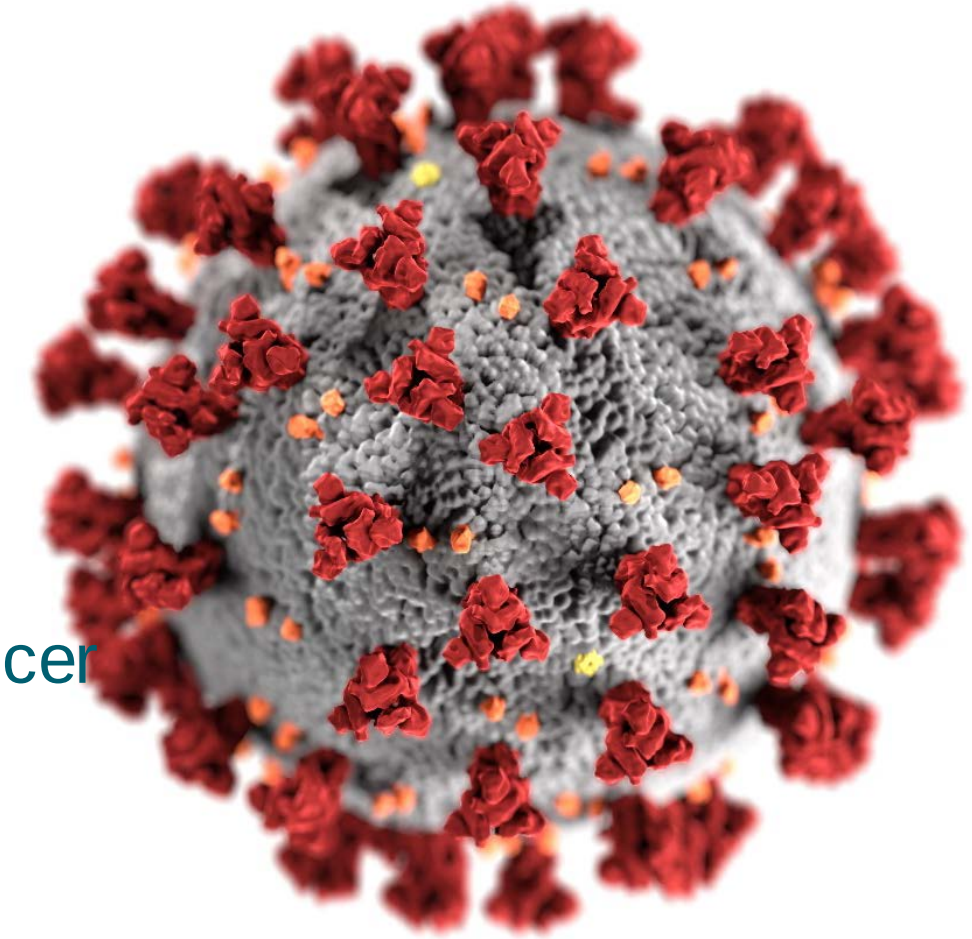
Vaccines and Related Biological Products Advisory Committee October 22, 2020 Meeting Presentation

Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please send an e-mail to: ocod@fda.hhs.gov and include 508 Accommodation and the title of the document in the subject line of your e-mail.

Epidemiology, Virology, and Clinical Features of COVID-19



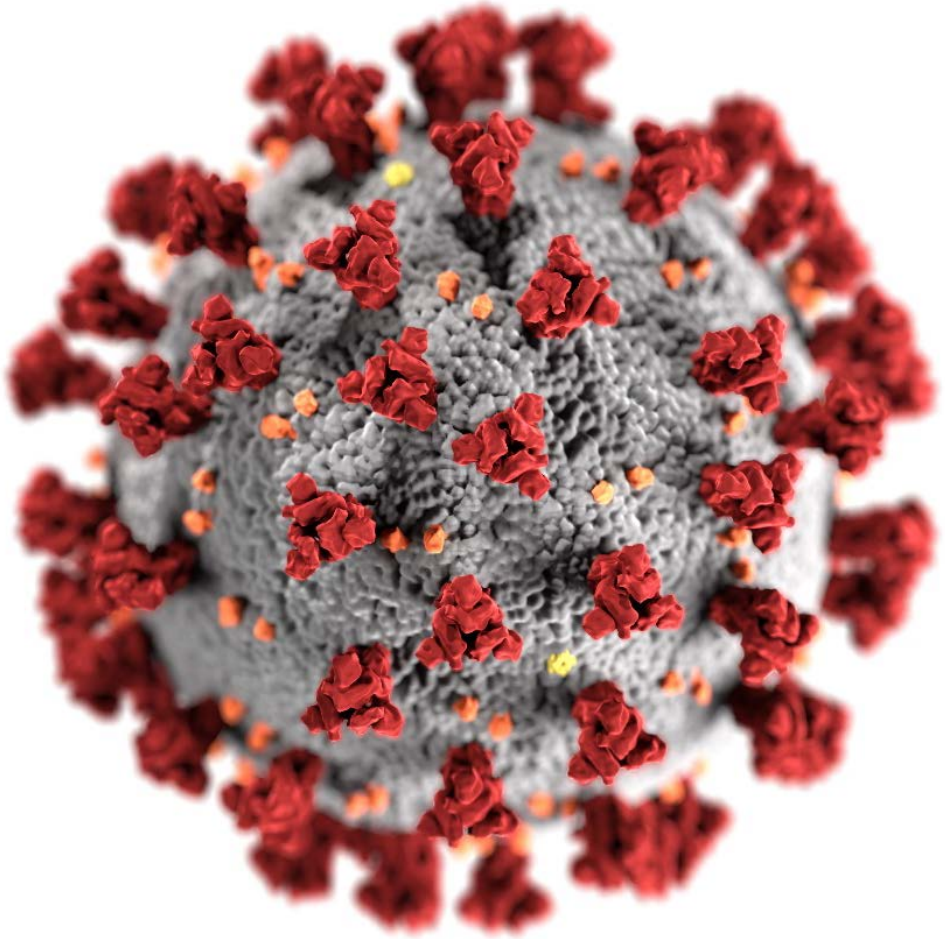
L. Clifford McDonald, MD – Chief Medical Officer
CDC, COVID-19 Emergency Response
VRBPAC Meeting
October 22, 2020

For more information: **www.cdc.gov/COVID19**

Valid as of October 15, 2020

COVID 19
CORONAVIRUS DISEASE

Dr. McDonald has no relevant financial affiliations to disclose



Acknowledgement: Dr. John Brooks

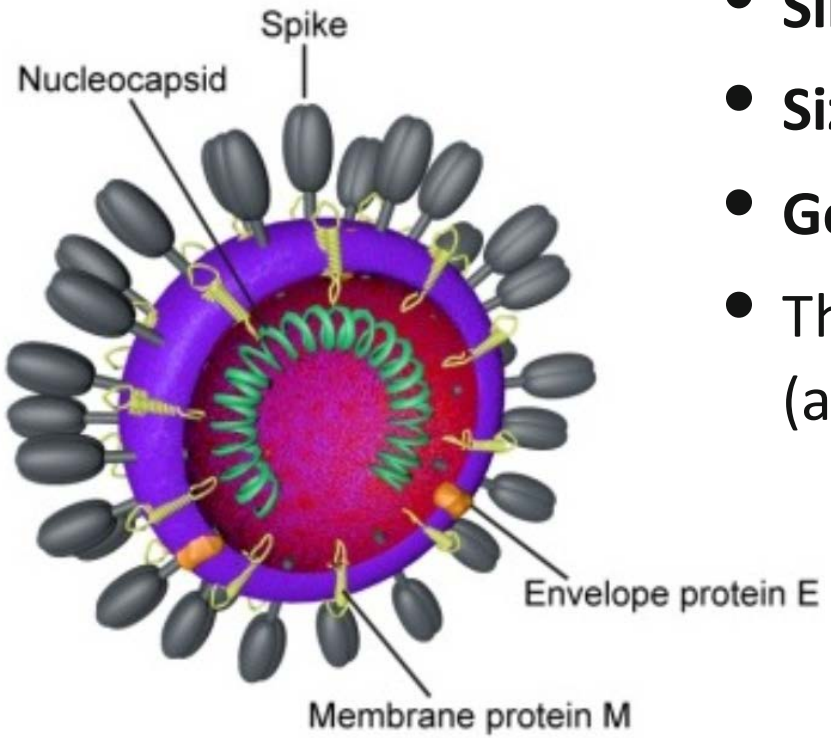
For more information: **www.cdc.gov/COVID19**

