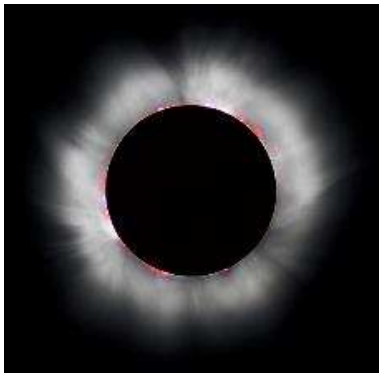
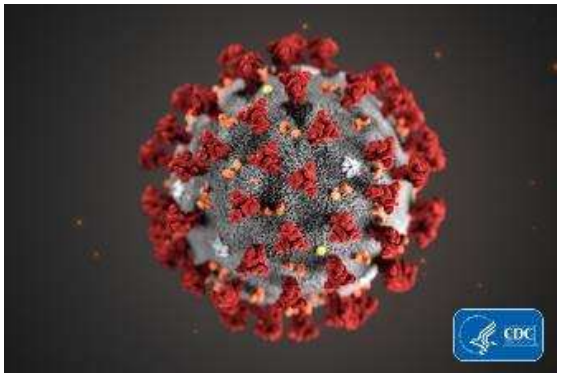
3-17-2020

# Covid-19 Clinical Update 3/17/2020

George Washington University






# COVID-19

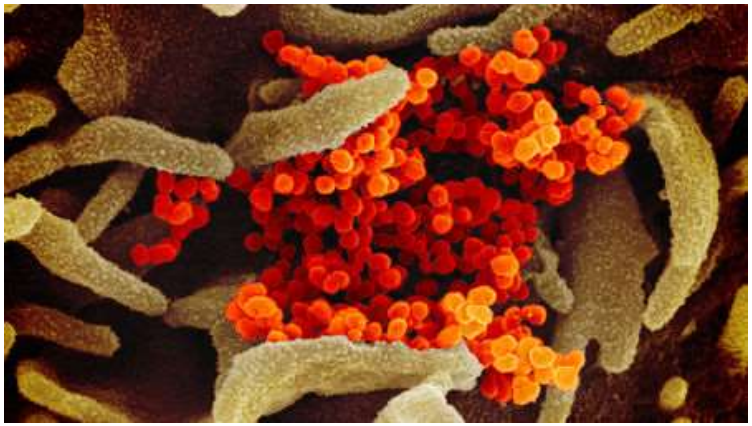
CURRENT AS OF 03.17.2020

HANA AKSELROD, MD, MPH

GW DIVISION OF INFECTIOUS DISEASES

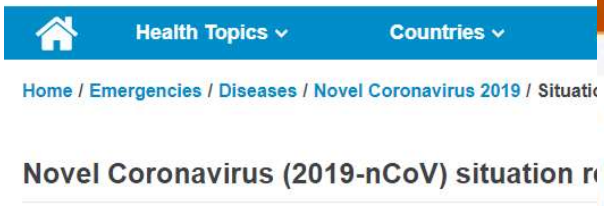
# Outline

1. Background
2. Pathophysiology and Transmission
3. Clinical Data
4. Diagnostics
5. Interventions
6. GW Preparedness and Response

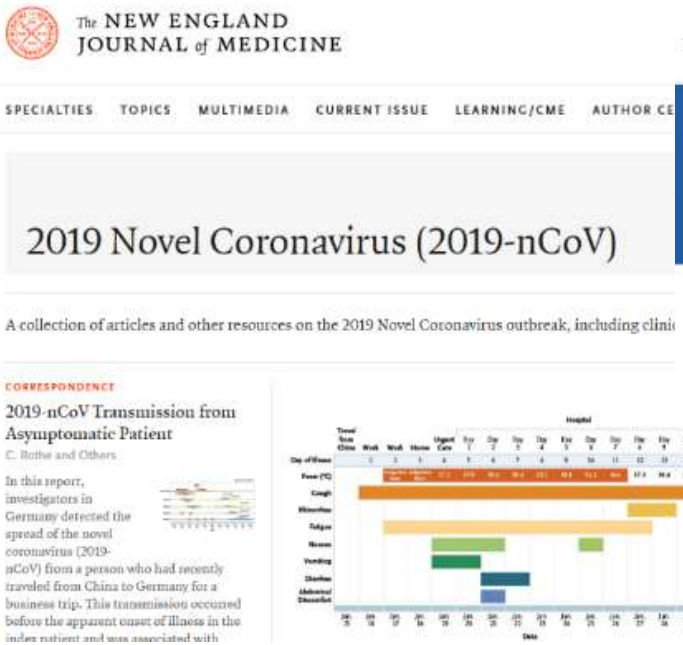


No commercial conflicts of interest.

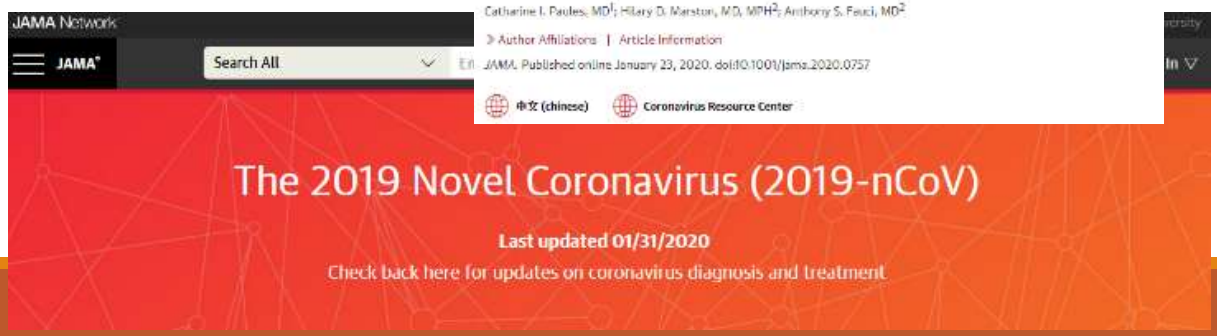










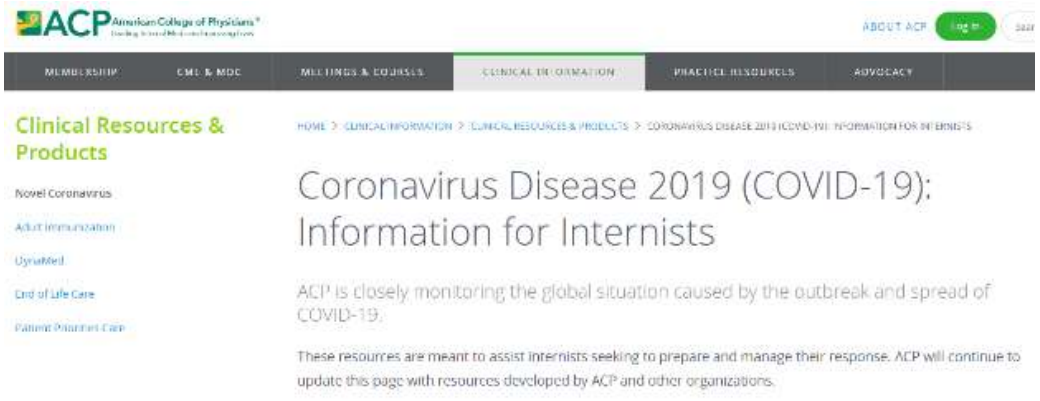



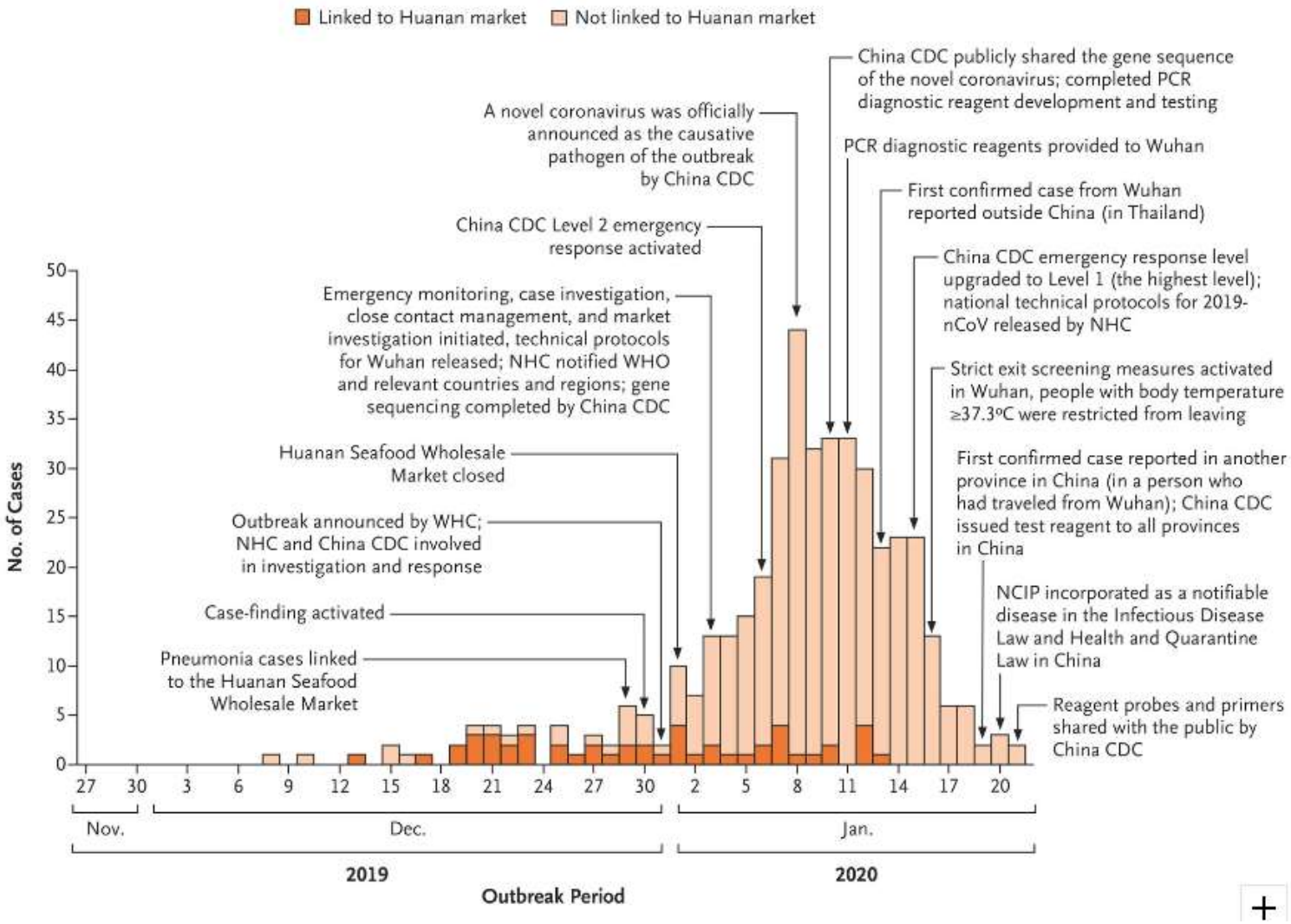

Some investigational data and use discussed


Society of Critical Care Medicine
ABOUT SCCM
COMMUNICATIONS
EDUCATION CENTER
FUNDAMENTALS
MEMBER CENTER
COVID-19 Resources
Access complimentary resources for managing COVID-19 patients


