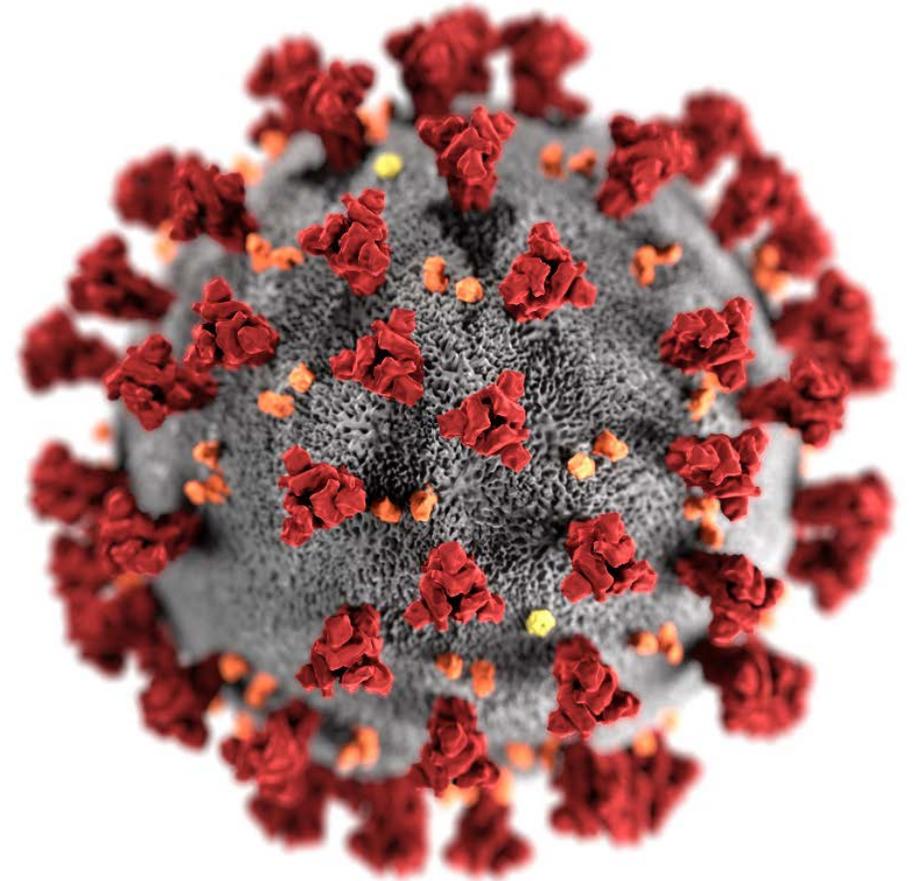


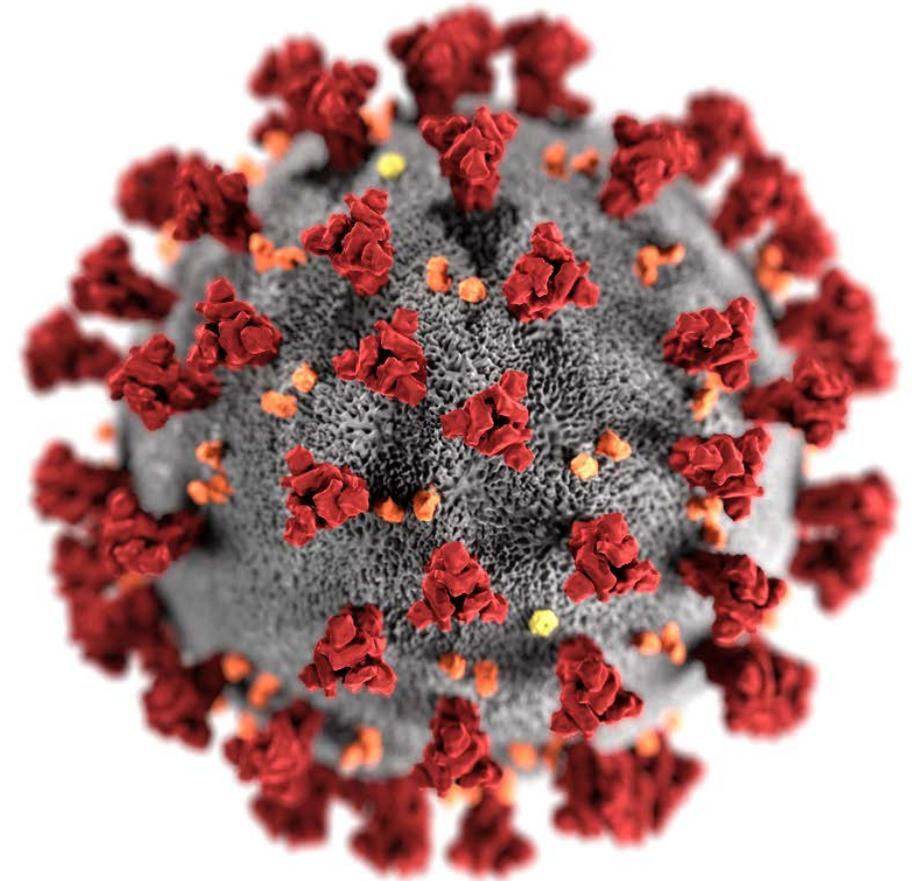
Overview of COVID-19 Disease

John T. Brooks MD – Chief Medical Officer
CDC, Division of HIV/AIDS Prevention
CDC, COVID-19 Response

