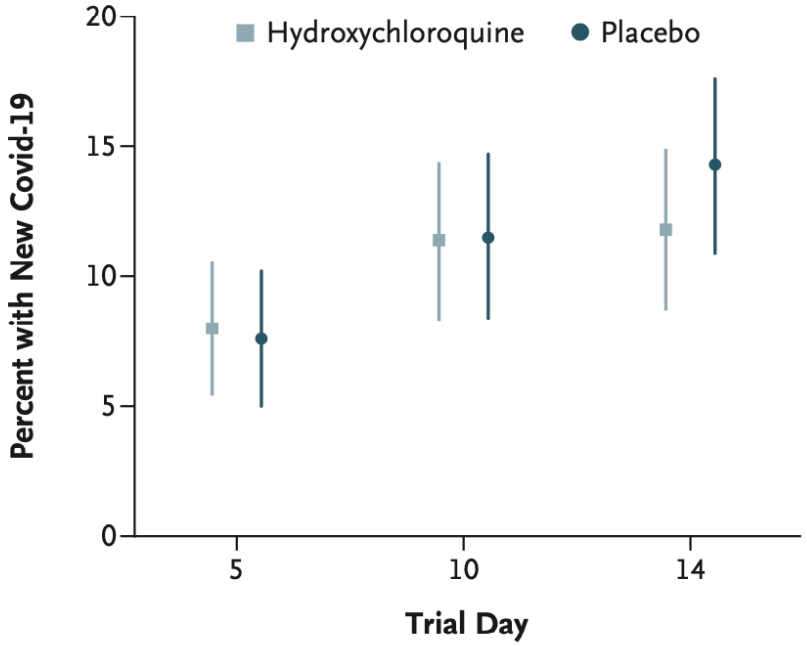
the bmj | BMJ 2020;369:m1844 | doi: 10.1136/bmj.m1844

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

Matthieu Mahévas,[1] Viet-Thi Tran,[2] Mathilde Roumier,[3] Amélie Chabrol,[4] Romain Paule,[3] Constance Guillaud,[1] Elena Fois,[1] Raphael Lepeule,[5] Tali-Anne Szwebel,[6] François-Xavier Lescure,[7] Frédéric Schlemmer,[8] Marie Matignon,[9] Mehdi Khellaf,[1] Etienne Crickx,[1] Benjamin Terrier,[6] Caroline Morbieu,[6] Paul Legendre,[6] Julien Dang,[2] Yoland Schoindre,[3] Jean-Michel Pawlotsky,[10] Marc Michel,[1] Elodie Perrodeau,[2] Nicolas Carlier,[11] Nicolas Roche,[11] Victoire de Lastours,[12] Clément Ourghanlian,[13] Solen Kerneis,[14] Philippe Ménager,[15] Luc Mouthon,[6] Etienne Audureau,[16] Philippe Ravaud,[2] Bertrand Godeau,[1] Sébastien Gallien,[17] Nathalie Costedoat-Chalumeau[2,6]

HCQ: **To randomized controlled trials…**

Post-exposure prophylaxis



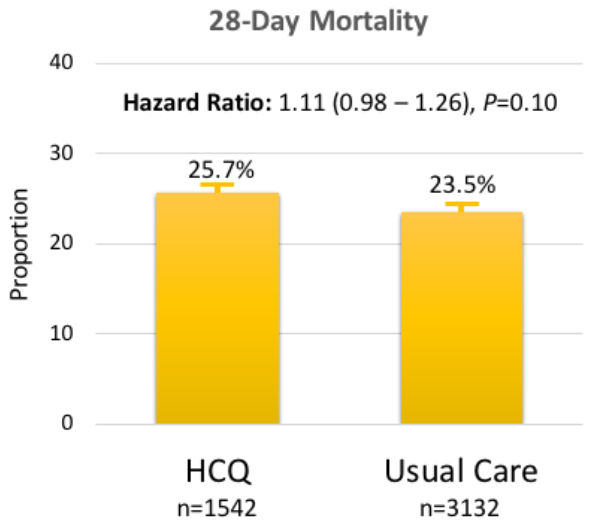
Limitation: only 2-3% confirmed dx

Hospitalized patients

RECOVERY
Randomised Evaluation of COVID-19 Therapy

Statement from the Chief Investigators of the Randomised Evaluation of COVid-19 thERapY (RECOVERY) Trial on hydroxychloroquine, 5 June 2020

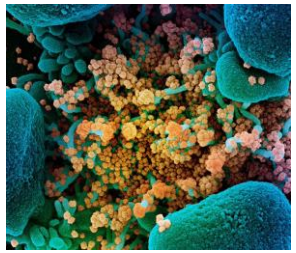
No clinical benefit from use of hydroxychloroquine in hospitalised patients with COVID-19



Media Advisory Saturday, June 20, 2020

NIH halts clinical trial of hydroxychloroquine

Study shows treatment does no harm, but provides no benefit



Boulware et al, NEJM 2020

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

- Re-purposed in 2015 for Ebola: inhibited viral replication in rhesus macaques.

- 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

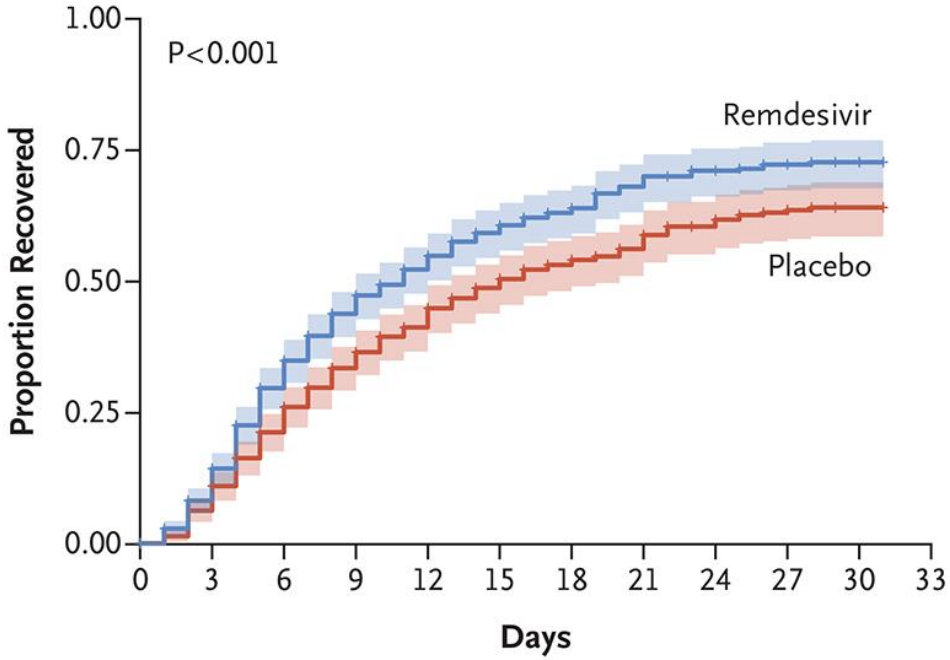
- Inhibits viral replication in cell cultures: SARS CoV, MERS-CoV, SARS CoV2 → human trials for COVID-19

nature
https://doi.org/10.1038/s41586-020-2423-5
Accelerated Article Preview

Clinical benefit of remdesivir in rhesus macaques infected with SARS-CoV-2

Received: 23 April 2020
Accepted: 2 June 2020
Accelerated Article Preview Published online 9 June 2020