Valid as of October 15, 2020

COVID-19 Virology

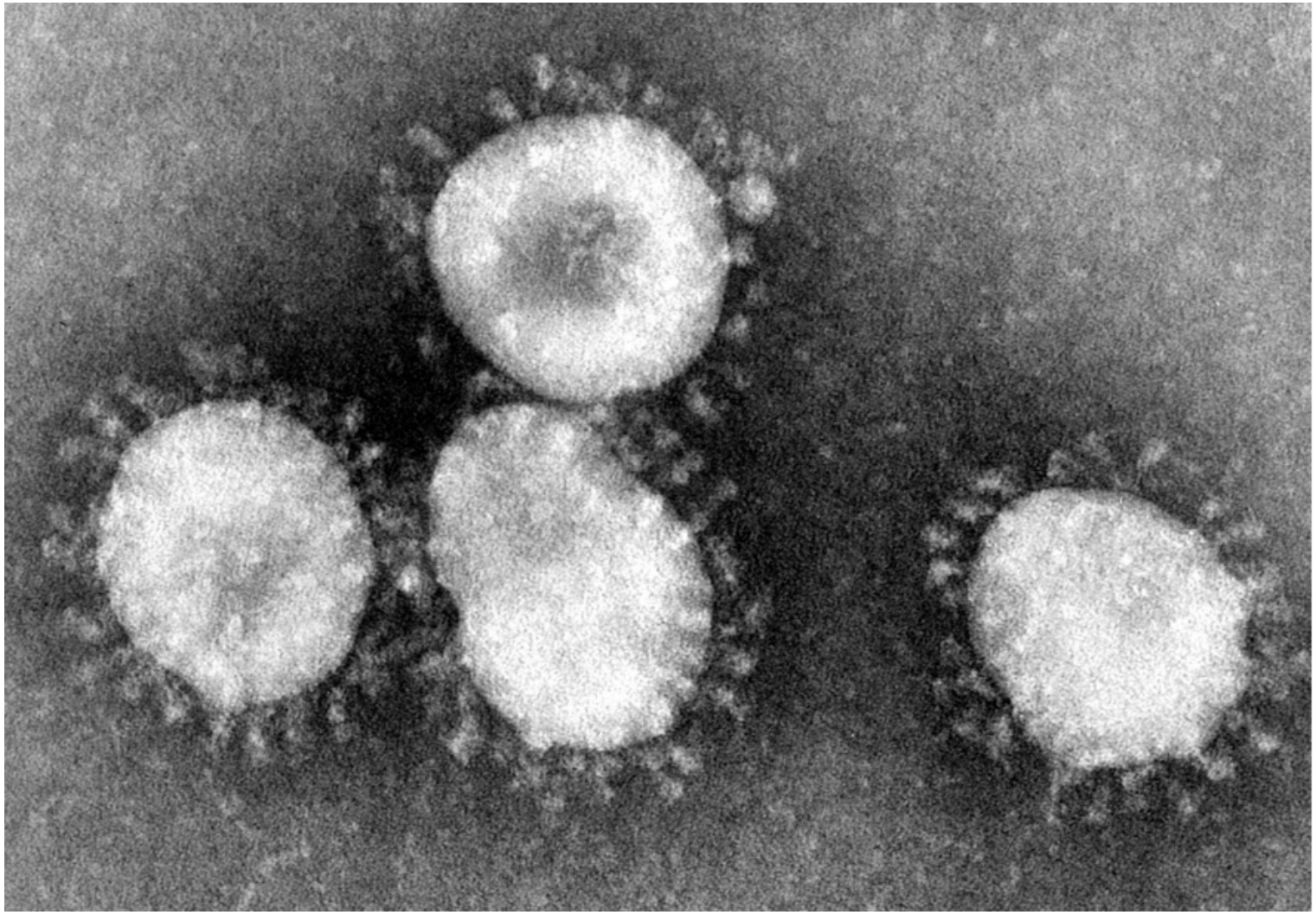
Valid as of October 15, 2020

Basic Structure of *Coronavirinae*



- **Single-stranded RNA viruses**
- **Sizes range from 65-125 nanometers**
- **Genomes range from 25 to 32 kilobases**
- The coronaviral genome encodes **4 major structural proteins** (all required to produce a structurally complete viral particle)
  - Spike (S) protein: *binding*
  - Nucleocapsid (N) protein: *RNA synthesis*
  - Membrane (M) protein: *organization/assembly*
  - Envelope (E) protein: *organization/assembly*

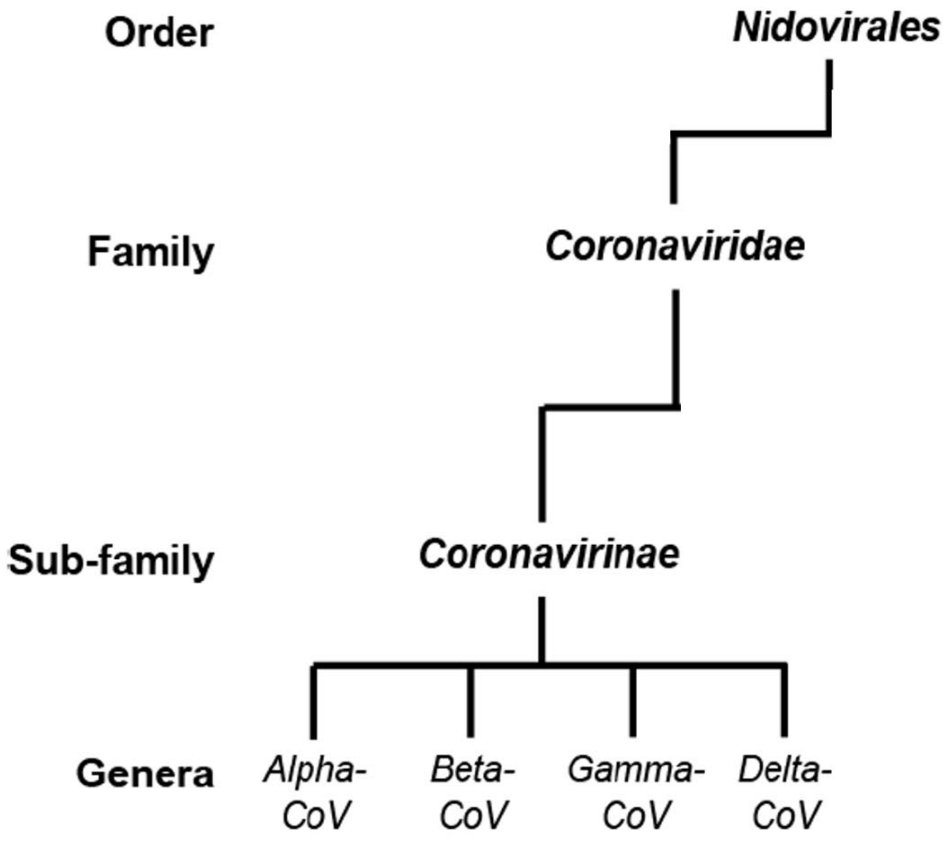
Electron Micrograph of Coronavirus Virions



Centers for Disease Control and Prevention's Public Health Image Library (PHIL), with identification number #4814.

Valid as of October 15, 2020

Coronaviridae/-virinae Belong to Order Nidovirales



Infect a wide variety of mammals and birds

- Alpha and beta: "mammals"
  - flying bats to beluga whales
- Gamma and delta: "birds"
  - sparrows to ostriches

Cause a variety of lethal diseases, with well-studied impact on the agricultural sector

- Illness is usually **respiratory or enteric**

Cong 2017, Viruses 9(182), doi:10.3390/v9070182

Seven Human Coronaviruses (HCoVs)

- **Common HCoVs (lower pathogenicity):**
  - HCoV-229E (alpha)
  - HCoV-NL63 (alpha)
  - HCoV-OC43 (beta)
  - HCoV-HKU1 (beta)
- **Other HCoVs (higher pathogenicity):**
  - SARS-CoV-1 (beta)
  - MERS-CoV (beta)
  - **SARS-CoV-2** (beta)

The illness COVID-19 is caused by SARS-CoV-2, which is more like SARS-CoV-1 than MERS-CoV