ACIP 2020 – June 24, 2020



**Dr. Brooks has no relevant
financial affiliations to disclose**

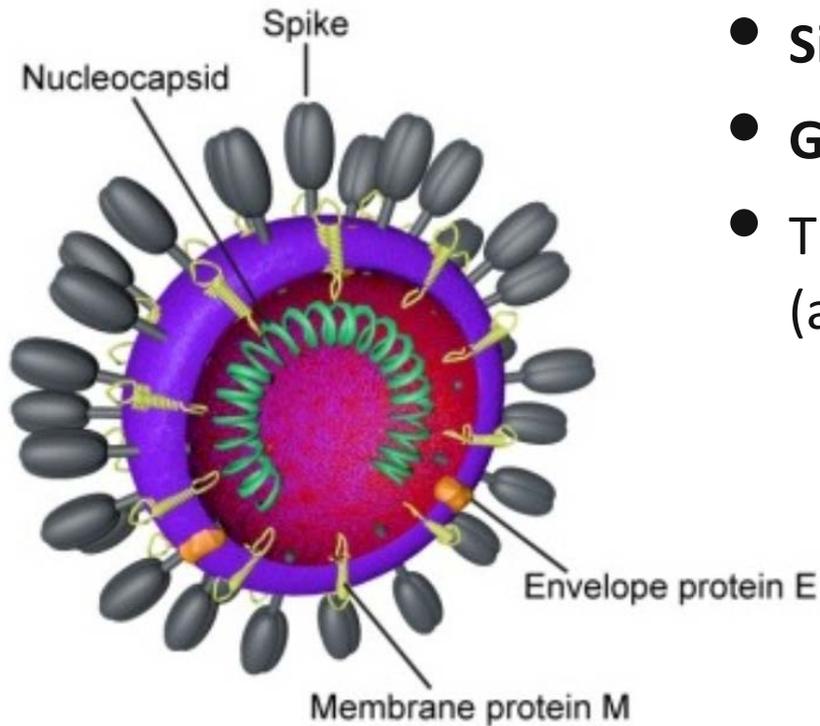


For more information: www.cdc.gov/COVID19

COVID-19 Virology

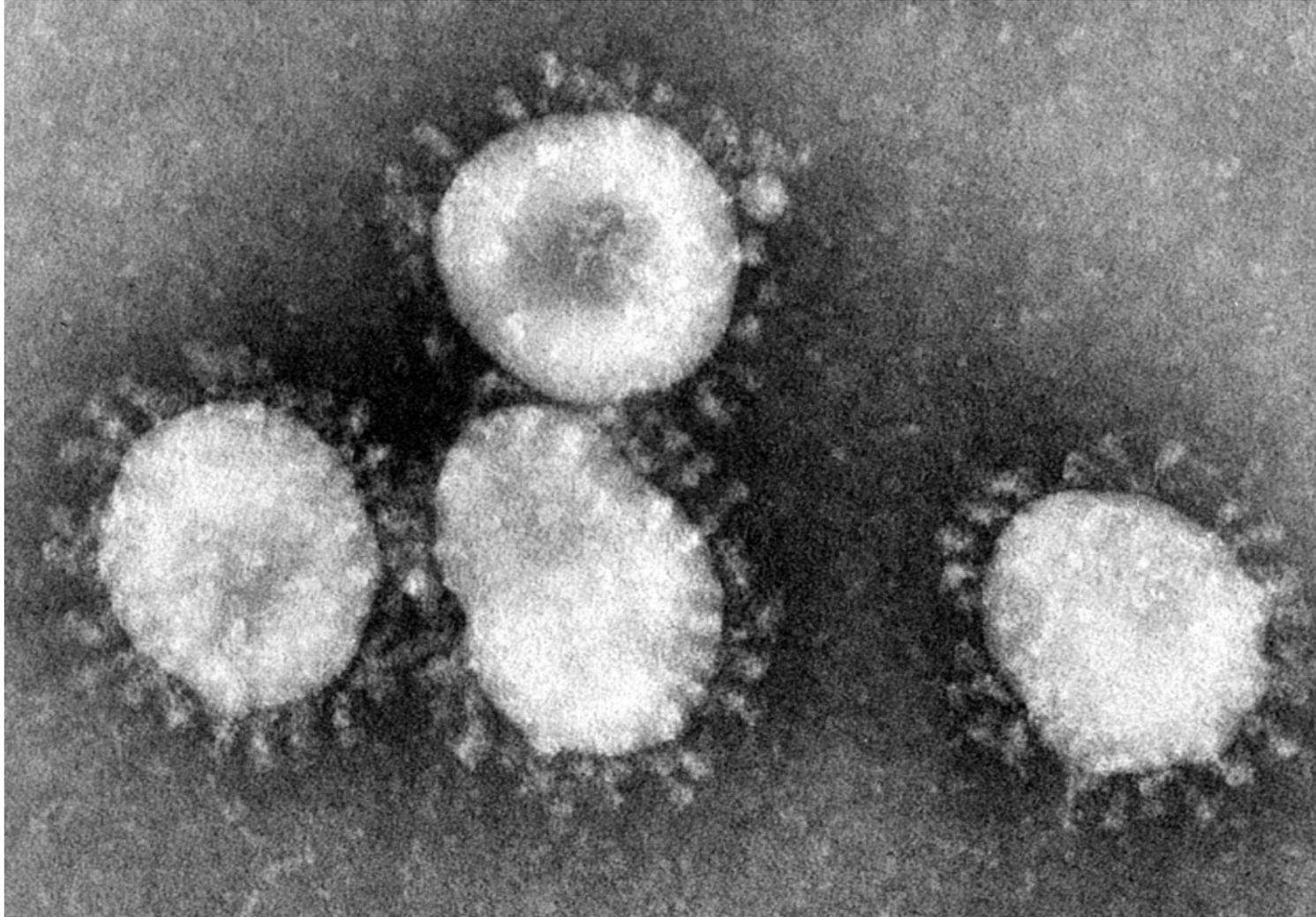


Basic Structure of *Coronavirinae*

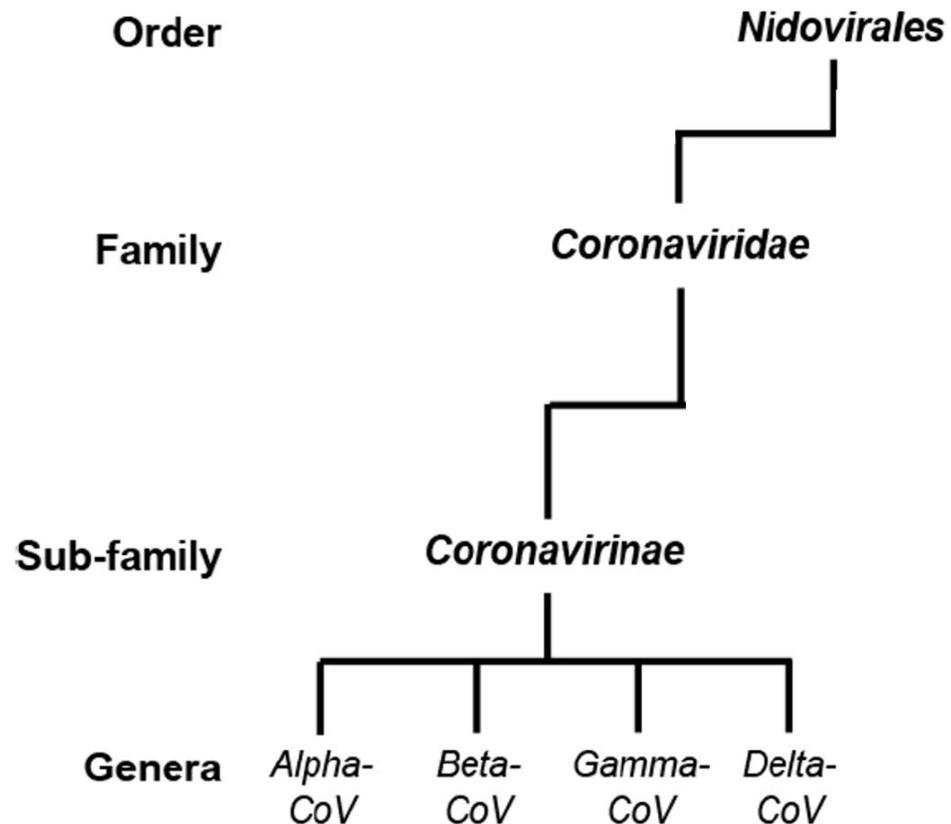


- **Single-stranded RNA viruses**
- **Genomes range from 25 to 32 kilobases**
- The coronaviral genome encodes **four major structural proteins** (all are required to produce a structurally complete viral particle)
 - Spike (S) protein: *binding*
 - Nucleocapsid (N) protein: *RNA synthesis*
 - Membrane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