IDSA
Guidelines
Public Health
Clinical Practice
Research
Professional Development
Policy
COVID-19: What You Need to Know
NEW EPISODE
MARCH 11, 2020
PODCAST
COVID-19
WHAT'S HAPPENING NOW
IDSA

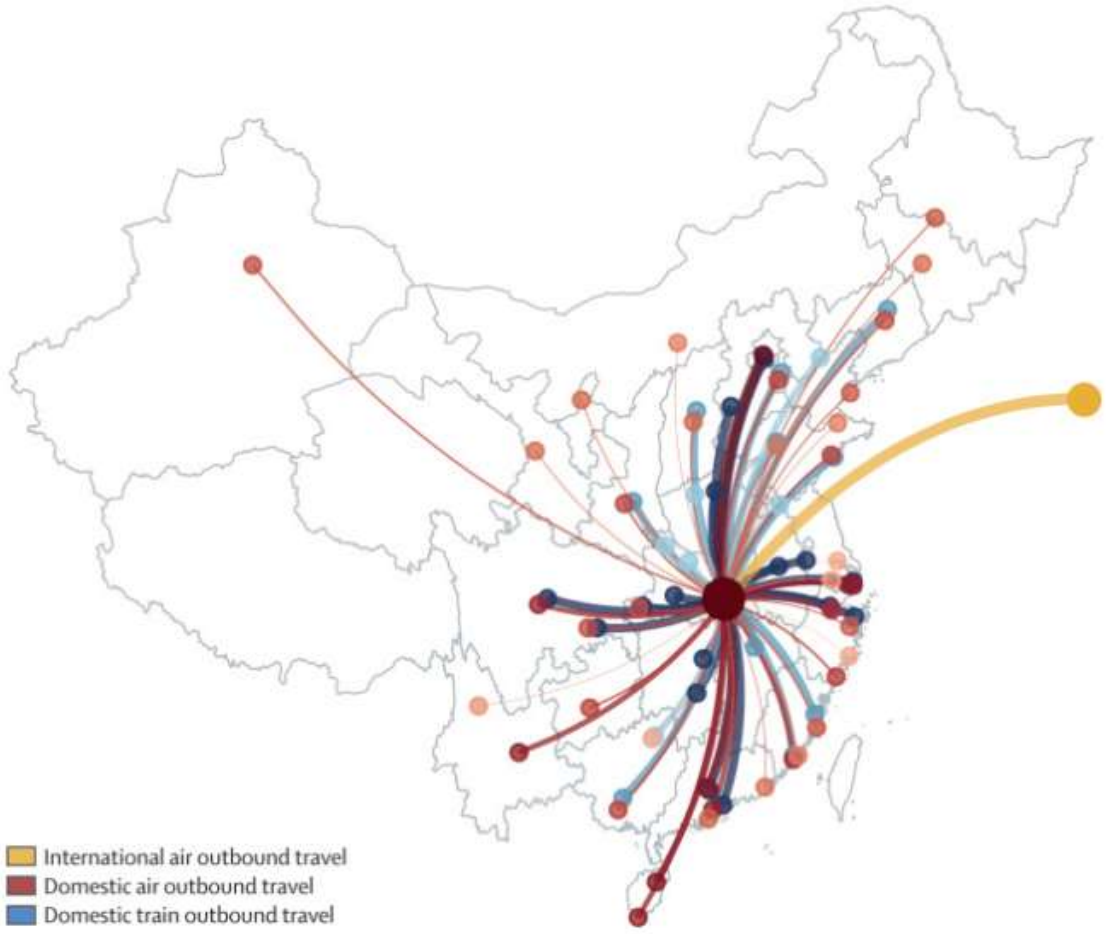

AMERICAN SOCIETY FOR MICROBIOLOGY
Home / Press Releases / Novel Coronavirus (COVID-19) Resources
Novel Coronavirus (COVID-19) Resources
March 11, 2020
Background: A new strain of coronavirus causing pneumonia-like symptoms was recently identified in Wuhan, China, marking the beginning of the spread of the virus across the globe. Coronaviruses (CoV), so named for their "crown-like" appearance, are a large family of viruses that spread from animals to humans and include diseases like Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). Researchers have now confirmed that the virus can spread via human to human transmission, though the original source of the virus has not been identified. Unlike other coronaviruses, COVID-19 has a much larger global spread and has infected more individuals than SARS and MERS combined.


ACP American College of Physicians
ABOUT ACP
MEMBERSHIP
CME & MOC
MEETINGS & COURSES
CLINICAL INFORMATION
PRACTICE RESOURCES
ADVOCACY
Clinical Resources & Products
Novel Coronavirus
Adult Immunization
UpToDate
End of Life Care
Patient Centered Care
HOME > CLINICAL INFORMATION > CLINICAL RESOURCES & PRODUCTS > CORONAVIRUS DISEASE 2019 (COVID-19): INFORMATION FOR INTERNISTS
Coronavirus Disease 2019 (COVID-19): Information for Internists
ACP is closely monitoring the global situation caused by the outbreak and spread of COVID-19.
These resources are meant to assist internists seeking to prepare and manage their response. ACP will continue to update this page with resources developed by ACP and other organizations.




(Li Q, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. *New England Journal of Medicine.* January 29, 2020.)

https://www.christianpost.com/news/christian-group-sends-face-masks-food-to-china-as-coronavirus-death-toll-rises-above-1000.html



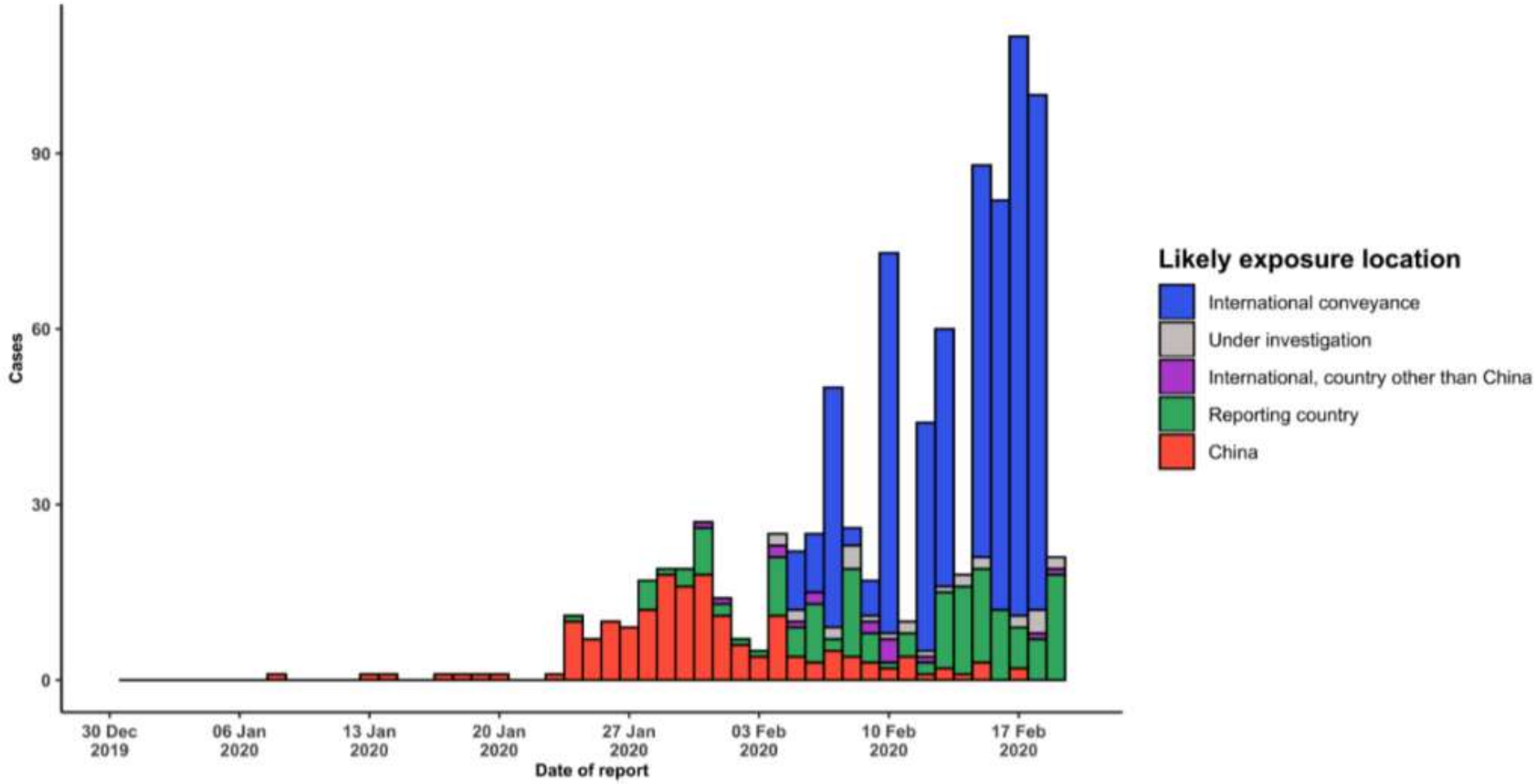

(Wu JT, Leung K, Leung GM. *Lancet*. January 31, 2020)

https://www.sciencenews.org/article/who-says-coronavirus-wuhan-china-outbreak-not-global-emergency-yet


http://www.cidrap.umn.edu/news-perspective/2020/02/china-covid-19-cases-rise-do-worries-over-diamond-princess-risk

