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
  - 4 of these circulate regularly and cause common cold
Coronaviruses of Importance

• **MERS CoV** in 2012 (and ongoing)
  o Arabian Peninsula
  o WHO: 2,499 lab-confirmed cases in 27 countries w/ 861 deaths
    ▪ Case-fatality rate ~34%
  o In Saudi Arabia alone: 1831 cases and 787 deaths

• **SARS CoV** in 2002-2003
  o Infected >8,000 people w/ 774 deaths in 32 countries in 2002-2003
    ▪ Case fatality rate ~9-10%
  o HCWs accounted for 20% of all cases
  o Many “Super Spreading” events
  o Outbreak ended through use of containment and mitigation strategies
Zoonotic Disease

- Can jump between animals and humans
- Animal reservoir for COVID-19 is unknown

Source: Timothy Sheahan, University of North Carolina
https://www.wsj.com/articles/what-we-know-about-the-wuhan-virus-11579716128
Novel viruses are of particular concern because of the lack of herd immunity.
Total Confirmed: 83,862

(as of 2/28/2020)

Total Deaths: 2,867
Total Recovered: 36,686
Current data on COVID-19: Infectiousness

• Probably about as infectious as SARS
  o $R_0$ estimates: 2.2-4.2

• More infectious than influenza
  o $R_0$ estimates pandemic flu: 1.46-1.8
  o $R_0$ estimate for seasonal flu: 1.28
    ▪ Biggerstaff et al. BMC ID. 2014

• $R_0$ estimates for COVID-19:
  o 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)
  o **5.1 days**
    ▪ Chan et al. Lancet. 2020
  o **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)
  o Donnelly et al. Lancet. 2003

• Serial interval (onset-to-onset): 7.5 days (95% CI: 5.3-19 days)
  o Li et al. NEJM. 2020

*Li et al. Early Transmission Dynamics in Wuhan, China of Novel Coronavirus–Infected Pneumonia. NEJM. 2020*
Current data on COVID-19: Severity

• Case Fatality Rate: between 2-4% in Hubei province
  o Lower than SARS (9-10%) or MERS (≈34%)
  o Higher than seasonal influenza (0.1%-0.2% among symptomatic cases)
    ▪ https://www.cdc.gov/flu/about/burden/past-seasons.html
  o 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:
  o 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 >80y; 8% among 70-79y
    ▪ Wu et al. JAMA 2020
  o Age: Only 2% of cases were <20 years of age
  o 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)
  o At the time of the study:
    ▪ 4.3% had died
    ▪ 34% were discharged, median hospital stay was 10 days
    ▪ 62% were still inpatient
  o Median age 56y (IQR, 42-68)
  o Median time from onset => hospital admission was 7 days
  o 41% were presumed to be HAIs
  o 46% had comorbidities
  o 29% were HCWs
  o 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)
  - Median age 47y
    - <1% were 0-14 years of age
  - 2.1% HCWs
  - 23% had comorbidity
  - 79% had pneumonia; median time from onset => PNA was 4 days
  - 6% mechanical ventilation
  - 5% admitted to ICU
  - 1.4% had died at the time of the study; 94% still inpatient
Wuhan coronavirus
Most estimates put the fatality rate below 3%, and the number of transmissions between 1.5 and 3.5.

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.

Current data on COVID-19: Symptoms

• Fever, cough, shortness of breath (ILI)
• GI symptoms occasionally reported
• Some confirmed cases have not had any symptoms
  o 10 yo child from early family cluster (Chan et al. Lancet. 2020)
  o Infant from Wuhan
  o Many news reports

• Asymptomatic transmission is possible
  o Germany cluster w/ 3 documented asymptomatic transmission events (Rothe et al. NEJM. 2020)
  o Family cluster in China (Bai et al. JAMA. 2020)
Asymptomatic Transmission:

- **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
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>
<thead>
<tr>
<th>Specimen</th>
<th>Illness Day 4</th>
<th>Illness Day 7</th>
<th>Illness Day 11</th>
<th>Illness Day 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngeal swab</td>
<td>Positive (Ct, 18–20)</td>
<td>Positive (Ct, 23–24)</td>
<td>Positive (Ct, 33–34)</td>
<td>Positive (Ct, 37–40)</td>
</tr>
<tr>
<td>Oropharyngeal swab</td>
<td>Positive (Ct, 21–22)</td>
<td>Positive (Ct, 32–33)</td>
<td>Positive (Ct, 36–40)</td>
<td>Negative</td>
</tr>
<tr>
<td>Serum</td>
<td>Negative</td>
<td>Negative</td>
<td>Pending</td>
<td>Pending</td>
</tr>
<tr>
<td>Urine</td>
<td>NT</td>
<td>Negative</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Stool</td>
<td>NT</td>
<td>Positive (Ct, 36–38)</td>
<td>NT</td>
<td>NT</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>&amp;</th>
<th>Epidemiologic Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever$^1$ or signs/symptoms of lower respiratory illness (e.g., cough or shortness of breath)</td>
<td>AND</td>
<td>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</td>
</tr>
<tr>
<td>Fever$^1$ and signs/symptoms of a lower respiratory illness (e.g., cough or shortness of breath) requiring hospitalization</td>
<td>AND</td>
<td>A history of travel from affected geographic areas$^5$ (see below) within 14 days of symptom onset</td>
</tr>
<tr>
<td>Fever$^1$ with severe acute lower respiratory illness (e.g., pneumonia, ARDS) requiring hospitalization$^6$ and without alternative explanatory diagnosis (e.g., influenza)$^7$</td>
<td>AND</td>
<td>No source of exposure has been identified</td>
</tr>
</tbody>
</table>