Electron Micrograph of Coronavirus Virions



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**

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)

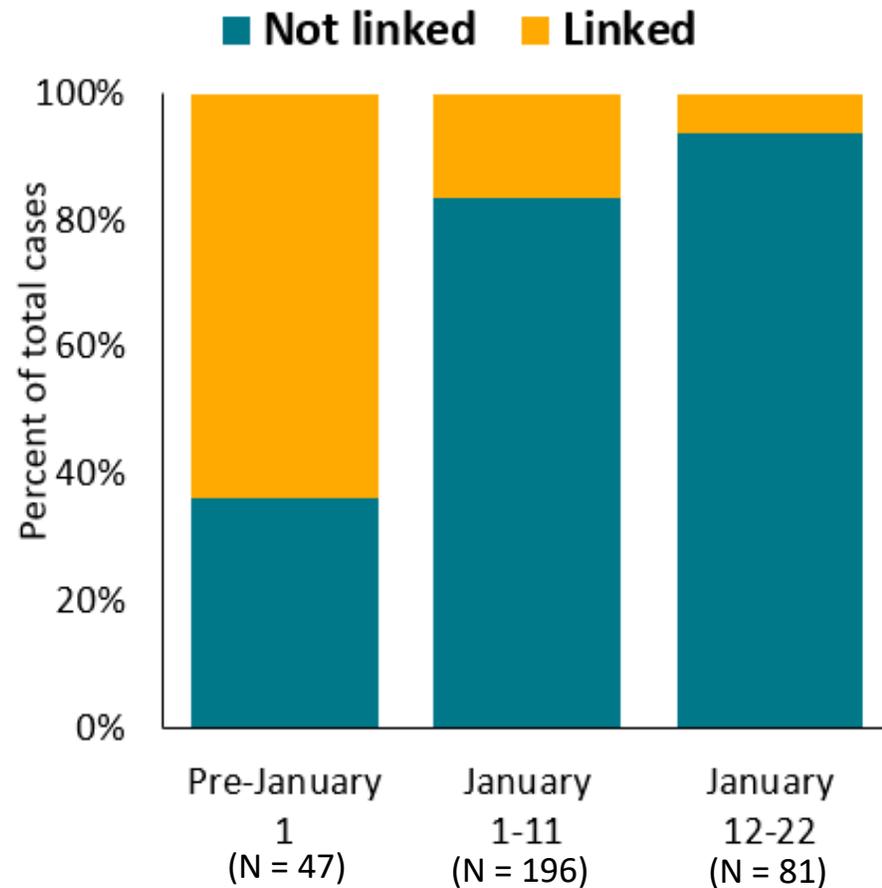
The illness COVID-19 is caused by SARS-CoV-2, which is more like SARS-CoV-1 than MERS-CoV



COVID-19 Transmission



Linkage of Early COVID-19 Cases* to Huanan Seafood Wholesale Market – Wuhan, China



<https://www.healthpolicy-watch.org/>



Adapted from Li 2020, *N Engl J Med*; DOI: 10.1056/NEJMoa2001316.

* Total N=324 persons with complete exposure histories among 425 total cases

Valid as of June 20, 2020

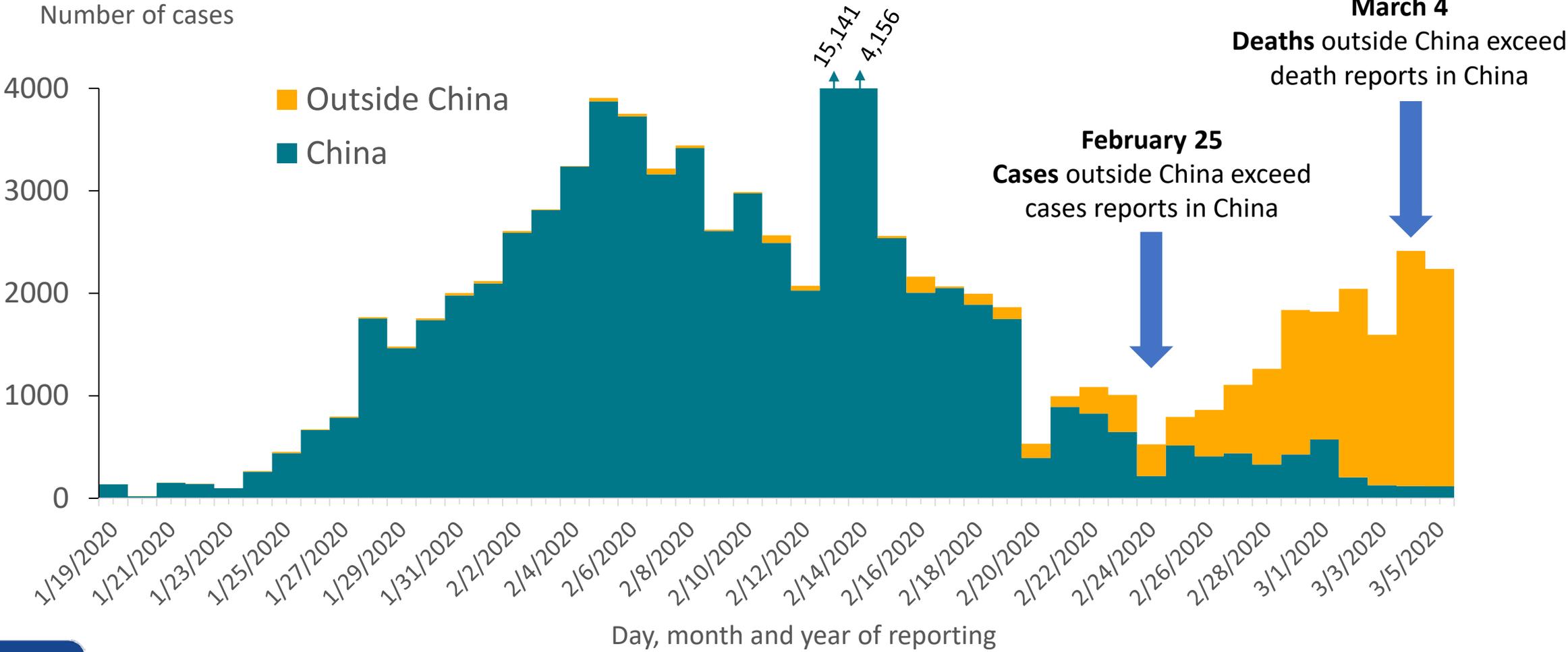
Early Distribution of Cases: China as of 20-Jan-2020