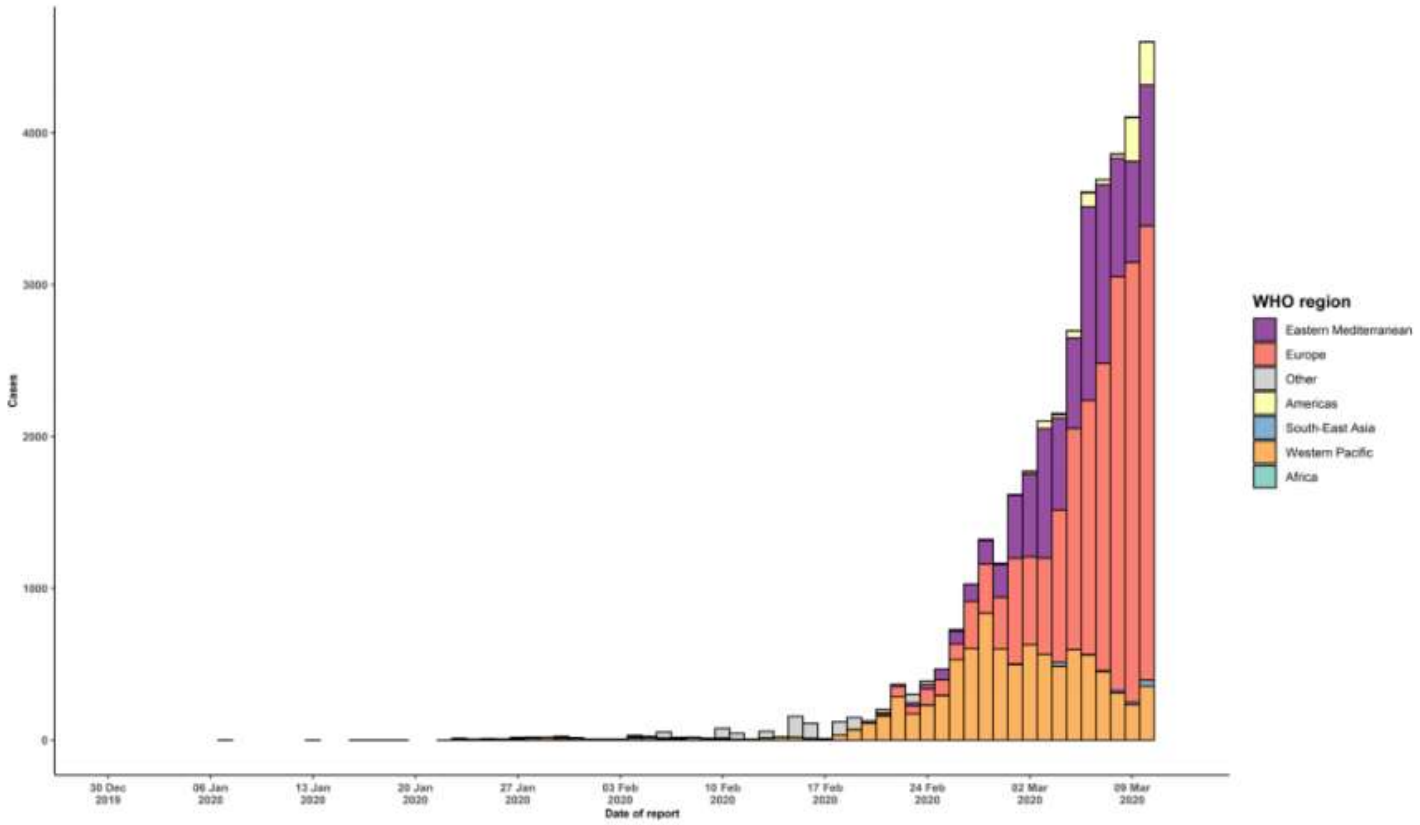

https://www.straitstimes.com/asia/east-asia/chinas-wuhan-to-build-second-designated-hospital-to-treat-coronavirus-patients

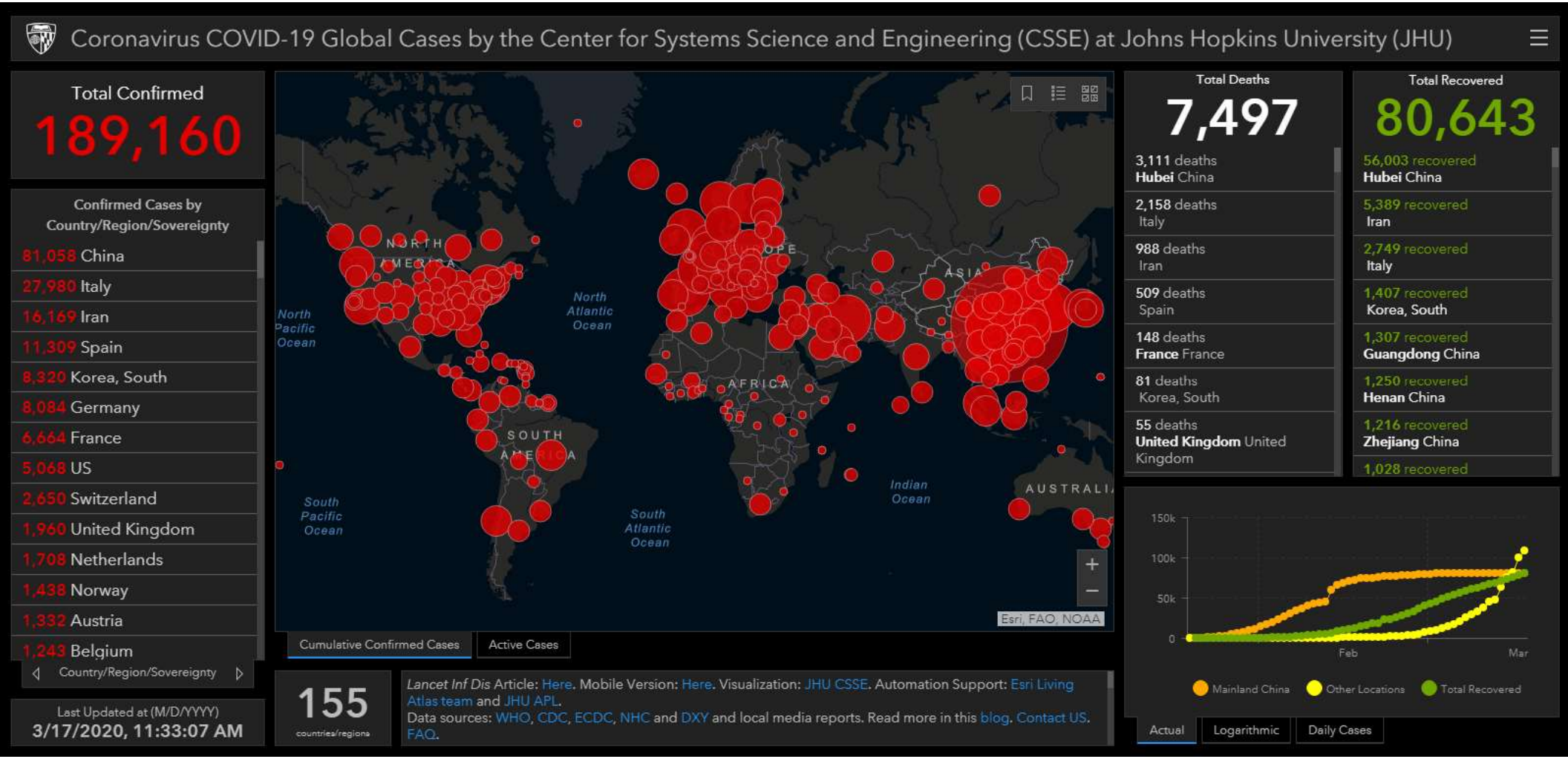
**Figure 3. Epidemic curve of COVID-19 cases (n=924) identified outside of China, by date of report and likely exposure location, 19 February 2020**