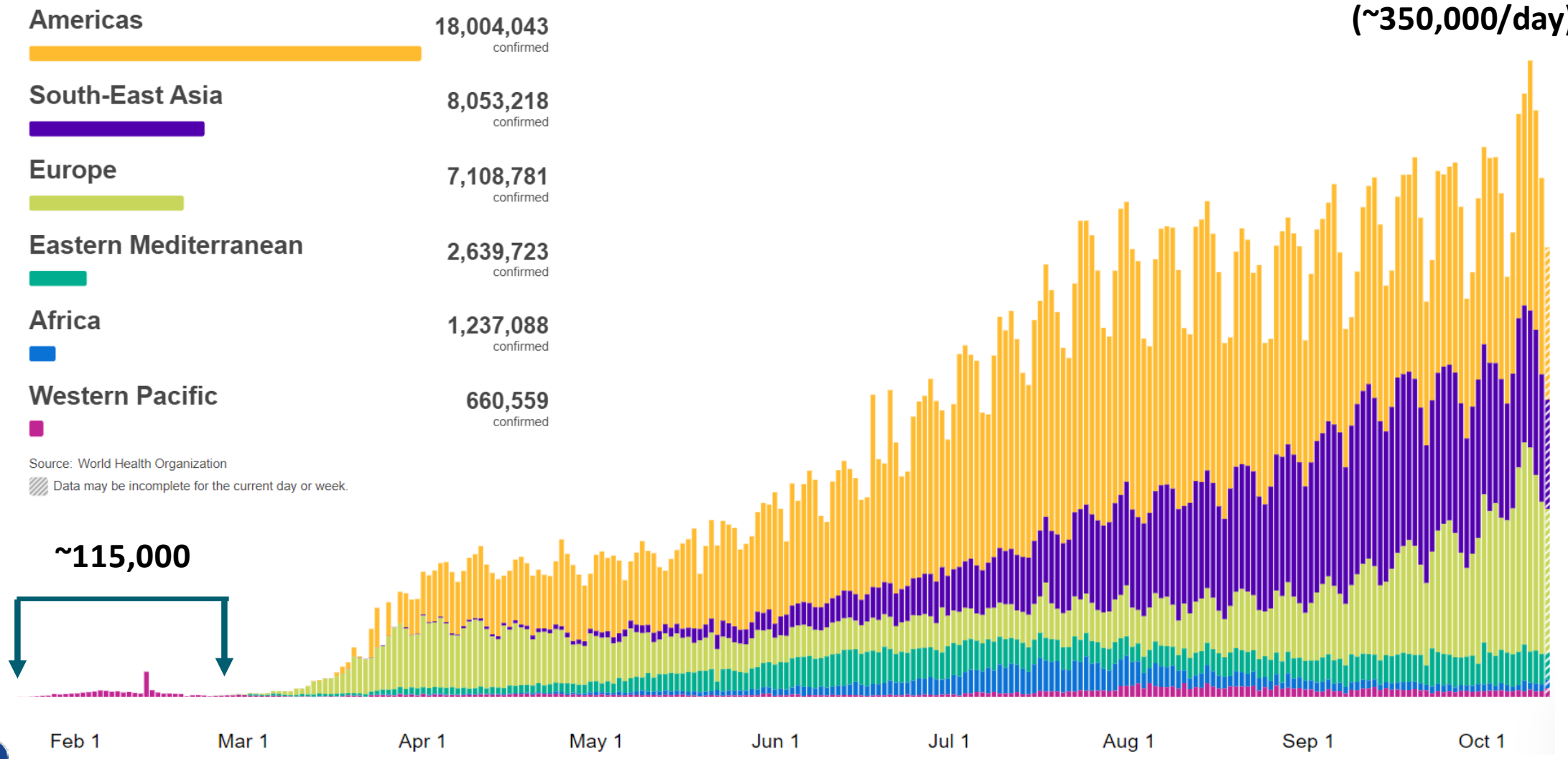
Song 2019, Viruses 11, 59; doi:10.3390/v11010059
https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it

COVID-19 Epidemiology

Valid as of October 15, 2020

Number of confirmed COVID-19 cases, by date of report and WHO region, 30 December 2019 through 13 October 2020

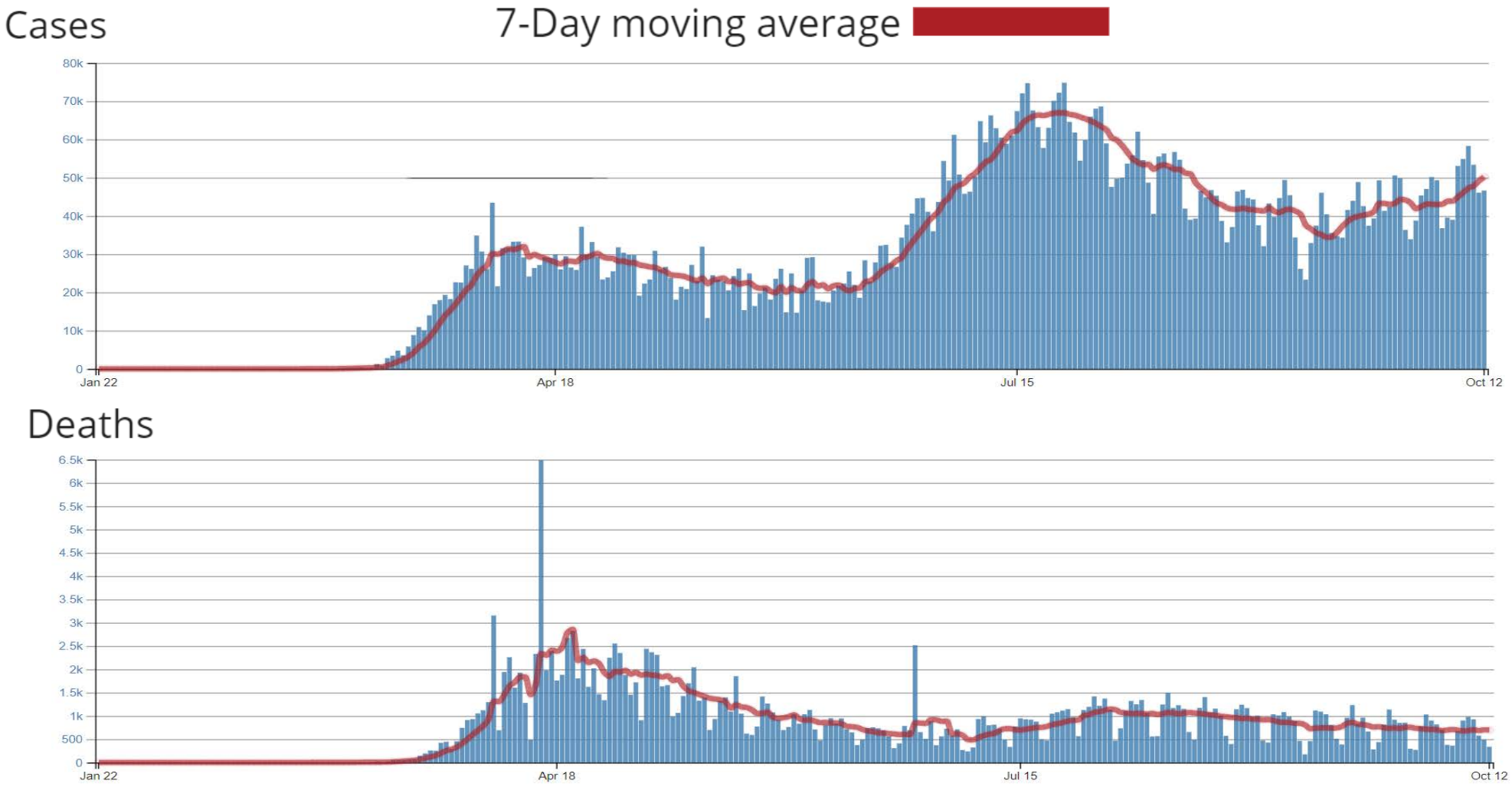
~38,000,000 total (~350,000/day)



https://covid19.who.int/

Valid as of October 15, 2020

Daily number of COVID-19 cases and deaths, U.S. through 13 October 2020
CDC COVID Data Tracker



https://covid.cdc.gov/covid-data-tracker/#trends_dailytrends

Valid as of October 15, 2020

Transmission Dynamics of Pathogenic Human *Coronavirinae* (CoV)

	SARS-CoV-1	MERS-CoV	SARS-CoV-2
Incubation period, median (range)	4-6 days (up to 16)	4-6 days (range 2-14)	4-6 days (range 2-14)
Infectious before ill	No	No	**Yes**

SARS-CoV-2

- Peak infectiousness days before symptom onset (***pre-symptomatic***) and shortly thereafter
- A substantial fraction of infections, **estimated 15-45%, are *asymptomatic***

Lauer 2020, Ann Intern Med; doi:10.7326/M20-0504. Du 2020, Emerg Infect Dis; doi.org/10.3201/eid2606.200357.
Nichiura 2020, Int J Infect Dis; doi.org/10.3201/eid2606.200357. Lipsitch 2003, Science;300(5627):1966-70.
Park 2018, BMC Public Health; doi.org/10.1186/s12889-018-5484-8

