COVID-19

Novel Coronavirus: Guidance for Health-care Providers

March 3, 2020



Coronaviruses

- RNA virus that mutates easily
- Largest genome of RNA viruses
- Infect wide range of hosts including mammals & birds
- 7 have known to infect humans
 - o 4 of these circulate regularly and cause common cold



Coronaviruses of Importance

• MERS CoV in 2012 (and ongoing)

Arabian Peninsula

- WHO: 2,499 lab-confirmed cases in 27 countries w/ 861 deaths
 - Case-fatality rate ~34%
- $_{\rm o}\,$ In Saudi Arabia alone: 1831 cases and 787 deaths

• SARS CoV in 2002-2003

- Infected >8,000 people w/ 774 deaths in 32 countries in 2002-2003
 - Case fatality rate ~9-10%
- $_{\rm \circ}\,$ HCWs accounted for 20% of all cases
- Many "Super Spreading" events
- Outbreak ended through use of containment and mitigation strategies



Source: Timothy Sheahan, University of North Carolina https://www.wsj.com/articles/what-we-know-about-the-wuhan-virus-11579716128

Zoonotic Disease

Can jump between animals and humans

Animal reservoir for COVID-19 is unknown



Novel viruses are of particular concern because of the lack of herd immunity

Coronavirus COVID-19 Global Cases by Johns Hopkins CSSE



https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6

Current data on COVID-19: Infectiousness

- Probably about as infectious as SARS
 - R₀ estimates: 2.2-4.2
 - Lipsitch et al. Science. 2003; Riely et al. Science 2003; Wallinga & Teunis. AJE. 2004
- More infectious than influenza
 - R₀ estimates pandemic flu: 1.46-1.8
 - \circ R₀ estimate for seasonal flu: 1.28
 - Biggerstaff et al. BMC ID. 2014
- R₀ estimates for COVID-19:
 - **2.2** (95% CI: 1.4-3.9)
 - Early disease reporting data (Li et al. NEJM. 2020)
 - o 2.24 (95% CI: 1.96-2.55)
 - When assuming 8-fold increase in reporting rate
 - o 3.58 (95% CI: 2.89-4.39)
 - When assuming 2-fold increase in reporting rate
 - Modeling paper using data from Jan 10-24th in China (Zhao et al. International Journal of Infectious Diseases, 2020)
 - o **2.8-3.9**
 - Modeling paper using data before 1/26 in China (Zhou et al. Journal of Evidenced Based Medicine. 2020)

Current data on COVID-19: Incubation Period

- Most likely 2-14 days (CDC)
 - $_{\rm O}$ 5.1 days
 - Chan et al. Lancet. 2020
 - 5.2 days (95% CI: 4.1-7.0)
 - Li et al. NEJM. 2020
- Similar to SARS, which was 6.4 days
 - (5.2-7.7 days)
 - Donnelly et al. Lancet. 2003
- Serial interval (onset-to-onset): 7.5 days (95% CI: 5.3-19 days)
 - $_{\circ}~$ Li et al. NEJM. 2020



The estimated incubation period distribution (i.e., the time from infection to illness onset) is shown in Panel A. The estimated serial interval distribution (i.e., the time from illness onset in successive cases in a transmission chain) is shown in Panel B. The estimated distributions of times from illness onset to first medical visit are shown in Panel C. The estimated distributions of times from illness onset to hospital admission are shown in Panel D.

Current data on COVID-19: Severity

- Case Fatality Rate: between 2-4% in Hubei province
 - Lower than SARS (9-10%) or MERS (~34%)
 - Higher than seasonal influenza (0.1%-0.2% among symptomatic cases)
 - https://www.cdc.gov/flu/about/burden/past-seasons.html
 - Possibly similar to 1918 pandemic influenza (2-3%)
 - Taubenberger et al. EID. 2006
- Study of 72,000 COVID-19 cases in China; of ~45K (62%) lab-confirmed:
 - 2.3% fatal (Severity: 81% mild disease; 14% severe disease; 5% critically ill)
 - Fatality higher among those with preexisting conditions: 10.5% CVD; 7.3% DM; 6.3% chronic respiratory disease; 6% HTN; 5.6% cancer
 - Fatality higher among elderly: 14.8% among <u>>80y</u>; 8% among 70-79y
 - Wu et al. JAMA 2020
 - $_{\circ}\,$ Age: Only 2% of cases were <20 years of age
 - HCW: 3.8% of confirmed cases, including 5 deaths