Brandi N. Williamson, Friederike Feldmann, Benjamin Schwarz, Kimberly Meade-White, Danielle P. Porter, Jonathan Schulz, Neeltje van Doremalen, Ian Leighton, Claude Kwe Yinda, Lizzette Pérez-Pérez, Atsushi Okumura, Jamie Lovaglio, Patrick W. Hanley, Greg Saturday, Catharine M. Bosio, Sarah Anzick, Kent Barbian, Tomas Cihlar, Craig Martens, Dana P. Scott, Vincent J. Munster & Emmie de Wit



Beigel JH, NEJM 2020

Remdesivir Clinical Trials

NIH U.S. National Library of Medicine

ClinicalTrials.gov

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)

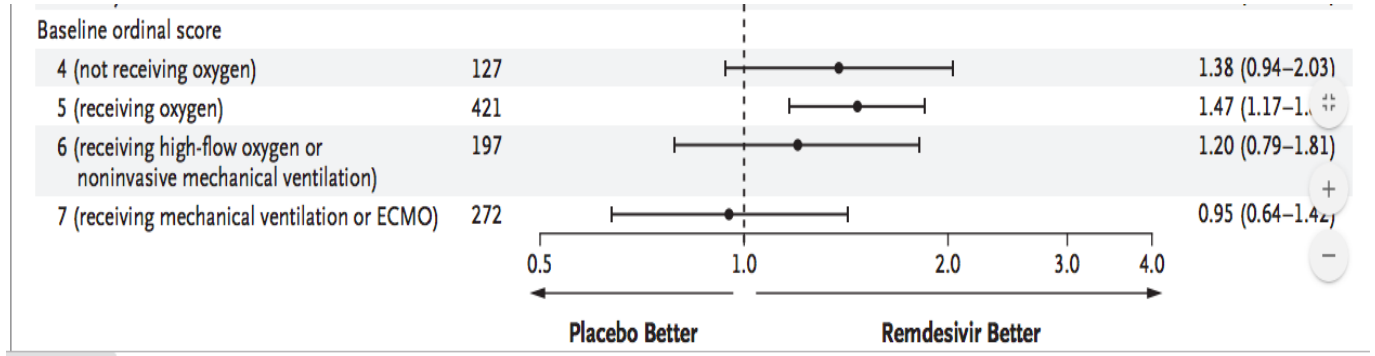
Remdesivir for the Treatment of Covid-19 — Preliminary Report

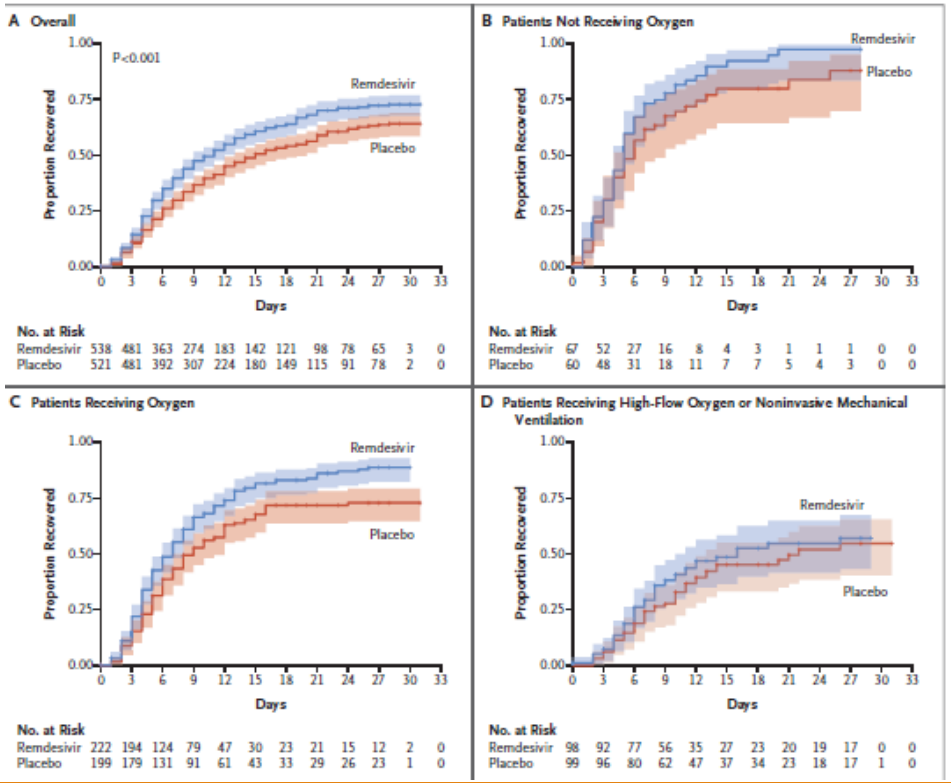
J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

The NEW ENGLAND JOURNAL of MEDICINE

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

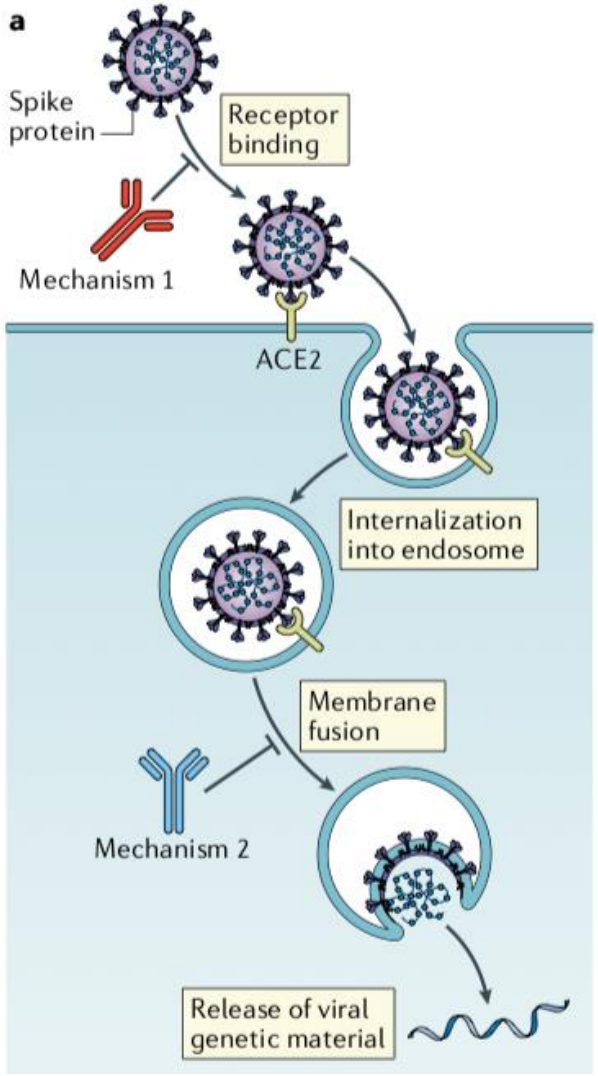
DOI: 10.1056/NEJMoa2007764





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

Decrease inflammation

Steroids: Case of Dexamethasone

RECOVERY
Randomised Evaluation of COVID-19 Therapy
Open label, 175 NHS Hospitals in the UK

- 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

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

Conclusion: Dexamethasone associated with decreased mortality among those on supplemental oxygen or on mechanical ventilation/ECMO. No benefit in those not requiring oxygen.

