# COVID-19/SARS-CoV-2

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# Topics

- General info
- What can we learn from SARS and MERS
- COVID-19 symptoms and signs
- Infection control/How should health care staff protect themselves
- Possible treatments
- Summary and speculations

# Caveats

- I’m not involved in the hospital’s COVID-19 preparation

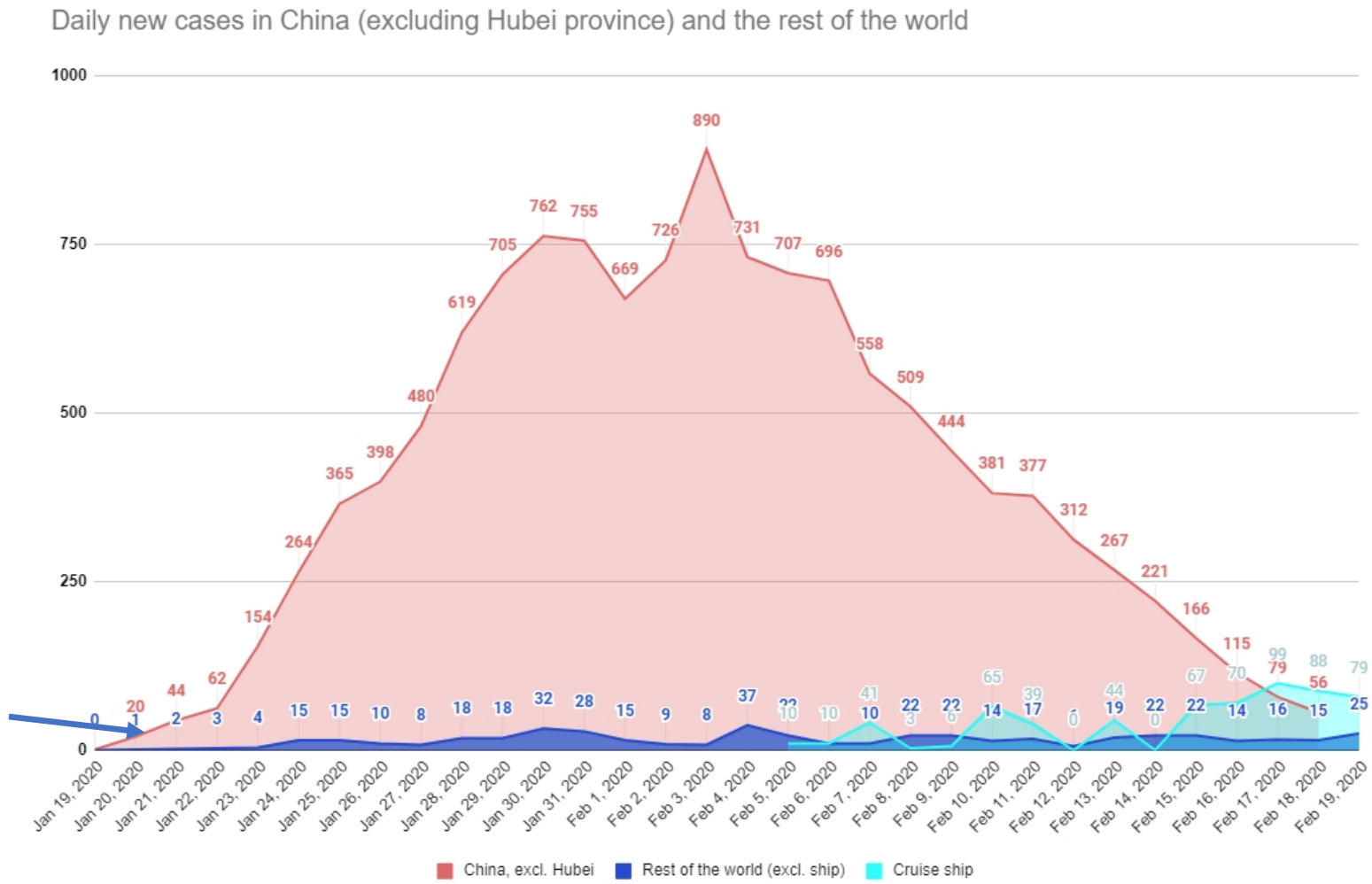
# We Aren’t Seeing The Whole Picture

Cases we are seeing right now

Cases we are not seeing right now

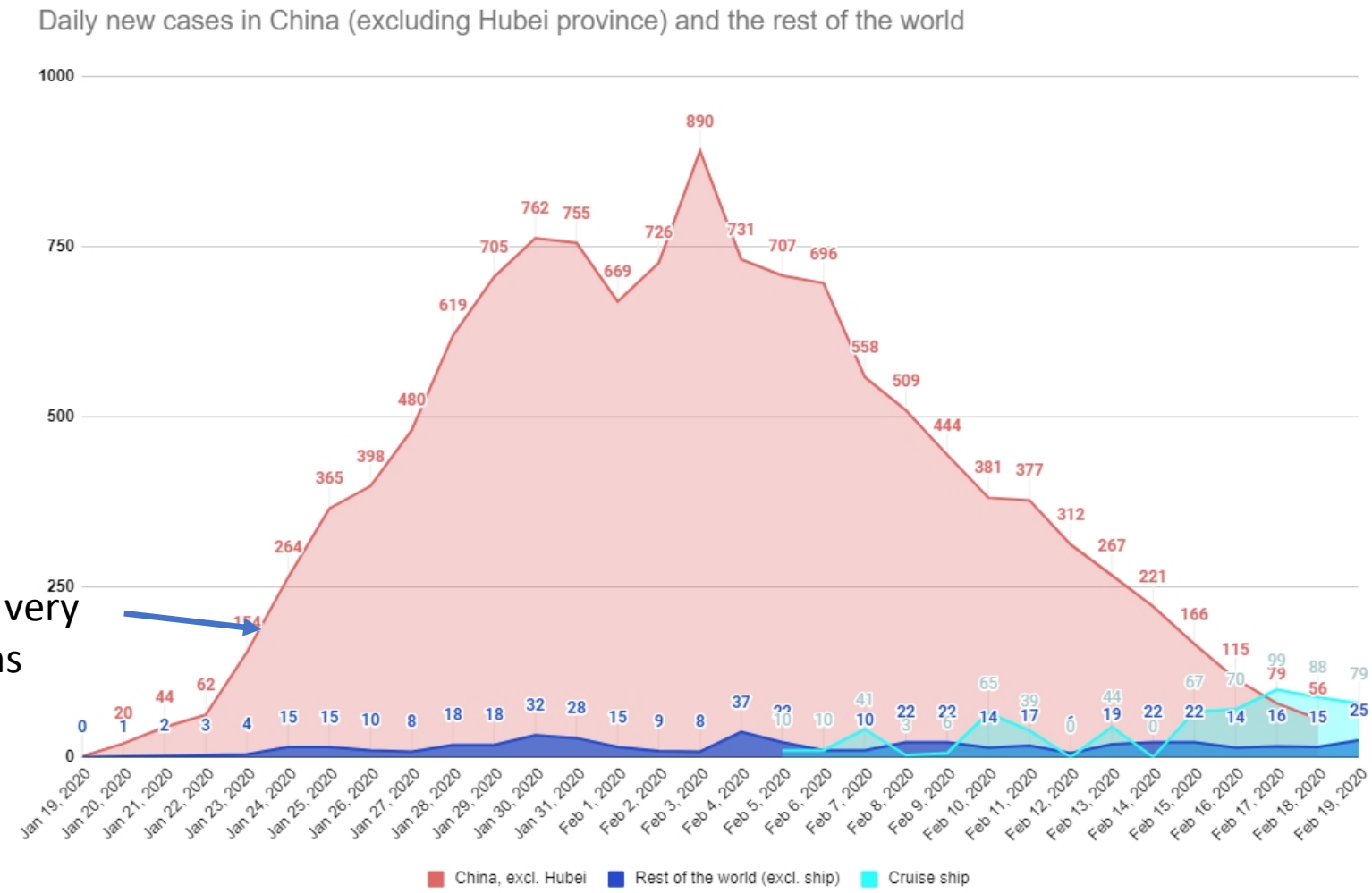
# General Epidemic Curve

Hmm, interesting