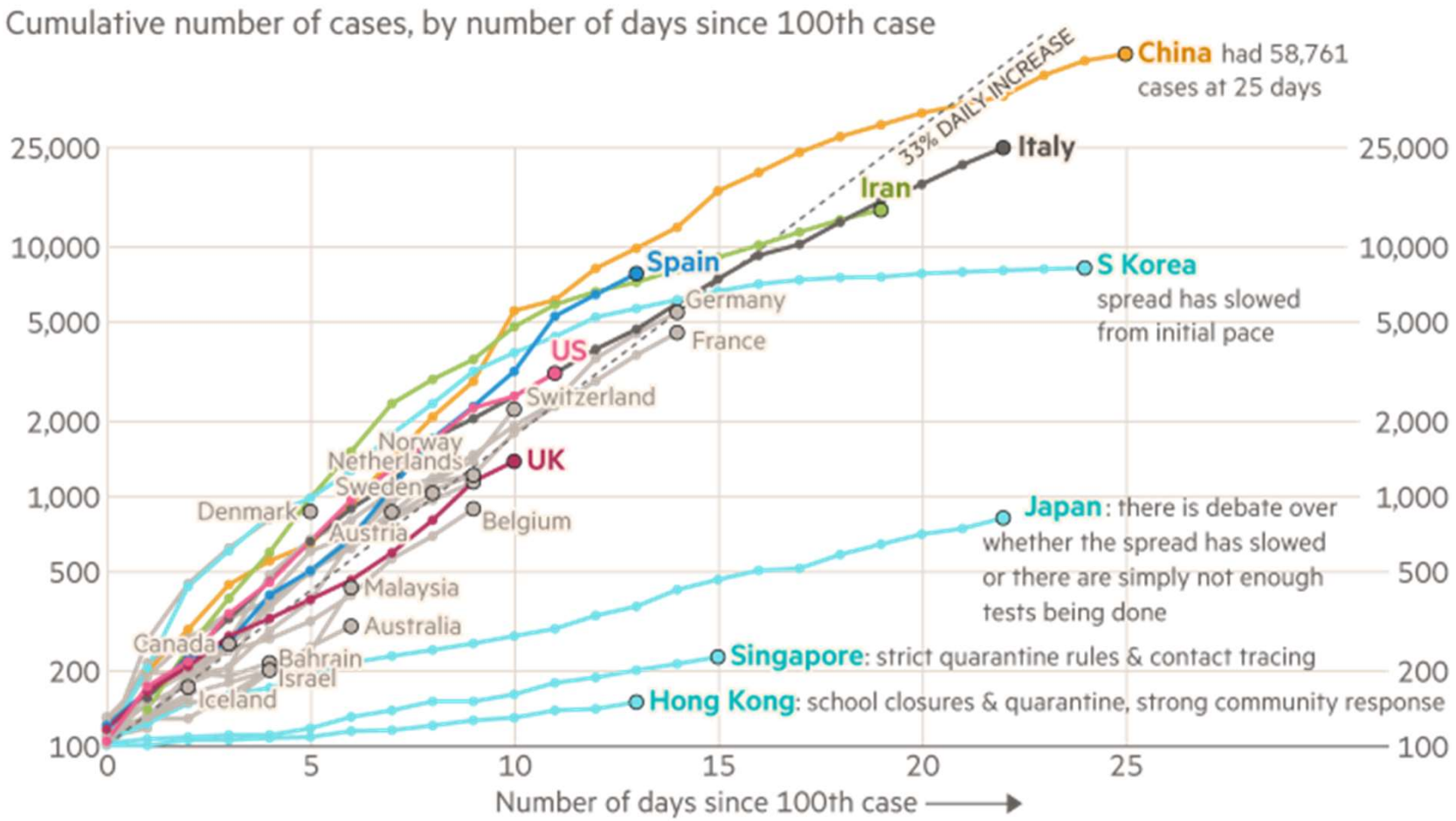



https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports

**Figure 2. Epidemic curve of confirmed COVID-19 cases reported outside of China , by date of report and WHO region through 11 March 2020**



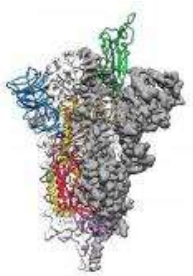

Coronavirus COVID-19 Global Cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)
Total Confirmed
189,160
Confirmed Cases by Country/Region/Sovereignty
81,058 China
27,980 Italy
16,169 Iran
11,309 Spain
8,320 Korea, South
8,084 Germany
6,664 France
5,068 US
2,650 Switzerland
1,960 United Kingdom
1,708 Netherlands
1,438 Norway
1,332 Austria
1,243 Belgium
Country/Region/Sovereignty
Last Updated at (M/D/YYYY)
3/17/2020, 11:33:07 AM
NORTH AMERICA
EUROPE
ASIA
AFRICA
SOUTH AMERICA
AUSTRALIA
North Pacific Ocean
North Atlantic Ocean
South Pacific Ocean
South Atlantic Ocean
Indian Ocean
Esri, FAO, NOAA
Cumulative Confirmed Cases
Active Cases
155
countries/regions
Lancet Inf Dis Article: Here. Mobile Version: Here. Visualization: JHU CSSE. Automation Support: Esri Living Atlas team and JHU APL.
Data sources: WHO, CDC, ECDC, NHC and DXY and local media reports. Read more in this blog. Contact US. FAQ.
Total Deaths
7,497
3,111 deaths Hubei China
2,158 deaths Italy
988 deaths Iran
509 deaths Spain
148 deaths France France
81 deaths Korea, South
55 deaths United Kingdom United Kingdom
Total Recovered
80,643
56,003 recovered Hubei China
5,389 recovered Iran
2,749 recovered Italy
1,407 recovered Korea, South
1,307 recovered Guangdong China
1,250 recovered Henan China
1,216 recovered Zhejiang China
1,028 recovered
150k
100k
50k
0
Feb
Mar
Mainland China
Other Locations
Total Recovered
Actual
Logarithmic
Daily Cases

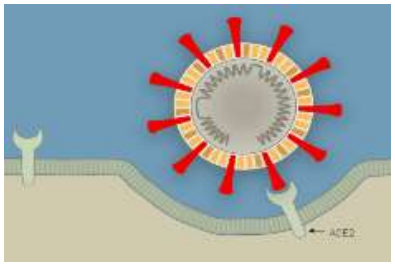



FT graphic: John Burn-Murdoch / @jburnmurdoch
Source: FT analysis of Johns Hopkins University, CSSE. Data updated March 15, 17:00 GMT


https://www.ft.com/content/a26fbf7e-48f8-11ea-aeb3-955839e06441

# SARS-CoV-2





**Family *Coronaviridae:***

- (+)RNA viruses
- 120-160 nm nucleocapsules
- High RNA replication error rate – 1 : $10^4$
- Common cause of respiratory illness: **229E**, **OC43**, **NL63**, and **HKU1**

**SARS-CoV-2:**

- S spike glycoprotein binds ACE2 with higher affinity than in SARS-CoV
- Limited antibody cross-reactivity

**Table 1**
Case fatality rate and $R_0$ value of commonly known emerging virus infections.

| Virus | Case Fatality Rate (%) | $R_0$ |
|---|---|---|
| 2019-nCoV | 3 | 1.4–5.5[a] |
| SARS-CoV | 10 | 2–5 |
| MERS-CoV | 40 | <1 |
| Avian H7N9 (2013) | 40 | <1 |
| H1N1 (2009) | 0.03 | 1.2–1.6 |
| H1N1 (1918) | 3 | 1.4–3.8 |
| Measles Virus | 0.3 | 12–18 |
| Rhinovirus | <0.01 | 6 |
| Ebola Virus | 70 | 1.5–2.5 |
| HIV | 80[b] | 2–4 |
| Small Pox Virus | 17 | 5–7 |

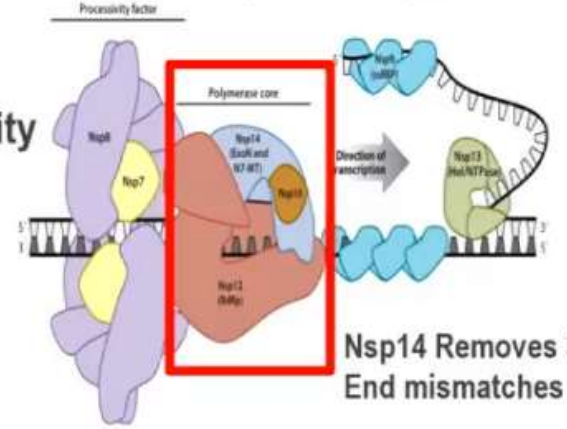
[a] WHO: 1.4–2.5; S. Zhao et al.: 3.3–5.5; J. Read et al.: 3.6–4.0; M. Shen et al.: 4.5–4.9.
[b] Without therapy.

(Chen, Pathogenicity and transmissibility of 2019-nCoV, *Microb Inf*, 2020)

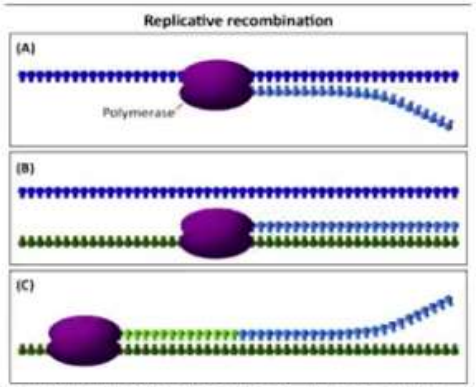
# Drivers of CoV Evolution

- CoV Genome Size: 32Kb
- CoV Mutation Rate
  - $10^{-6}$ → Regulated Fidelity (nsp14: ExoN)
  - Environmental Change
    - Fidelity rates change
- High Rates RNA Recombination
  - 25% during mixed infections
  - Modular evolution

CoV Replicase Complex




Nsp14 Removes 3' End mismatches

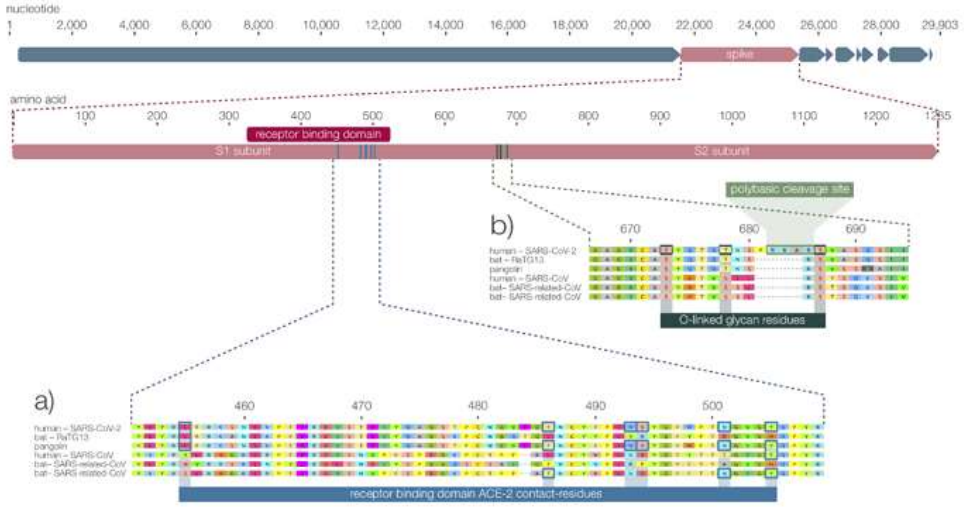



**Position Piece**: CoV: An RNA Proofreading Machine Regulates Replication and Fidelity (RNA Biol, 2011), Dudas G. Virus Evolution 2016; Eckerle et al., Plos Pathogens 2010; Graham et al., Nature Medicine 2012; Smith et al., Plos Path 2014