Current data on COVID-19: Severity

- Study of 138 hospitalized patients in Wuhan in January (Wang et al. JAMA. 2020)
 - $_{\circ}$ At the time of the study:
 - 4.3% had died
 - 34% were discharged, median hospital stay was 10 days
 - 62% were still inpatient
 - Median age 56y (IQR, 42-68)
 - Median time from onset => hospital admission was 7 days
 - $_{\circ}~$ 41% were presumed to be HAIs
 - $_{\circ}$ 46% had comorbidities
 - \circ 29% were HCWs
 - $_{\circ}~$ 26% admitted to ICU
 - 72% had comorbidities
 - Median age 66y (IQR, 57-78)
 - 47% required invasive mechanical ventilation; 11% received ECMO

Current data on COVID-19: Severity

- Study of 1,099 hospitalized patients from 552 hospitals in China in January (Guan & Ni. not published)
 - $_{\circ}$ Median age 47y
 - <1% were 0-14 years of age</p>
 - $_{\odot}$ 2.1% HCWs
 - $_{\circ}$ 23% had comorbidity
 - 79% had pneumonia; median time from onset => PNA was 4 days
 - 6% mechanical ventilation
 - $_{\circ}$ 5% admitted to ICU
 - 1.4% had died at the time of the study; 94% still inpatient



Average number of people infected by each sick person

Note: Average case-fatality rates and transmission numbers are shown. Estimates of case-fatality rates can vary, and numbers for the new coronavirus are preliminary estimates.

https://www.nytimes.com/interactive/2020/world/asia/china-coronavirus-contain.html

Current data on COVID-19: Symptoms

- Fever, cough, shortness of breath (ILI)
- GI symptoms occasionally reported
- Some confirmed cases have not had any symptoms
 - $_{\circ}$ 10 yo child from early family cluster (Chan et al. Lancet. 2020)
 - $_{\circ}$ Infant from Wuhan
 - Many news reports
 - https://www.gpbnews.org/post/atlanta-couple-tests-positive-coronavirus-aboard-cruise-ship
- Asymptomatic transmission is possible
 - Germany cluster w/ 3 documented asymptomatic transmission events (Rothe et al. NEJM. 2020)
 - Family cluster in China (Bai et al. JAMA. 2020)

Asymptomatic Transmission:

Rothe et al. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. NEJM. 2020.



- Index Patient: Shanghai resident, businesswoman visited Germany between 1/19 and 1/22. No s/s of disease in Germany; became ill on flight back to China on 1/22; PCR+ 1/26
- Patient 1: 33 healthy German businessman; became ill with a sore throat, chills, and myalgias on 1/24. The following day, developed a fever of 102.4°F and productive cough. By the evening of the next day, he started feeling better and went back to work on 1/27.
- Patients 3 & 4 only had contact with Patient 1 prior to him developing symptoms

contact tracing started 1/27

Current data on COVID-19: Viremia

- Specimens for diagnosis include NP, OP, BAL, aspirate,
- NP PCR may remain positive for at least 12 days (Holshu et al. NEJM. 2020)
- Virus can be shed in feces; may be more prevalent later in course of illness (Zhang et al. EMI. 2020)
 Table 2. Molecular detection of 2019-nCoV in swabs from two

| Table 2. Results of Real-Time Reverse-Transcriptase–Polymerase-Chain-Reaction Testing for the 2019 Novel Coronavirus (2019-nCoV).* | | | | |
|--|-------------------------|-------------------------|-------------------------|-------------------------|
| Specimen | Illness Day 4 | Illness Day 7 | Illness Day 11 | Illness Day 12 |
| Nasopharyngeal swab | Positive (Ct, 18–20) | Positive (Ct, 23–24) | Positive (Ct, 33–34) | Positive (Ct, 37–40) |
| Oropharyngeal swab | Positive (Ct, 21–22) | Positive (Ct, 32–33) | Positive (Ct, 36–40) | Negative |
| Serum | Negative | Negative | Pending | Pending |
| Urine | NT | Negative | NT | NT |
| Stool | NT | Positive (Ct, 36–38) | NT | NT |

* Lower cycle threshold (Ct) values indicate higher viral loads. NT denotes not tested.