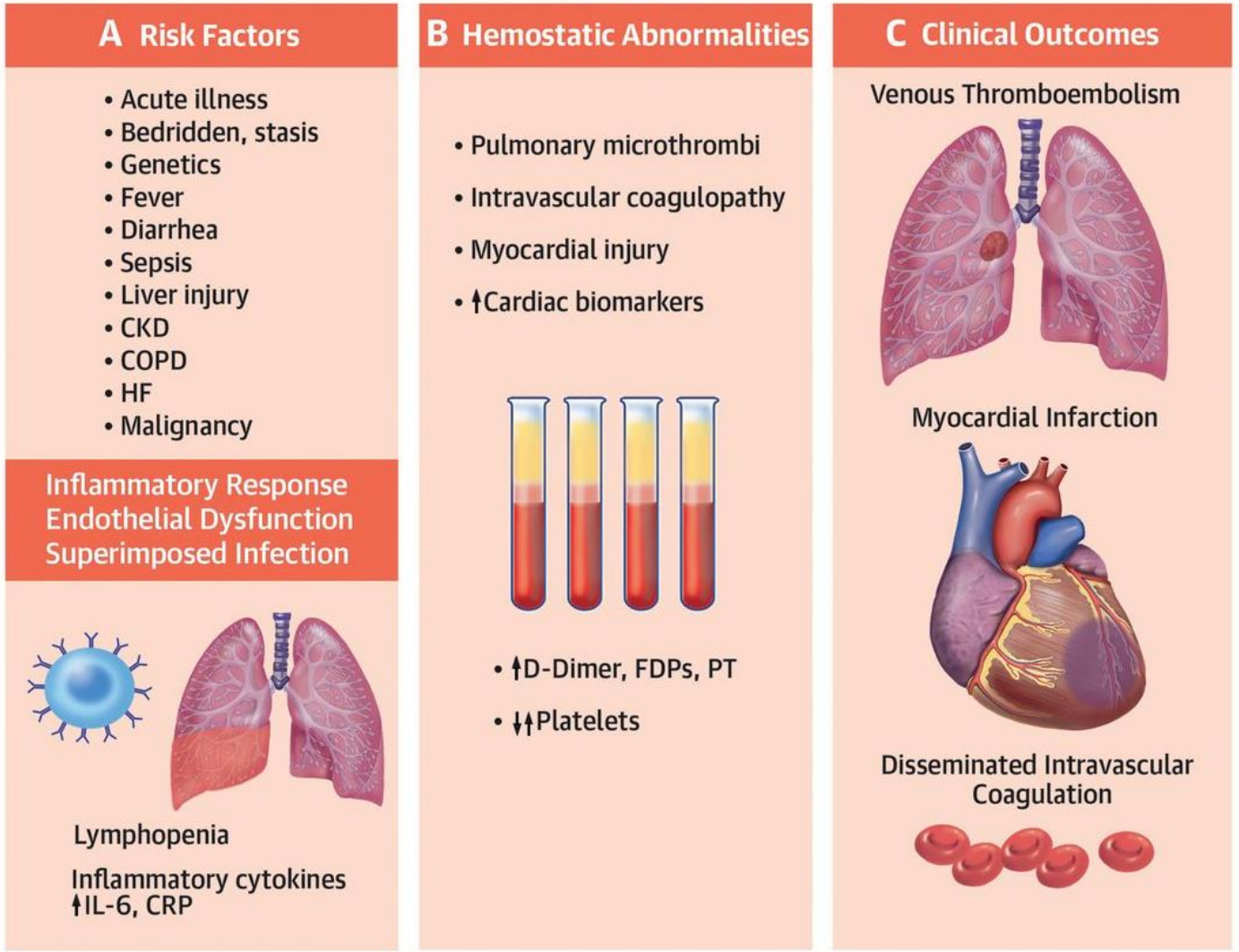
Treating Complications: Role of Anticoagulation

- 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



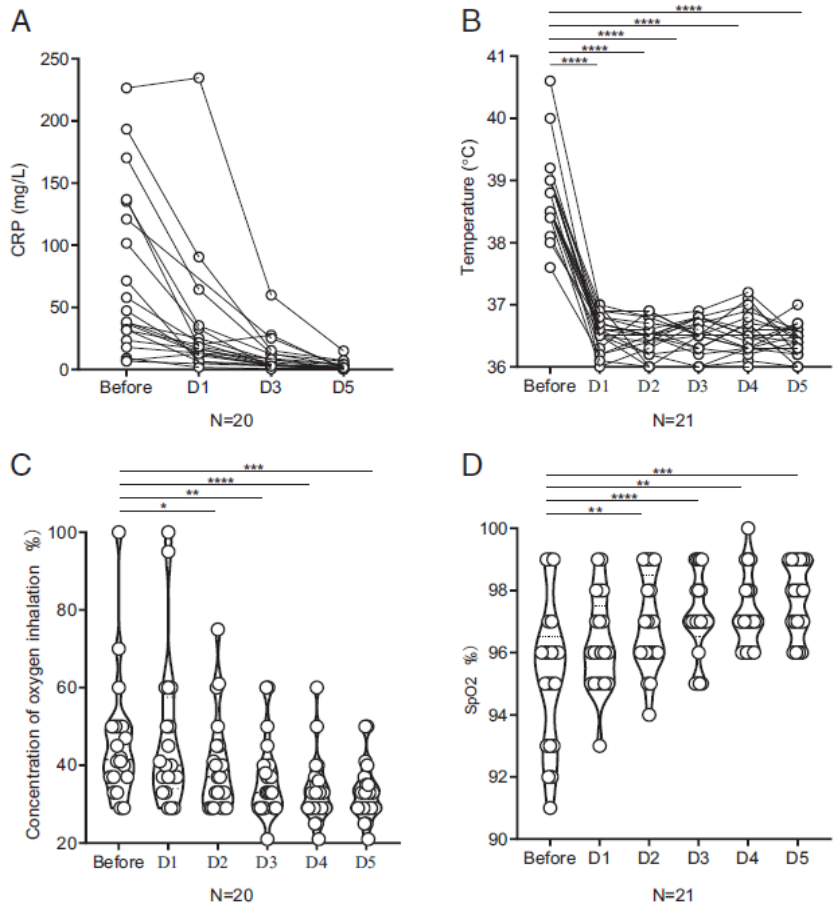
NIH Covid-19 Treatment Guidelines; Bikdeli B et al JACC 2020