CNN Source: National Health Commission of the PRC. Data correct as of January 26, 08:30 P.M. ET
 Graphic: Natalie Leung and Henrik Pettersson, CNN



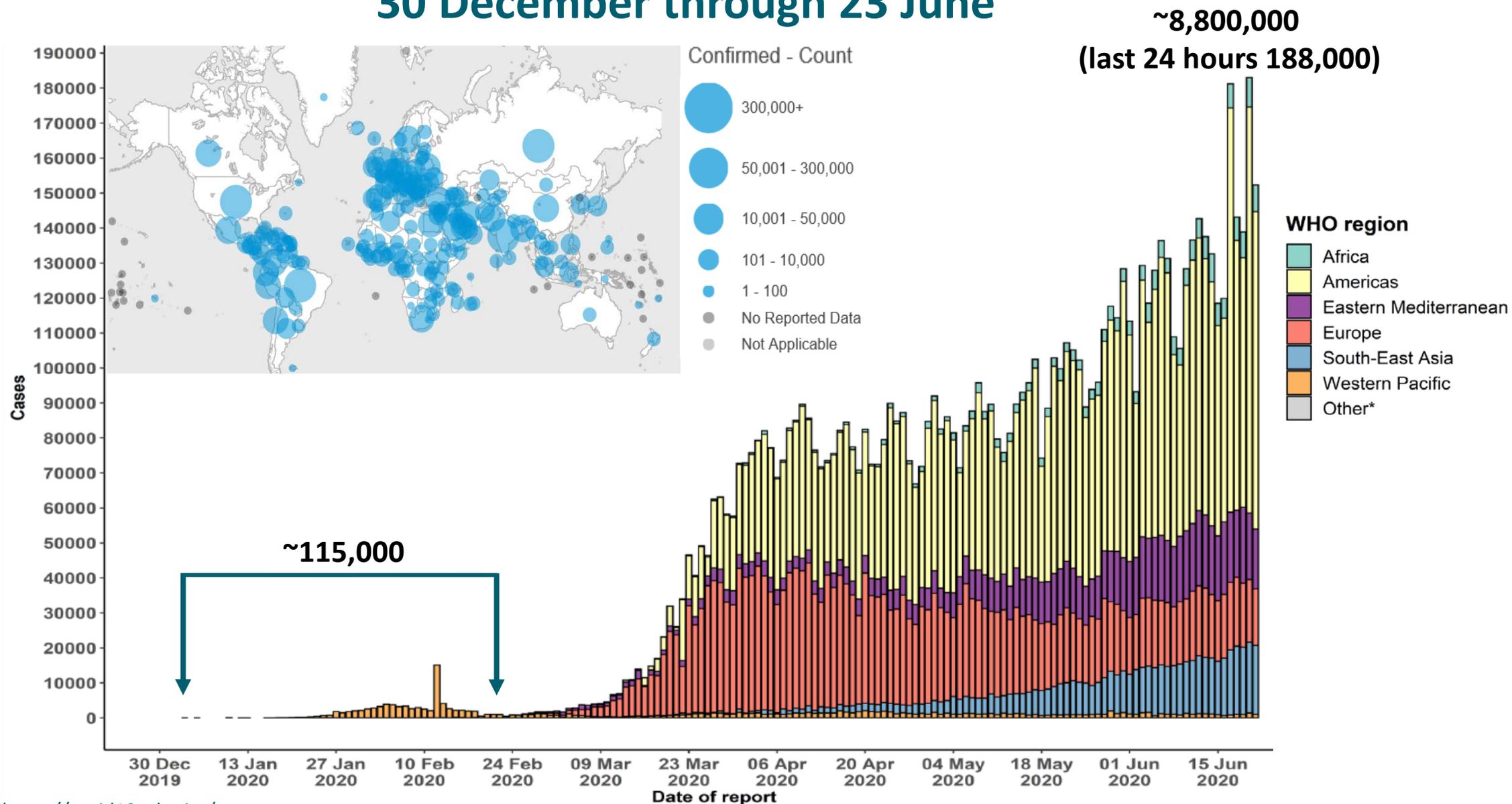
Distribution of COVID-19 cases in accordance with the applied case definitions in the affected countries, as of 05 March 2020



Courtesy of European CDC

Valid as of June 20, 2020

Number of confirmed COVID-19 cases, by date of report and WHO region, 30 December through 23 June



<https://covid19.who.int/>

Valid as of June 20, 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)	5 days (range 2-14)
Serial interval (days)	> Incubation (8)	> Incubation (12-14)	< Incubation (4)
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 30-35%, are asymptomatic**

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
Urine	URINARY	No	Not yet reported	Not yet reported
Blood/serum	TRANSFUSION	Not reliably	No	Not yet reported
Amniotic fluid	PERINATAL	No	Not yet reported	Not yet reported
Umbilical cord blood		No	Not yet reported	Not yet reported
Breast milk		Not reliably	No	Not yet reported
Cervicovaginal fluid		No	Not yet reported	Not yet reported
Semen		SEXUAL	Yes, but likely rare	Not yet reported