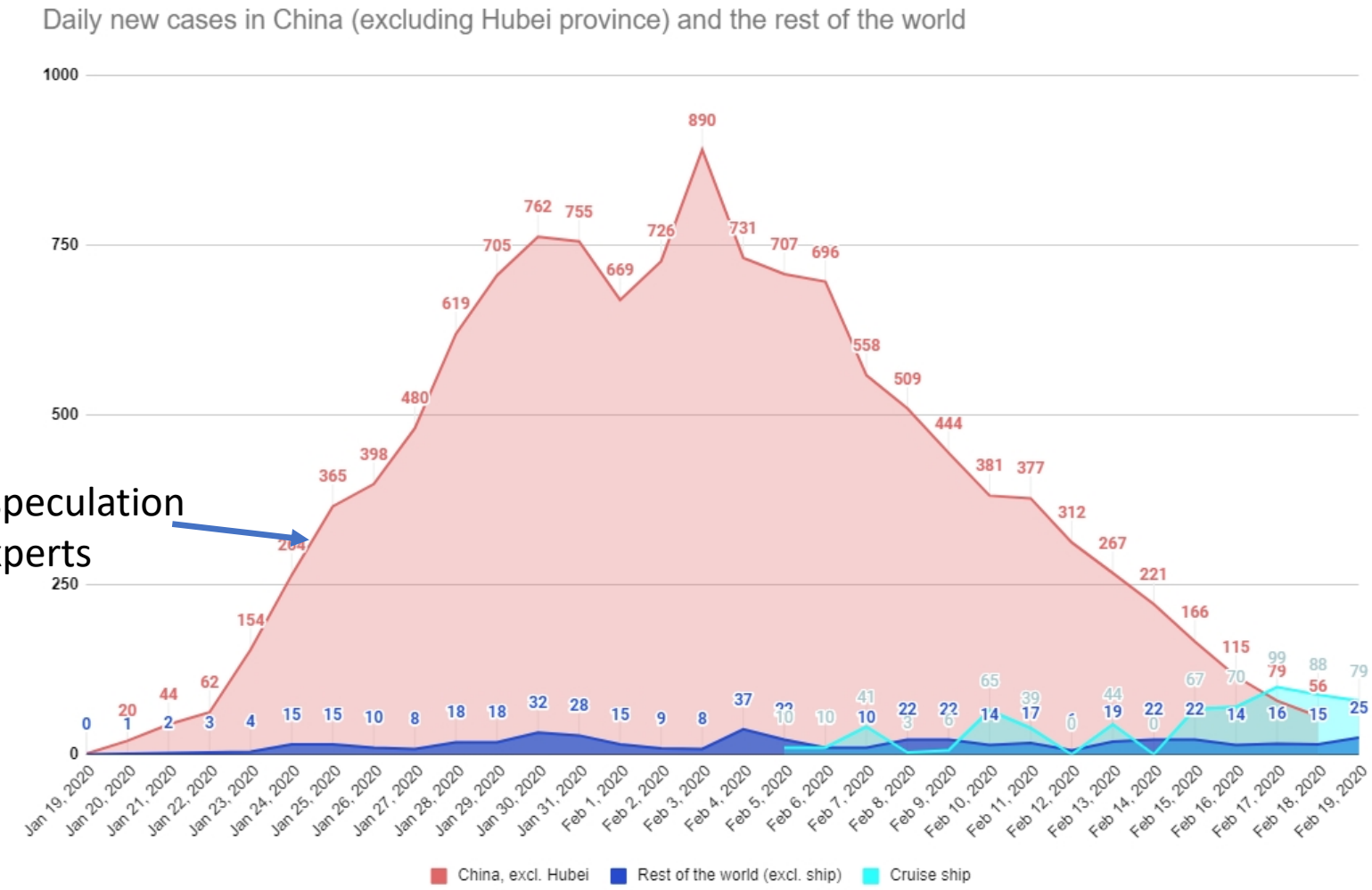
# General Epidemic Curve

Death rate looks very high, panic begins



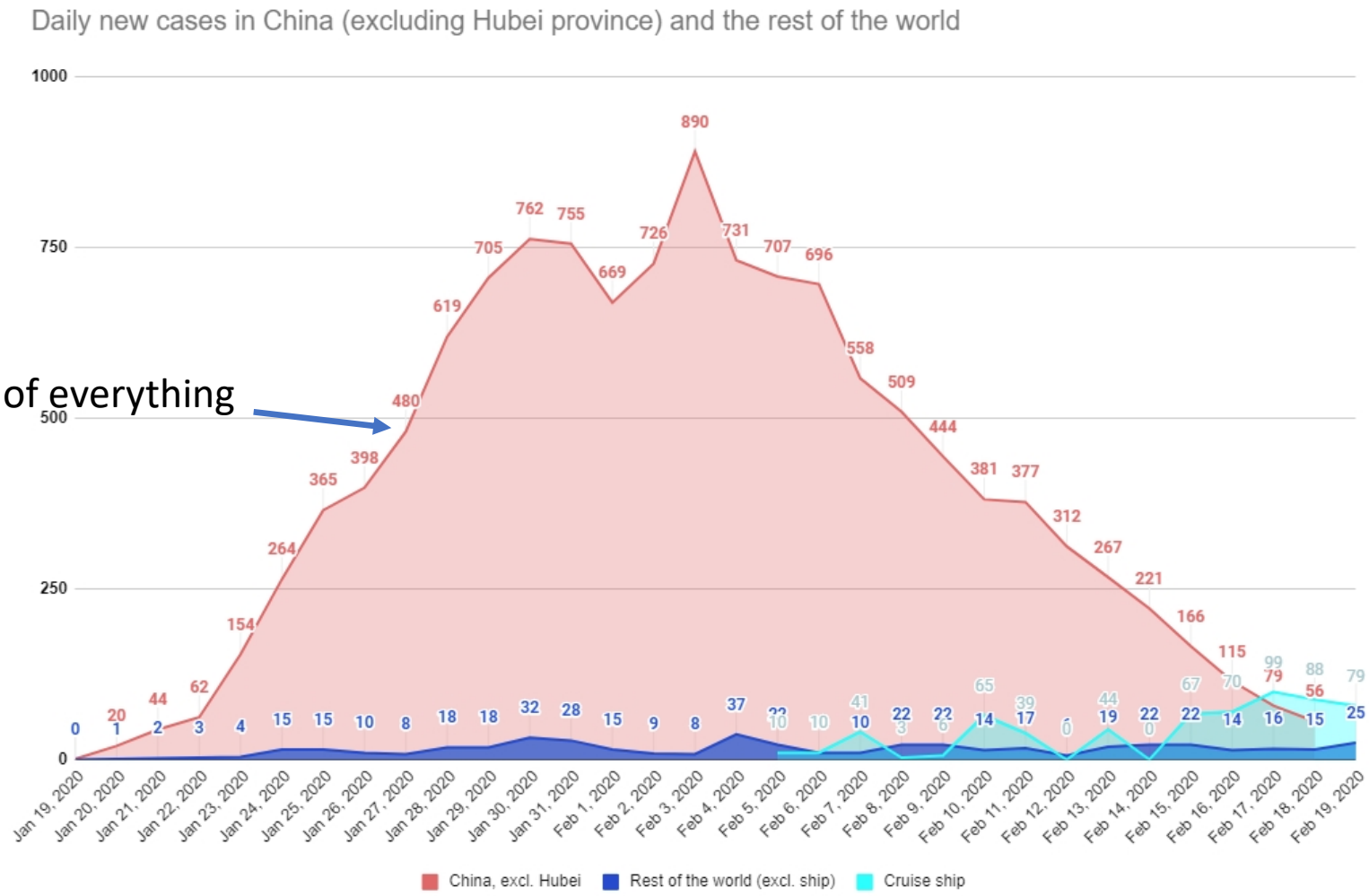
# General Epidemic Curve

Wildly inaccurate speculation by public health experts

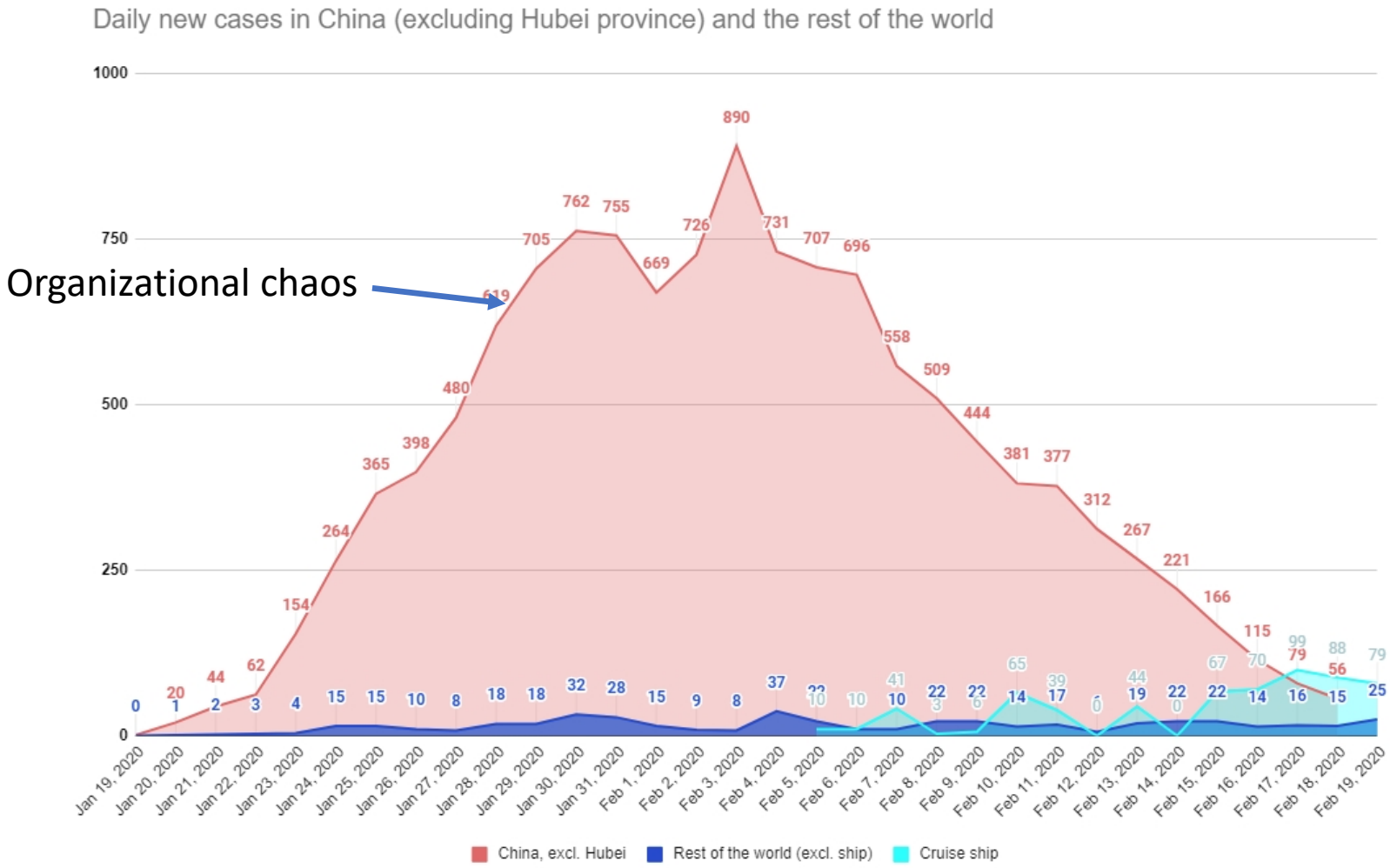


# General Epidemic Curve

Run out of everything



# General Epidemic Curve



# General Epidemic Curve

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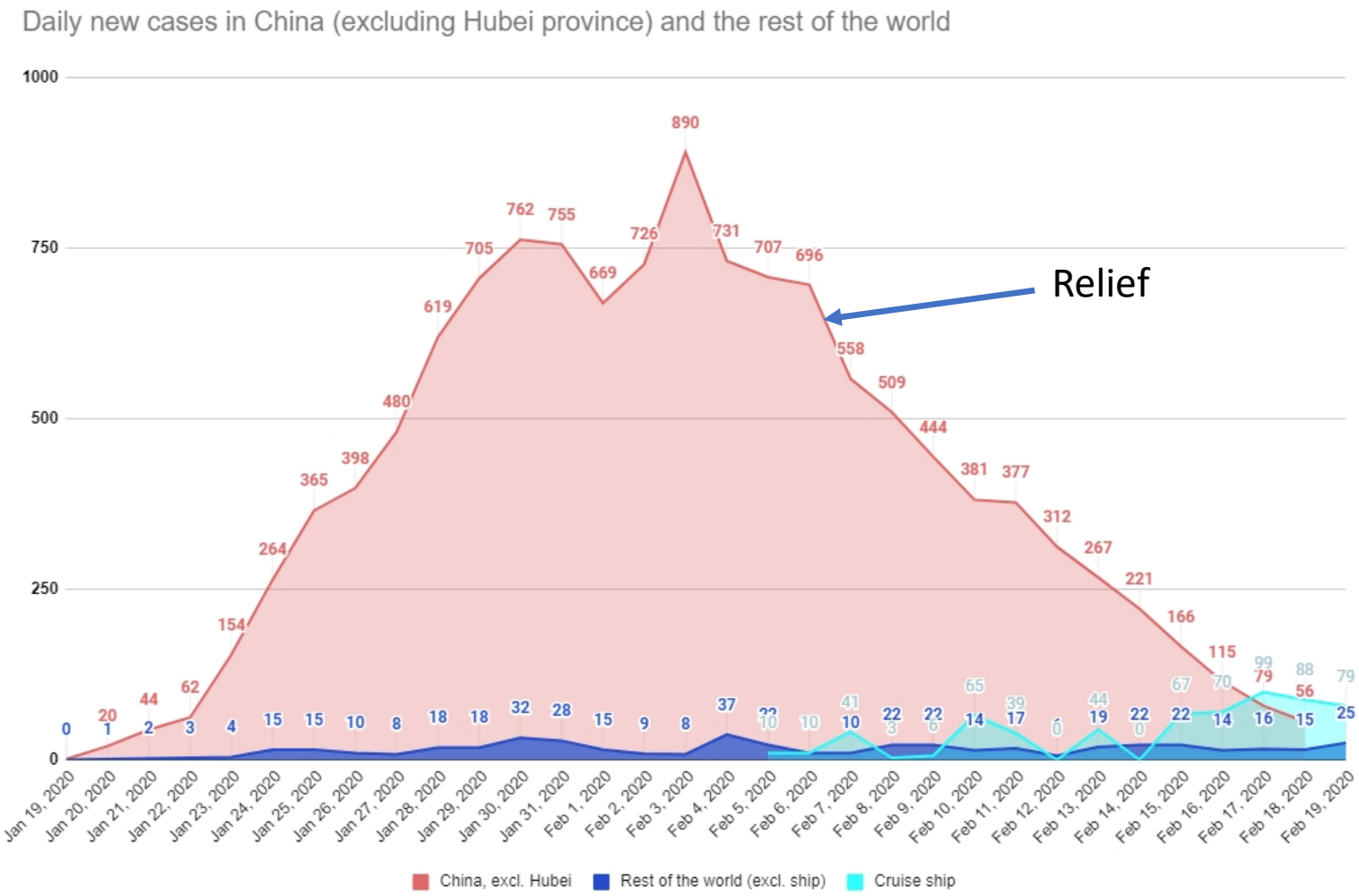

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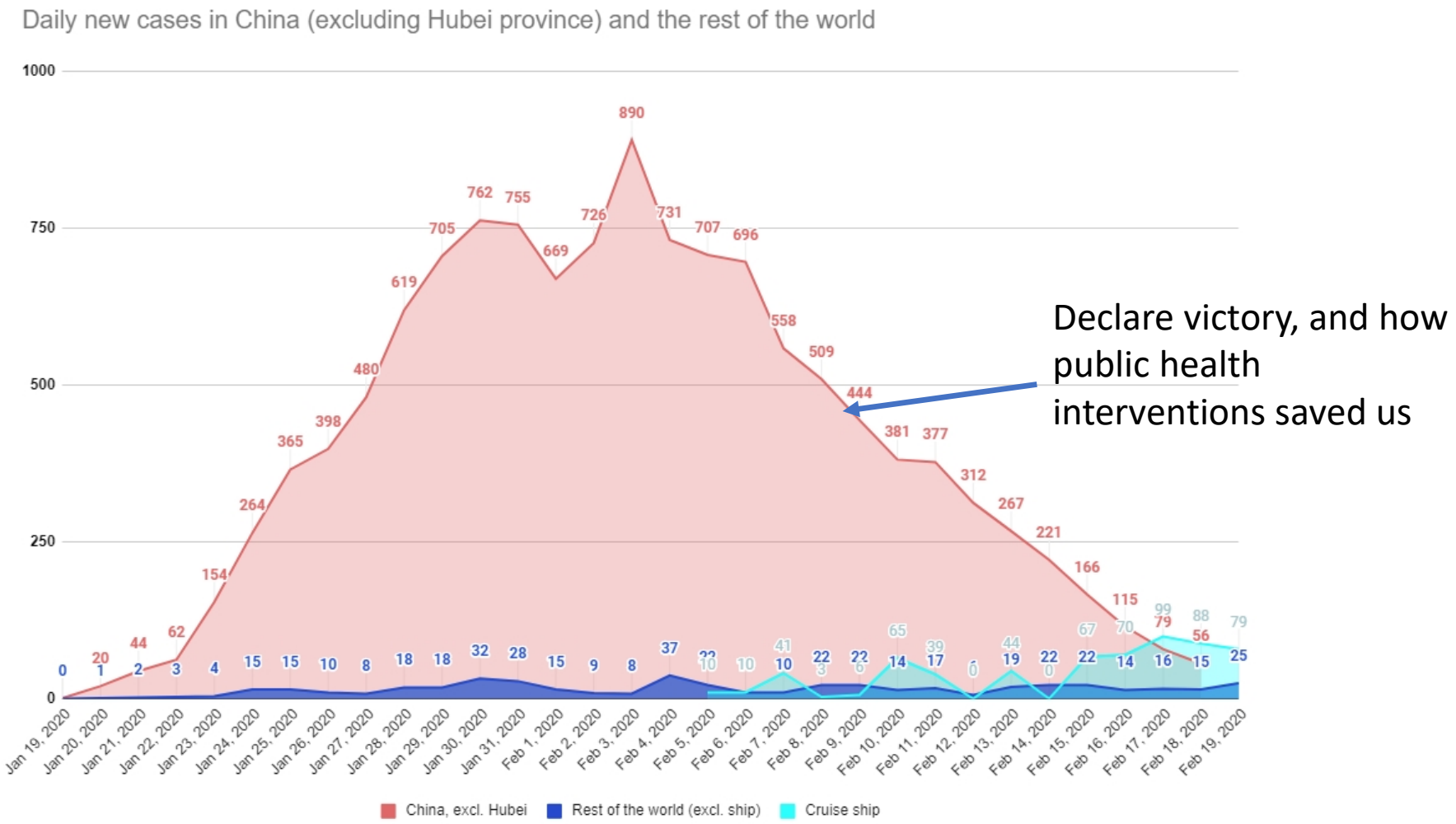
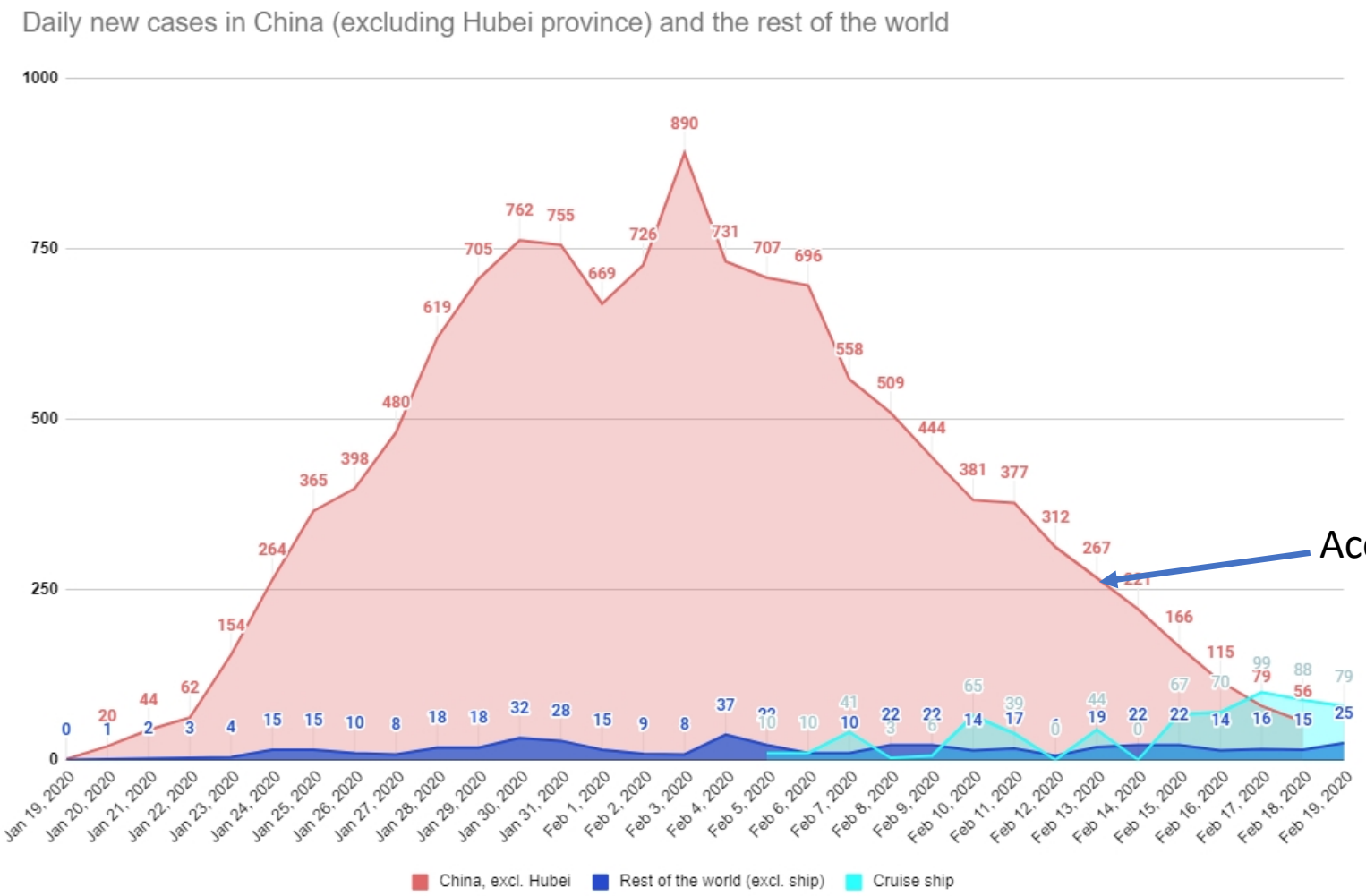