Valid as of October 15, 2020

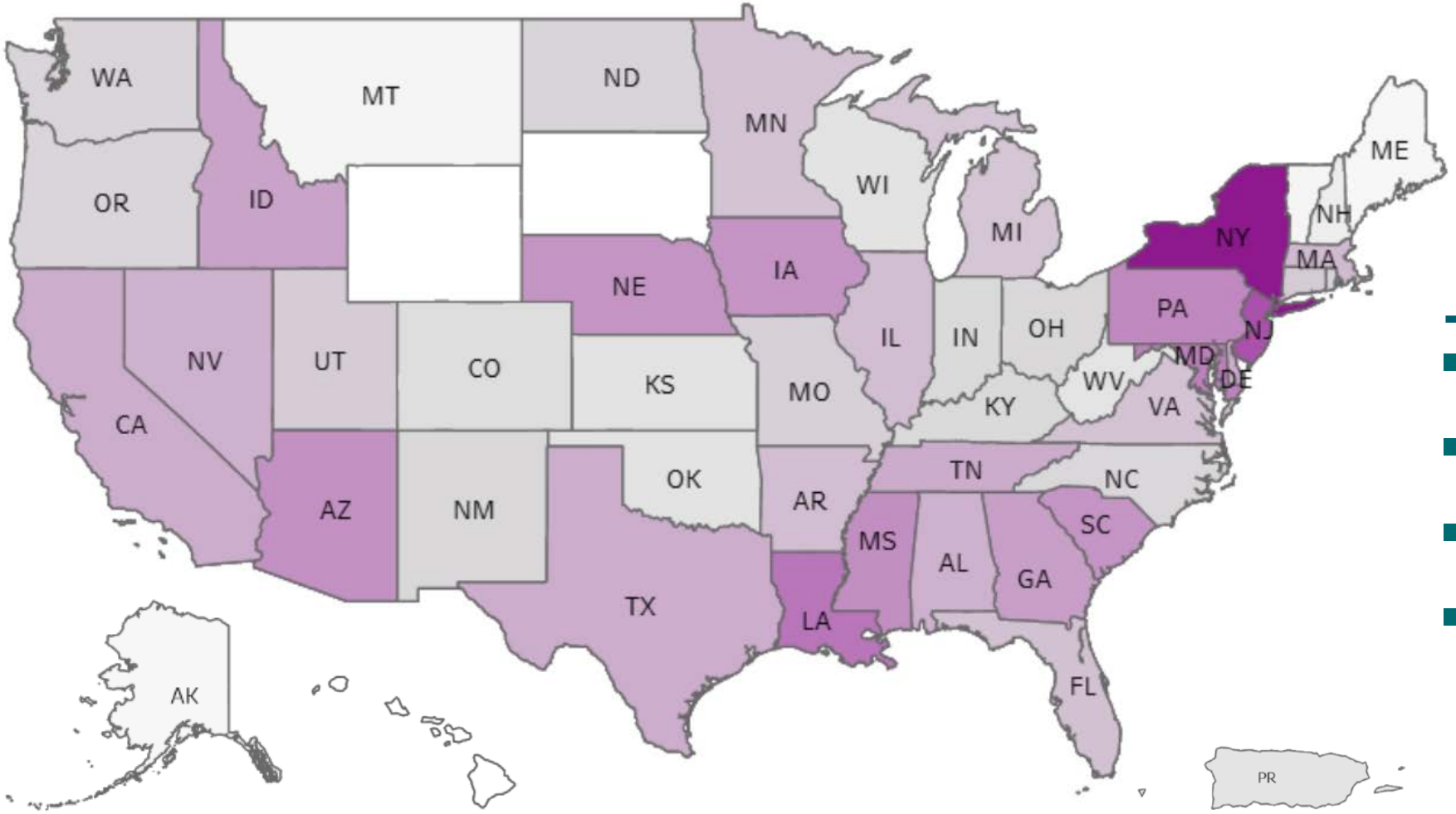
SARS-CoV-2 in Human Samples and Transmission

Sample	Mode of transmission	Detected by PCR	Isolated by culture	Observed mode of transmission
Nasopharyngeal swab	**RESPIRATORY**	**Yes**	**Yes**	**Yes**
Oropharyngeal swab		**Yes**	**Yes**	**Yes**
Sputum		**Yes**	**Yes**	**Yes**
Stool	**FECAL**	**Yes**	Yes but likely rare	Not yet reported
Blood/serum	**TRANSFUSION**	**Yes**	**No**	Not yet reported
Cervicovaginal fluid	**SEXUAL**	**No**	Not yet reported	Not yet reported
Semen		Yes, but likely rare	Not yet reported	Not yet reported
Urine	**URINARY**	**No**	Not yet reported	Not yet reported

Zou 2020, N Engl J Med; DOI: 10.1056/NEJMc2001737. Pan 2020, Lancet Infect Dis; https://doi.org/10.1016/S1473-3099(20)30113-4. Zhang 2020; China CDC Weekly: http://weekly.chinacdc.cn/en/article/id/ffa97a96-db2a-4715-9dfb-ef662660e89d. Chen 2020; Lancet: https://doi.org/10.1016/ S0140-6736(20)30360-3. Zhu 2020, Transl Pedtr; http://dx.doi.org/10.21037/tp.2020.02.06. Li 2020, JAMA Network Open; doi:10.1001/jamanetworkopen.2020.8292. Yu 2020, Lancet Infect Dis; doi.org/10.1016/S1473-3099(20)30320-0. Chang 2020, Emerg Infect Dis; in press. Xiao 2020, Emerg Infect Dis; August 26(8). Xiao 2020, Gastroentrol; doi.org/10.1053/j.gastro.2020.02.055. Wang 2020, JAMA, 323(18):1843-4. Andersson 2020, Wellcome Open Research: https://doi.org/10.12688/wellcomeopenres.16002.1 v1

Valid as of October 15, 2020

U.S. COVID-19 Seroprevalence Estimate, By State



As of August 2020

- New York - 22%
- New Jersey - 15%
- Louisiana - 11%
- All others - <10%

https://covid.cdc.gov/covid-data-tracker/#national-lab

Valid as of October 15, 2020

Role of Serologic Testing

Role of serology

- Utility of serologic testing to establish the absence or presence of infection or reinfection, as well as immunity, remains undefined
- Data that will inform serologic testing guidance are rapidly evolving
- Serologic or other correlates of immunity have not yet been established
- Serologic testing should not be used to establish presence or absence of:
  - infection or reinfection
  - immunity

Credit: NIH

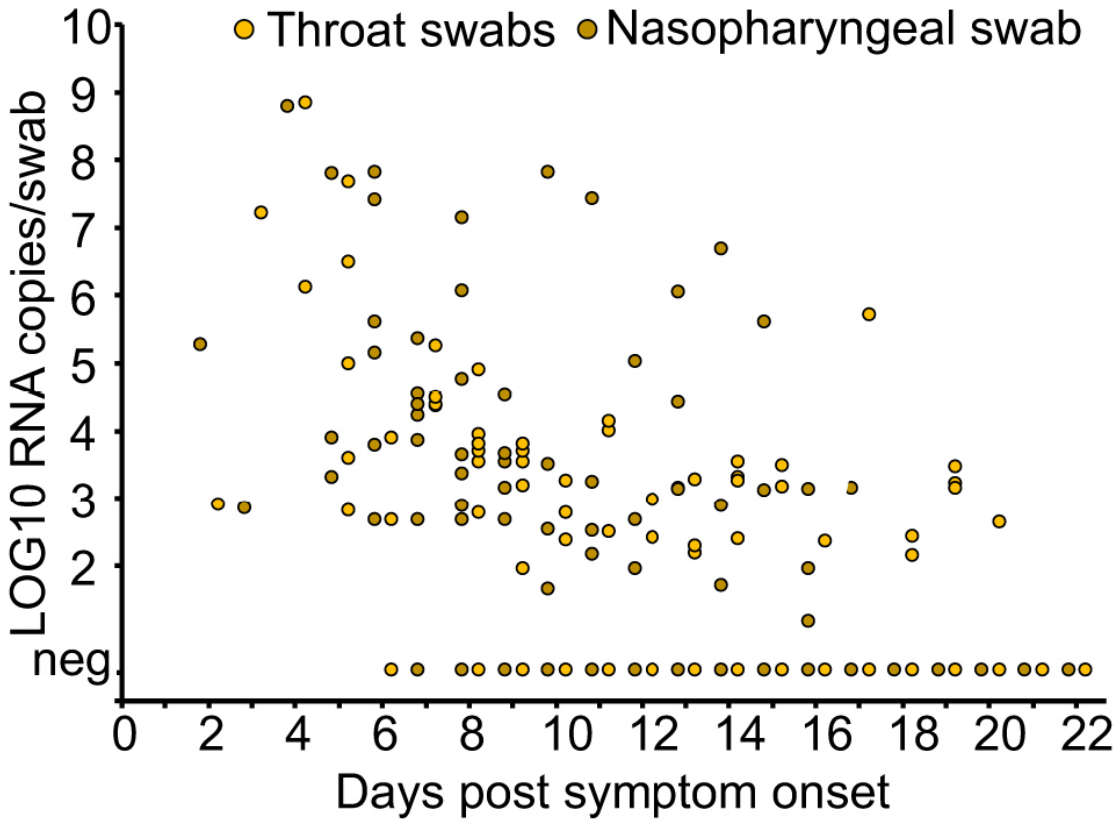
https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html