Effective treatment of severe COVID-19 patients with tocilizumab

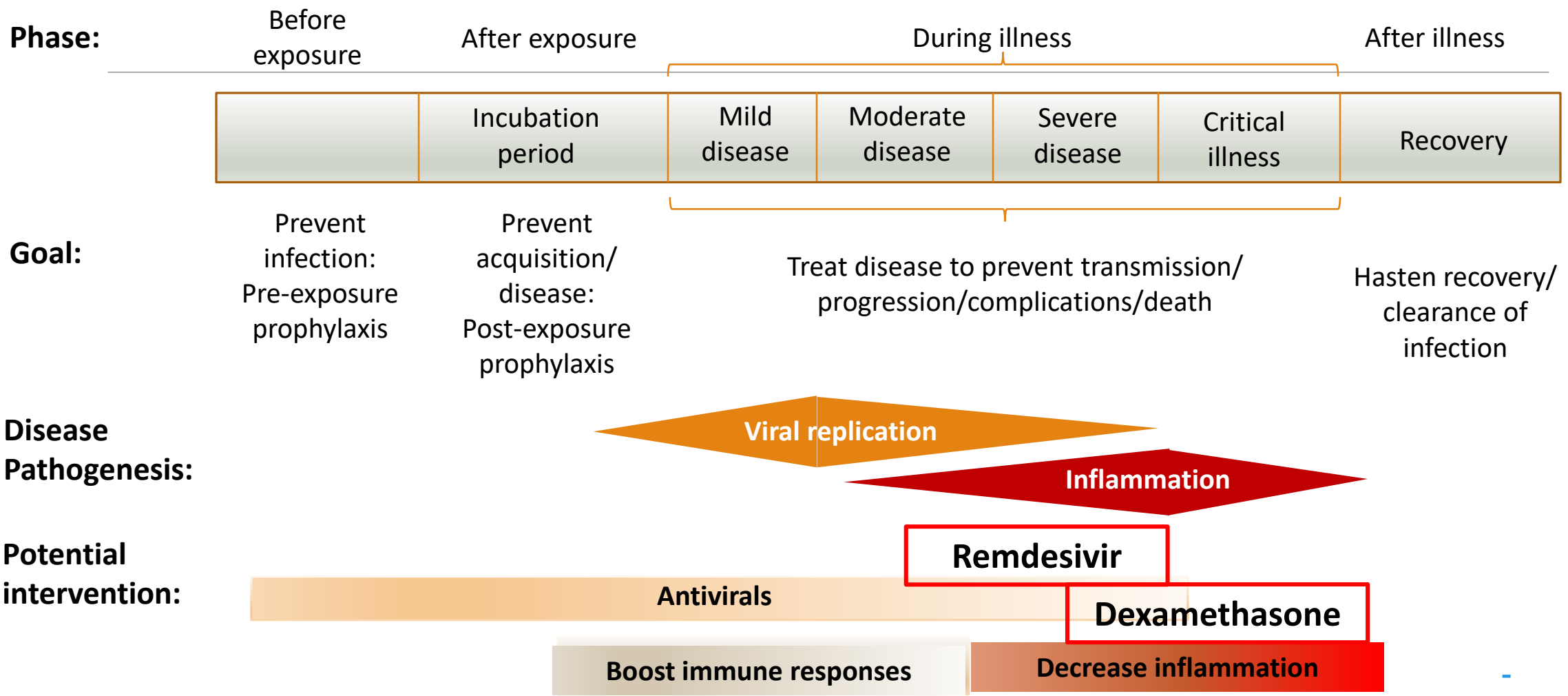
Xiaoling Xu[a,1,2], Mingfeng Han[b,1], Tiantian Li[a], Wei Sun[b], Dongsheng Wang[a], Binqing Fu[c,d], Yonggang Zhou[c,d], Xiaohu Zheng[c,d], Yun Yang[e], Xiuyong Li[f], Xiaohua Zhang[b], Aijun Pan[e], and Haiming Wei[c,d,2]

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 monoclonal 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.

10970–10975 | PNAS | May 19, 2020 | vol. 117 | no. 20



Goals of Treatment Across the **COVID-19 Infection Spectrum**



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

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

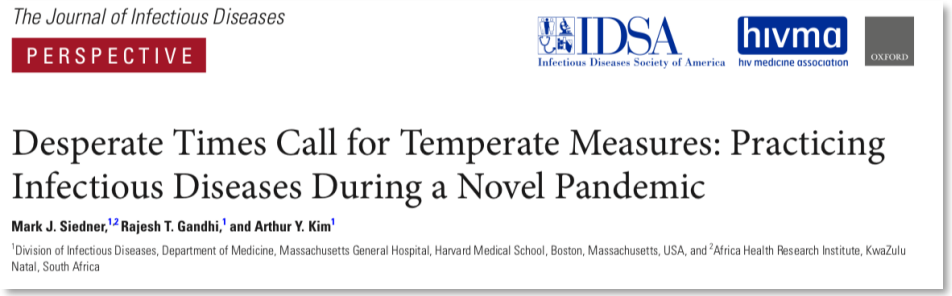
Adarsh Bhimraj*, Rebecca L. Morgan**, Amy Hirsch Shumaker, Valery Lavergne**, Lindsey Baden, Vincent Chi-Chung Cheng, Kathryn M. Edwards, Rajesh Gandhi, William J. Muller, John C. O'Horo, Shmuel Shoham, M. Hassan Murad**, Reem A. Mustafa**, Shahnaz Sultan**, Yngve Falck-Ytter**

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

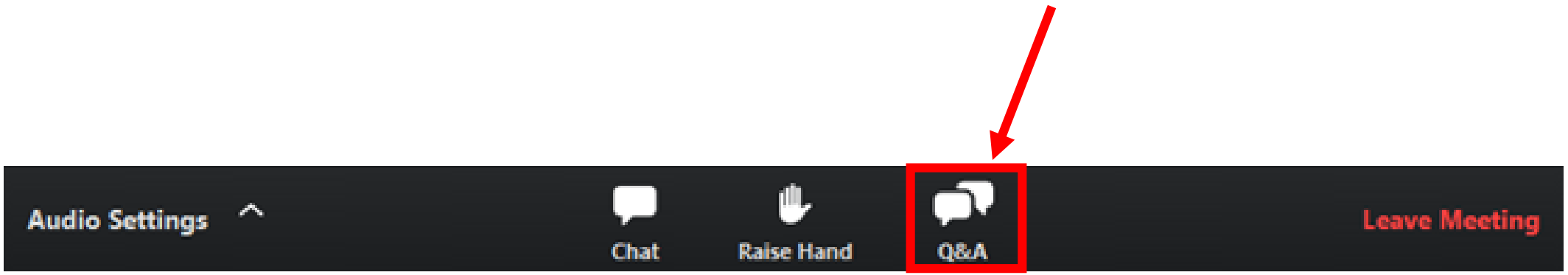
Question & Answer

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



NAM Leadership Consortium

Collaboration for a Value & Science-Driven Health System

BREAK

Resume at 12:15 PM EST

NATIONAL ACADEMY OF MEDICINE

NAM Leadership Consortium

Collaboration for a Value & Science-Driven Health System

Evidence Generation During the COVID-19 Pandemic:

Mobilizing Evidence and the General Public

NATIONAL ACADEMY OF MEDICINE

Dietram A. Scheufele
University of Wisconsin- Madison

UNDERSTANDING “INFODEMICS”