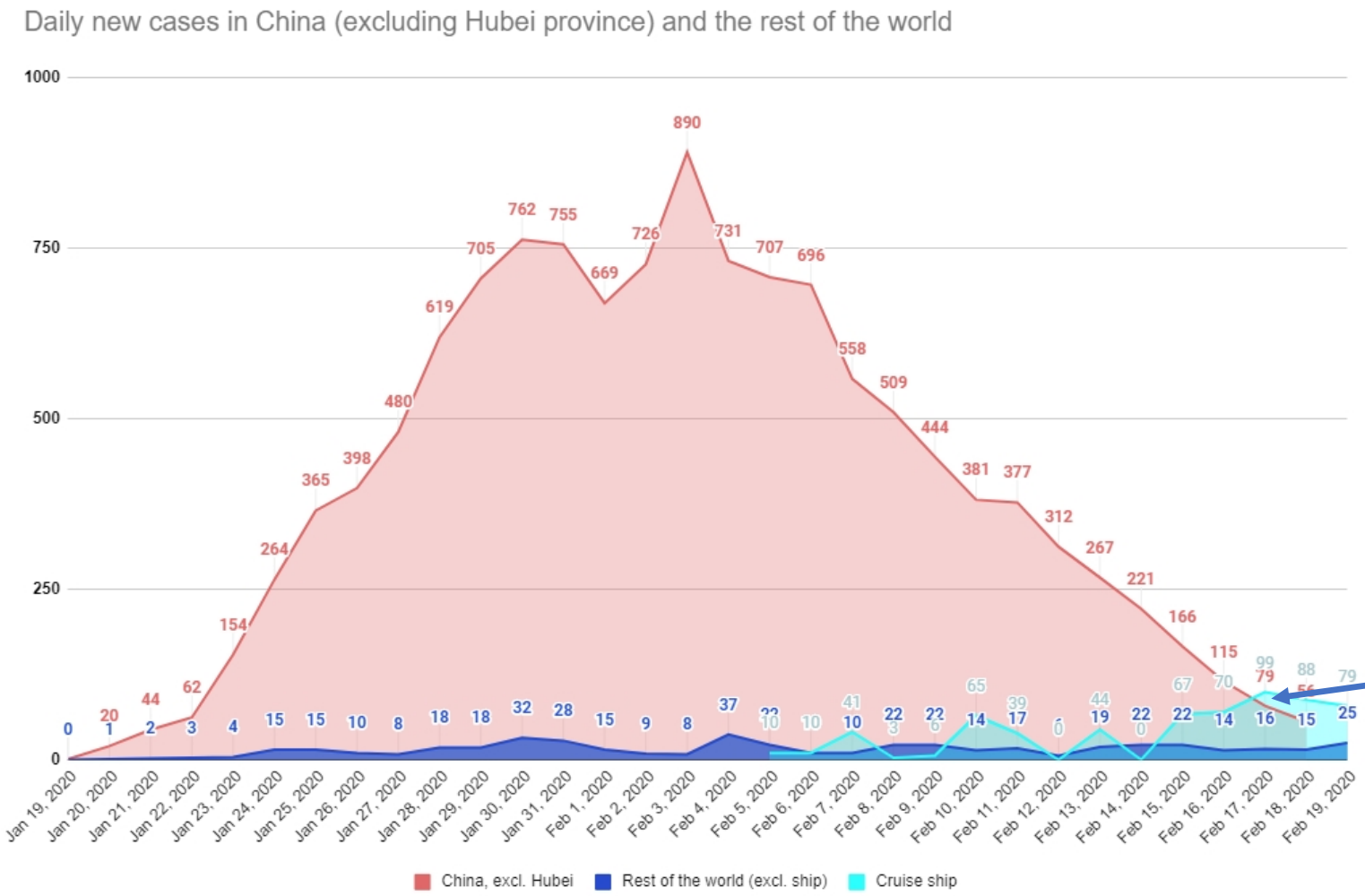

Declare victory, and how public health interventions saved us

# General Epidemic Curve




Accurate data arrives

# General Epidemic Curve




Fall guy is fired

# Neither Minimize Nor Maximize

# Coronaviruses

- Enveloped, positive-strand RNA viruses
- Largest genome size of any RNA virus (~30 kilobases)
- 4 genera: alpha, beta, delta, and gamma
  - Alpha and beta infect humans
- Wide host range – bats as reservoir for many
- Primarily cause respiratory illness in humans, GI illness in animals

## Coronavirus Structure

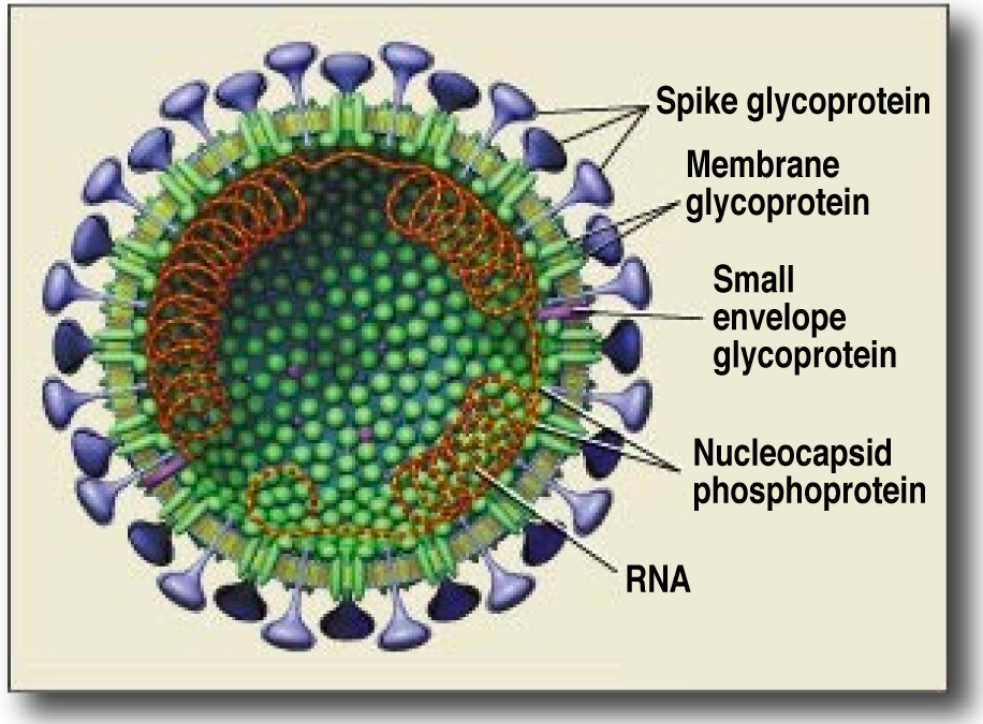



Image credit: JM Drazen *New Eng. Journ. Med.* 2003.

# Coronavirus

- 4 typical human coronaviruses (15-30% of common colds)
- 3 emergent ones
- Most diversity in bats
- Virus Name = SARS-CoV-2
- Disease caused by virus = COVID-19

# SARS History

- The first known cases of SARS occurred in Guangdong province, China, in November 2002
- WHO reported that the last human chain of transmission of SARS in that epidemic had been broken on 5 July 2003.
- SARS coronavirus (SARS-CoV) appears to be a bat virus that crossed over to humans
- By July 2003, the international spread of SARS-CoV resulted in 8098 SARS cases in 26 countries, with 774 deaths.

# SARS Receptor

- The surface spike (S) glycoprotein is critical for binding of host cell receptors and is believed to represent a key determinant of host range restriction
- The predominant receptor for SARS S glycoprotein is angiotensin-converting enzyme 2 (ACE2)
  - found primarily in the lower respiratory tract compared to upper airway
  - receptor distribution may explain **lack of upper respiratory tract symptoms** and that peak viral shedding occurs about 10 days into illness (nosocomial spread)

# SARS Symptoms

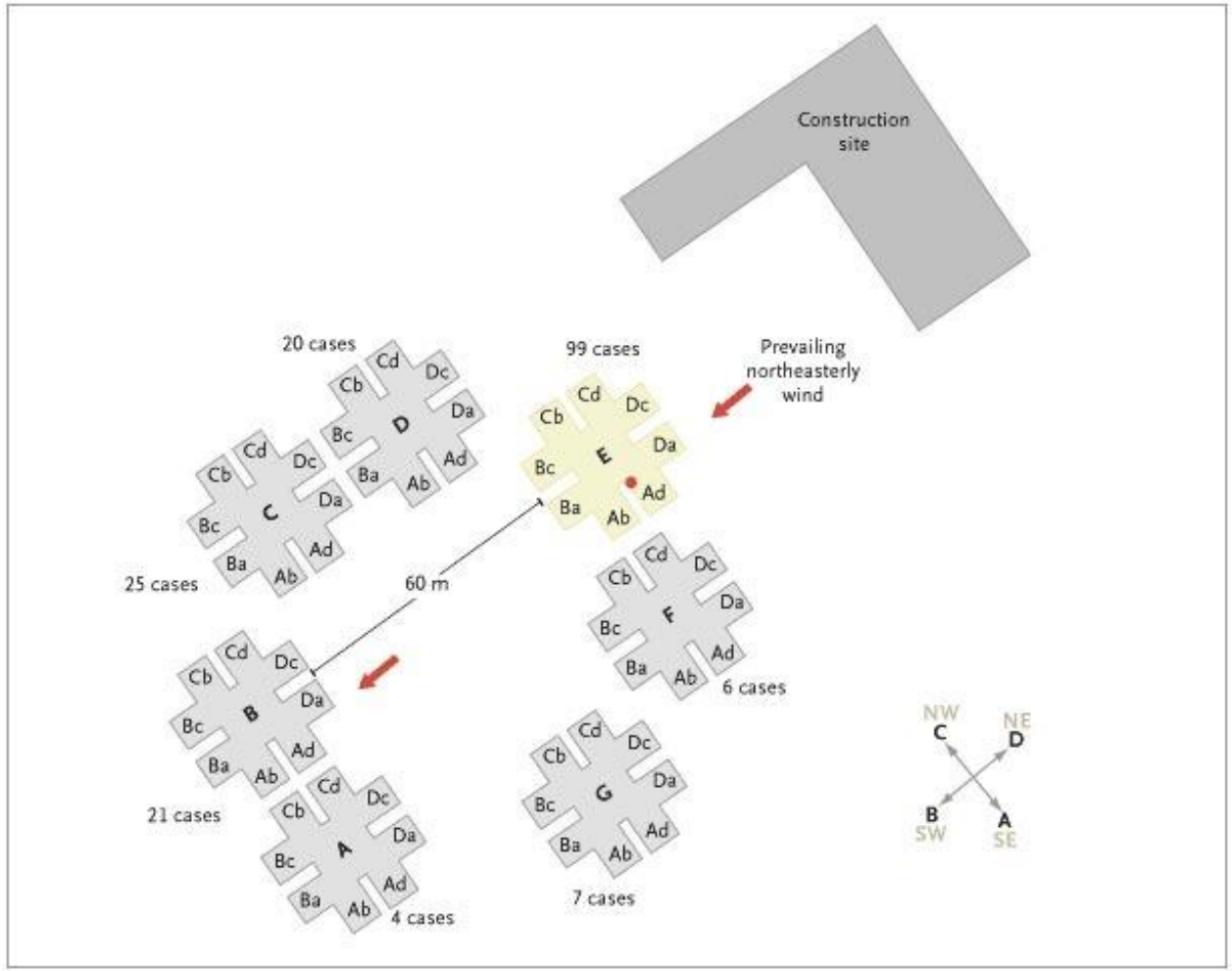
- Common symptoms of SARS included fever, cough, dyspnea, and occasionally watery diarrhea
- Of infected patients, 20% to 30% required mechanical ventilation
- 10% died, with higher fatality rates in older patients and those with medical comorbidities