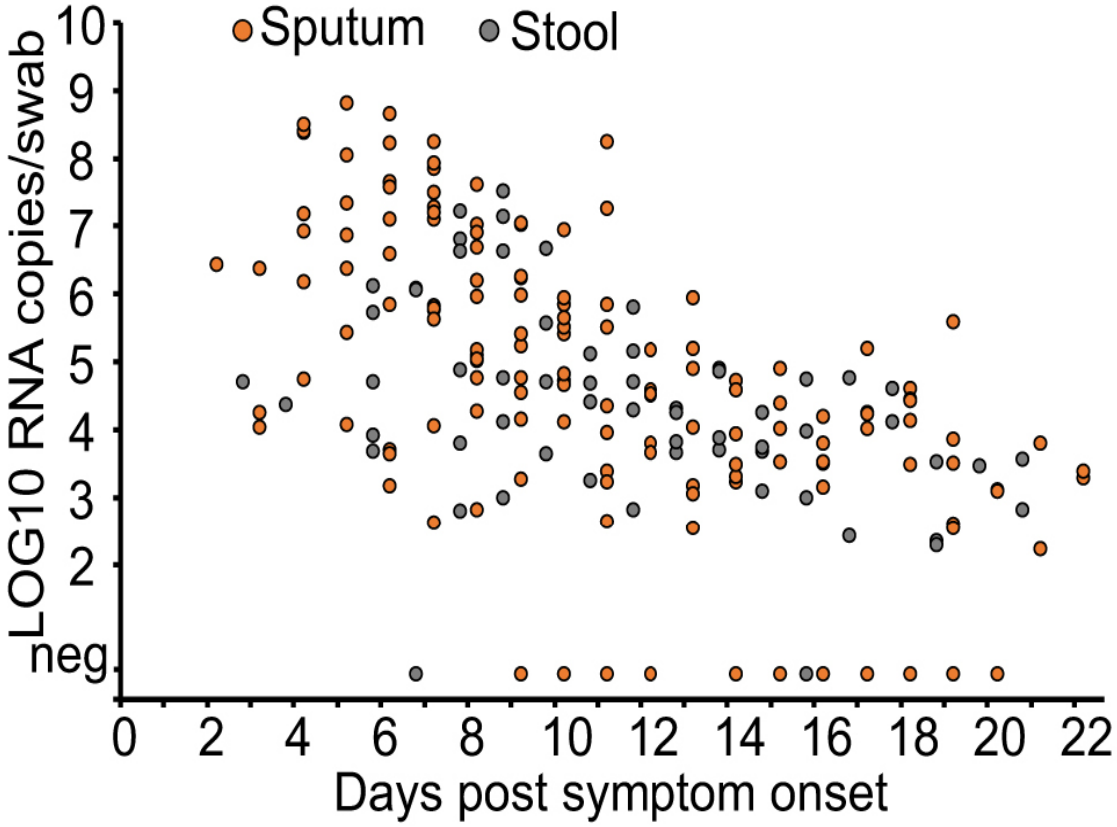
Valid as of October 15, 2020

COVID-19
Response to Infection

Valid as of October 15, 2020

Viral Burden Declines Steadily After Illness Onset

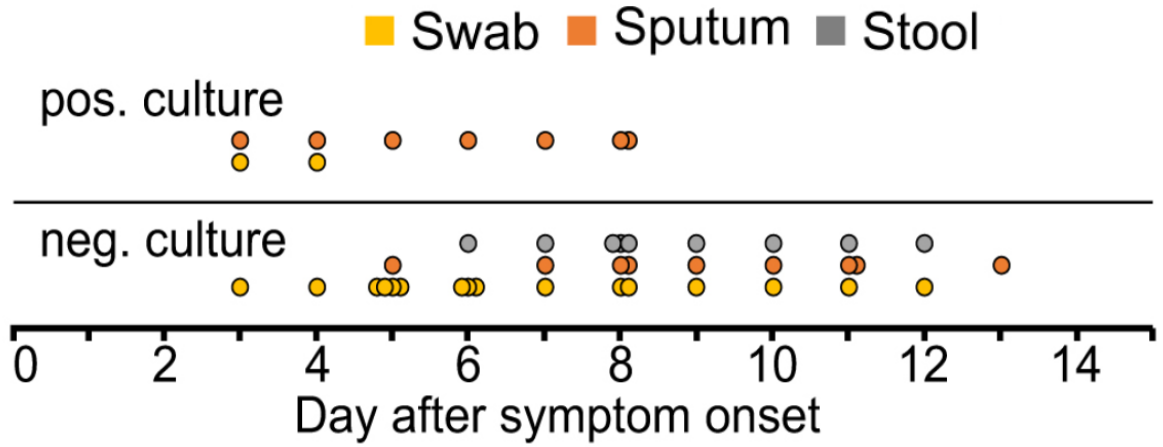




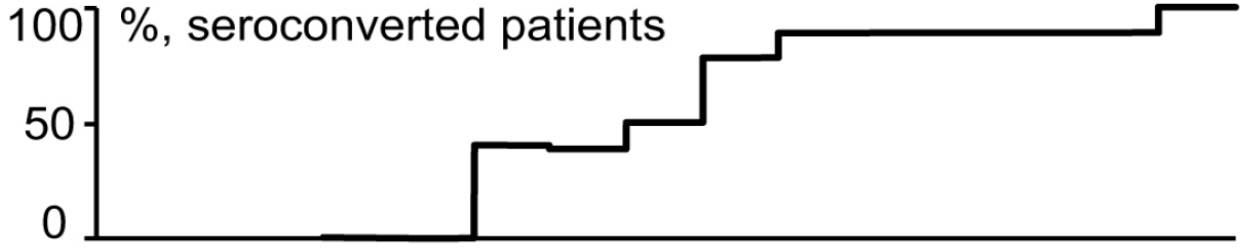
Wölfel 2020, Nature; doi.org/10.1038/s41586-020-2196-x.

Valid as of October 15, 2020

Ability to Culture Virus from Specimens Declines as Serologic Response to Infection Grows



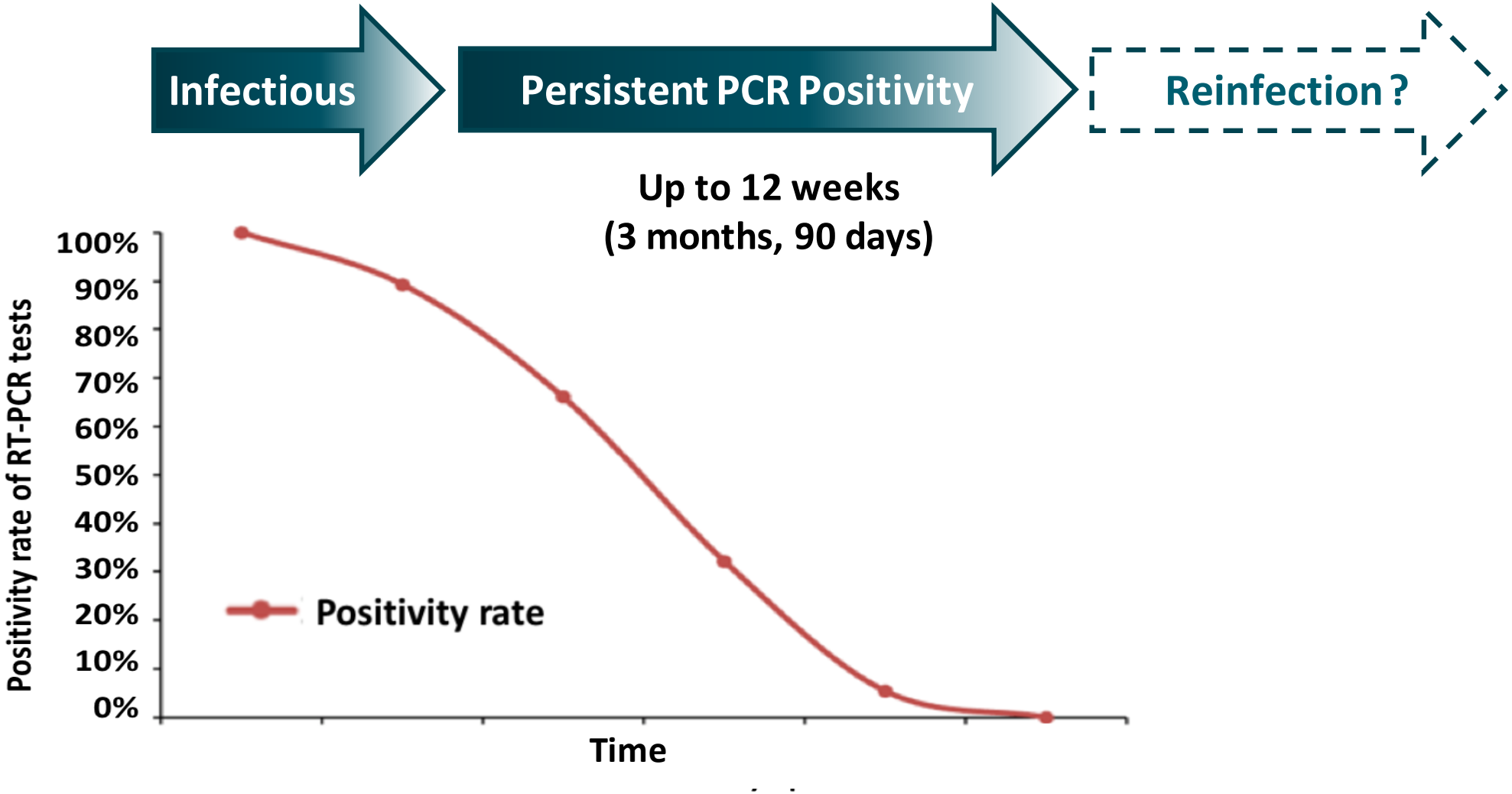
- After 8-10 days, replication-competent virus longer present in respiratory tract specimens, in otherwise healthy persons with mild to moderate illness.
- In severely ill persons, shedding of live virus may persist up to 20 days



- Within days after symptom onset, patients being to develop serologic response to infection that includes IgM, IgG, and IgA.
- IgG response includes neutralizing antibodies.