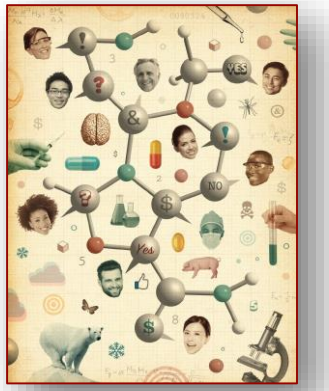
Dietram A. Scheufele
Taylor-Bascom Chair, and
Vilas Distinguished Achievement Professor

University of Wisconsin—Madison and
Morgridge Institute for Research

@scheufele
/scheufele

UNDERSTANDING "INFODEMICS"

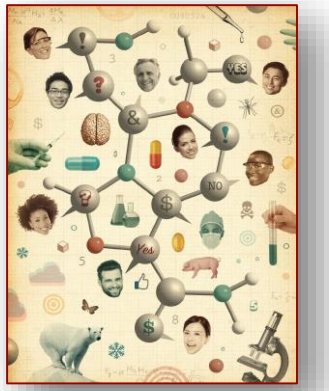
Scheufele, D. A., Krause, N. M., Freiling, I., & Brossard, D. (2020). How not to lose the COVID-19 communication war. *Issues in Science and Technology, April 17*. Retrieved from https://issues.org/covid-19-communication-war/



- 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"

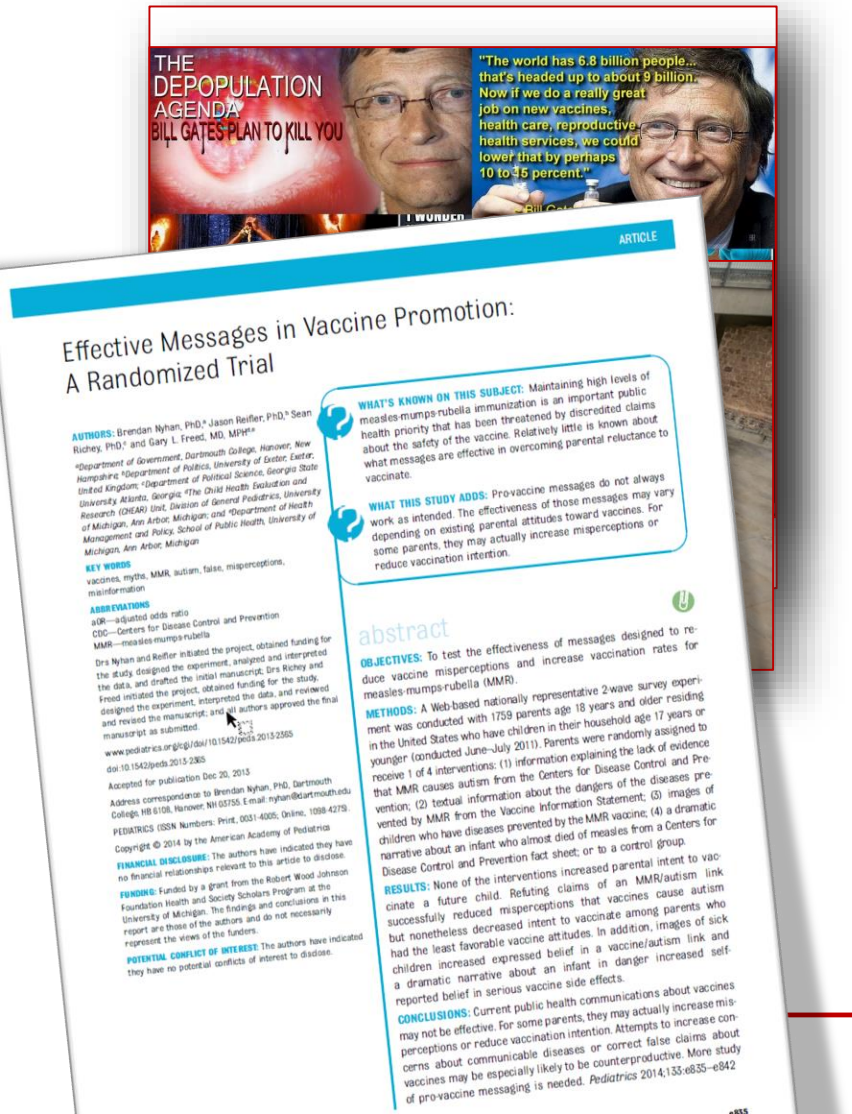
Scheufele, D. A., Krause, N. M., Freiling, I., & Brossard, D. (2020). How not to lose the COVID-19 communication war. *Issues in Science and Technology, April 17*. Retrieved from https://issues.org/covid-19-communication-war/



- 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

UW-MADISON LSC

LITTLE SYSTEMATIC SOCIAL SCIENTIFIC EVIDENCE OF A UNIQUE COVID-19 "INFODEMIC"

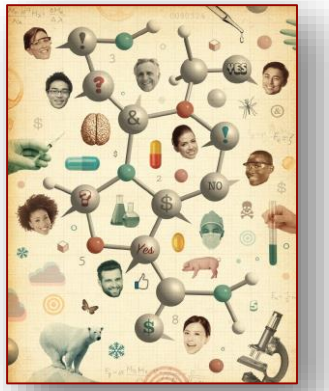


- Is there really an "infodemic?"
  - Is public trust in (COVID) science declining?
  - Is mis/disinformation more prevalent or for COVID-19 than for other areas of science, politics, etc.?
  - Does misinformation impact relevant behavioral outcomes, i.e., social distancing, wearing masks, vaccine hesitancy,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

UW-MADISON LSC

UNDERSTANDING "INFODEMICS"

Scheufele, D. A., Krause, N. M., Freiling, I., & Brossard, D. (2020). How not to lose the COVID-19 communication war. *Issues in Science and Technology, April 17*. Retrieved from https://issues.org/covid-19-communication-war/