CROI
Conference on Retroviruses and Opportunistic Infections

# A novel bat coronavirus reveals natural insertions at the S1/S2 cleavage site of the Spike protein and a possible recombinant origin of HCoV-19

Hong Zhou[1,8], Xing Chen[2,8], Tao Hu[1,8], Juan Li[1,8], Hao Song[3], Yanran Liu[1], Peihan Wang[1], Di Liu[4], Jing Yang[5], Edward C. Holmes[6], Alice C. Hughes[2,*], Yuhai Bi[5,*], Weifeng Shi[1,7,*]




# Clinical Features – Summary Data

- **Symptom severity at diagnosis:**
  - 80% mild-moderate
  - 15% severe (hospitalized)
  - 5% critical
- **Average time from exposure to onset of symptoms: 5 days (range: 2-14)**
- Duration of illness: 1-2 weeks if mild, 4-6 if severe
- Virus shedding is highest in early days of illness, continues for 7-12 days
- **Viral shedding can occur 24-48 hours prior to onset of symptoms**
- Attack rate among close contacts: 10%
- **Truly asymptomatic infection rates: unknown without serology**

# Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China

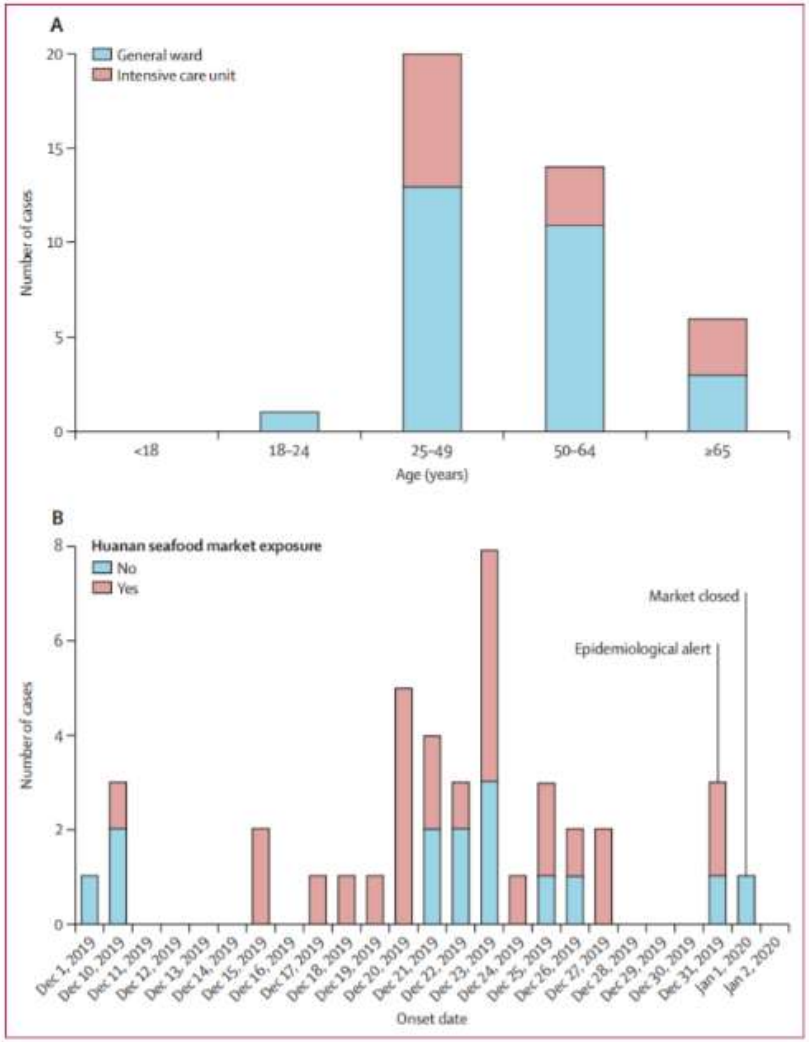
Prof Chaolin Huang, MD * • Yeming Wang, MD * • Prof Xingwang Li, MD * • Prof Lili Ren, PhD * • Prof Jianping Zhao, MD * • Yi Hu, MD * • et al. Show all authors • Show footnotes

## Summary

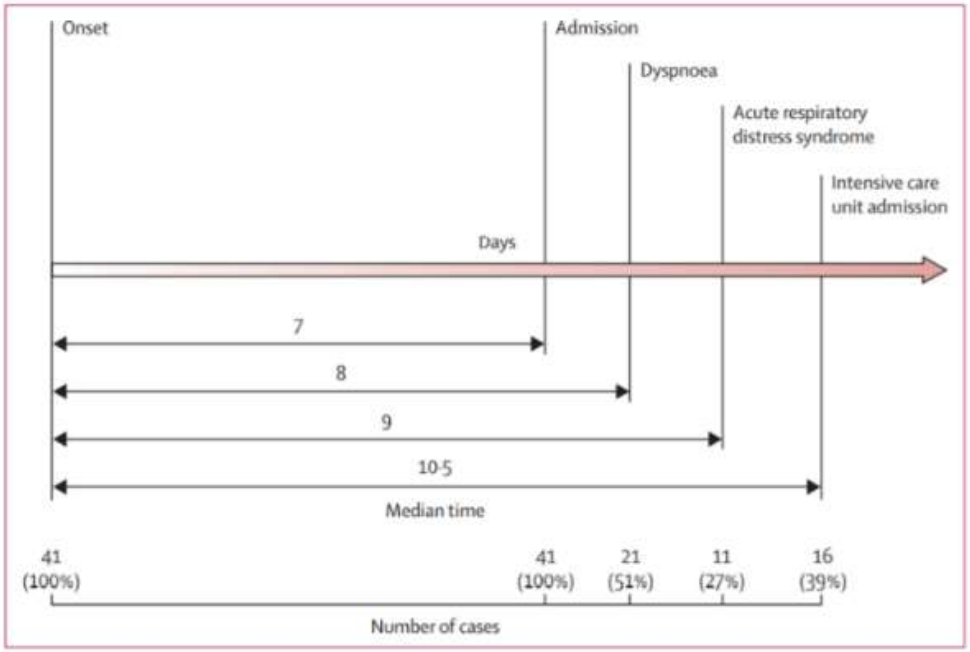
**Background** A recent cluster of pneumonia cases in Wuhan, China, was caused by a novel betacoronavirus, the 2019 novel coronavirus (2019-nCoV). We report the epidemiological, clinical, laboratory, and radiological characteristics and treatment and clinical outcomes of these patients.

**Methods** All patients with suspected 2019-nCoV were admitted to a designated hospital in Wuhan. We prospectively collected and analysed data on patients with laboratory-confirmed 2019-nCoV infection by real-time RT-PCR and next-generation sequencing. Data were obtained with standardised data collection forms shared by WHO and the International Severe Acute Respiratory and Emerging Infection Consortium from electronic medical records. Researchers also directly communicated with patients or their families to ascertain epidemiological and symptom data. Outcomes were also compared between patients who had been admitted to the intensive care unit (ICU) and those who had not.

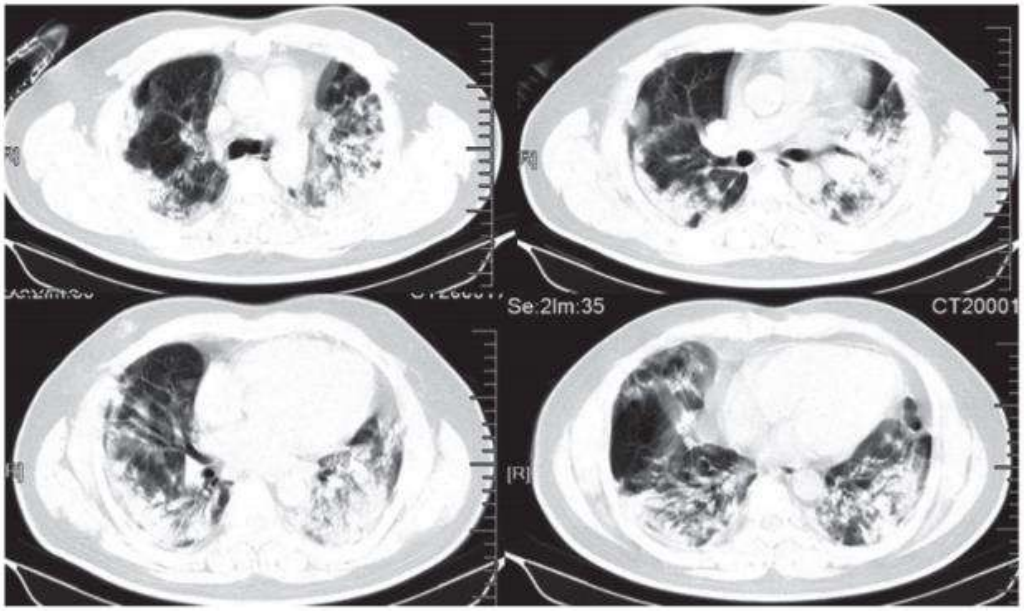
**Findings** By Jan 2, 2020, 41 admitted hospital patients had been identified as having laboratory-confirmed 2019-nCoV infection. Most of the infected patients were men (30 [73%] of 41); less than half had underlying diseases (13 [32%]), including diabetes (eight [20%]), hypertension (six [15%]), and cardiovascular disease (six [15%]). Median age was 49·0 years (IQR 41·0–58·0). 27 (66%) of 41 patients had been exposed to Huanan seafood market. One family cluster was found. Common symptoms at onset of illness were fever (40 [98%] of 41 patients), cough (31 [76%]), and myalgia or fatigue (18 [44%]); less common symptoms were sputum production (11 [28%] of 39), headache (three [8%] of 38), haemoptysis (two [5%] of 39), and diarrhoea (one [3%] of 38). Dyspnoea developed in 22 (55%) of 40 patients (median time from illness onset to dyspnoea 8·0 days [IQR 5·0–13·0]). 26 (63%) of 41 patients had lymphopenia. All 41 patients had pneumonia with abnormal findings on chest CT. Complications included acute respiratory distress syndrome (12 [29%]), RNAaemia (six [15%]), acute cardiac injury (five [12%]) and secondary infection (four [10%]). 13 (32%) patients were admitted to an ICU and six (15%) died. Compared with non-ICU patients, ICU patients had higher plasma levels of IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, and TNFα.