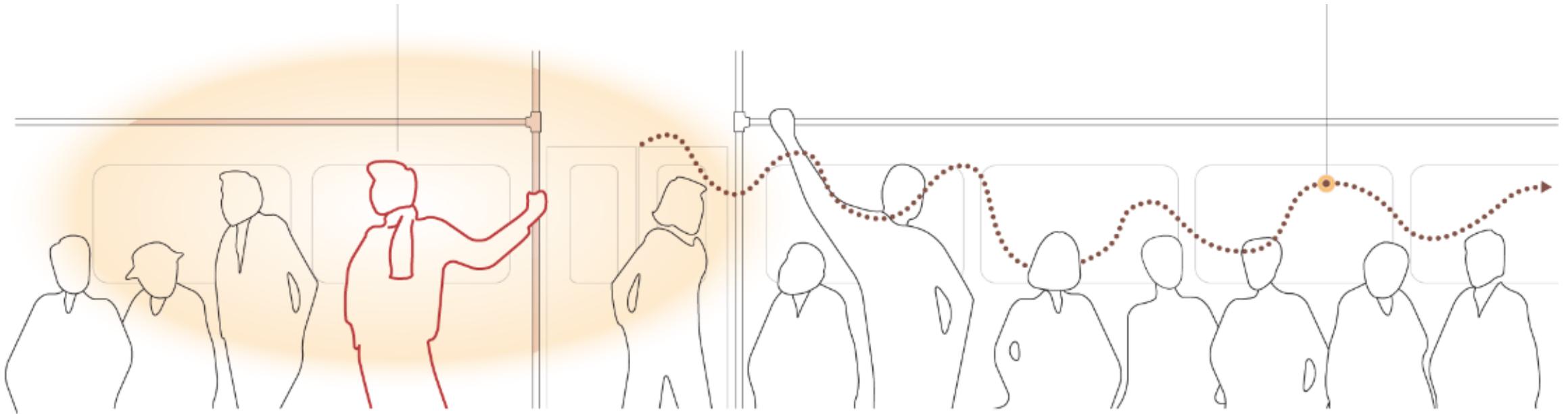
Zou 2020, *N Engl J Med*; DOI: 10.1056/NEJMc2001737. Pan 2020, *Lancet Infect Dis*; [https://doi.org/10.1016/S1473-3099\(20\)30113-4](https://doi.org/10.1016/S1473-3099(20)30113-4). Zhang 2020; *China CDC Weekly*; <http://weekly.chinacdc.cn/en/article/id/ffa97a96-db2a-4715-9dfb-ef662660e89d>. Chen 2020; *Lancet*; [https://doi.org/10.1016/S0140-6736\(20\)30360-3](https://doi.org/10.1016/S0140-6736(20)30360-3). Zhu 2020, *Transl Pediatr*; <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, *Gastroenterol*; doi.org/10.1053/j.gastro.2020.02.055



How Far Can SARS-CoV-2 Travel?

Respiratory droplets
About 6 feet (2 meters)

Airborne/aerosolized
Many meters

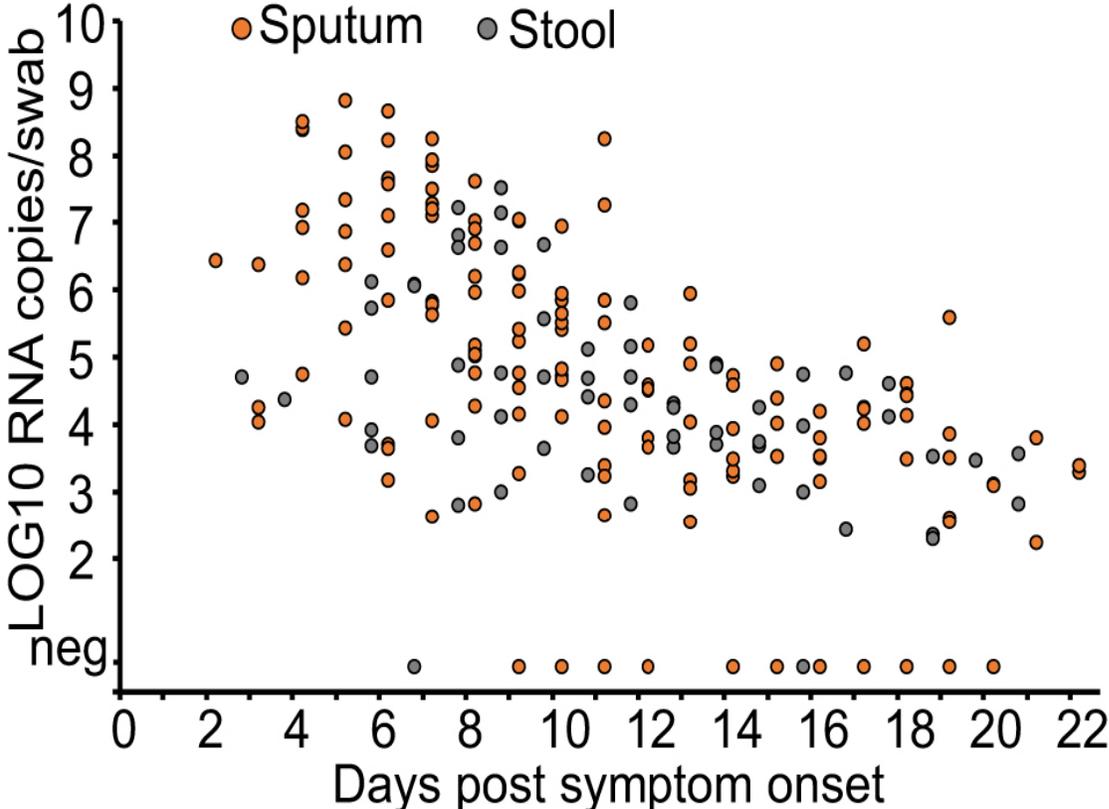
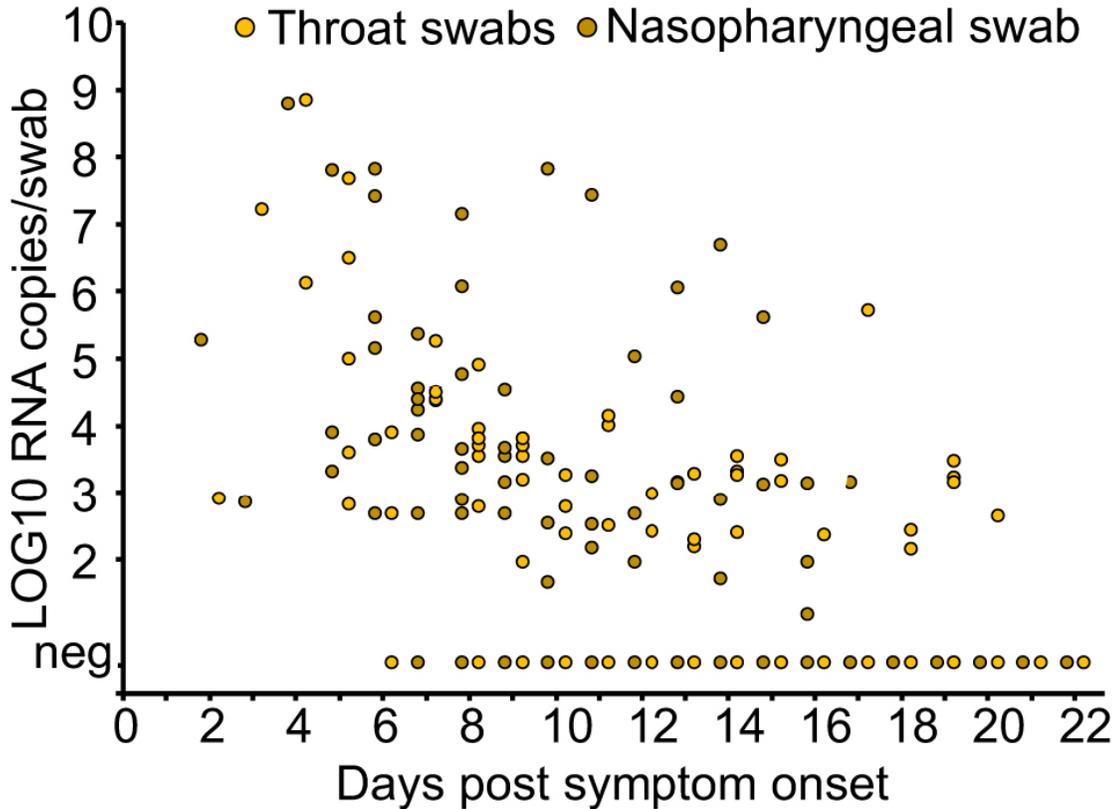