Wölfel 2020, Nature; doi.org/10.1038/s41586-020-2196-x. van Kampen 2020, medRxiv; doi.org/10.1101/2020.06.08.20125310

PCR Can Remain Positive for Weeks After Recovery Even Though Live Virus Cannot be Isolated



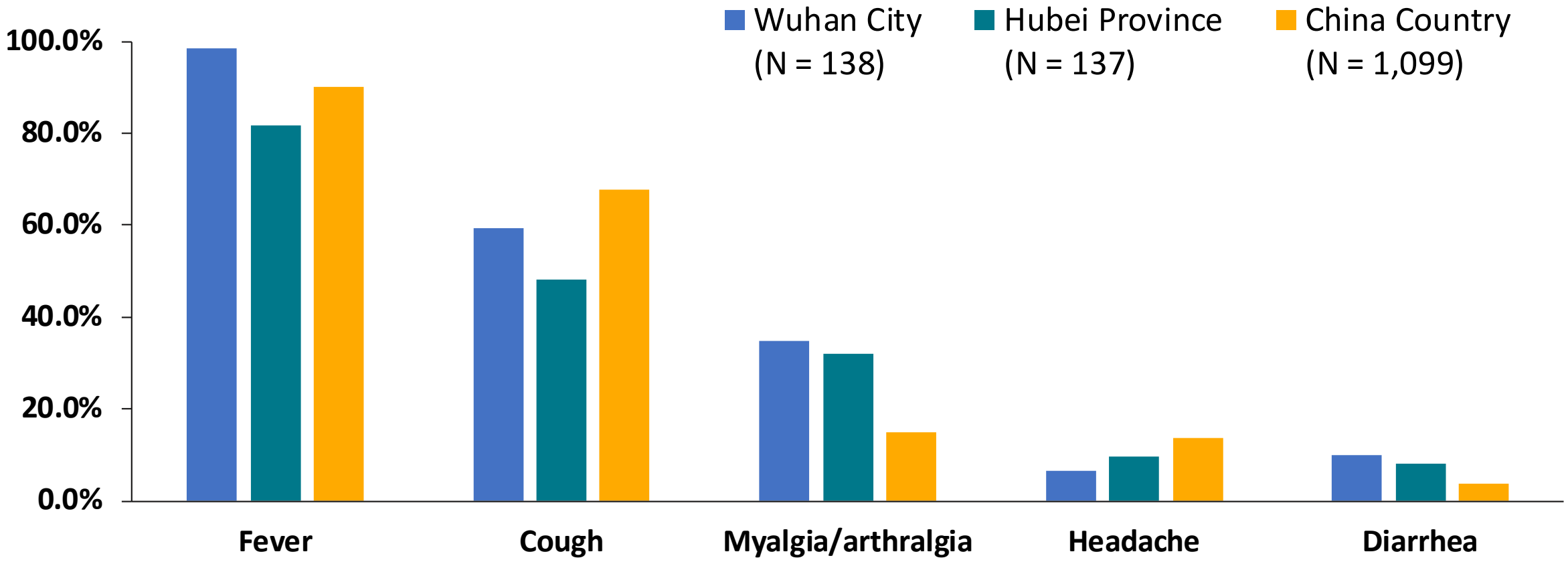
Xiao 2020, Clin Infect Dis; doi.org/10.1093/cid/ciaa460. Li 2020, J Med Virol; doi: 10.1002/jmv.25952. Kiyuka 2018, J Infect Dis; 217:1728-39.

Valid as of October 15, 2020

COVID-19
Clinical Epidemiology

Valid as of October 15, 2020

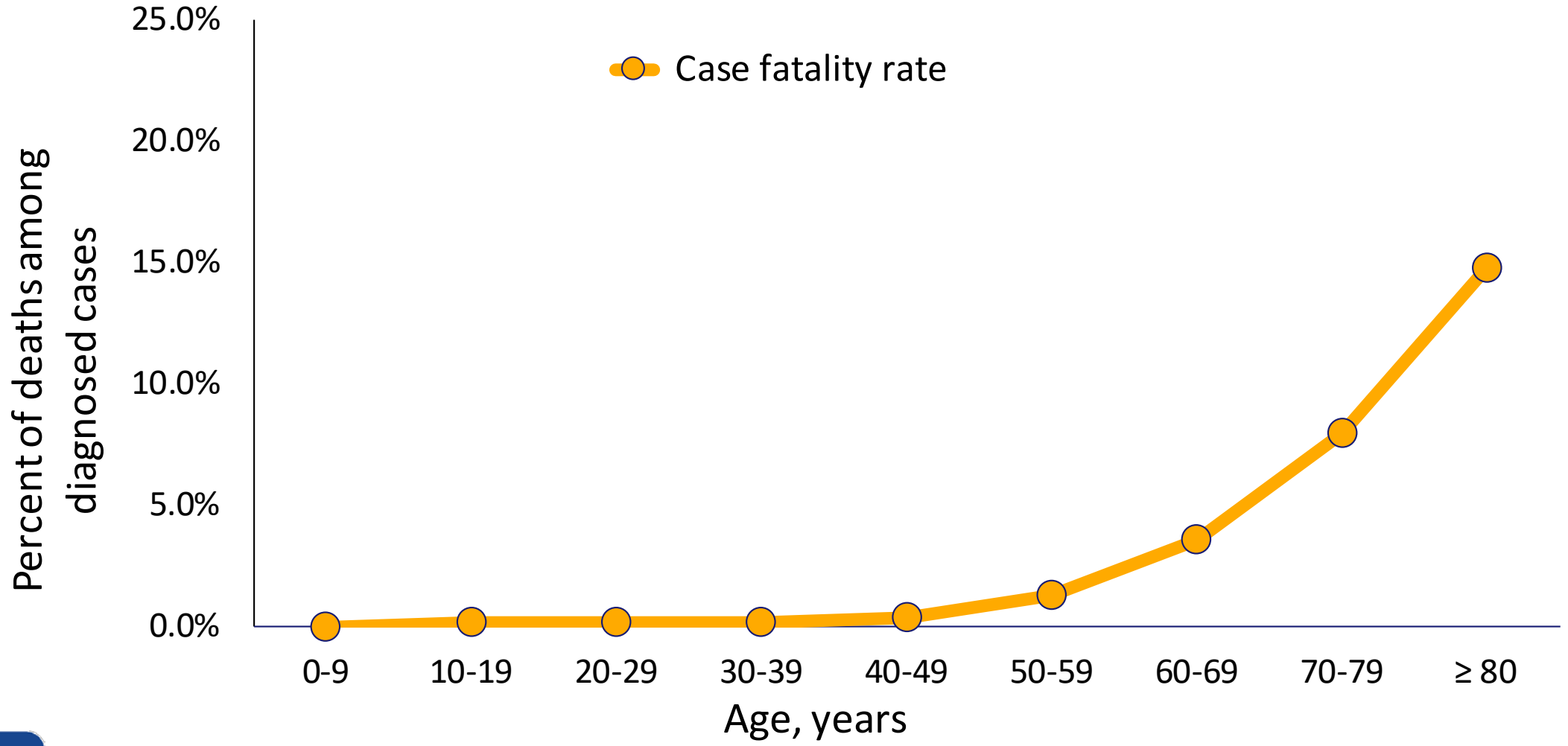
Signs/Symptoms of COVID-19



Liu 2020, Chinese Med J; DOI: 10.1097/CM9.0000000000000744. Wang 2020, JAMA; doi:10.1001/jama.2020.1585.
Guan 2020, N Engl J Med; DOI: 10.1056/NEJMoa2002032.