# SARS Hosts

- The natural reservoir of SARS-CoV has not been identified, but:
- Himalayan masked palm civet (Paguma larvata)*
- Chinese ferret badger (Melogale moschata)
- Raccoon dog (Nyctereutes procyonoides)
- Domestic cat

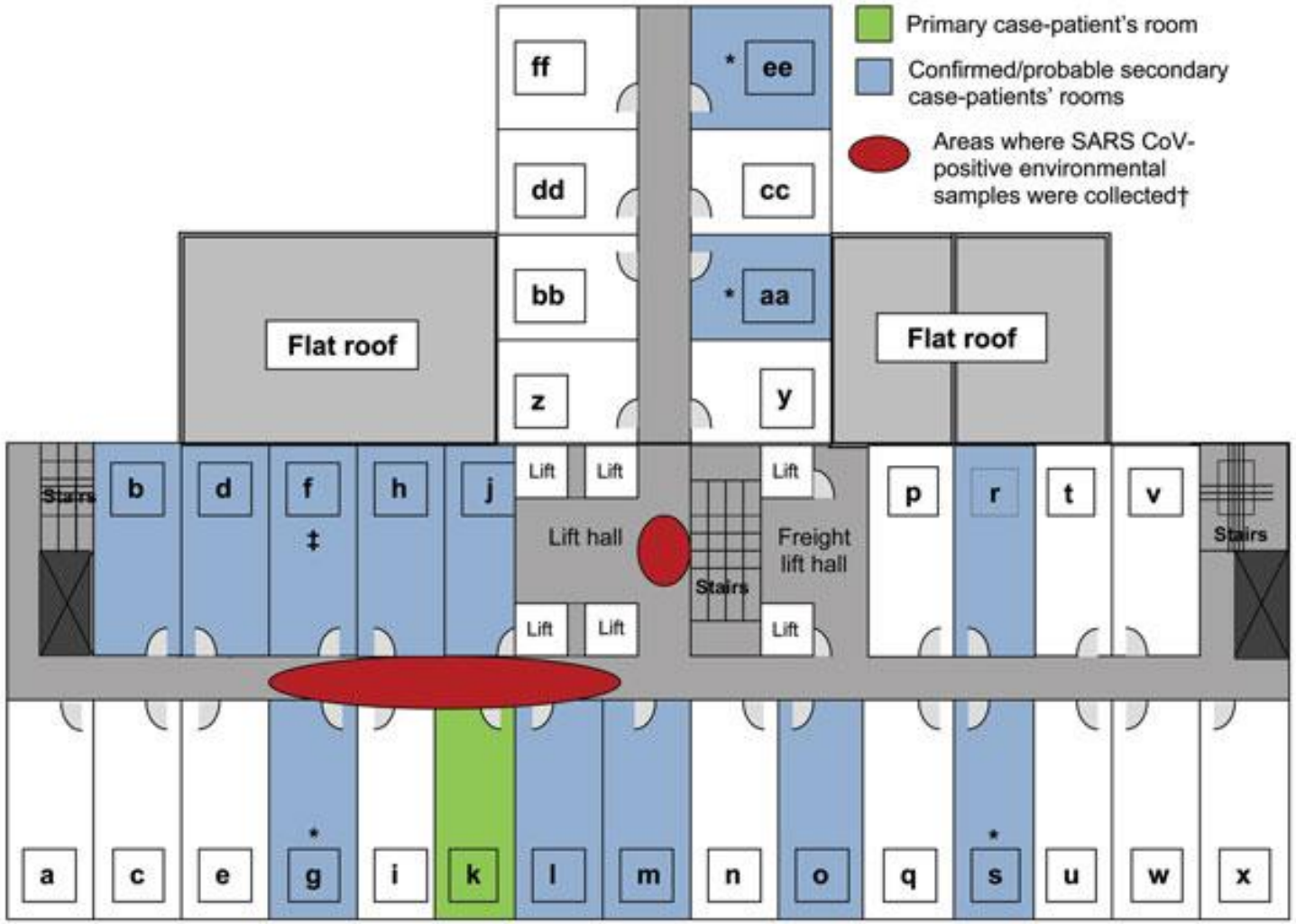

*The masked palm civet is species most often associated with animal-to-human transmission

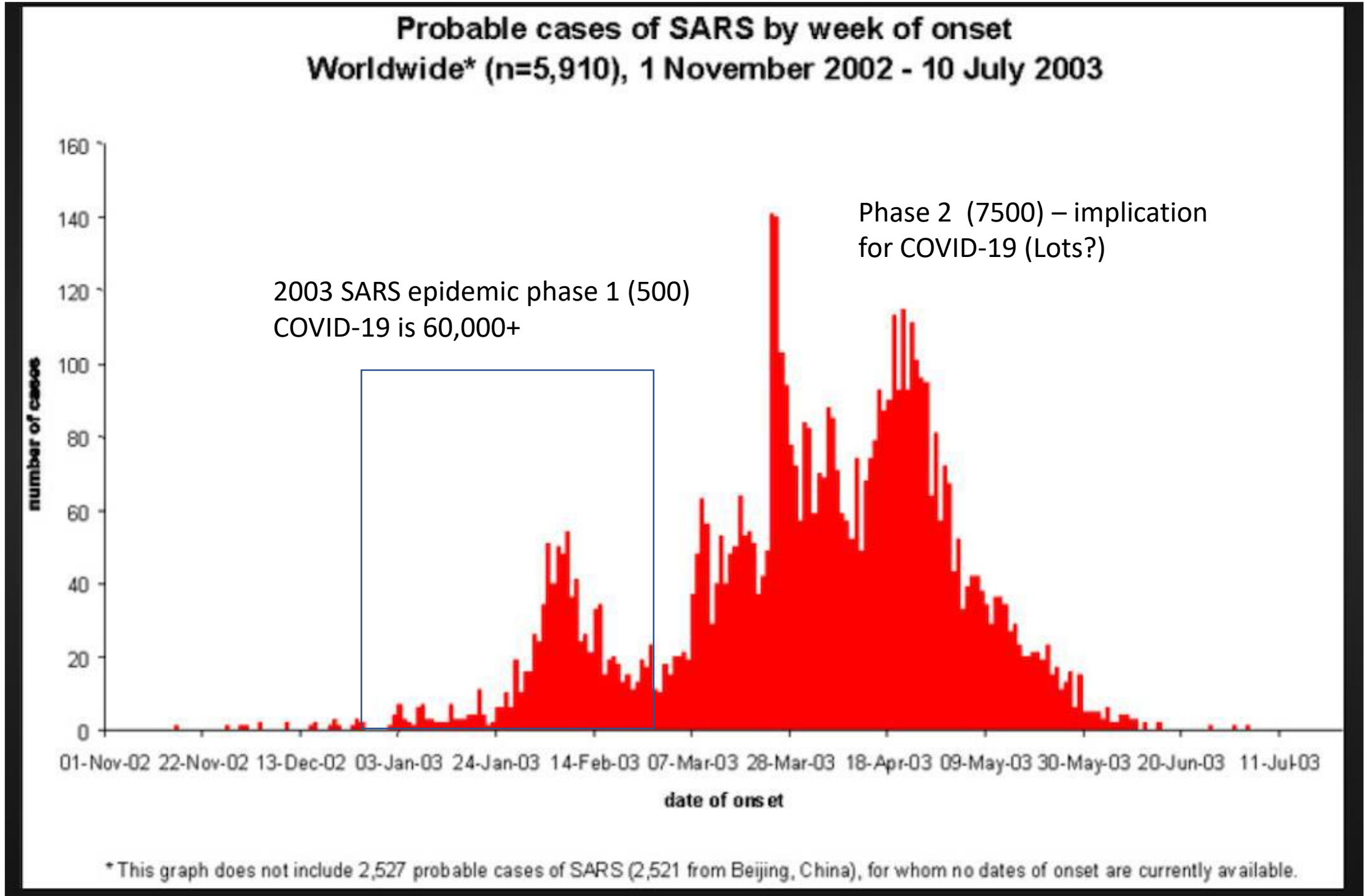
# Airborne spread of SARS: Amoy Gardens




N Engl J Med 2004; 350:1731-1739
DOI: 10.1056/NEJMoa032867

# Hotel Metropole 9th Floor: SARS Airborne spread



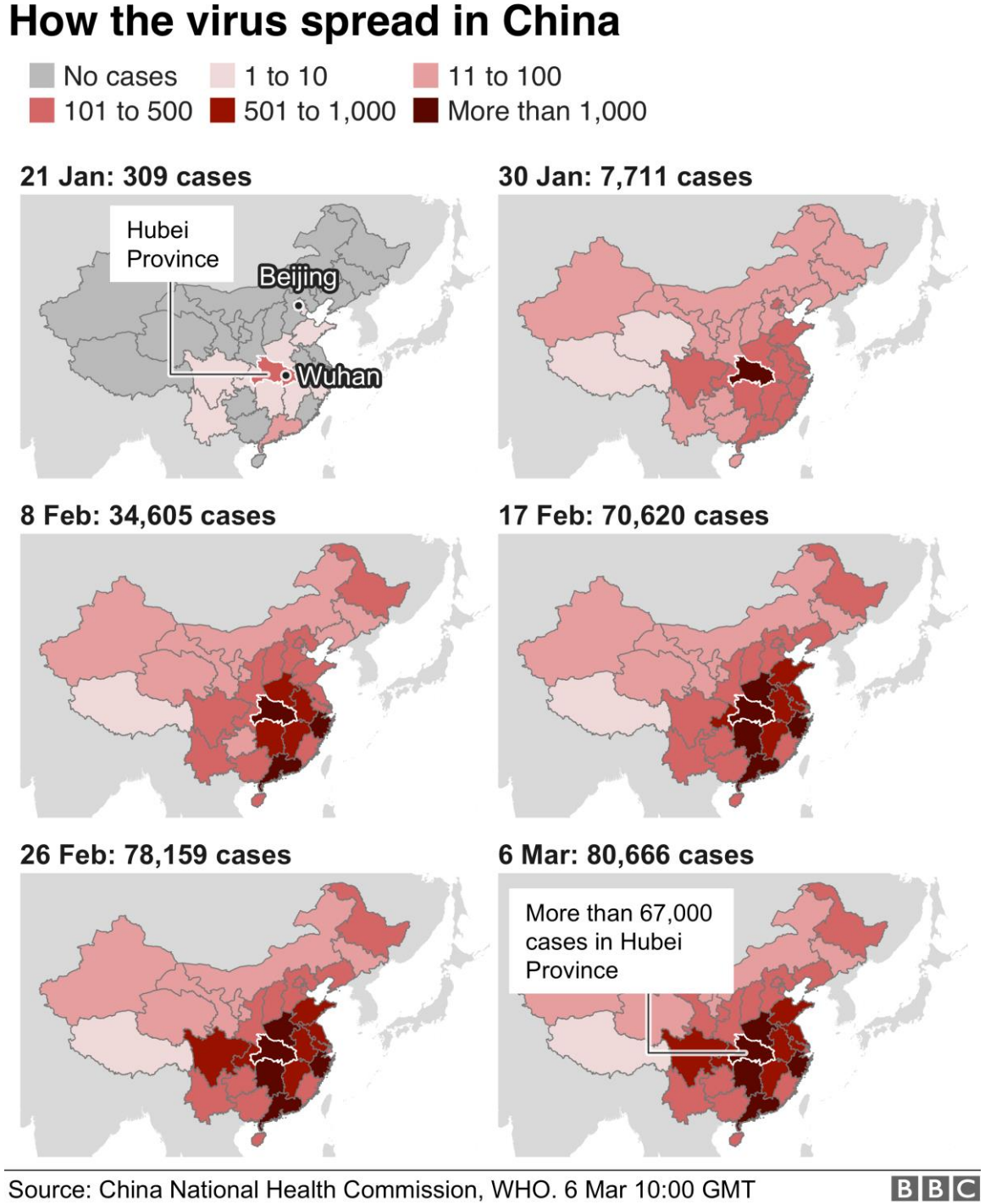

Probable cases of SARS by week of onset
Worldwide* (n=5,910), 1 November 2002 - 10 July 2003
2003 SARS epidemic phase 1 (500)
COVID-19 is 60,000+
Phase 2 (7500) – implication for COVID-19 (Lots?)
number of cases
0
20
40
60
80
100
120
140
160
01-Nov-02
22-Nov-02
13-Dec-02
03-Jan-03
24-Jan-03
14-Feb-03
07-Mar-03
28-Mar-03
18-Apr-03
09-May-03
30-May-03
20-Jun-03
11-Jul-03
date of onset
*This graph does not include 2,527 probable cases of SARS (2,521 from Beijing, China), for whom no dates of onset are currently available.