COVID-19

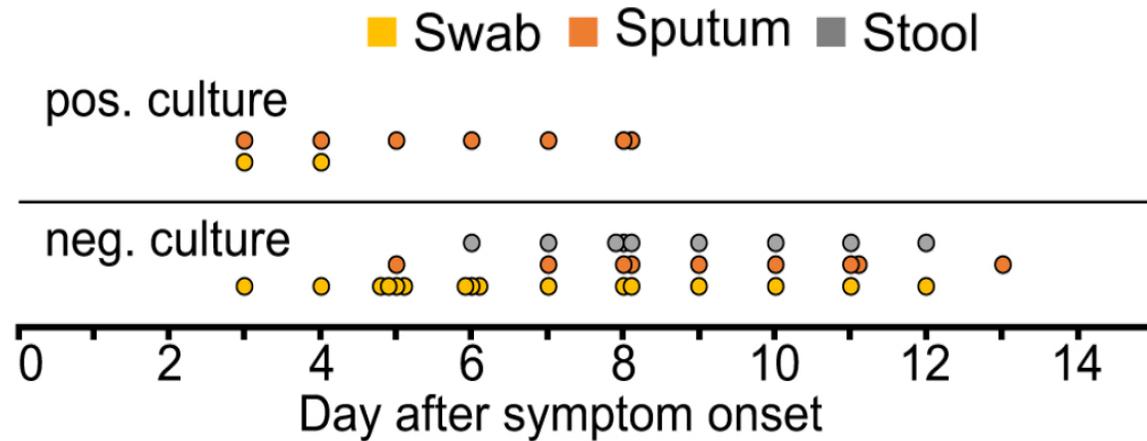
Response to Infection



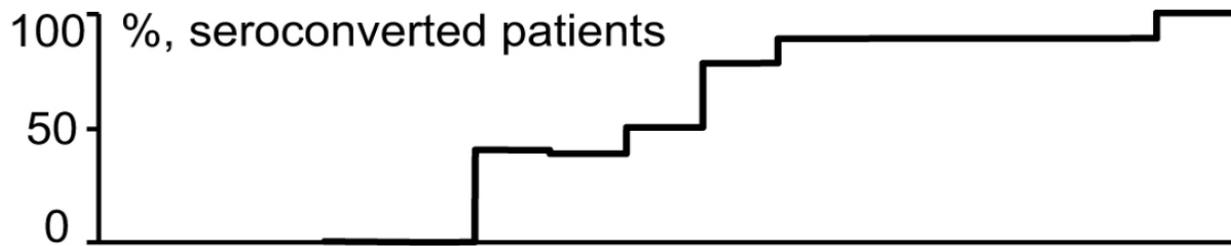
Viral Burden Declines Steadily After Illness Onset



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



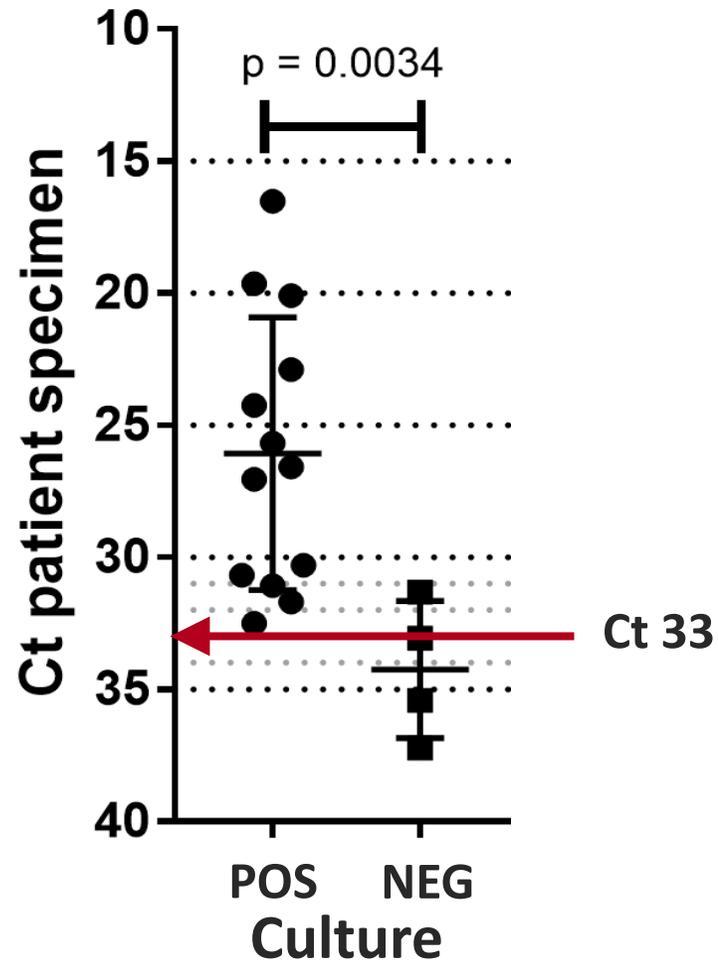
- After 8-10 days, replication-competent virus can no longer be recovered from respiratory tract specimens, in otherwise healthy persons with mild to moderate illness.
- In severely ill and immunocompromised persons, shedding of culturable virus may persist up to 20 days