(Huang C, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. January 24, 2020.)

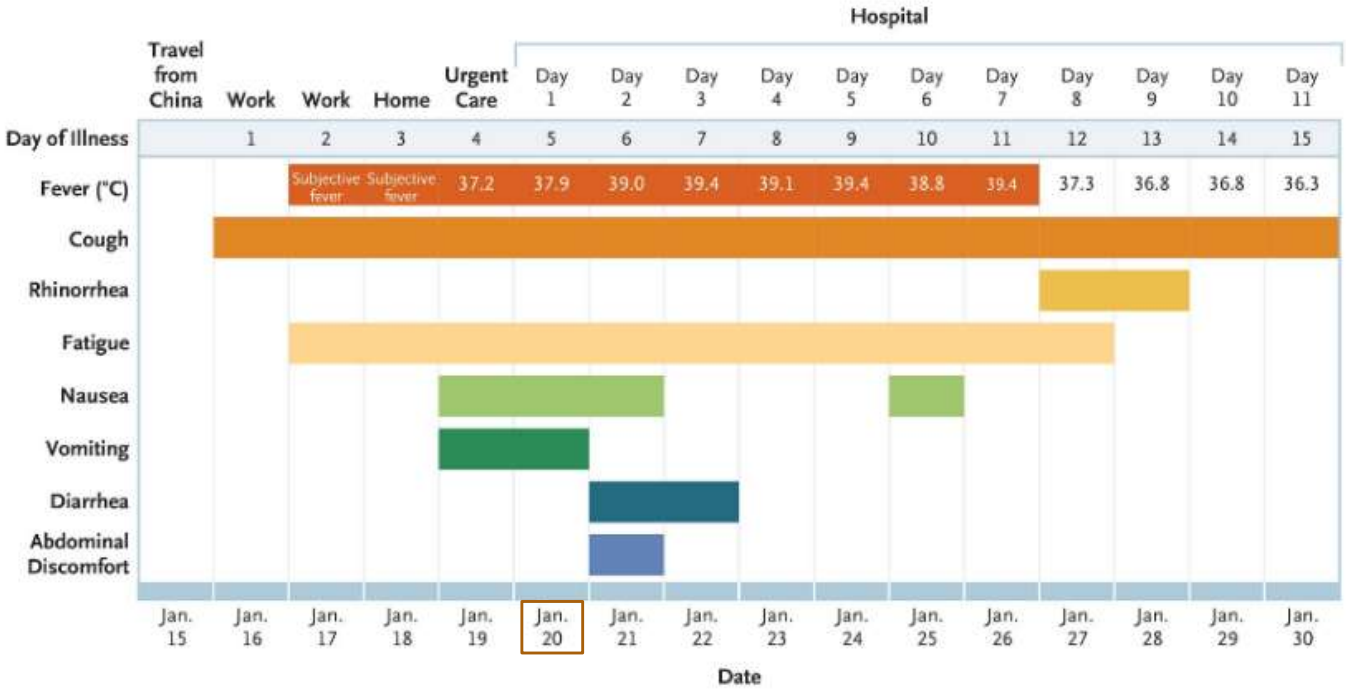



| | | | |
|---|---|---|---|
| Bilateral involvement of chest radiographs | 40/41 (98%) | 13/13 (100%) | 27/28 (96%) |




(Huang C, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. January 24, 2020.)

# First US Case Report

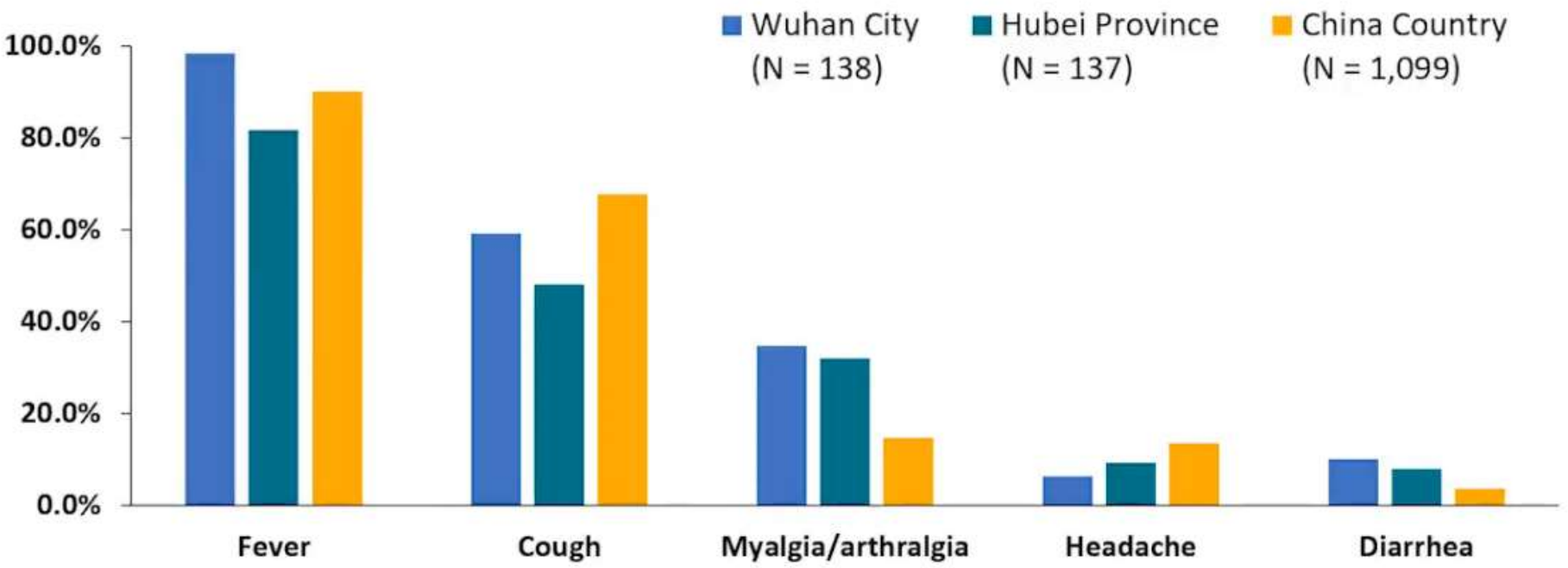



1/19/2020: WA State DOH and CDC contacted

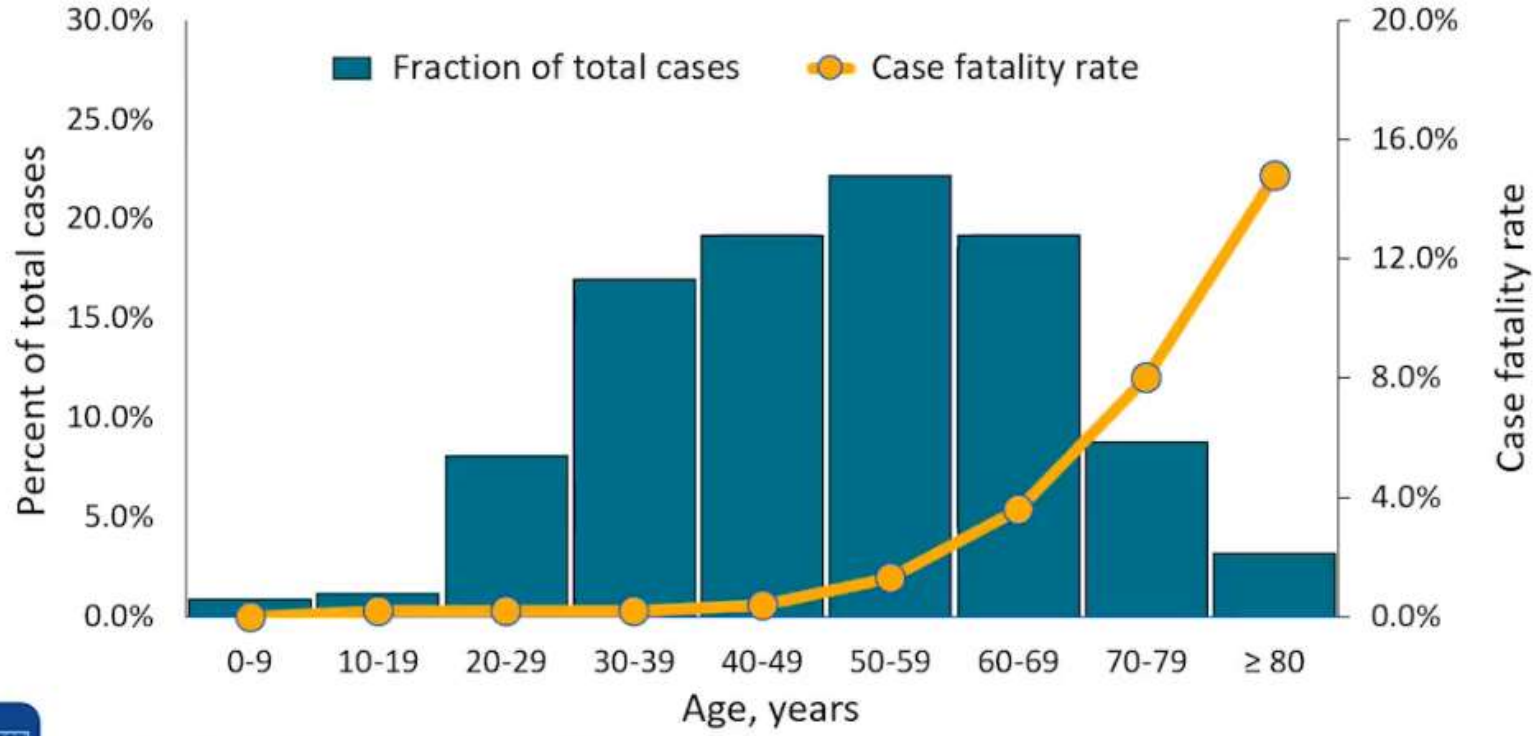
1/20/2020: CDC confirms that his nasopharyngeal and oropharyngeal swabs tested positive for 2019-nCoV by RT-PCR assay

Holshue ML, et al. First Case of 2019 Novel Coronavirus in the United States. New Engl J Med. January 31, 2020.