Table 2. Molecular detection of 2019-nCoV in swabs from two investigations. Samples were from oral swabs (OS), anal swabs (AS) and blood. Data were shown as qPCR Ct values.

| | Date 0-OS | Date 0-AS | Date 5-OS | Date 5-AS |
|------------|-----------|-----------|-----------|-----------|
| Patient 1 | | | 23.2 | |
| Patient 2 | 30.3 | | | |
| Patient 3 | | 19.5 | | |
| Patient 4 | 32.7 | 30.2 | | |
| Patient 5 | | 33.1 | | |
| Patient 6 | 31.1 | | 30.0 | 31.4 |
| Patient 7 | 27.3 | | | |
| Patient 8 | | | 27.0 | |
| Patient 9 | 32.9 | 33.6 | | |
| Patient 10 | | | | 23.8 |
| Patient 11 | 31.9 | | | |
| Patient 12 | 32.3 | | | |
| Patient 13 | | | | 17.8 |
| Patient 14 | | | | 25.5 |
| Patient 15 | | | | 30.0 |
| Patient 16 | 33.8 | | 26.9 | 27.5 |

| Clinical Features | & | Epidemiologic Risk |
|--|-----|---|
| Fever ¹ or signs/symptoms of lower respiratory illness (e.g. cough or shortness of breath) | AND | Any person, including health care workers ² , who has had close contact ³ with a laboratory- confirmed ⁴ COVID-19 patient within 14 days of symptom onset |
| Fever ¹ and signs/symptoms of a lower respiratory illness (e.g., cough or shortness of breath) requiring hospitalization | AND | A history of travel from affected geographic areas (see below) within 14 days of symptom onset |
| Fever ¹ with severe acute lower respiratory illness (e.g., pneumonia, ARDS) requiring hospitalization ⁶ and without alternative explanatory diagnosis (e.g., influenza) ⁷ | AND | No source of exposure has been identified |

Who is getting tested for COVID-19 in the U.S.?

Affected Geographic Areas with Widespread or Sustained Community Transmission

- China
- Iran
- Italy
- Japan
- South Korea

https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-criteria.html

In the U.S. – as of 2/26/2020

- 15 confirmed COVID-19 cases in the U.S.; 14 have direct epidemiologic links to Wuhan
 - 12 travel-related; 3 person-to-person
- 451 PUIs have been tested
- An additional 46 cases have occurred among persons repatriated to the U.S.
 - o 3 from Wuhan; 43 from *Diamond Princess* cruise ship

How do you stop an outbreak?



Good contact tracing

Good case identification

Containment & Mitigation

Isolate the sick

Quarantine the exposed

Reduce social mixing

Containment & Mitigation

Isolate the sick

Quarantine the exposed

Reduce social mixing

- Hospital triage & COVID-19 treatment facilities
- Restrict transit
 - Trains, busses, ferries
 - $_{\circ}$ Some airlines have suspended flights to affected areas
 - $_{\circ}$ Border crossings closed
 - Visas and entrance restricted
- Closure of:
 - $_{\circ}$ Public transit
 - Schools (China, Japan, Iran)
 - $_{\circ}$ Major store chains
 - Major companies (Google, Apple, Airbnb, Amazon, FB, MS...)
- Canceling of public events
 - $_{\rm o}~$ Lunar New Year and other festivals

Control Measures in the U.S.