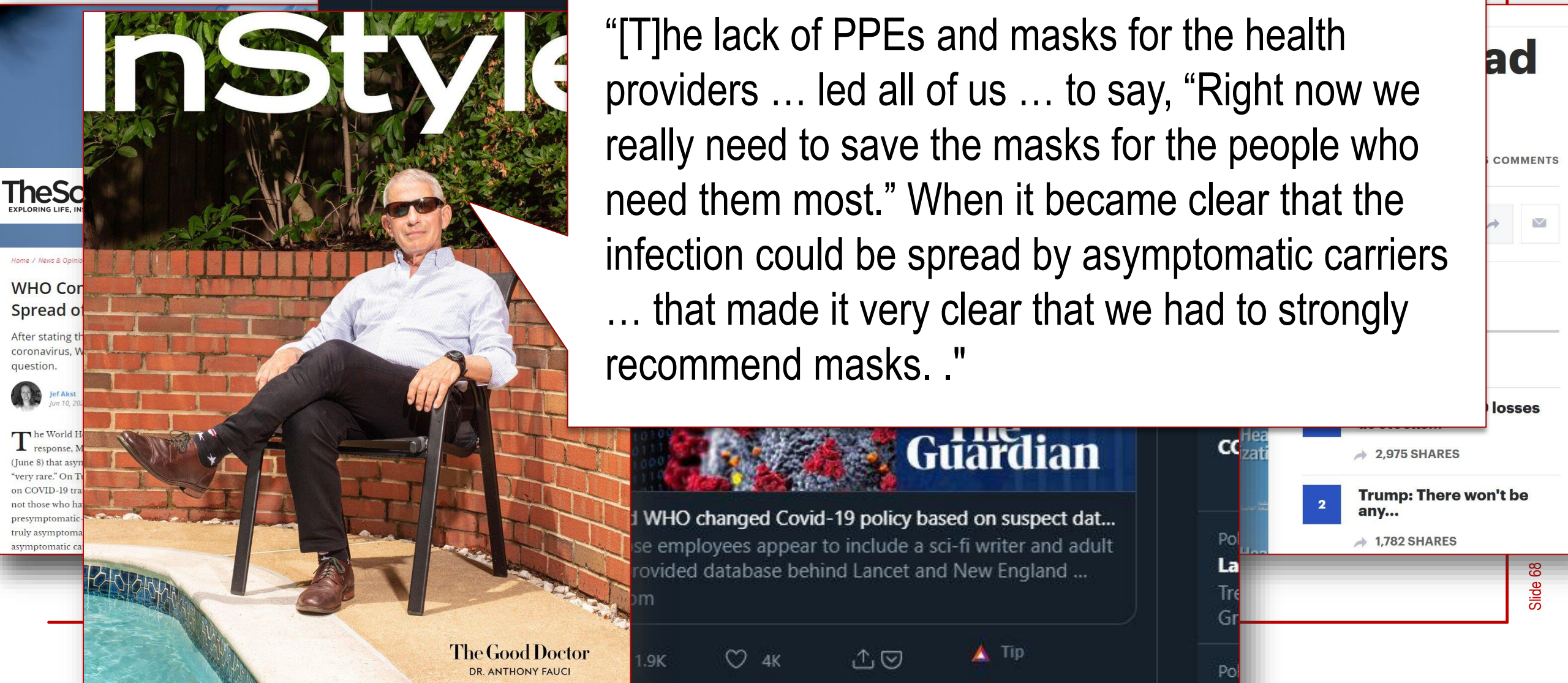


- A closer look at the COVID-19 "infodemic"
- "Facts" are elusive during pandemics
- When facts are what each of us wants them to be
- The "accelerated" wickedness of COVID-19

UW-MADISON LSC

WHAT THE "SCIENCE" OF MASKS LOOK

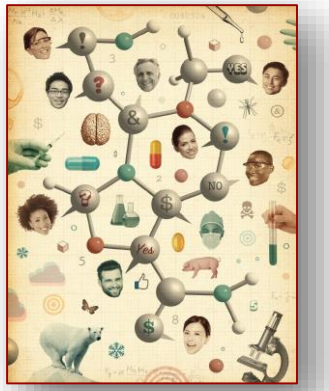
"[T]he lack of PPEs and masks for the health providers … led all of us … to say, "Right now we really need to save the masks for the people who need them most." When it became clear that the infection could be spread by asymptomatic carriers … that made it very clear that we had to strongly recommend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



UW-MADISON LSC

UNDERSTANDING "INFODEMICS"

Scheufele, D. A., Krause, N. M., Freiling, I., & Brossard, D. (2020). How not to lose the COVID-19 communication war. *Issues in Science and Technology, April 17*. Retrieved from https://issues.org/covid-19-communication-war/



- 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

ABILITY OR MOTIVATION TO ENGAGED IN BIASED REASONING?

Scheufele, D. A. (2014). Science communication as political communication. *Proceedings of the National Academy of Sciences, 111*(Supplement 4), 13585-13592. doi:10.1073/pnas.1317516111

- 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 …

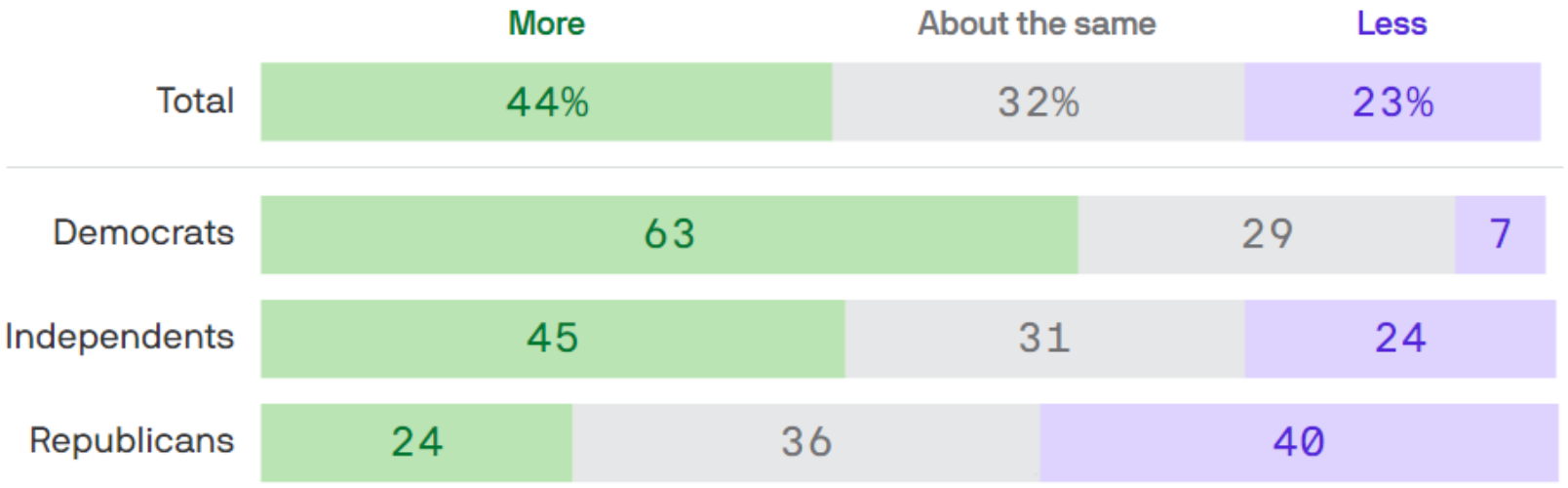
UW-MADISON LSC

WE EVEN DISAGREE ON THE MOST BASIC FACTS

https://www.axios.com/axios-ipsos-coronavirus-week-8-5a1947d5-9850-4e58-9583-9b617e6fdc1b.html

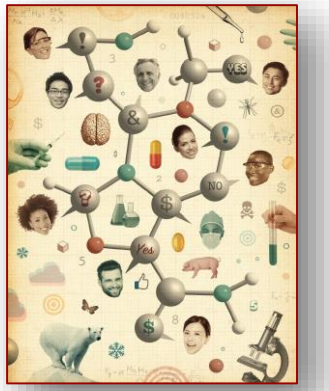
Do you believe the number of Americans dying from COVID-19 is more, less, or about the same as the reported number?