# Current COVID-19 Status

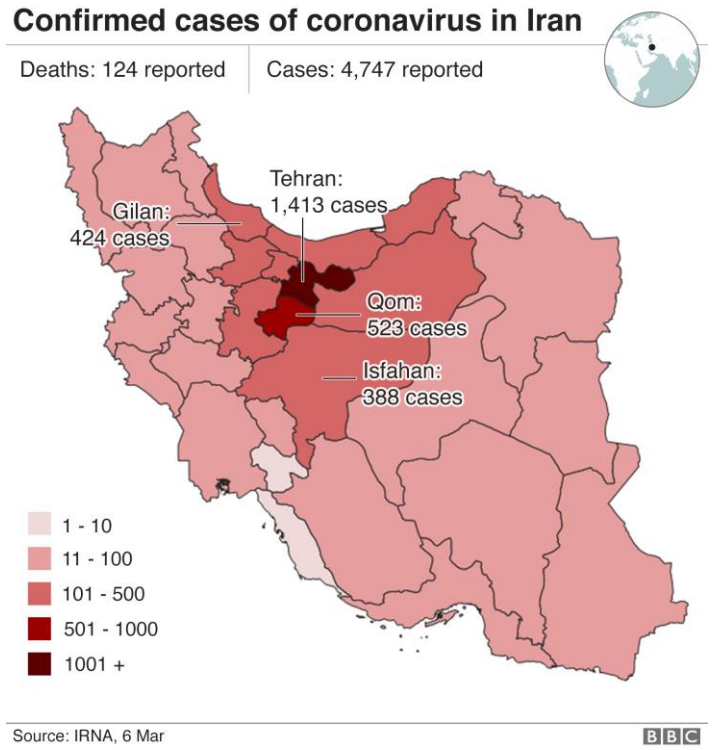
- 126,369 cases
- 4,633 deaths

- Annual global influenza pandemic results in 3-5 million severe cases and 250,000-500,000 deaths/year

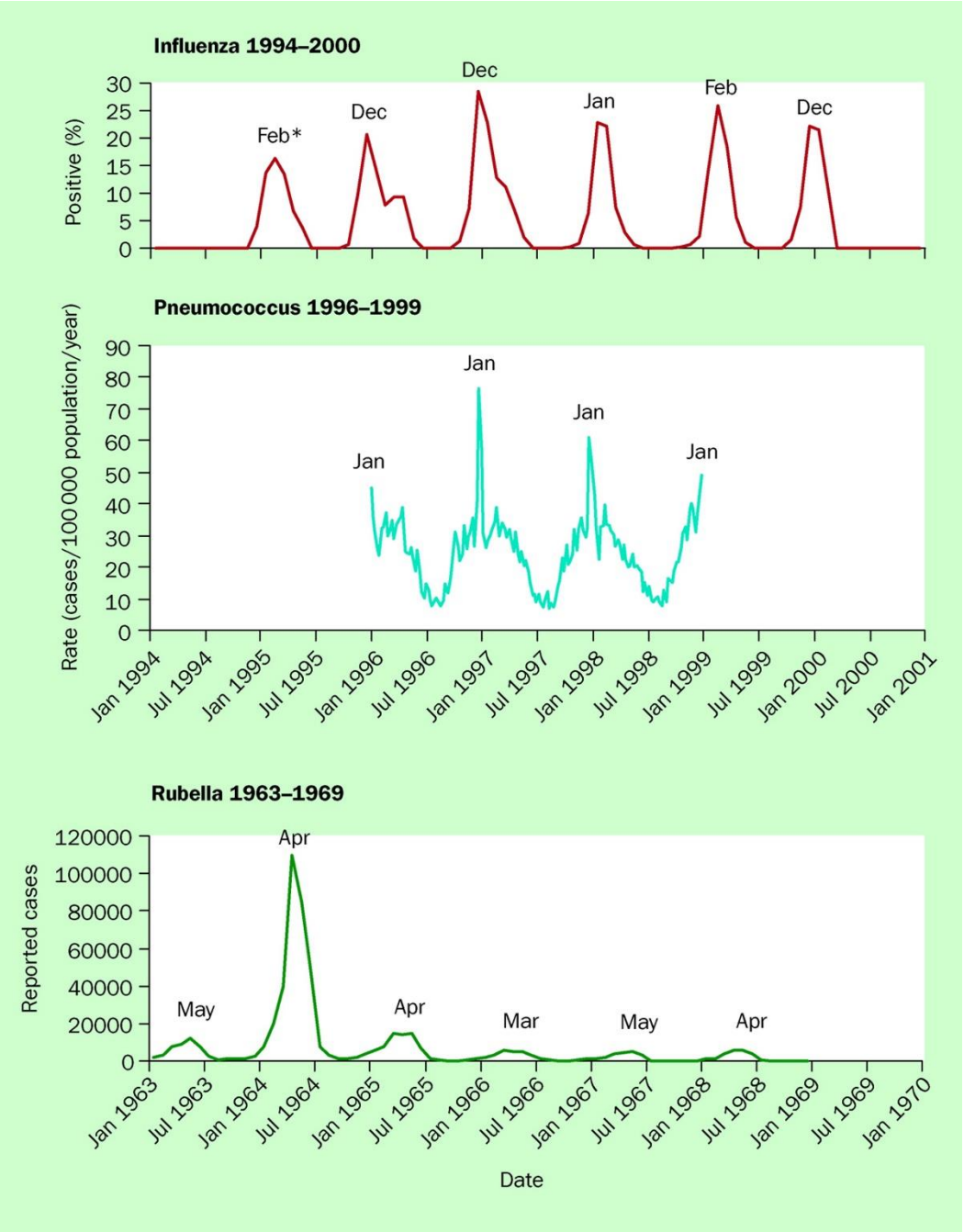
# Geography of COVID-19



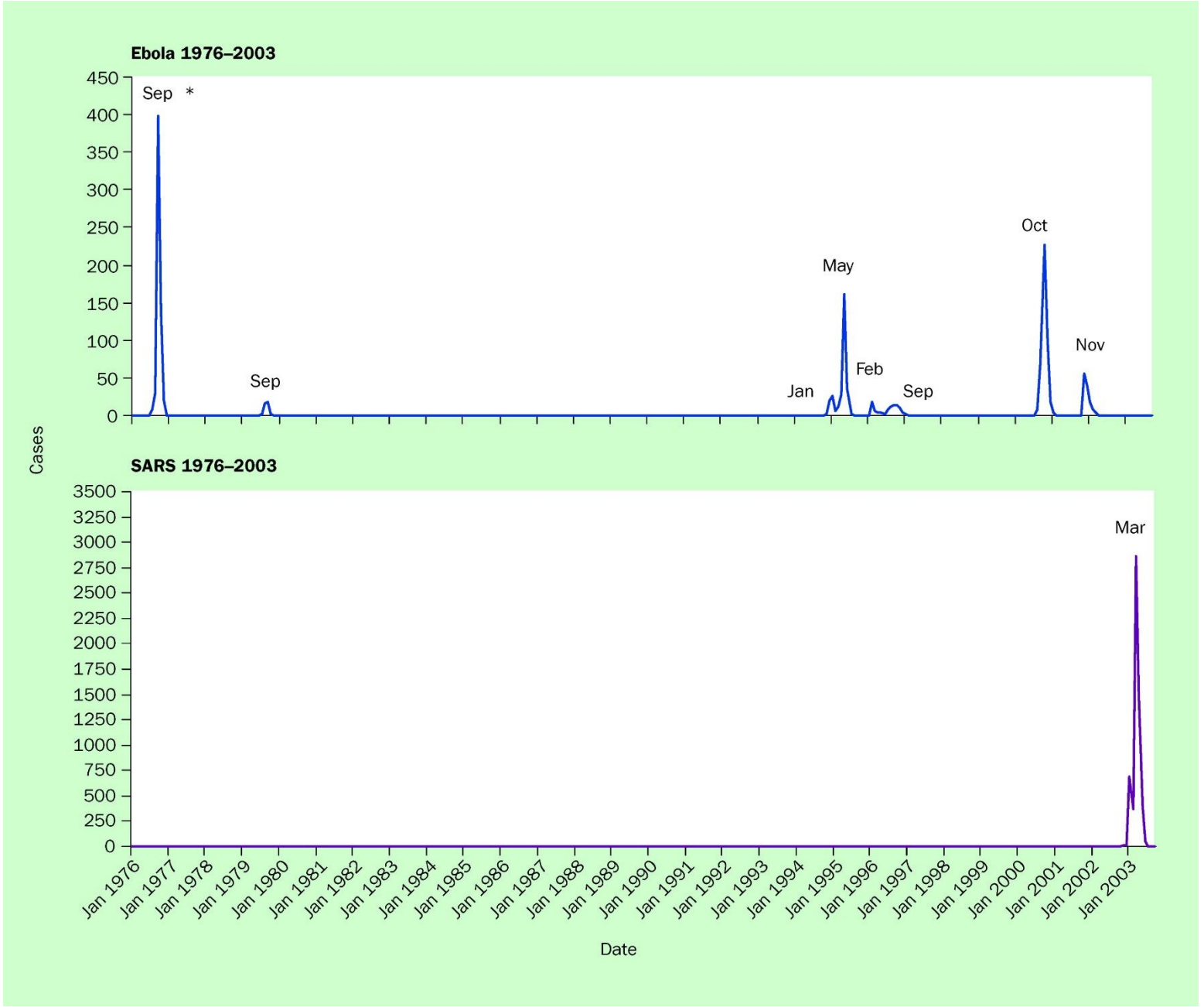




# Seasonality of Select Agents




ELSEVIER


Ebola 1976–2003
Sep *
Sep
Jan
May
Feb
Sep
Oct
Nov
SARS 1976–2003
Mar
Cases
Date
0
50
100
150
200
250
300
350
400
450
0
250
500
750
1000
1250
1500
1750
2000
2250
2500
2750
3000
3250
3500
Jan 1976
Jan 1977
Jan 1978
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Jan 1982
Jan 1983
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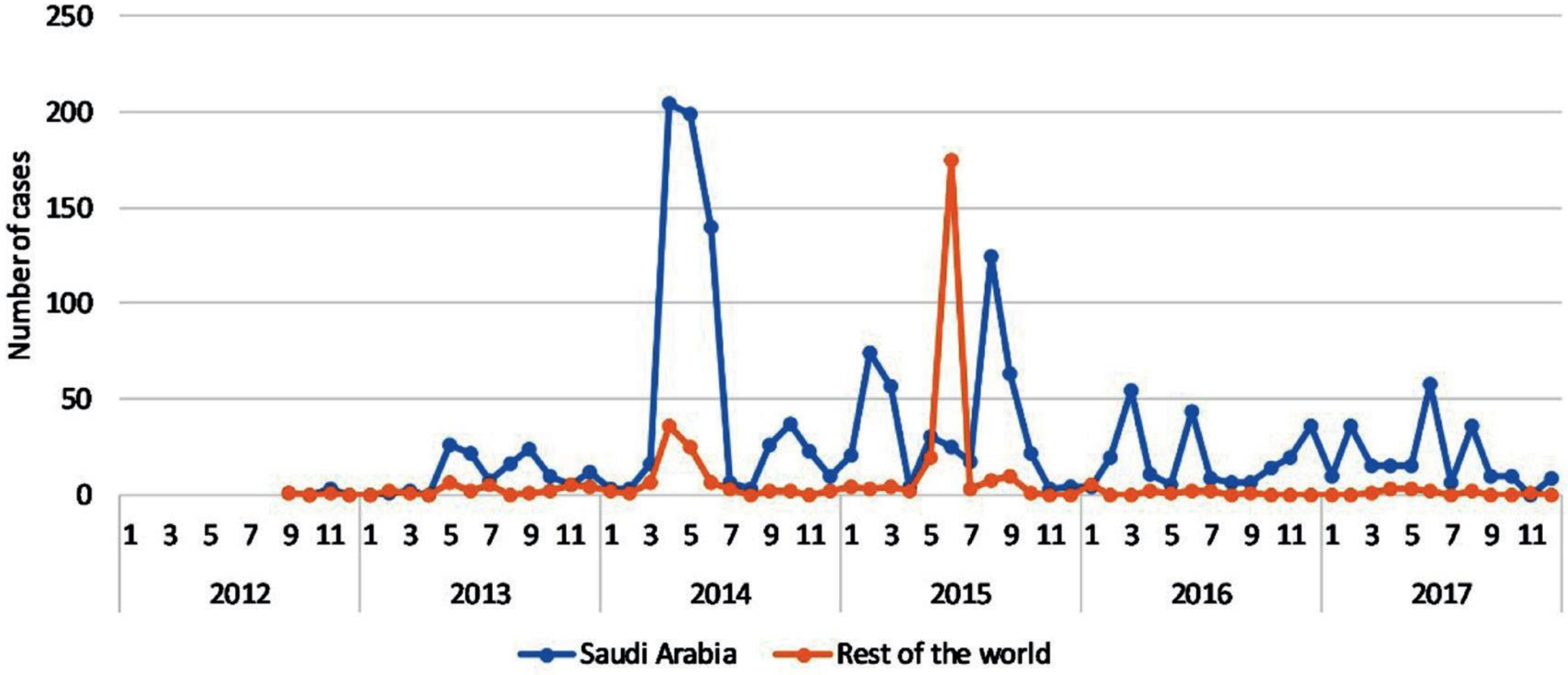
Jan 1998
Jan 1999
Jan 2000
Jan 2001
Jan 2002
Jan 2003