# Signs/Symptoms of COVID-19



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



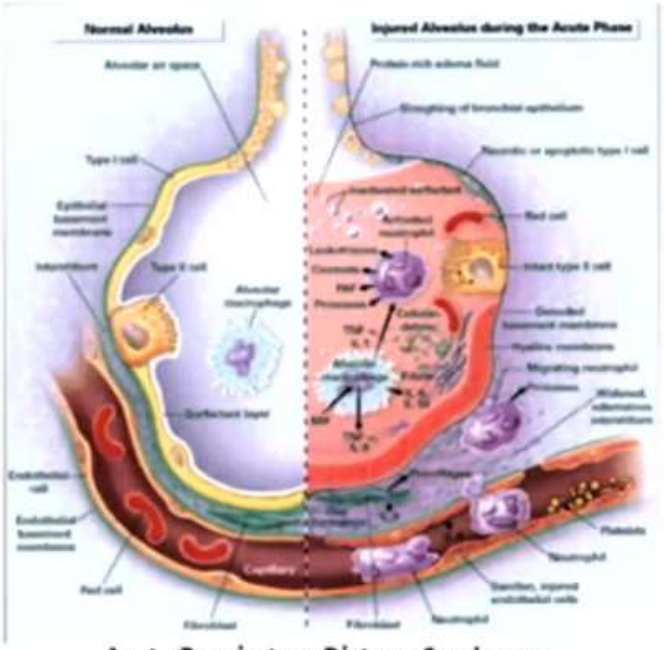

adapted from Zhang 2020, China CDC Weekly Rep; 2(8):113-122.

# COVID-19 in High-Risk Groups

- **Comorbidity and advanced age increase risk for severe illness and death**
  - Cardiovascular disease, diabetes, chronic respiratory disease (CFR >5%)
- **Immunocompromised (medical, acquired) – no data at present**
  - For persons with HIV, risk likely greatest at low CD4 cell counts or if not virally suppressed
  - Nonetheless all should take precautions given this is a new virus
  - CDC estimates that ≥ 50% of people with HIV are more than 50 years old
- **Pregnancy**
  - Current observational data only exist for women infected in third trimester
  - Maternal morbidity similar to that of uninfected women without COVID-19
  - No definitive evidence infection transmitted perinatally

# Cause of Death: ARDS

- **Emerging CoV and IAV**
  - **SARS-CoV** **H7N9** **2019-nCoV**
    H1N1-2009 **1918 H1N1**
  - **MERS-CoV** **H5N1**
- **Acute Respiratory Distress Syndrome (ARDS) (SARS, MERS, 2019-nCoV)**
  - End stage lung disease
  - ~30% mortality, ~17% require respiratory assistance (13% invasive ventilators)
  - Little evidence 2nd bacterial infections
- **ARDS:**
  - **~75,000 deaths in US**
  - **1 million deaths worldwide**
  - **Progress: Pulmonary Fibrosis**
  - **5 million deaths/worldwide**




**Acute Respiratory Distress Syndrome (hypoxia, oxygen insufficiency, organ failure, death)**

**Infections in children generally mild, males generally develop more serious disease**

Wang et al., 2020, JAMA Clinical Characteristics of 138 Hospitalized Patients With2019 NovelCoronavirus–Infected Pneumoniain Wuhan, China

CROI

CORRESPONDENCE

# Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany

January 30, 2020
DOI: 10.1056/NEJMc2001468

ACCEPTED MANUSCRIPT

# A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period

Ping Yu, Jiang Zhu, Zhengdong Zhang, Yingjun Han, Lihong Huang

*The Journal of Infectious Diseases*, jiaa077, https://doi.org/10.1093/infdis/jiaa077

Rapid communication

# Effectiveness of airport screening at detecting travellers infected with novel coronavirus (2019-nCoV)

Billy J Quilty[1], Sam Clifford[1], CMMID nCoV working group2[1,2,3], Stefan Flasche[1,3], Rosalind M Eggo[1,3]

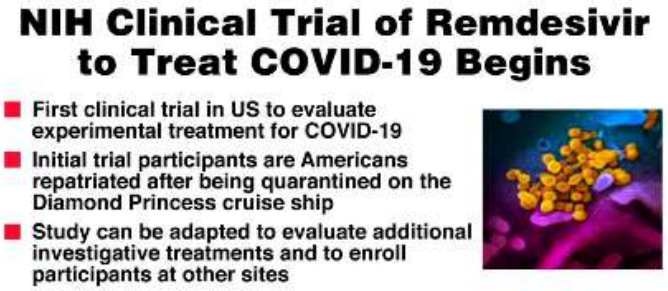
# Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes

Wei Zhang, Rong-Hui Du, Bei Li, Xiao-Shuang Zheng, Xing-Lou Yang, Ben Hu ... show all

# Pharmacologic Treatment

Ongoing trials to establish safety and efficacy in COVID-19

- Lopinavir/ritonavir (AbbVie)
  - Studied in combination with IFN-β1b against MERS
- Ribavirin (Merck)
  - Studied in combination with IFN-α against MERS
- Remdesivir (Gilead)
  - Studied in Ebola
  - https://clinicaltrials.gov/ct2/show/NCT04257656
- Tocilizumab (Actemra) (Genentech)
- Others



# Vaccine Development

## HHS partners with drug makers on COVID-19 vaccine, drugs

Filed Under: **COVID-19**

Stephanie Soucheray | News Reporter | CIDRAP News | Feb 18, 2020

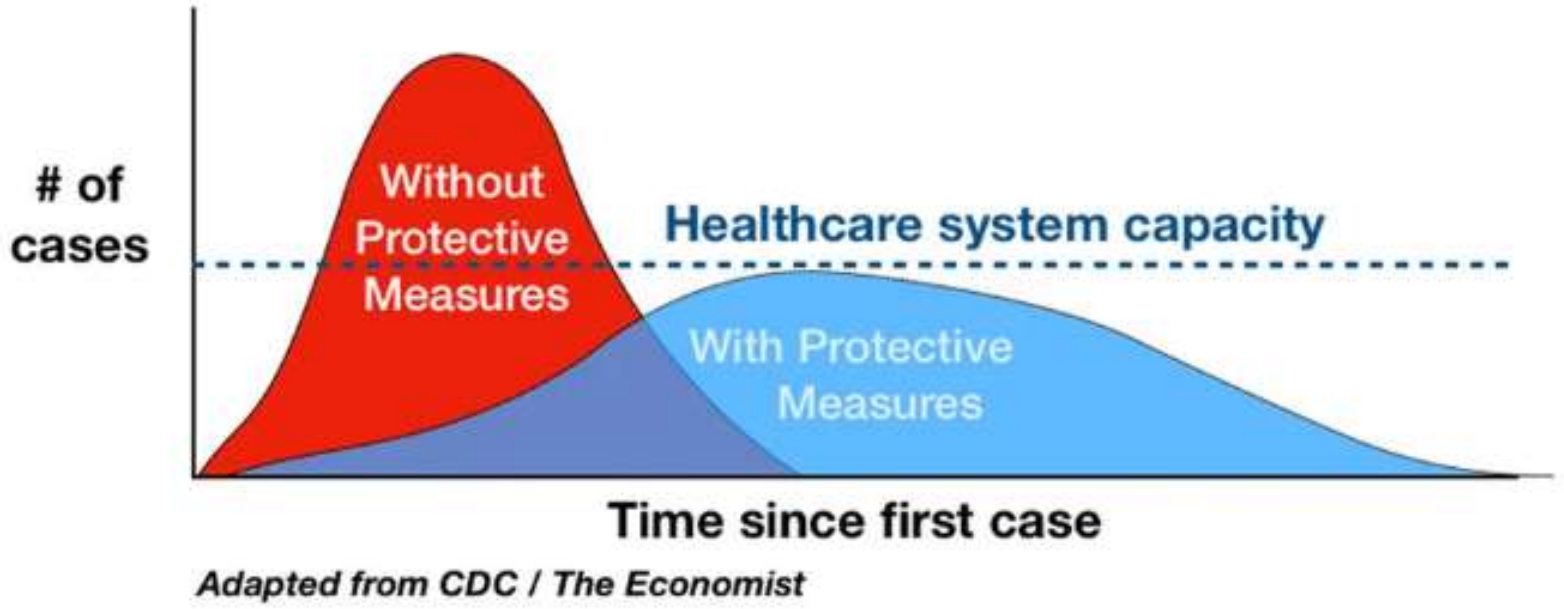
Share Tweet LinkedIn Email Print & PDF

The US Department of Health and Human Services (HHS) is partnering with Sanofi Pasteur and Johnson & Johnson to develop vaccines and therapeutics to use against COVID-19, according to press releases from the drug makers and HHS today.

Sanofi announced it will be revisiting previous development work for a SARS (severe acute respiratory syndrome) vaccine to examine a path for COVID-19 vaccine development. Both SARS and COVID-19 are coronaviruses that originated in China, with SARS appearing in 2002 and largely disappearing by 2004.