- Travel notices:
 - Level 3: China, South Korea, Iran, Italy
 - Level 2: Japan
 - $_{\circ}$ Level 1: Hong Kong
- Airports:
 - $_{\circ}$ Passenger screening at 11 airports (where all flights from China being directed)
 - Among travelers from China, entry limited to U.S. citizens and permanent residents; screened for fever, cough, SOB at arrival
- Isolation & quarantine
- Contact tracing

Covid-19: Cases and Persons Under Quarantine among Repatriated Persons from Diamond Princess, by Location

| Location | Currently Under Quarantine [§] | Cases |
|--|---|-------|
| Travis Air Force Base | 149 | 12 |
| Lackland Air Force Base | 134 | 8 |
| University of Nebraska Medical Center | 2 | 13 |
| Providence Sacred Heart Medical Center | 0 | 4 |
| Medically cleared in Japan | N/A | 1 |
| Other [±] | 0 | 5 |
| Total | 285 | 43 |

As of 2/26/2020

Footnotes

⁺ Cases have laboratory confirmation and may or may not have been symptomatic.

[§] <u>Quarantine information</u>

Contact Tracing

January

| Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday |
|--------|--------|-------------|-----------|---------------------|-----------------------|----------|
| | | | | 1 | 2 | 3 |
| 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 11 | 12 | 13 | 14 | 15 | 16 | 17 |
| 18 | 19 | 20 | 21 | 22 | 23 | 24 |
| 25 | 26 | 27 Onset | 28 | 29 Flight | 30 ER visit | 31 |
| - | | Unset | | Flight | | |

- Where did you go?
 - Work/school
 - Store/restaurant
 - Medical visits

• How did you travel there?

- Public transit
- Taxi/ride share
- Personal vehicle
- Who were you with?
 - Household/close contacts
 - Social/transient contacts
 - HCW contacts

Assessing Exposure Risk

- High Risk:
 - Travel from Hubei Province, China
 - Same household or intimate partner of, or providing care in a non-healthcare setting (such as a home) without using recommended precautions for home care and home isolation for a person with
 - a) Symptomatic laboratory-confirmed COVID-19 infection or
 - b) A person diagnosed clinically with COVD-19 infection outside of the U.S. who did not have laboratory testing.

Assessing Exposure Risk

- Medium Risk:
 - Travel from mainland China outside Hubei Province AND not having any exposures that meet a high-risk definition
 - Close contact, but no high-risk exposures, to a person with:
 - a) Symptomatic laboratory-confirmed COVID-19 infection
 - b) Clinical diagnosis of COVID-19 infection outside of the United States who did not have laboratory testing.
 - Close contact and with high-risk exposures to a person with symptomatic laboratory-confirmed COVID-19 infection *while consistently using recommended precautions* for <u>home care</u> and <u>home isolation</u>
 - On an aircraft, being seated within 6 feet (two meters) of a traveler with symptomatic laboratory-confirmed COVID-19 infection; this distance correlates approximately with 2 seats in each direction

Assessing Exposure Risk - Airplane





Assessing Exposure Risk

- Low Risk:
 - Being in the same indoor environment (e.g., a classroom, a hospital waiting room) as a person with symptomatic laboratory-confirmed COVID-19 infection for a prolonged period of time but not meeting the definition of close contact
 - On an aircraft, being seated within two rows of a traveler with symptomatic laboratory-confirmed COVID-19 infection but not within 6 feet (2 meters) AND not having any exposures that meet a medium- or a high-risk definition

Assessing Severity



Asymptomatic infection

Assessing Infectiousness

• Reproduction number (R₀)

The number of people that one sick person will infect (on average) is called R_0 . Here are the maximum R_0 values for a few viruses.



https://www.npr.org/sections/health-shots/2014/10/02/352983774/no-seriously-how-contagious-is-ebola

Infectiousness

• Determined by:

• Environmental factors

- $_{\rm O}$ Agent factors
- $_{\circ}$ Host factors



Infectiousness

• Determined by:

Environmental factors

oAgent factors

Host factors

Where in body

Durability outside body

Infective dose

Infectiousness

- Determined by:
 - Environmental factors
 - $_{\rm O}$ Agent factors
 - •Host Factors

Symptoms

Behaviors

Host immunity/health

Super Spreaders



*Huang et al. Clinical features of patients with 2019 novel coronavirus in Wuhan, China. Lancet. 2020.