Valid as of October 15, 2020

Case Fatality Rate COVID-19
China through 11-Feb-2020 (N = 44,672 confirmed cases)

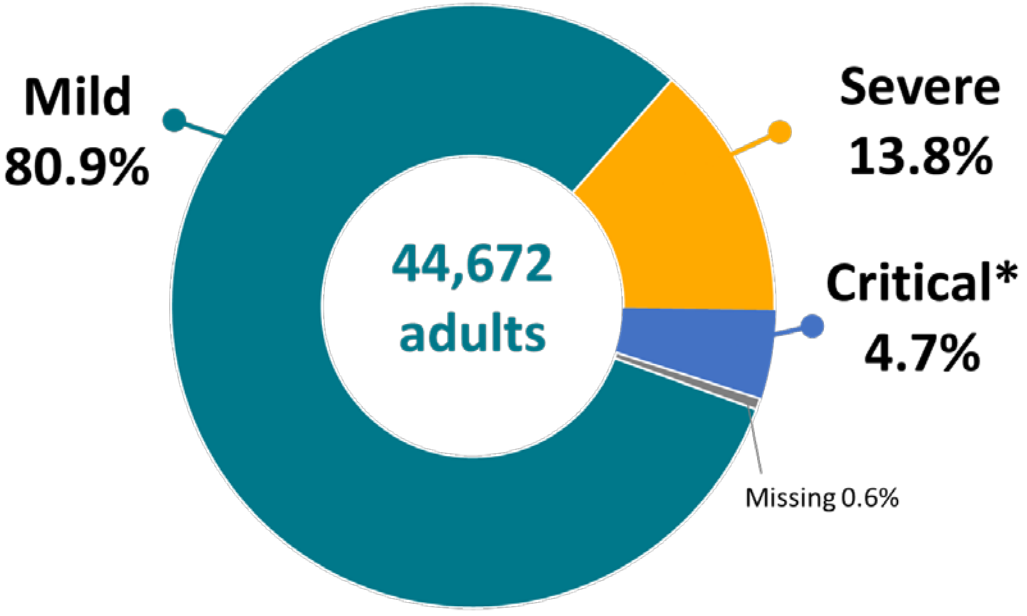


adapted from Zhang 2020, China CDC Weekly Rep; 2(8):113-122.

Valid as of October 15, 2020

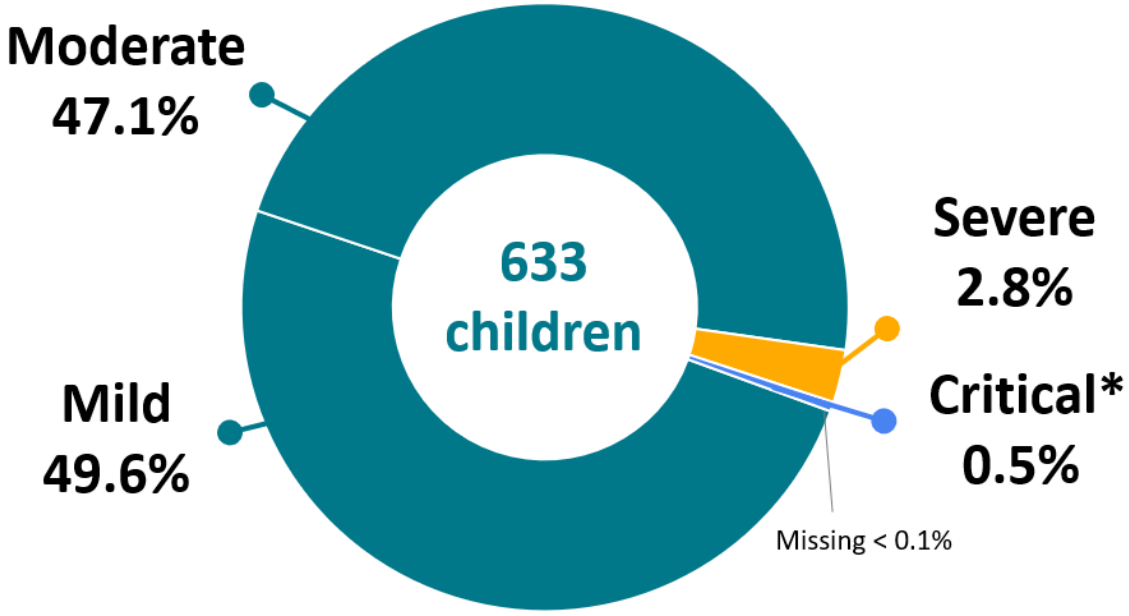
Illness Severity in Adults and Children with COVID-19, China

Severity of Illness, Adult COVID-19 (N = 44,672 confirmed cases)



* 1,023 (49%) deaths among 2,087 critically ill adults

Severity of Illness, Pediatric COVID-19 (N = 633 confirmed cases)



* 1 deaths among critically ill children

adapted from Zhang 2020, China CDC Weekly Report; 2(8):113-122 and Dong 2020, Pediatrics; doi 10.1542/peds.2020-0702. (symptomatic cases only

Valid as of October 15, 2020

Signs/Symptoms of COVID-19

- No particular set of signs or symptoms can reliably discriminate COVID-19 from other respiratory viral illnesses such as influenza
  - Anosmia/dysgeusia
- Most people will recover spontaneously with supportive care
- Typical complications include pneumonia, respiratory failure, multiorgan system failure, and death

Liu 2020, Chinese Med J; DOI: 10.1097/CM9.0000000000000744. Wang 2020, JAMA; doi:10.1001/jama.2020.1585.
Guan 2020, N Engl J Med; DOI: 10.1056/NEJMoa2002032.

Severity of Illness Categories for SARS-CoV-2 Infection

NIH COVID-19 Clinical Guideline	
ASYMPTOMATIC	No signs or symptoms
MILD	Any sign or symptom without shortness of breath, dyspnea, or abnormal chest imaging
MODERATE	Evidence of lower respiratory disease by clinical assessment or imaging and SpO_2 ≥94%*
SEVERE	Respiratory frequency >30 breaths per minute, SpO2 <94%*, PaO_2/FiO_2 <300 mmHg, or lung infiltrates >50%
CRITICAL	Respiratory failure, septic shock, or multiple organ dysfunction

* on room air at sea level

https://www.covid19treatmentguidelines.nih.gov/overview/clinical-presentation/

Valid as of October 15, 2020

COVID-19 in High-Risk Groups

- **Comorbidity and advanced age increase risk for severe illness and death**
  - Cancer
  - Chronic kidney disease
  - COPD (chronic obstructive pulmonary disease)
  - Immunocompromise (weakened immune system) from solid organ transplant
  - Obesity (body mass index [BMI] of 30 or higher)
  - Serious heart conditions (e.g., heart failure, coronary artery disease, cardiomyopathies)
  - Sickle cell disease
  - Type 2 diabetes mellitus

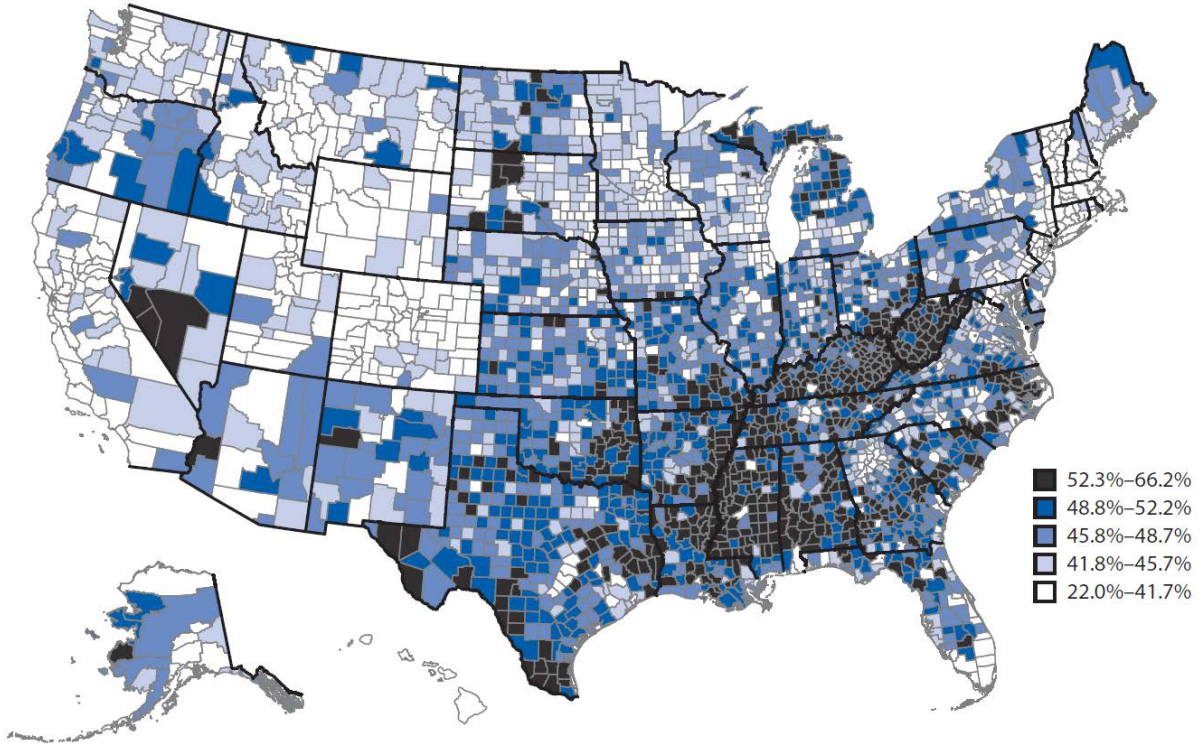
https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-increased-risk.html