# Seasonality of MERS Virus



# MERS

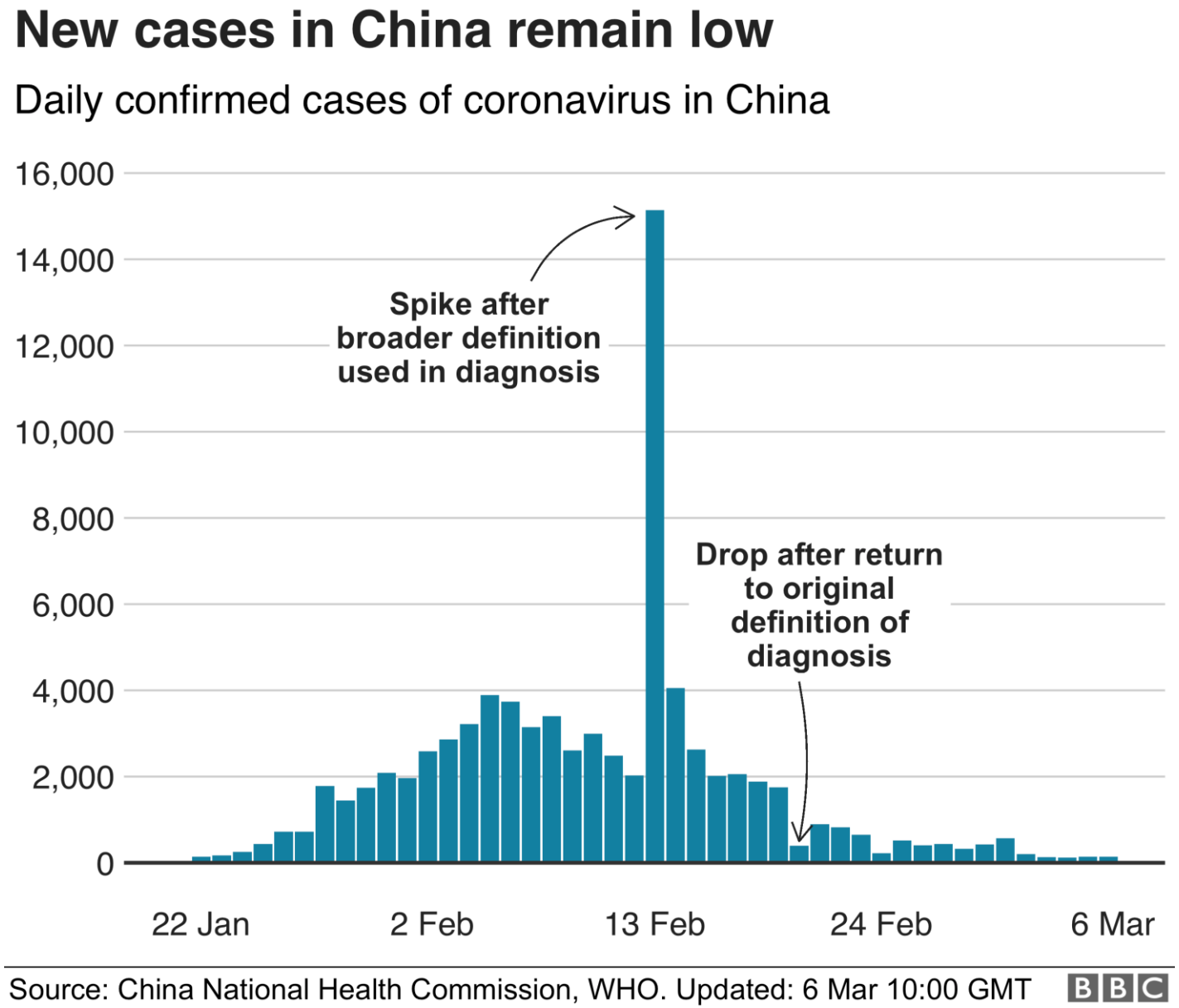
- As of end November 2019, MERS-CoV has caused a total of 2494 cases and 858 deaths, the majority in Saudi Arabia
- The natural reservoir of MERS-CoV is presumed to be bats
  - human cases have been associated with the dromedary camel
- MERS causes severe atypical pneumonia like SARS
- Gastrointestinal symptoms and acute kidney failure are common in MERS
  - MERS-CoV S glycoprotein binds to dipeptidyl peptidase 4 (DPP4), present in the lower airway, gastrointestinal tract and renal tissue
- Mechanical ventilation required in 50% to 89% of patients and has a case fatality rate of 36%

# Epidemiological Findings and Clinical Outcomes of 2015 MERS-CoV Outbreak in the Republic of Korea

**Treatment Regimen**:
IFN-alpha+
Ribavirin+
Lopinavir/ritonavir

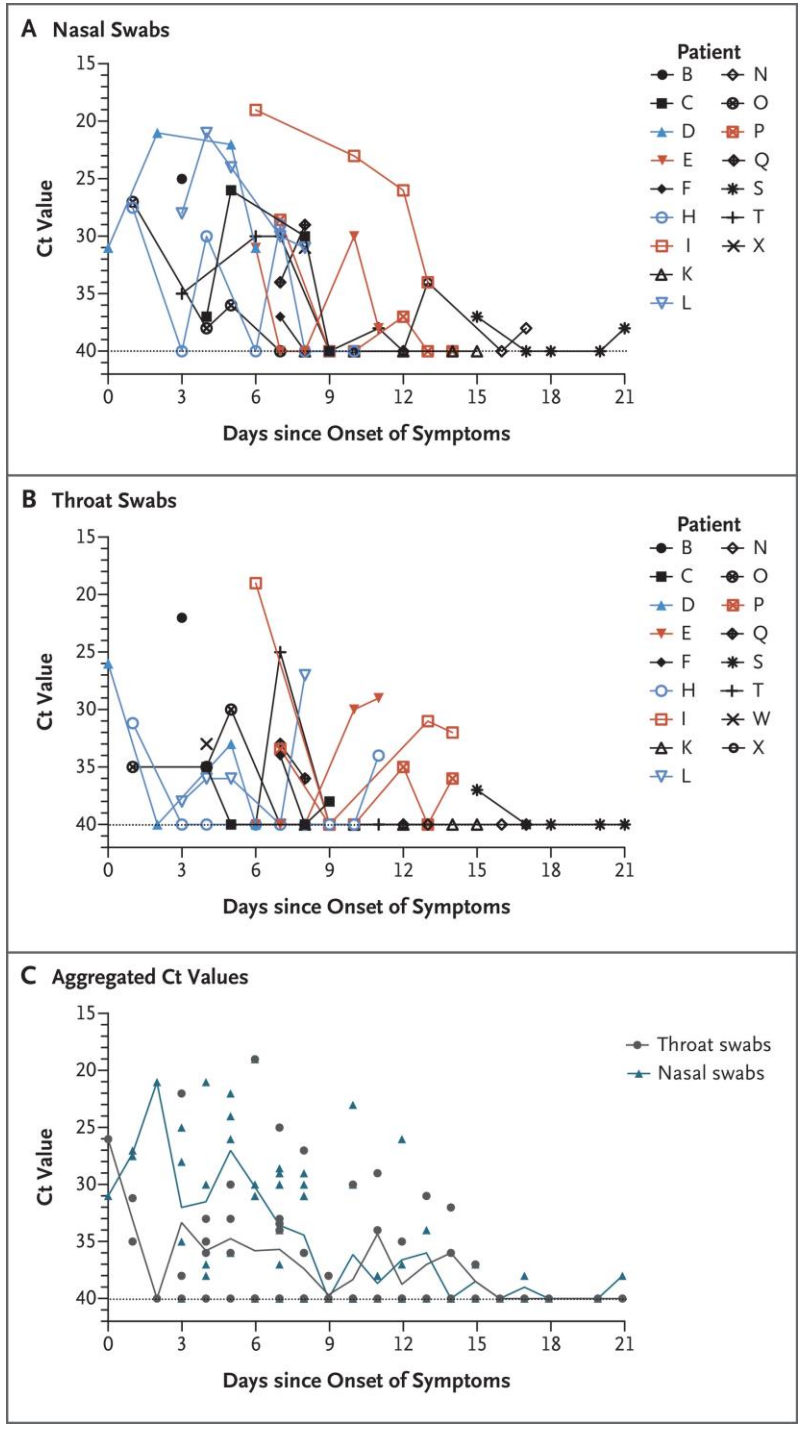
| |
|---|
| Incubation time: 2–14 days |
| Infectious period: 1–11 day of illness onset |
| Duration of fever: 8 days (median) |
| Symptom onset to rRT-PCR (–) conversion: 17 days (median) |
| Five superspreaders infected 83% of cases |
| Pneumonia (CXR infiltrates): 80.8% of the laboratory confirmed MERS-CoV (+) patients |
| Pneumonia progressed suddenly at around day 7 of illness onset |
| Symptom onset to mechanical ventilation: 9 days (median) |
| Mechanical ventilation required in 24.5% of the laboratory confirmed MERS-CoV (+) patients |
| Symptom onset to death: 14 days (median) |
| Case fatality ratio: 20.4% (38/186) |

# How Long Will It Last?

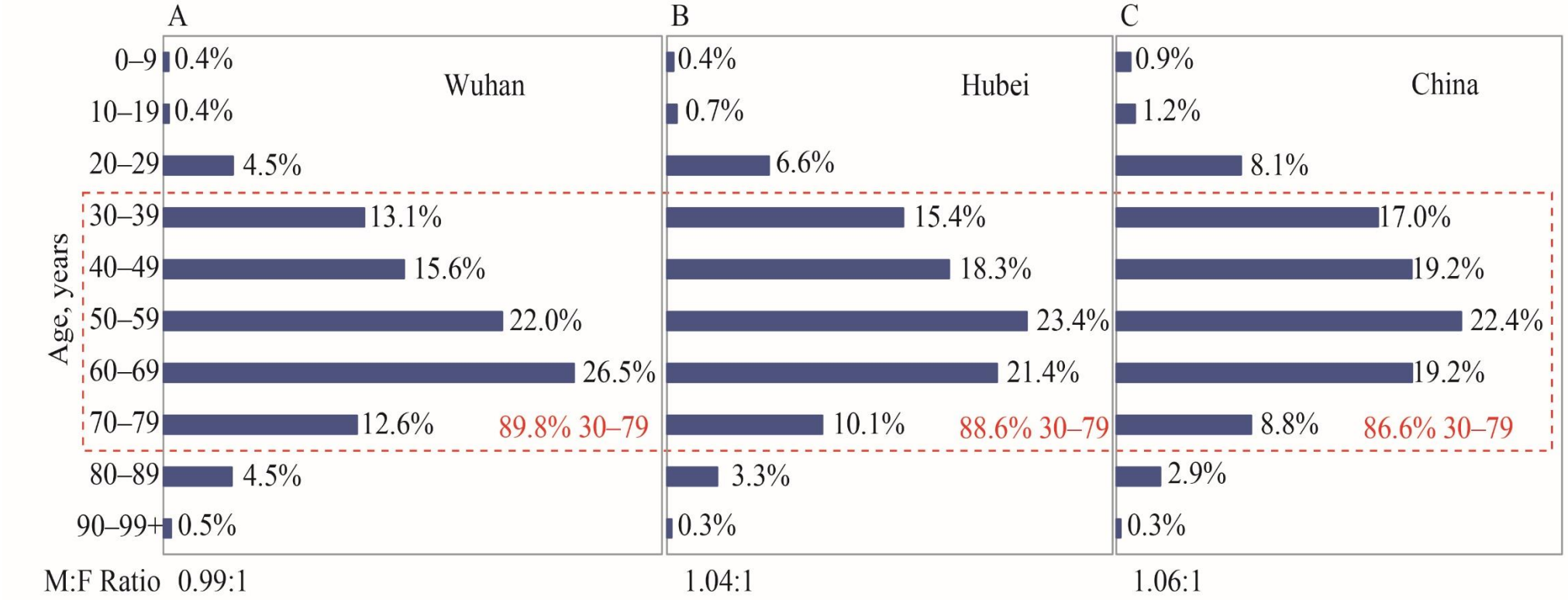


# SARS-CoV-2 VL

- Viral load high at onset of illness
- Asymptomatic case has equivalent VL
- Nasal VL higher than throat



# Age Distribution of Cases in Wuhan, Hubei, and China




Age distribution and sex ratio of all confirmed COVID-19 cases in China through February 11, 2020. (A) patients diagnosed in the city of Wuhan only; (B) patients diagnosed in Hubei Province, which includes Wuhan as its capital city; and (C) patients diagnosed in China overall, including Hubei Province and all 30 other provincial-level administrative divisions (PLADs). Dashed red line highlights the proportion of patients in the 30–79 years age range. Sex ratio (i.e. male-to-female [M:F] ratio) is shown below each graph.

The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team

**The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020**

China CDC Weekly,2020, 2(8)

http://dx.doi.org/null

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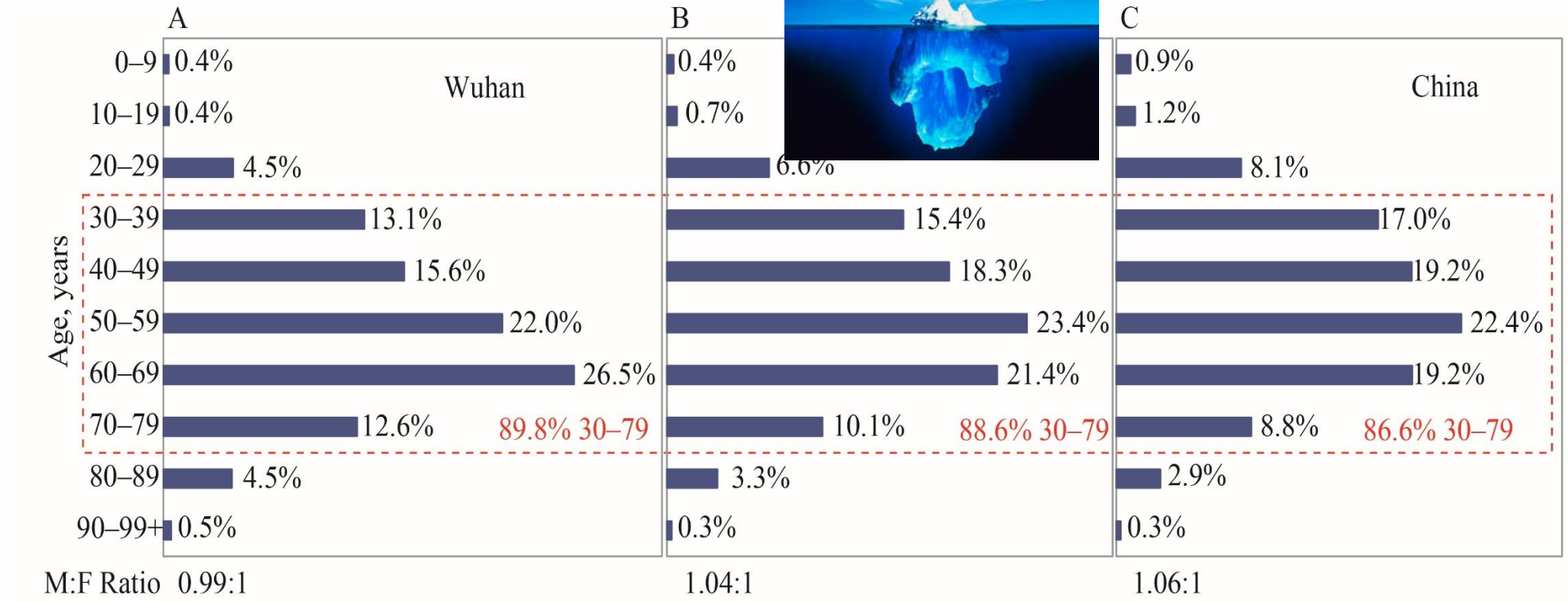