Wuhan, China

- 11M people
- Major transportation hub
- Earliest hospitalized case had onset December 1, 2019
- Wet market likely source
- Case series of first 41 hospitalized: 13 had no contact to market*

Passengers flying form Wuhan to other countries





RUSSIAN FEDERATION KAZAKHSTAN HELIONGJIANG MONGOLIA Harbin Changchun **NEI MONGOL ZIZHIQU** Urumgi (INNER MONGOLIA) JILIN LIAONING KYRGYZSTAN Shenyang HEBEI Hohhot_ **XINJIANG UYGHUR** BEIJING NORTH KOREA BEIJING Sea of Japan (East Sea) TIANJIN= Tianji **Yinchuan** AJIKISTAN Taiyuan Xining, SOUTH KOREA N. AFGHANISTAN SHAN-DONG Yellow JAPAN Sea. Xi'an Zhengzhou -SHAANXI PAKISTAN mel ð Q 60 MCHUAN Hefei Nanjina **XIZANG ZIZHIQU** (TIBET) CHONGO' PACIFIC he biggest pub Hangzhou a East China Sea - Thor OCEAN INDIA ZHEJIANG Nanchang Changsha GUIZHOU HUNAN JIANGXI FUJIAN LEGEND Guiyang Fuzhou ary International Boun GUANGXI BANGLADESH Province Boundary GUANGDONG ZHUANG YUNNAN National Capital 0 TAJWAN Guangzhoù Nanning Province Capital HONGKONG (SAR) MYANMAR Province (22) VIETNAM MACAU (SAR) 250 500 Miles Autonomous Region (5) Bay of LAOS Haikou Municipality (4) Bengal 500 Kilometers 250 Special Administrative HAINAN South China Sea (THAILAND) Region (SAR) (2) PHILIPPINES Copyright © 2019 www.mapsofworld.com

CHINA Political Map



The Year of the Rat

- The largest annual human migration on Earth
 - In 2019; nearly 7 million Chinese tourists traveled abroad for Lunar New Year
- Lunar New Year was 1/25; celebrations last 15 days
- Wuhan restrictions started 1/23; ~5M people left before this
- Events canceled all over the world



1/30/2020: WHO declared the outbreak a "public health emergency of international concern" (PHEIC)

- PHEIC is an "extraordinary event" that "constitutes a public health risk to other States" and "potentially requires a coordinated international response"
- Provides formal recommendations to China and all countries re: outbreak control and mitigation
- WHO's Contingency Fund for Emergencies => optional

CDC/HHS





- 1/31/2020 HHS declared a Public Health Emergency (PHE) for the US
 - "An emergency need for health care services to respond to a disaster, significant outbreak of an infectious disease, bioterrorist attack or other significant or catastrophic event."
 - Releases resources (\$, stockpile), waivers for CMS requirements
- 2/26/2020 VP Pence to lead administration response
- At most State and Local levels, Public Health Activations already in place
 - $_{\rm o}\,$ Level 3 (lowest) to Level 1 (highest)
 - Emergency Operation Centers
 - Incident Management Systems (Incident Command System)