Valid as of October 15, 2020

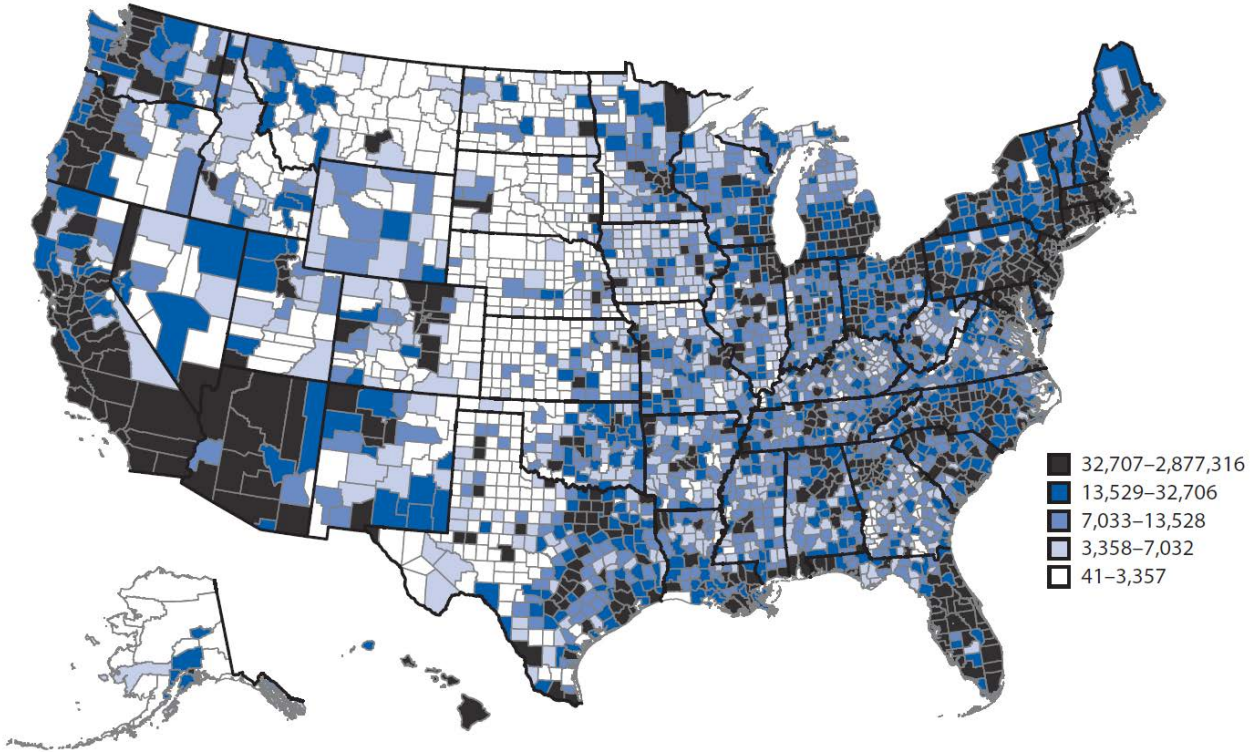
COVID-19 in High-Risk Groups

Estimated County-Level Adult Prevalence of Selected Underlying Medical Conditions* Associated with Increased Risk for Severe COVID-19 Illness — U.S., 2018

Prevalence: 41% nationally



Number: median 9,642/county



* BMI ≥30 kg/m² (31%), diabetes (11%), COPD (7%), heart disease (7%), chronic kidney disease (3%). Does not include cancer, immunocompromise, or sickle cell disease.

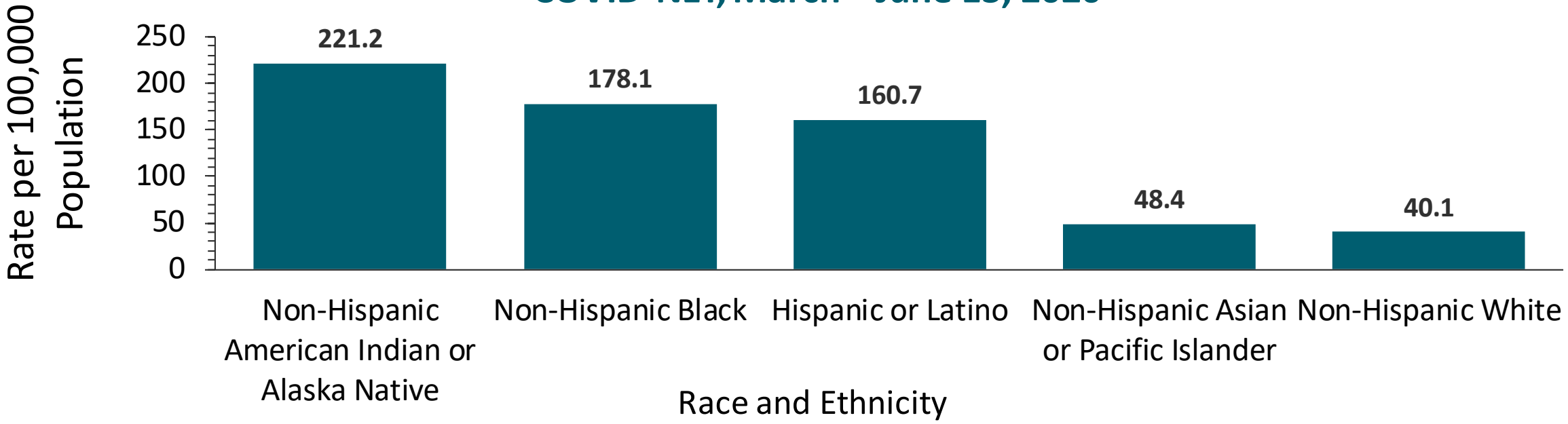
Razzaghi 2020, MMWR: 69(29):945-50.

Valid as of October 15, 2020

COVID-19 and Race and Ethnicity

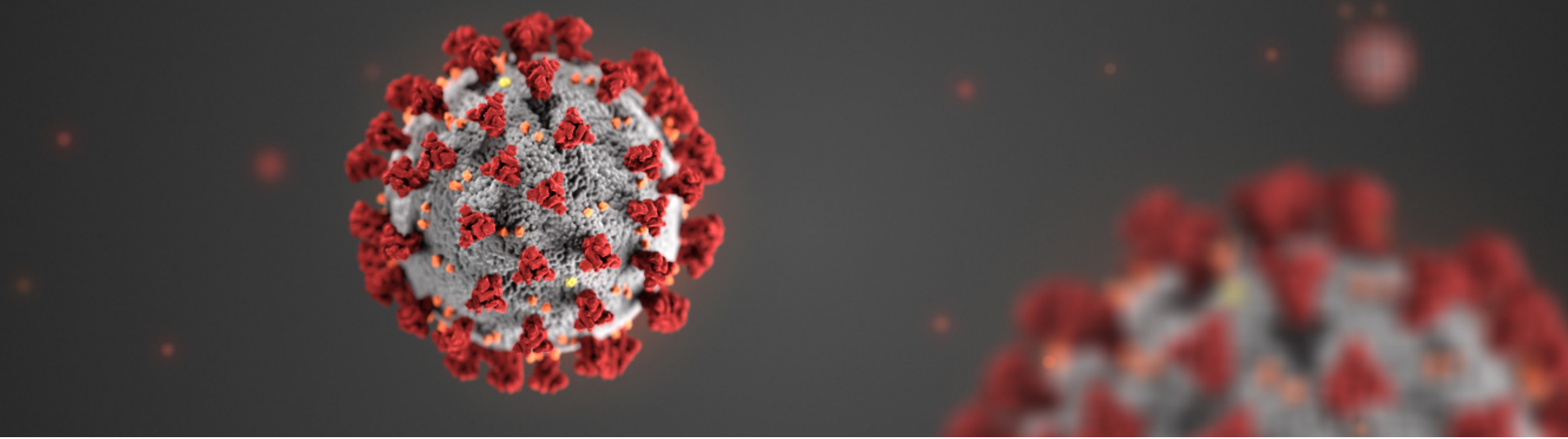
- **Long-standing systemic health and social inequities** have put some members of racial and ethnic minority groups at increased risk

Age-adjusted COVID-19-associated hospitalization rates by race and ethnicity, COVID-NET, March – June 13, 2020



https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/racial-ethnic-minorities.html

Valid as of October 15, 2020



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.