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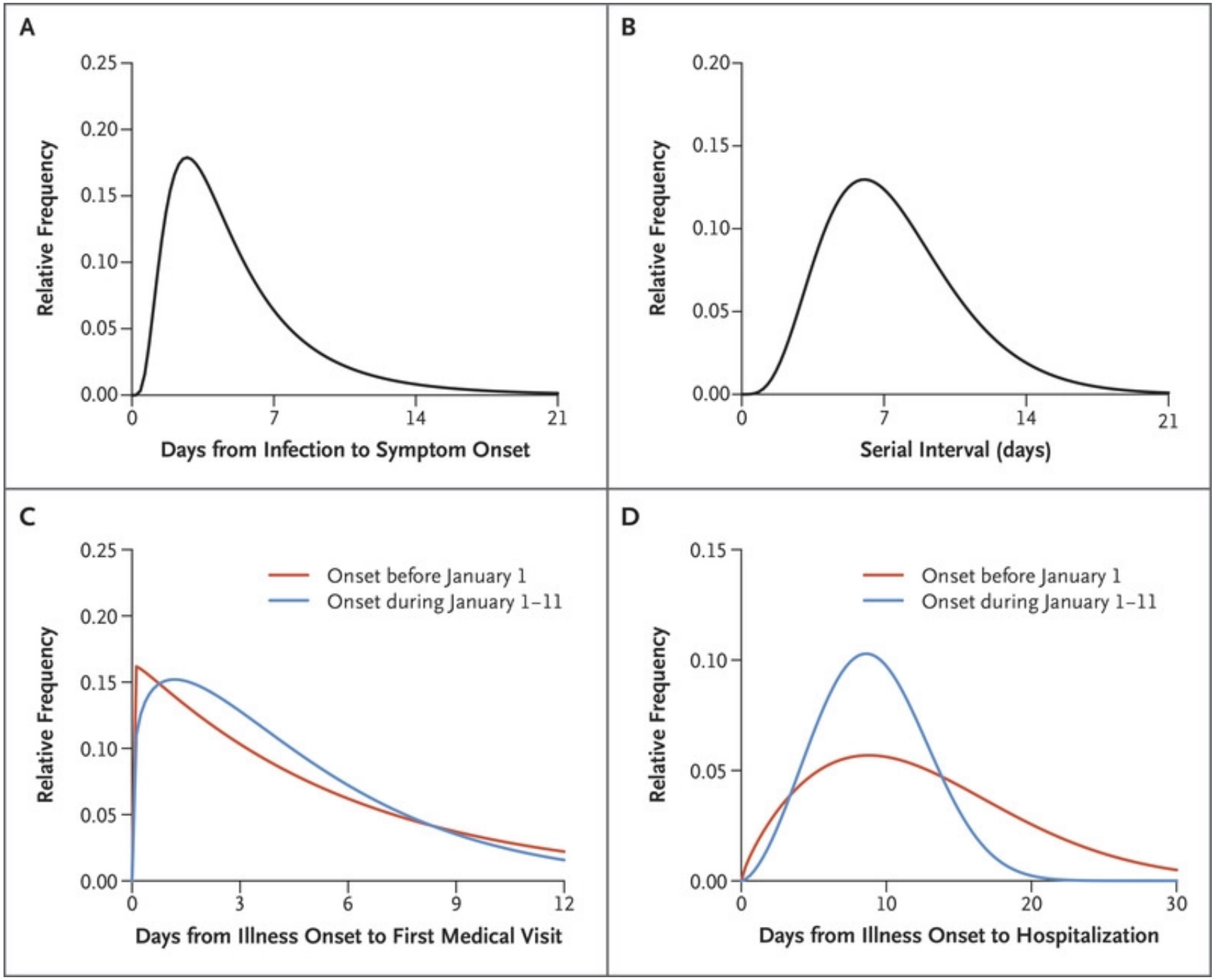
# COVID-19

## Incubation Period



# Incubation Period and other

- From NEJM paper
- 4 days
- IQR 2-7

- Mean interval of 9.1 to 12.5 days between the onset of illness and hospitalization
- Symptom onset to recovery/death
  - 2 weeks for mild
  - 3-6 weeks severe
  - 2-8 weeks from symptom onset to death

# Role of Asymptomatic Transmission

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

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

**TO THE EDITOR:** The novel coronavirus (2019-nCoV) from Wuhan is currently causing concern in the medical community as the virus is spreading around the world.[1] Since identification of the virus in late December 2019, the number of cases from China that have been imported into other countries is on the rise, and the epidemiologic picture is changing on a daily basis. We are reporting a case of 2019-nCoV infection acquired outside Asia in which transmission appears to have occurred during the incubation period in the index patient.

A 33-year-old otherwise healthy German businessman (Patient 1) became ill with a sore throat, chills, and myalgias on January 24, 2020. The following day, a fever of 39.1°C (102.4°F) developed, along with a productive cough. By the evening of the next day, he started feeling better and went back to work on January 27.

Before the onset of symptoms, he had attended meetings with a Chinese business partner at his company near Munich on January 20 and 21. The business partner, a Shanghai resident, had tive for 2019-nCoV on January 26 (index patient in Fig. 1) (see Supplementary Appendix, available at NEJM.org, for details on the timeline of symptom development leading to hospitalization).

On January 27, she informed the company about her illness. Contact tracing was started, and the above-mentioned colleague was sent to the Division of Infectious Diseases and Tropical Medicine in Munich for further assessment. At presentation, he was afebrile and well. He reported no previous or chronic illnesses and had no history of foreign travel within 14 days before the onset of symptoms. Two nasopharyngeal swabs and one sputum sample were obtained and were found to be positive for 2019-nCoV on quantitative reverse-transcriptase–polymerase-chain-reaction (qRT-PCR) assay.[2] Follow-up qRT-PCR assay revealed a high viral load of $10^8$ copies per milliliter in his sputum during the following days, with the last available result on January 29.

On January 28, three additional employees at the company tested positive for 2019-nCoV (Patients 2 through 4 in Fig. 1). Of these patients

# Asymptomatic Spread Example

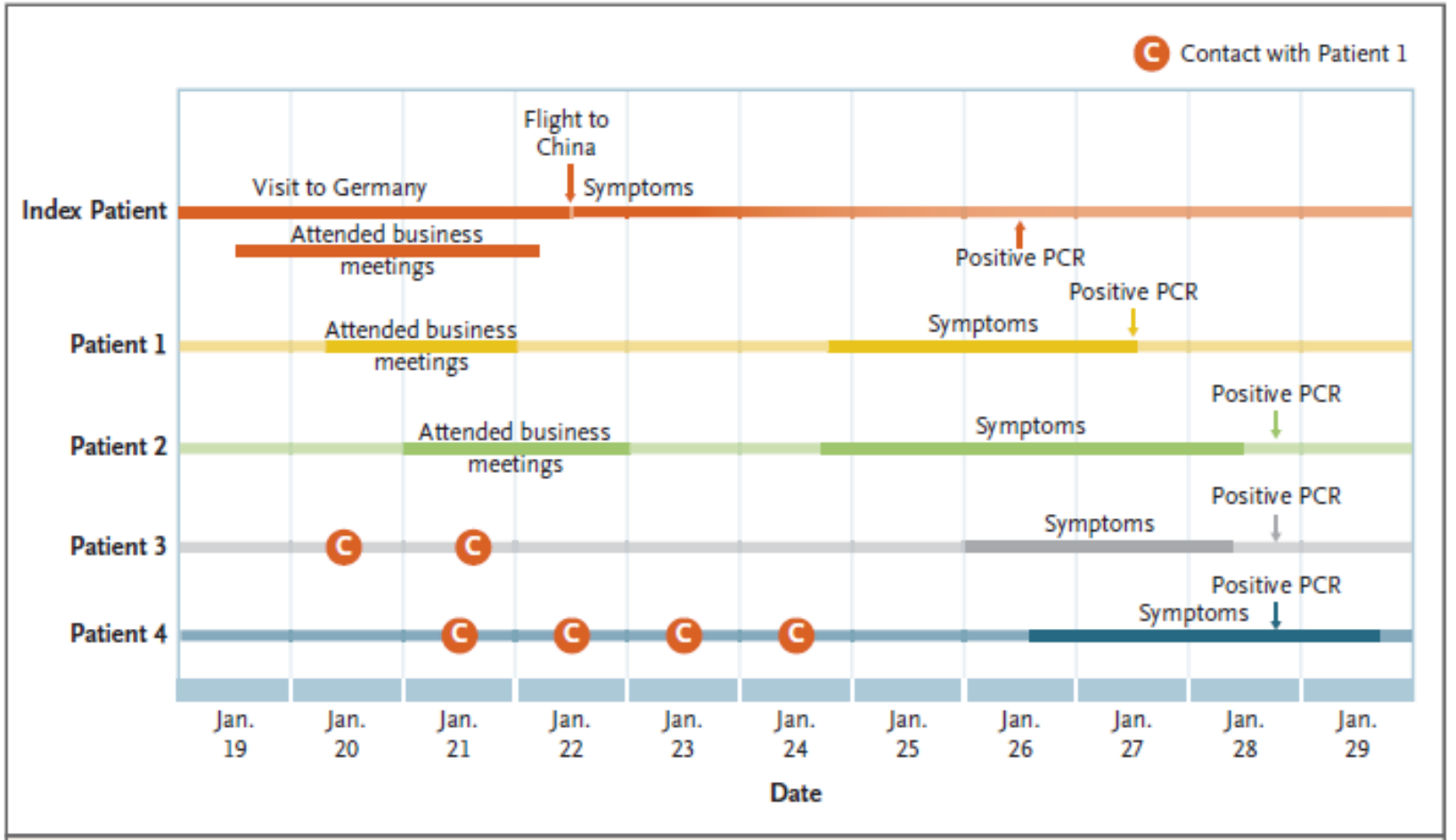



**Figure 1.** Timeline of Exposure to Index Patient with Asymptomatic 2019-CoV Infection in Germany.

# Symptoms

- Fever, cough, dyspnea
- Pneumonia
- 81 percent mild
- 14 percent severe (>50 percent lung involvement, hypoxia)
- 5 percent critical (multiorgan failure, mechanical vent)

# 1099 Compiled Cases

**Table 1. Clinical Characteristics of the Study Patients, According to Disease Severity and the Presence or Absence of the Primary Composite End Point.***