### Affected Geographic Areas with Widespread or Sustained Community Transmission

Last updated February 26, 2020

- China
- Iran
- Italy
- Japan
- South Korea

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
  o 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 disease surveillance

“Classic public health measures”
-Dr. Fauci, director of NIAID

Good contact tracing

Good case identification
Containment & Mitigation

Isolate the sick
Quarantine the exposed
Reduce social mixing
Containment & Mitigation

- Hospital triage & COVID-19 treatment facilities
- Restrict transit
  - Trains, busses, ferries
  - Some airlines have suspended flights to affected areas
  - Border crossings closed
  - Visas and entrance restricted
- Closure of:
  - Public transit
  - Schools (China, Japan, Iran)
  - Major store chains
  - Major companies (Google, Apple, Airbnb, Amazon, FB, MS...)
- Canceling of public events
  - Lunar New Year and other festivals
Control Measures in the U.S.

• Travel notices:
  o Level 3: China, South Korea, Iran, Italy
  o Level 2: Japan
  o Level 1: Hong Kong

• Airports:
  o Passenger screening at 11 airports (where all flights from China being directed)
  o 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

<table>
<thead>
<tr>
<th>Location</th>
<th>Currently Under Quarantine</th>
<th>Cases¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Travis Air Force Base</td>
<td>149</td>
<td>12</td>
</tr>
<tr>
<td>Lackland Air Force Base</td>
<td>134</td>
<td>8</td>
</tr>
<tr>
<td>University of Nebraska Medical Center</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Providence Sacred Heart Medical Center</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Medically cleared in Japan</td>
<td>N/A</td>
<td>1</td>
</tr>
<tr>
<td>Other²</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>285</td>
<td>43</td>
</tr>
</tbody>
</table>

As of 2/26/2020

## Footnotes

¹ Cases have laboratory confirmation and may or may not have been symptomatic.

² Quarantine information
## Contact Tracing

**January**

<table>
<thead>
<tr>
<th>Sunday</th>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
<th>Thursday</th>
<th>Friday</th>
<th>Saturday</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
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<tr>
<td>22</td>
<td>23</td>
<td>24</td>
<td>25</td>
<td>26</td>
<td>27</td>
<td>28</td>
</tr>
</tbody>
</table>

- **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

Onset Flight ER visit

- 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:
  o Travel from Hubei Province, China
  o 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 COVID-19 infection outside of the U.S. who did not have laboratory testing.
Assessing Exposure Risk

• Medium Risk:
  o Travel from mainland China outside Hubei Province AND not having any exposures that meet a high-risk definition
  o 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.
  o Close contact and with high-risk exposures to a person with symptomatic laboratory-confirmed COVID-19 infection while consistently using **recommended precautions** for **home care** and **home isolation**
  o 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

- Infected Traveler
- Medium Risk (Close Contact)
- Low Risk
- No Identifiable Risk
Assessing Exposure Risk

• Low Risk:
  o 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
  o 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
- Non-severe symptomatic disease
- Severe disease
- Death
Assessing Infectiousness

• Reproduction number ($R_0$)

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.

- Hepatitis C (2)
- Ebola (2)
- HIV (4)
- SARS (4)
- Mumps (10)
- Measles (18)

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

• Determined by:
  o Environmental factors
    o Agent factors
    o Host factors
  o Air temp/humidity
  o Sanitation
  o Population
  o Herd Immunity
Infectiousness

• Determined by:
  o Environmental factors
  o Agent factors
  o Host factors

Where in body
Durability outside body
Infective dose
Infectiousness

- Determined by:
  - Environmental factors
  - Agent factors
  - Host Factors

- Symptoms
- Behaviors
- Host immunity/health
- Super Spreaders
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 from Wuhan to other countries
October to November 2019

Note: Map shows passenger volume from October to November 2019, the most recent data available.

LOCKDOWN

>60M in quarantine

The biggest public health experiment
The Year of the Rat

• The largest annual human migration on Earth
  o 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
• 1/31/2020 HHS declared a Public Health Emergency (PHE) for the US
  o “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.”
  o 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
  o Level 3 (lowest) to Level 1 (highest)
  o Emergency Operation Centers
  o Incident Management Systems (Incident Command System)
Travel Advisories

China
People's Republic of China

China - Level 4: Do Not Travel
February 2, 2020

Do not travel to China due to the novel coronavirus first identified in Wuhan, China. On January 30, the World Health Organization (WHO) determined the rapidly spreading outbreak constitutes a Public Health Emergency of International Concern (PHEIC). Travelers should be prepared for the possibility of travel restrictions with little or no advance notice. Most commercial air carriers have reduced or suspended routes to and from China.

[READ MORE]

Travel Advisory Levels

1. Exercise normal precautions
2. Exercise increased caution
3. Reconsider travel
4. Do not travel

Assistance for U.S. Citizens

U.S. Embassy Beijing
No. 55 An Jia Lui Road
Chaoyang District, Beijing 100600
China

Telephone:
+86 (10) 6531-4000
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
  - Isolation and quarantine
  - Mandatory medical screening
  - Cancelling of school and public events
Quarantine

• Reality is that quarantine is used frequently for infectious diseases

• Often voluntary, though official orders are sometimes issued at local level
PANDEMIC
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
• *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
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