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



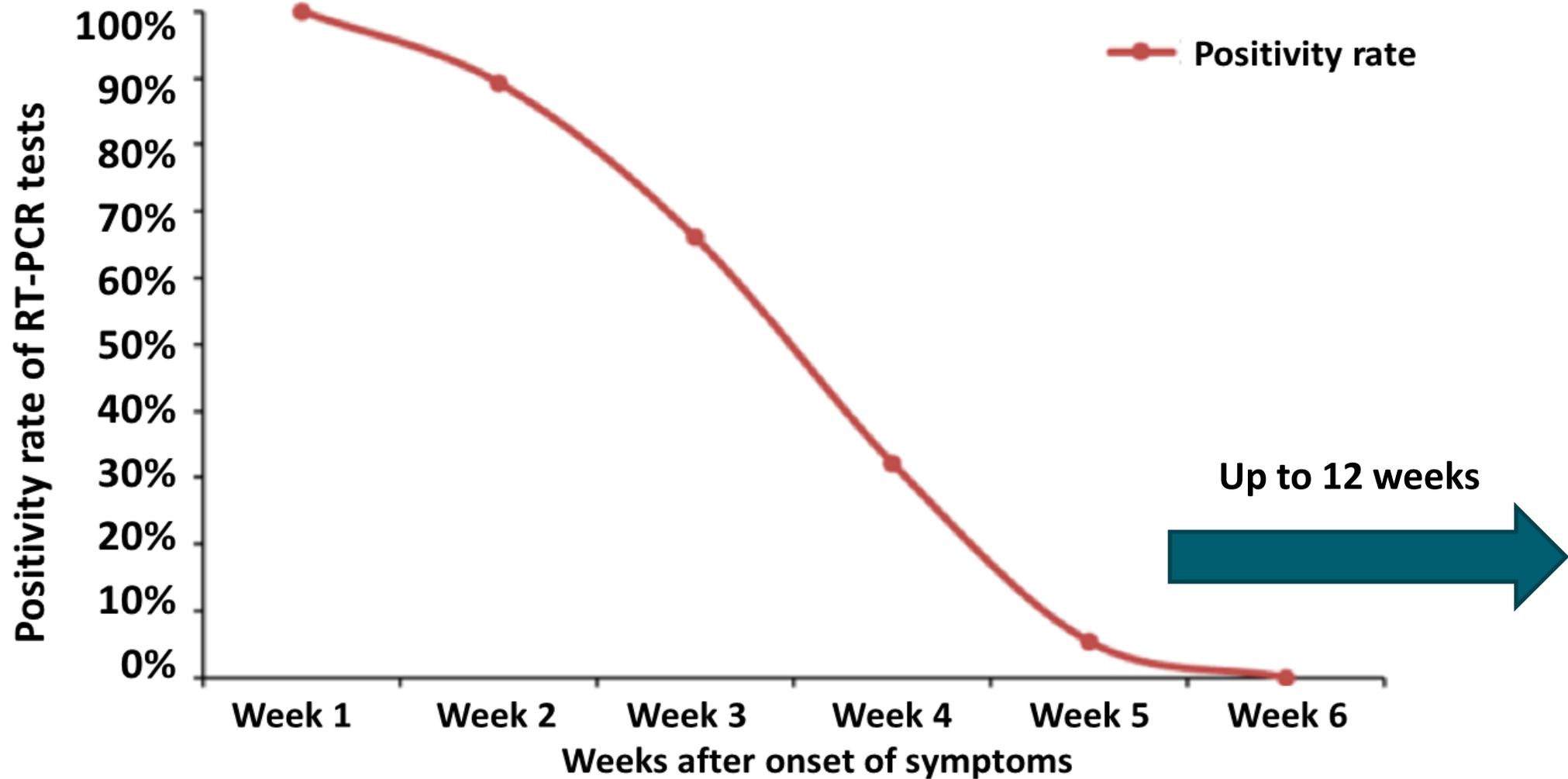
Ability to Culture Virus from Specimens Declines with Decreasing Viral Burden



CDC, unpublished data.