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



UNDERSTANDING “INFODEMICS”

Scheufele, D. A., Krause, N. M., Freiling, I., & Brossard, D. (2020). How not to lose the COVID-19 communication war. *Issues in Science and Technology, April 17*. Retrieved from https://issues.org/covid-19-communication-war/



- 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

THERE IS NO SINGLE SILVER #SCICOMM BULLET …

- … 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

UW-MADISON LSC

THANK YOU

@scheufele
/scheufele

Funding:

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

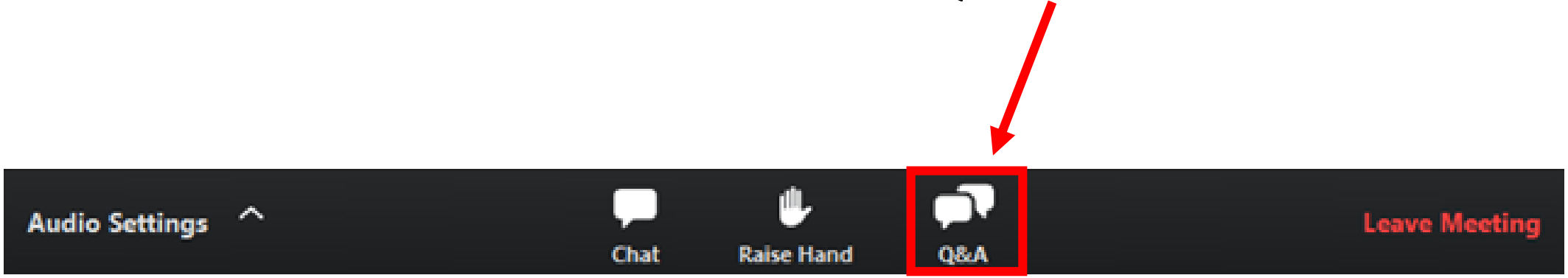
Question & Answer

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



NAM Leadership Consortium

Collaboration for a Value & Science-Driven Health System

FDA Evidence Accelerator

NATIONAL ACADEMY OF MEDICINE

Amy Abernethy
Food and Drug Administration

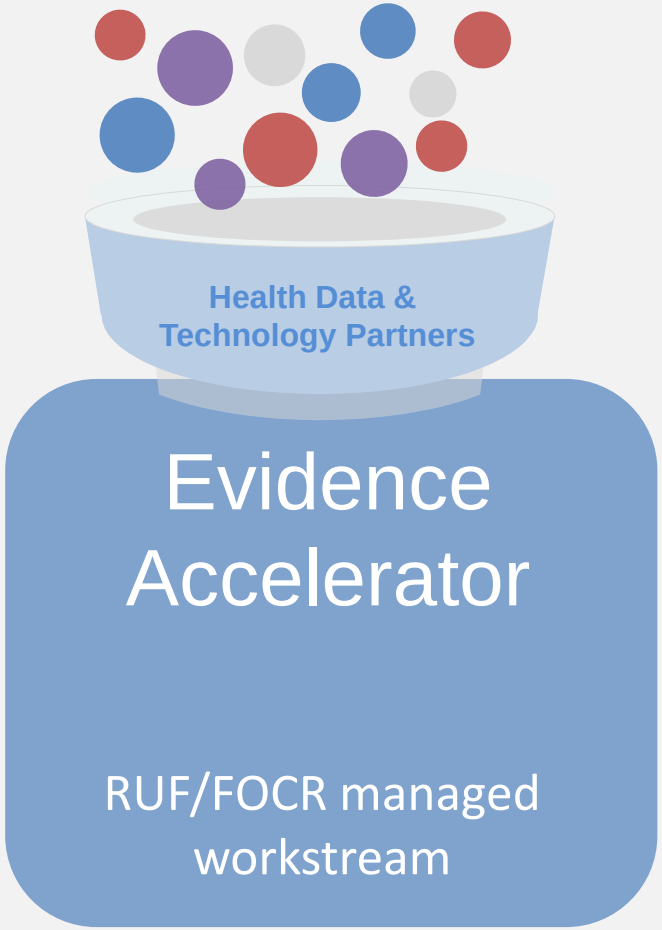
Real-world Evidence Accelerator – Lessons Learned from COVID-19

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 RUF/FOCR* Evidence Accelerator

REAGAN-UDALL FOUNDATION for the Food and Drug Administration

FRIENDS of CANCER RESEARCH

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

https://evidenceaccelerator.org/

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-turn-around 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 deploy 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 (3) 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 RUF/FOCR* Evidence Accelerator

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

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?

The RUF/FOCR* Evidence Accelerator

Collaborative group effort to align and work on a common research question

*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

The RUF/FOCR* Evidence Accelerator

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

Lab Meeting

COVID-19 EVIDENCE ACCELERATOR
LAB MEETING 1

REAGAN-UDALL FOUNDATION for the Food and Drug Administration

FRIENDS of CANCER RESEARCH

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

Tailored to Specific Topics

Crowdsourcing the Question

How can RWE inform OCE's efforts?

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?

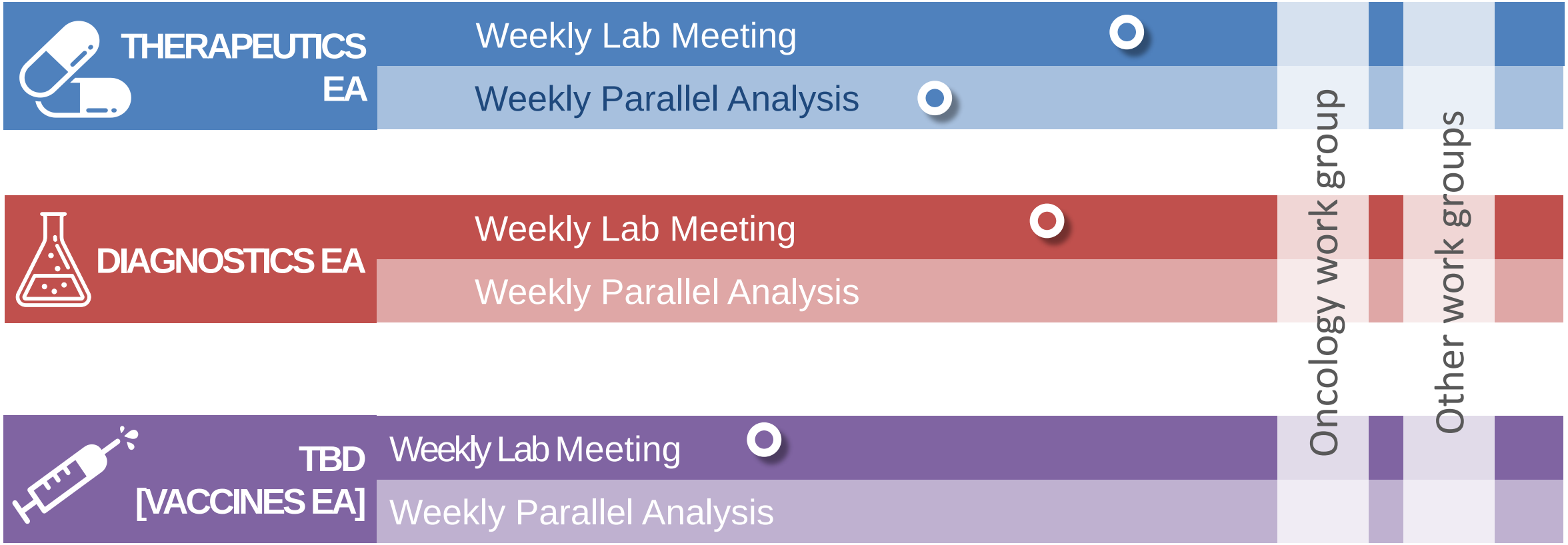
And the list goes on….