| Emergency Notification February 20, 2020 | | Emergency Alert: Novel Coronavirus |
|--|---|---|
| | | Home Travel Advisories Newsroom About Us Contact Us Careers 🎝 MyTravelGov 🔤 Find U.S. Embassies & Consulates |
| US. DEPARTM | S tate.Gov Ient of state — Bureau of Consular A | AFFAIRS Search |
| U.S. Passports Intern | ational Travel U.S. Visas | Intercountry Adoption International Parental Child Records and Abduction Authentications |
| Before You Go Country Inf | ormation While Abroad | Emergencies |
| Travel.State.Gov > International Travel | > <u>Country Information</u> > China International Trav | vel Information 🖶 Print 🔤 Email 🕈 Facebook 🈏 Twitter 🕂 More |
| People's Republic of China Travel Advisory C | hina - Level 4: Do Not Travel | H O Travel Advisory Levels |
| February 2, 2020 Do not travel to China du zation (WHO) determine (PHEIC). Travelers shoul ercial air carriers have re | le to the novel coronavirus first identifi d the rapidly spreading outbreak const d be prepared for the possibility of trav educed or suspended routes to and from | tied in Wuhan, China. On January 30, the World Health Organi titutes a Public Health Emergency of International Concern avel restrictions with little or no advance notice. Most comm om China. [READ MORE] |
| Embassy Messages Alerts | | 4 Do not travel |
| COVID-19 Information Update to Travel Advisory The U.S. Department of S | Mon, 24 Feb 2020 <u>for China (February 19, 2020)</u> Tue, 1 tate – <u>China Travel Advisory Level 4 – 1</u> | 18 Feb 2020 Do Not Travel Sat, 08 Feb 2020 Assistance for U.S. Citizens |
| Suspension of Entry of Pe | rsons who Pose a Risk of Transmitting | g COVID-19 Sat, 08 Feb 2020 View Alerts and Messages Archive No. 55 An Jia Lou Road Chaoyang District, Beijing 100600 China |

Telephone +(86)(10) 8531-4000 Travel

Advisories

Quick Facts

Public Health Service Act



- Enacted 1944; signed by FDR
- Gives US PHS broad powers to prevent introduction, transmission, and spread of communicable diseases
 - Just-in-time appointment of scientists, clinicians, and public health professionals
 - Travel restrictions
 - $_{\rm \circ}\,$ Isolation and quarantine
 - Mandatory medical screening
 - $_{\rm o}\,$ Cancelling of school and public events

PUBLIC HEALTH

Coronavirus: CDC Puts Americans Who Left Wuhan Into 'Unprecedented' 14-Day Quarantine

January 31, 2020 · 1:44 PM ET

BILL CHAPPELL



A chartered jet carrying U.S. citizens being evacuated from Wuhan, China, landed at March Air Reserve Base in Riverside County, Calif., on Wednesday. The passengers are now under a quarantine, the CDC announced Friday. *Ringo H.W. Chiu/AP*

Updated 6:15 p.m. ET

The U.S. is placing 195 Americans who were evacuated from Wuhan, China, under a mandatory 14-day quarantine in an effort to limit the spread of a deadly new

Quarantine

- Reality is that quarantine is used frequently for infectious diseases
- Often voluntary, though official orders are sometimes issued at local level





PANDEMIC



The Atlantic

HEALTH We Don't Have Enough Masks

Pandemics will require deciding who needs respirators and surgical masks, and who doesn't.

JAMES HAMBLIN JANUARY 30, 2020



Passengers board trains at a Beijing railway station before the Lunar New Year, on January 23, 2020. (KEVIN FRAYER / GETTY)





 Diamond Princess quarantined in Yokohama; 3,700 passengers; >700 tested + for COVID-19, including 6 deaths

 M.S. Westerdam: 1,500 passengers and 800 crew; refused port by several countries until Cambodia; left Hong Kong 2/1/2020



Vaccine Development

- NIH working closely with researchers to fast-track development
- Candidate immunogen: receptor-binding domain of the "spike protein"
- Animal studies to assess safety ongoing
- First Phase I trial scheduled to be begin in a few weeks

Wash hands at least 20 seconds. If soap and water are not available, use an alcohol-based hand sanitizer.



Cover your mouth & nose with your sleeve or a tissue, when you cough or sneeze.



Clean and disinfect frequently used surfaces; door knobs, countertops, keyboards, and phones to remove germs.

> Stay home when you are sick.

Prevent the spread of **Respiratory Illnesses**

The Centers for Disease Control and Prevention & Imperial County Public Health Department recommend daily preventative actions to reduce the spread of respiratory viruses.



Get vaccinated to protect yourself and your family.



Avoid touching your eyes, nose, and mouth with unwashed hands.



Avoid close contact with people who are sick.



For more information, call (442) 265-1444 or visit www.icphd.org.



In Conclusion

- This pandemic is unprecedented in modern history
- No one knows what future spread will be
- No one knows how severe it will be

COVID-19

Novel Coronavirus:

Guidance for Health-care Providers