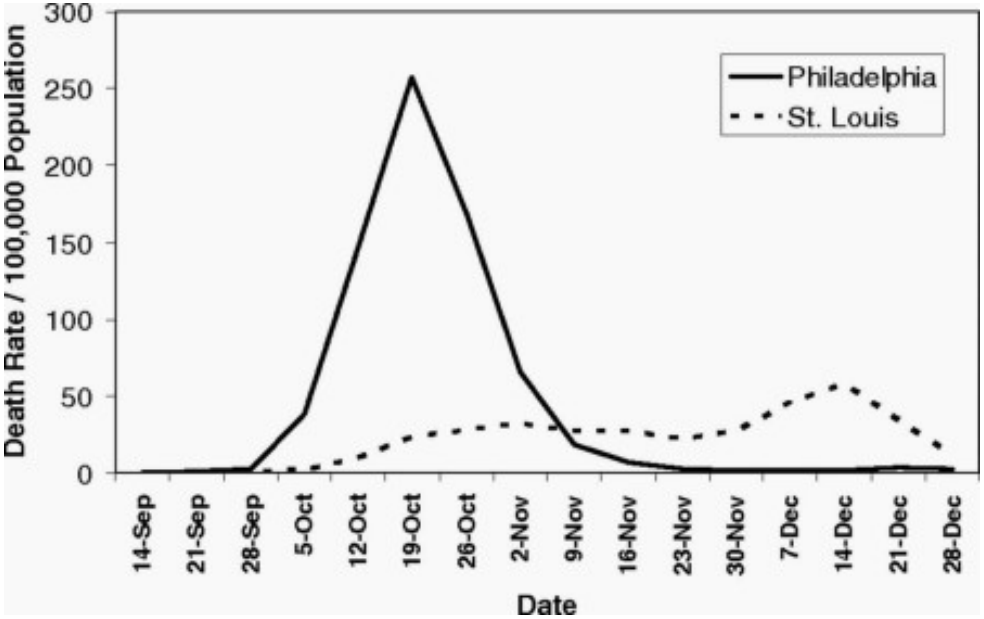
http://www.cidrap.umn.edu/news-perspective/2020/02/hhs-partners-drug-makers-covid-19-vaccine-drugs

# “Flattening the Curve”

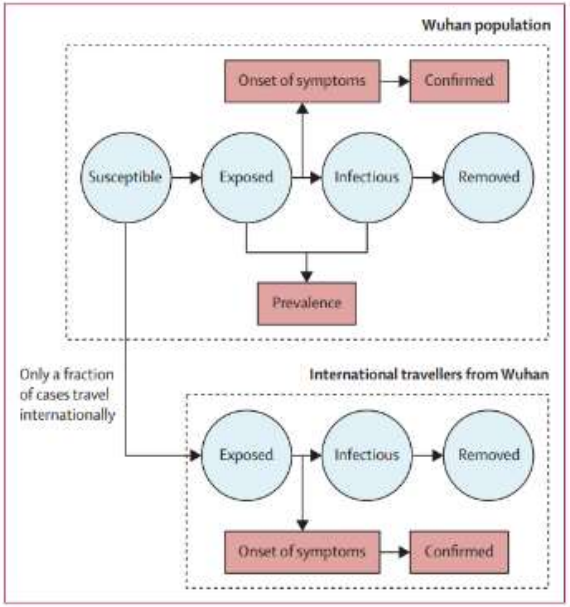


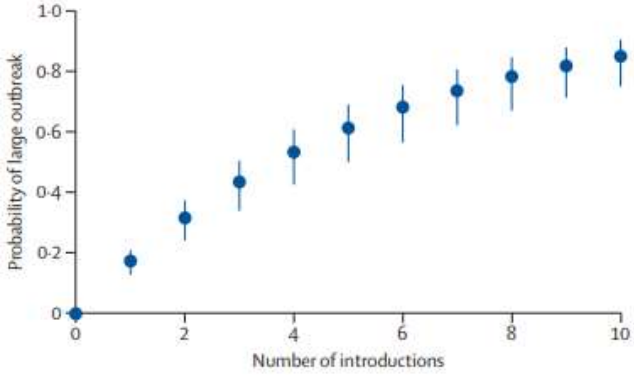

*Adapted from CDC / The Economist*

**Walter Reed Hospital Flu Ward**
In: Williams E. “The Forgotten Epidemic: A Century Ago, DC Lost Nearly 3,000 Residents to Influenza.” *The Washingtonian*. Oct. 31, 2018.



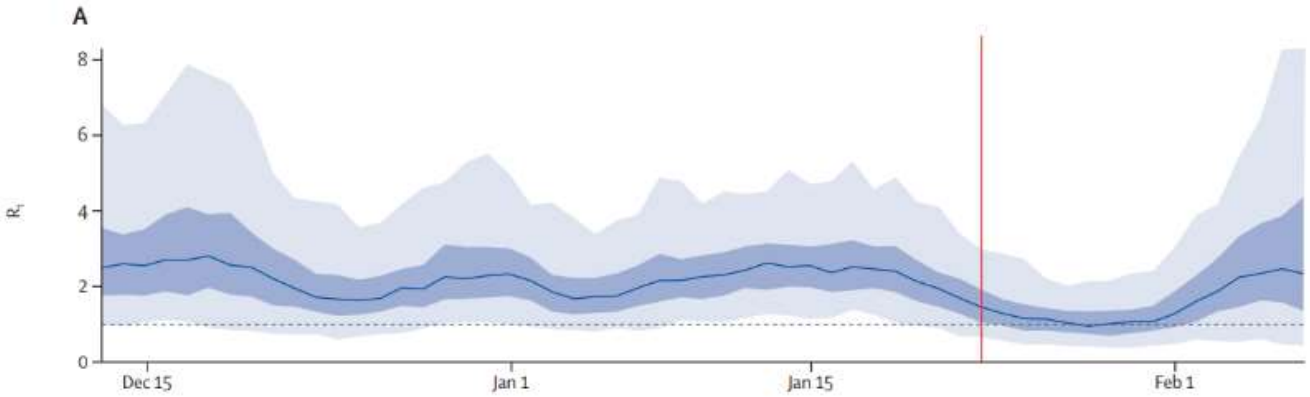

https://qz.com/1816060/a-chart-of-the-1918-spanish-flu-shows-why-social-distancing-works/
https://www.washingtonian.com/2018/10/31/the-forgotten-epidemic-a-century-ago-dc-lost-nearly-3000-residents-to-influenza/




## Early dynamics of transmission and control of COVID-19: a mathematical modelling study

*Adam J Kucharski, Timothy W Russell, Charlie Diamond, Yang Liu, John Edmunds, Sebastian Funk, Rosalind M Eggo, on behalf of the Centre for Mathematical Modelling of Infectious Diseases COVID-19 working group**

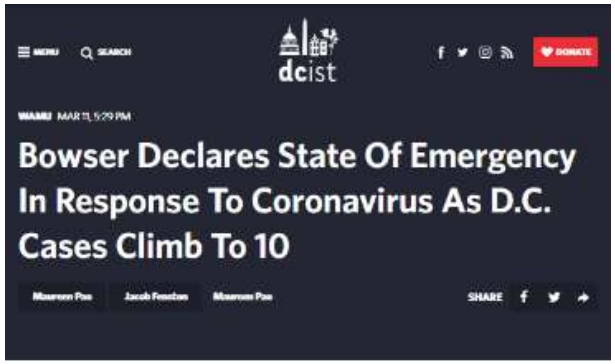



- COVID-19 transmission probably declined in Wuhan during late January, 2020, coinciding with the introduction of travel control measures.
- As more cases arrive in international locations with similar transmission potential to Wuhan before these control measures, it is likely many chains of transmission will fail to establish initially, but might lead to new outbreaks eventually.

(*Lancet Infect Dis*, March 11, 2020)

# Italy recorded its most deaths from the coronavirus in a single day, more evidence it's now the hardest-hit place on Earth

Mia Jankowicz Mar 11, 2020, 7:04 AM




# Maryland and Washington, DC: Latest updates on coronavirus

By Laura Geggel - Associate Editor an hour ago

Comments (0)

(Image: © Shutterstock)

*Last updated March 17 at 11:11 am E.D.T.*

There are 57 confirmed cases of the new coronavirus in Maryland and 17 in the nation's capitol, according to Maryland.gov and public health authorities in D.C. Of note, Maryland's numbers are updated daily, while the D.C. public health page was last updated March 15.

# Clinician Wellness

**Challenges:**

- Overload on top of existing burdens
- Stress from general public and family concerns
- Concern for family, own health, and security
- Child care and elder care
- Responsibility and guilt

**Suggestions:**

- Encourage physicians to acknowledge and validate their own personal concerns, without feeling that they are being selfish or taking away from the care of their patients
- We rely on our organization's leadership to put processes in place to protect us so that we can work to protect our patients
- Take a "time out" to disconnect from the information overload at times, and take necessary steps to remain centered
- Ask for help when we need it
- Keep lines of communication open


| DO'S | DON'TS |
| --- | --- |
| ☐ Practice sound hand hygiene (use the five-step approach: wet, lather, scrub, rinse, dry). | ☐ Rush out to buy facemasks. The common surgical facemasks are not effective in preventing an uninfected person from being infected. |
| ☐ Practice proper respiratory hygiene (cover coughs and sneezes with a tissue and dispose properly). | ☐ Go outside or into public if you're sick. |
| ☐ Routinely disinfect surfaces commonly touched by other people. | |
| ☐ Avoid contact with people who are known to be sick. | |
| ☐ Consult your health care provider when you develop symptoms of cold or flu and stay home unless advised to seek medical attention. | |
| ☐ Wearing a facemask should be reserved for when you are sick and in proximity to others (to avoid infecting them) or if advised by your health care provider. | |
| ☐ Get the flu vaccine. | |

https://news.yale.edu/2020/03/10/public-health-prof-albert-ko-protecting-yourself-against-coronavirus