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

RUF / FOCR* Evidence Accelerator Work Streams

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



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

COVID-19 Evidence Accelerator (EA) Launch

April 16, 2020

First “Lab” Meeting

Diagnostics EA Launch

May 28, 2020

Weekly Lab EA

Weekly Lab EA

Weekly Lab EA

Weekly Lab EA

Weekly Lab EA

Weekly Lab EA

Parallel Analysis Project 1

April 22, 2020

HCQ +/- azithromycin in hospitalized patients

Weekly Diagnostics Lab EA

Oncology Workgroup

June 2020

Weekly Therapeutics Lab EA

Dx Parallel Analysis

Project 1

PCR+, plus serology

July 2020

Parallel Analysis

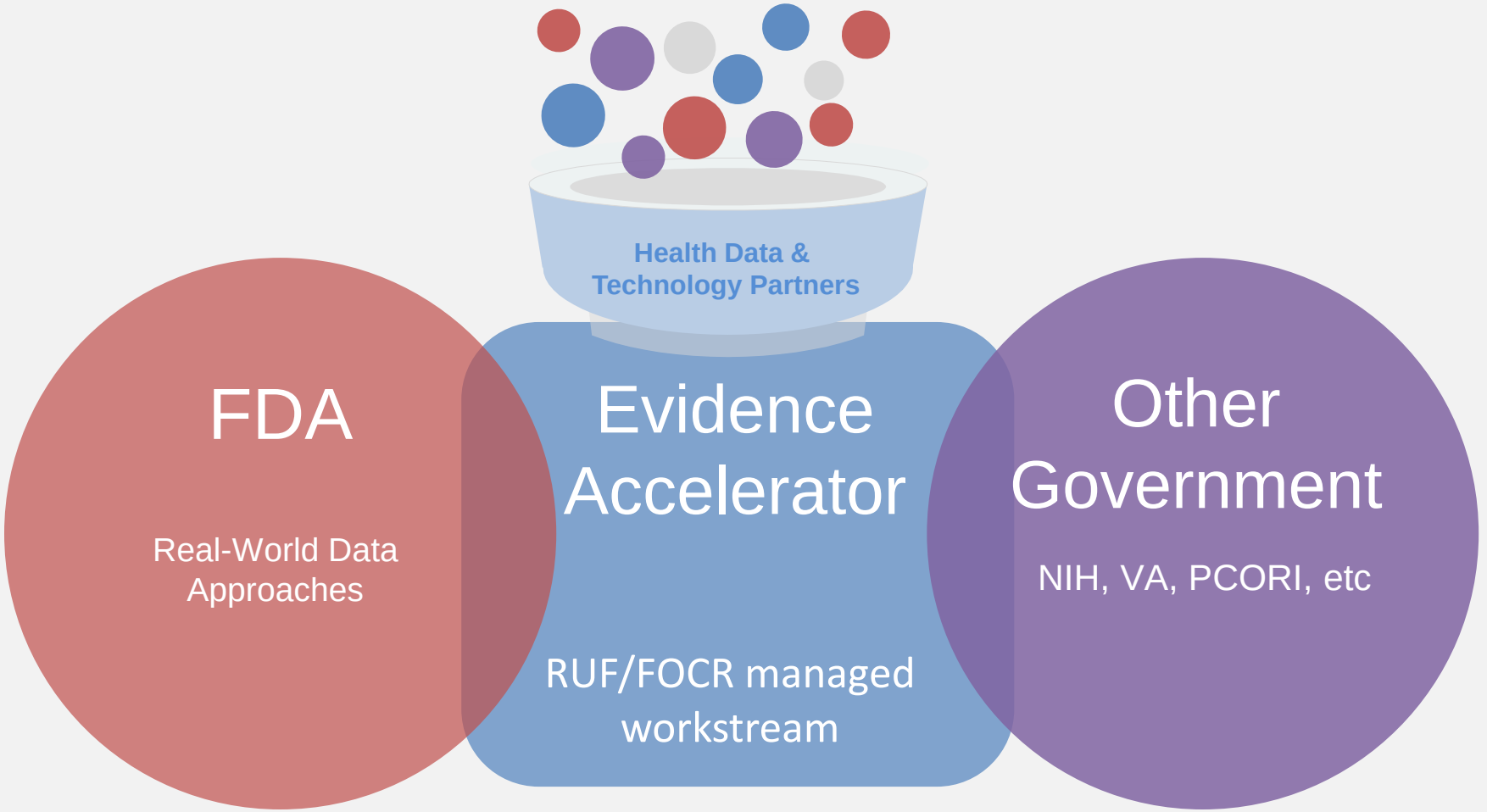
Next Projects:

Coagulopathy

Remdesivir

July 2020

Real-World Data for COVID-19



Sits within a larger RWD Community

Our Responsibility

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

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

RWD Priorities

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

DRAFT PRINCIPLES for the EA

01 **Respect for patient privacy**

02 **Act fast,** Traceability and provenance – understand data generation, processing, curation, and analytics

03 **Transparency,** ruthless transparency

04 **Traceability and provenance** – understand data generation, processing, curation, and analytics

05 **Sharing** – show process, explore limitations, pitfalls, and celebration successes – bring work and learnings to the community

06 **Build trust** – 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

07 Embrace **convergence and discordance** to facilitate understanding

08 Learning is **additive, and continuously integrated** to improve knowledge and understanding

09 **Dissemination** – responsible evidence generation (show what good looks like)

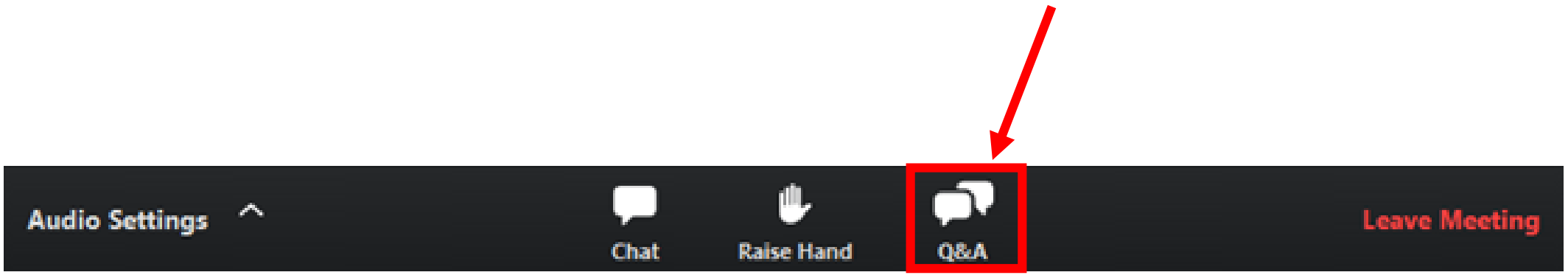
Question & Answer

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



NAM Leadership Consortium

Collaboration for a Value & Science-Driven Health System

Reflections From Speakers

NATIONAL ACADEMY OF MEDICINE

NAM Leadership Consortium

Collaboration for a Value & Science-Driven Health System

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

NATIONAL ACADEMY OF MEDICINE

Closing Remarks

Thank you for joining!

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