Valid as of June 20, 2020

PCR Can Remain Positive for Weeks After Recovery

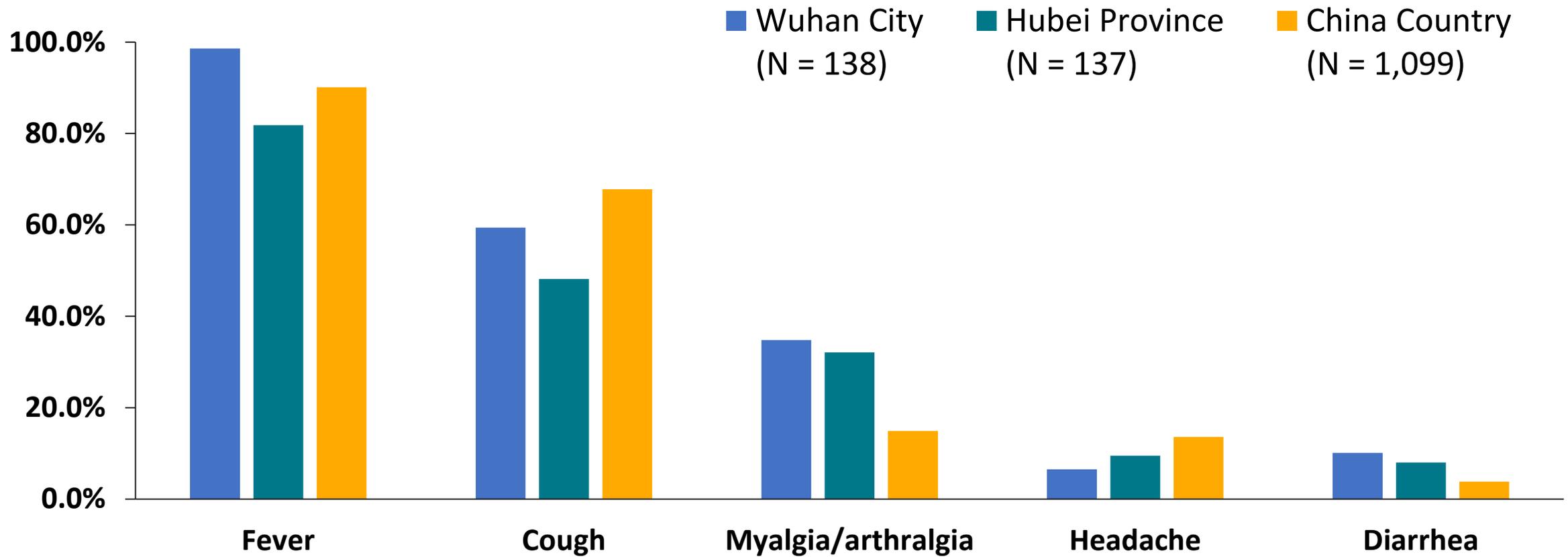


COVID-19

Clinical Epidemiology



Signs/Symptoms of COVID-19



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

Valid as of June 20, 2020

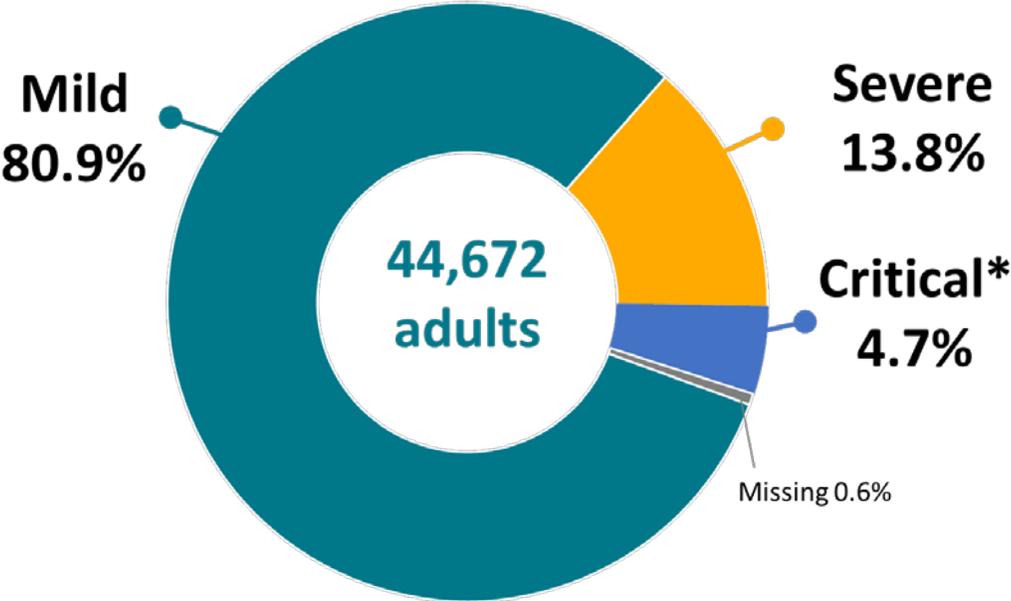
Signs/Symptoms of COVID-19

- 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



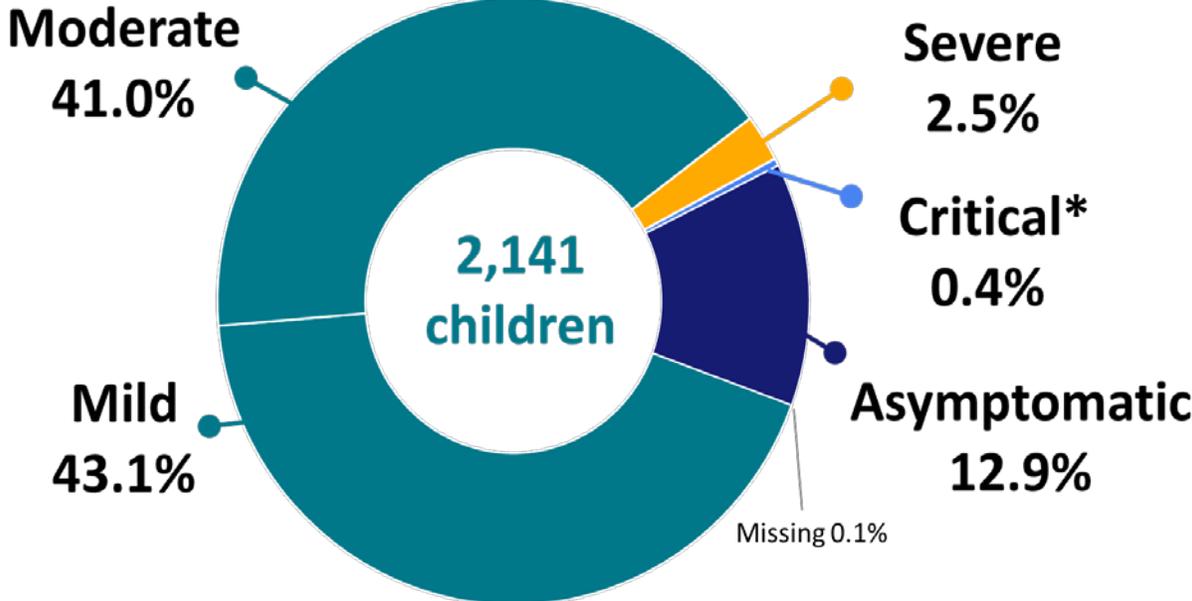
Illness Severity in Adults and Children with COVID-19, China

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 = 2,141 confirmed cases)



* 1 deaths among critically ill children



COVID-19 in High-Risk Groups

- **Comorbidity and advanced age increase risk for severe illness and death**
 - Cardiovascular disease, diabetes, chronic respiratory disease
- **Immunocompromised (medical, acquired) – emerging data reassuring**
 - For persons with HIV, risk likely greatest at low CD4 cell counts or not virally suppressed
 - No definitive evidence that cancer therapy worsens outcomes (incl. immunosuppressives)



Unique Complications of COVID-19

- **Diffuse endotheliitis**

- Viral tropism for endothelial cells with inflammatory cell injury and death

- **Hypercoagulability**

- Both local and embolic
- ARDS complicated by thromboemboli (especially pulmonary embolism)

- **Peri- and post-infectious hyperimmune reaction**

- Myocarditis (STEMI without coronary artery blockage)
- Multiorgan inflammatory syndrome in children (MIS-C)



SARS-CoV-2 and Influenza Coinfection, Coinfection with Influenza B More Deadly

- Patients from a single hospital outbreak in Wuhan during Jan-Feb 2020
- Diagnoses made by assaying SARS-CoV-2 RNA and influenza IgM
- No significant differences in age (median 50's-60's), sex (M:F, 1:1), illness severity