| Characteristic | All Patients (N=1099) | Disease Severity | | Presence of Primary Composite End Point† | |
|---|---|---|---|---|---|
| | | Nonsevere (N=926) | Severe (N=173) | Yes (N=67) | No (N=1032) |
| Age | | | | | |
| Median (IQR) — yr | 47.0 (35.0–58.0) | 45.0 (34.0–57.0) | 52.0 (40.0–65.0) | 63.0 (53.0–71.0) | 46.0 (35.0–57.0) |
| Distribution — no./total no. (%) | | | | | |
| 0–14 yr | 9/1011 (0.9) | 8/848 (0.9) | 1/163 (0.6) | 0 | 9/946 (1.0) |
| 15–49 yr | 557/1011 (55.1) | 490/848 (57.8) | 67/163 (41.1) | 12/65 (18.5) | 545/946 (57.6) |
| 50–64 yr | 292/1011 (28.9) | 241/848 (28.4) | 51/163 (31.3) | 21/65 (32.3) | 271/946 (28.6) |
| ≥65 yr | 153/1011 (15.1) | 109/848 (12.9) | 44/163 (27.0) | 32/65 (49.2) | 121/946 (12.8) |
| Female sex — no./total no. (%) | 459/1096 (41.9) | 386/923 (41.8) | 73/173 (42.2) | 22/67 (32.8) | 437/1029 (42.5) |
| Smoking history — no./total no. (%) | | | | | |
| Never smoked | 927/1085 (85.4) | 793/913 (86.9) | 134/172 (77.9) | 44/66 (66.7) | 883/1019 (86.7) |
| Former smoker | 21/1085 (1.9) | 12/913 (1.3) | 9/172 (5.2) | 5/66 (7.6) | 16/1019 (1.6) |
| Current smoker | 137/1085 (12.6) | 108/913 (11.8) | 29/172 (16.9) | 17/66 (25.8) | 120/1019 (11.8) |
| Exposure to source of transmission within past 14 days — no./total no. | | | | | |
| Living in Wuhan | 483/1099 (43.9) | 400/926 (43.2) | 83/173 (48.0) | 39/67 (58.2) | 444/1032 (43.0) |
| Contact with wildlife | 13/687 (1.9) | 10/559 (1.8) | 3/128 (2.3) | 1/41 (2.4) | 12/646 (1.9) |
| Recently visited Wuhan‡ | 193/616 (31.3) | 166/526 (31.6) | 27/90 (30.0) | 10/28 (35.7) | 183/588 (31.1) |
| Had contact with Wuhan residents‡ | 442/611 (72.3) | 376/522 (72.0) | 66/89 (74.2) | 19/28 (67.9) | 423/583 (72.6) |
| Median incubation period (IQR) — days§ | 4.0 (2.0–7.0) | 4.0 (2.8–7.0) | 4.0 (2.0–7.0) | 4.0 (1.0–7.5) | 4.0 (2.0–7.0) |
| Fever on admission | | | | | |
| Patients — no./total no. (%) | 473/1081 (43.8) | 391/910 (43.0) | 82/171 (48.0) | 24/66 (36.4) | 449/1015 (44.2) |
| Median temperature (IQR) — °C | 37.3 (36.7–38.0) | 37.3 (36.7–38.0) | 37.4 (36.7–38.1) | 36.8 (36.3–37.8) | 37.3 (36.7–38.0) |
| Distribution of temperature — no./total no. (%) | | | | | |
| <37.5°C | 608/1081 (56.2) | 519/910 (57.0) | 89/171 (52.0) | 42/66 (63.6) | 566/1015 (55.8) |
| 37.5–38.0°C | 238/1081 (22.0) | 201/910 (22.1) | 37/171 (21.6) | 10/66 (15.2) | 228/1015 (22.5) |
| 38.1–39.0°C | 197/1081 (18.2) | 160/910 (17.6) | 37/171 (21.6) | 11/66 (16.7) | 186/1015 (18.3) |
| >39.0°C | 38/1081 (3.5) | 30/910 (3.3) | 8/171 (4.7) | 3/66 (4.5) | 35/1015 (3.4) |
| Fever during hospitalization | | | | | |
| Patients — no./total no. (%) | 975/1099 (88.7) | 816/926 (88.1) | 159/173 (91.9) | 59/67 (88.1) | 916/1032 (88.8) |
| Median highest temperature (IQR) — °C | 38.3 (37.8–38.9) | 38.3 (37.8–38.9) | 38.5 (38.0–39.0) | 38.5 (38.0–39.0) | 38.3 (37.8–38.9) |
| <37.5°C | 92/926 (9.9) | 79/774 (10.2) | 13/152 (8.6) | 3/54 (5.6) | 89/872 (10.2) |
| 37.5–38.0°C | 286/926 (30.9) | 251/774 (32.4) | 35/152 (23.0) | 20/54 (37.0) | 266/872 (30.5) |
| 38.1–39.0°C | 434/926 (46.9) | 356/774 (46.0) | 78/152 (51.3) | 21/54 (38.9) | 413/872 (47.4) |
| >39.0°C | 114/926 (12.3) | 88/774 (11.4) | 26/152 (17.1) | 10/54 (18.5) | 104/872 (11.9) |
| Symptoms — no. (%) | | | | | |
| Conjunctival congestion | 9 (0.8) | 5 (0.5) | 4 (2.3) | 0 | 9 (0.9) |
| Nasal congestion | 53 (4.8) | 47 (5.1) | 6 (3.5) | 2 (3.0) | 51 (4.9) |
| Headache | 150 (13.6) | 124 (13.4) | 26 (15.0) | 8 (11.9) | 142 (13.8) |
| Cough | 745 (67.8) | 623 (67.3) | 122 (70.5) | 46 (68.7) | 699 (67.7) |
| Sore throat | 153 (13.9) | 130 (14.0) | 23 (13.3) | 6 (9.0) | 147 (14.2) |
| Sputum production | 370 (33.7) | 309 (33.4) | 61 (35.3) | 20 (29.9) | 350 (33.9) |
| Fatigue | 419 (38.1) | 350 (37.8) | 69 (39.9) | 22 (32.8) | 397 (38.5) |
| Hemoptysis | 10 (0.9) | 6 (0.6) | 4 (2.3) | 2 (3.0) | 8 (0.8) |
| Shortness of breath | 205 (18.7) | 140 (15.1) | 65 (37.6) | 36 (53.7) | 169 (16.4) |
| Nausea or vomiting | 55 (5.0) | 43 (4.6) | 12 (6.9) | 3 (4.5) | 52 (5.0) |
| Diarrhea | 42 (3.8) | 32 (3.5) | 10 (5.8) | 4 (6.0) | 38 (3.7) |
| Myalgia or arthralgia | 164 (14.9) | 134 (14.5) | 30 (17.3) | 6 (9.0) | 158 (15.3) |
| Chills | 126 (11.5) | 100 (10.8) | 26 (15.0) | 8 (11.9) | 118 (11.4) |
| Signs of infection — no. (%) | | | | | |
| Throat congestion | 19 (1.7) | 17 (1.8) | 2 (1.2) | 0 | 19 (1.8) |
| Tonsil swelling | 23 (2.1) | 17 (1.8) | 6 (3.5) | 1 (1.5) | 22 (2.1) |
| Enlargement of lymph nodes | 2 (0.2) | 1 (0.1) | 1 (0.6) | 1 (1.5) | 1 (0.1) |
| Rash | 2 (0.2) | 0 | 2 (1.2) | 0 | 2 (0.2) |
| Coexisting disorder — no. (%) | | | | | |
| Any | 261 (23.7) | 194 (21.0) | 67 (38.7) | 39 (58.2) | 222 (21.5) |
| Chronic obstructive pulmonary disease | 12 (1.1) | 6 (0.6) | 6 (3.5) | 7 (10.4) | 5 (0.5) |
| Diabetes | 81 (7.4) | 53 (5.7) | 28 (16.2) | 18 (26.9) | 63 (6.1) |
| Hypertension | 165 (15.0) | 124 (13.4) | 41 (23.7) | 24 (35.8) | 141 (13.7) |
| Coronary heart disease | 27 (2.5) | 17 (1.8) | 10 (5.8) | 6 (9.0) | 21 (2.0) |
| Cerebrovascular disease | 15 (1.4) | 11 (1.2) | 4 (2.3) | 4 (6.0) | 11 (1.1) |
| Hepatitis B infection¶ | 23 (2.1) | 22 (2.4) | 1 (0.6) | 1 (1.5) | 22 (2.1) |
| Cancer‖ | 10 (0.9) | 7 (0.8) | 3 (1.7) | 1 (1.5) | 9 (0.9) |
| Chronic renal disease | 8 (0.7) | 5 (0.5) | 3 (1.7) | 2 (3.0) | 6 (0.6) |
| Immunodeficiency | 2 (0.2) | 2 (0.2) | 0 | 0 | 2 (0.2) |

* The denominators of patients who were included in the analysis are provided if they differed from the overall numbers in the group. Percentages may not total 100 because of rounding. Covid-19 denotes coronavirus disease 2019, and IQR interquartile range.
† The primary composite end point was admission to an intensive care unit, the use of mechanical ventilation, or death.
‡ These patients were not residents of Wuhan.
§ Data regarding the incubation period were missing for 808 patients (73.5%).
¶ The presence of hepatitis B infection was defined as a positive result on testing for hepatitis B surface antigen with or without elevated levels of alanine or aspartate aminotransferase.
‖ Included in this category is any type of cancer.

# Clinical Symptoms (N=1099)

| Symptoms | All pts (1099) | Nonsevere (926) | Severe (173) | Composite Y (67) | Composite N (1032) |
|---|---|---|---|---|---|
| Conjunctival cong | 9 (0.8) | 5 (0.5) | 4 (2.3) | 0 | 9 (0.9) |
| Nasal congest | 53 (4.8) | 47 (5.1) | 6 (3.5) | 2 (3.0) | 51 (4.9) |
| Headache | 150 (13.6) | 124 (13.4) | 26 (15.0) | 8 (11.9) | 142(13.8) |
| Cough | 745 (67.8) | 623 (67.3) | 122 (70.5) | 46 (68.7) | 699 (67.7) |
| Sore throat | 153 (13.9) | 130 (14.0) | 23 (13.3) | 6 (9.0) | 147 (14.2) |
| Sputum product | 370 (33.7) | 309 (33.4) | 61 (35.3) | 20 (29.9) | 350 (33.9) |
| Fatigue | 419 (38.1) | 350 (37.8) | 69 (39.9) | 22 (32.8) | 397 (38.5) |
| Hemoptysis | 10 (0.9) | 6 (0.6) | 4 (2.3) | 2 (3.0) | 8 (0.8) |
| SOB | 205 (18.7) | 140 (15.1) | 65 (37.6) | 36 (53.7) | 169 (16.4) |
| N or V | 55 (5.0) | 43 (4.6) | 12 (6.9) | 3 (4.5) | 52 (5.0) |
| Diarrhea | 42 (3.8) | 32 (3.5) | 10 (5.8) | 4 (6.0) | 38 (3.7) |
| Myalgia/arthr | 164 (14.9) | 134 (14.5) | 30 (17.3) | 6 (9.0) | 158 (15.3) |
| Chills | 126 (11.5) | 100 (10.8) | 26 (15.0) | 8 (11.9) | 118 (11.4) |
| Fever on admit | 473 (43.8) | 391 (43.0) | 82 (48.0) | 24 (36.4) | 449 (44.2) |

composite = admission to an intensive care unit (ICU), the use of mechanical ventilation, or

# ATS/IDSA Criteria

## Severe vs Nonsevere

| **2007 Infectious Diseases Society of America/American Thoracic Society Criteria for Defining Severe Community-acquired Pneumonia** |
|---|
| **Validated definition includes either one major criterion or three or more minor criteria** |
| **Minor criteria** |
| Respiratory rate ≥ 30 breaths/min |
| $Pa_{O2}/Fi_{O2}$ ratio ≤ 250 |
| Multilobar infiltrates |
| Confusion/disorientation |
| Uremia (blood urea nitrogen level ≥ 20 mg/dl) |
| Leukopenia* (white blood cell count < 4,000 cells/µl) |
| Thrombocytopenia (platelet count < 100,000/µl) |
| Hypothermia (core temperature < 36°C) |
| Hypotension requiring aggressive fluid resuscitation |
| **Major criteria** |
| Septic shock with need for vasopressors |
| Respiratory failure requiring mechanical ventilation |

From: **Clinical Signs and Symptoms Predicting Influenza Infection**

Arch Intern Med. 2000;160(21):3243-3247. doi:10.1001/archinte.160.21.3243

**Table 3. Proportion of Pooled Participants With Baseline Symptoms**

| Symptom | Patients With Laboratory-Confirmed Influenza, % (n = 2470) | Patients Who Tested Negative for Influenza, % (n = 1274) |
|---|---|---|
| Fever (≥37.8°C)* | 68 | 40 |
| Feverishness* | 90 | 89 |
| Cough | 93 | 80 |
| Nasal congestion | 91 | 81 |
| Weakness | 94 | 94 |
| Loss of appetite | 92 | 86 |
| Sore throat | 84 | 84 |
| Headache | 91 | 89 |
| Myalgia | 94 | 94 |

**Fever was a body temperature of 37°C or higher, whereas feverishness was the patient's subjective feeling that they had a fever or chill.*

# Radiographic Findings

| Abnormalities on CXR | All | Nonsevere | Severe | Comp Y | Comp N |
|---|---|---|---|---|---|
| All | 162/274 (59.1) | 116/214 (54.2) | 46/60 (76.7) | 30/39 (76.9) | 132/235 (56.2) |
| GGO | 55/274 (20.1) | 37/214 (17.3) | 18/60 (30.0) | 9/39 (23.1) | 46/235 (19.6) |
| Local patchy shadowing | 77/274 (28.1) | 56/214 (26.2) | 21/60 (35.0) | 13/39 (33.3) | 64/235 (27.2) |
| Bilateral patchy shadowing | 100/274 (36.5) | 65/214 (30.4) | 35/60 (58.3) | 27/39 (69.2) | 73/235 (31.1) |
| Interstitial abnormalities | 12/274 (4.4) | 7/214 (3.3) | 5/60 (8.3) | 6/39 (15.4) | 6/235 (2.6) |
| Abnormalities on chest CT | | | | | |
| All | 840/975 (86.2) | 682/808 (84.4) | 158/167 (94.6) | 50/57 (87.7) | 790/918 (86.1) |
| GGO | 550/975 (56.4) | 449/808 (55.6) | 101/167 (60.5) | 30/57 (52.6) | 520/918 (56.6) |
| Local patchy shadowing | 409/975 (41.9) | 317/808 (39.2) | 92/167 (55.1) | 22/57 (38.6) | 387/918 (42.2) |
| Bilateral patchy shadowing | 505/975 (51.8) | 368/808 (45.5) | 137/167 (82.0) | 40/57 (70.2) | 465/918 (50.7) |
| Interstitial abnormalities | 143/975 (14.7) | 99/808 (12.3) | 44/167 (26.3) | 15/57 (26.3) | 128/918 (13.9) |

# Radiographic Findings

| Abnormalities on CXR | All | Nonsevere | Severe | Comp Y | Comp N |
|---|---|---|---|---|---|
| All | 162/274 (59.1) | 116/214 (54.2) | 46/60 (76.7) | 30/39 (76.9) | 132/235 (56.2) |
| GGO | 55/274 (20.1) | 37/214 (17.3) | 18/60 (30.0) | 9/39 (23.1) | 46/235 (19.6) |
| Local patchy shadowing | 77/274 (28.1) | 56/214 (26.2) | 21/60 (35.0) | 13/39 (33.3) | 64/235 (27.2) |
| Bilateral patchy shadowing | 100/274 (36.5) | 65/214 (30.4) | 35/60 (58.3) | 27/39 (69.2) | 73/235 (31.1) |
| Interstitial abnormalities | 12/274 (4.4) | 7/214 (3.3) | 5/60 (8.3) | 6/39 (15.4) | 6/235 (2.6) |
| Abnormalities on chest CT | | | | | |
| All | 840/975 (86.2) | 682/808 (84.4) | 158/167 (94.6) | 50/57 (87.7) | 790/918 (86.1) |
| GGO | 550/975 (56.4) | 449/808 (55.6) | 101/167 (60.5) | 30/57 (52.6) | 520/918 (56.6) |
| Local patchy shadowing | 409/975 (41.9) | 317/808 (39.2) | 92/167 (55.1) | 22/57 (38.6) | 387/918 (42.2) |
| Bilateral patchy shadowing | 505/975 (51.8) | 368/808 (45.5) | 137/167 (82.0) | 40/57 (70.2) | 465/918 (50.7) |
| Interstitial abnormalities | 143/975 (14.7) | 99/808 (12.3) | 44/167 (26.3) | 15/57 (26.3) | 128/918 (13.9) |

"No radiographic or CT abnormality was found in 157 of 877 patients (17.9%) with nonsevere disease and in 5 of 173 patients (2.9%) with severe disease."

JAMA Network™

From: **Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China**

JAMA. Published online February 07, 2020. doi:10.1001/jama.2020.1585

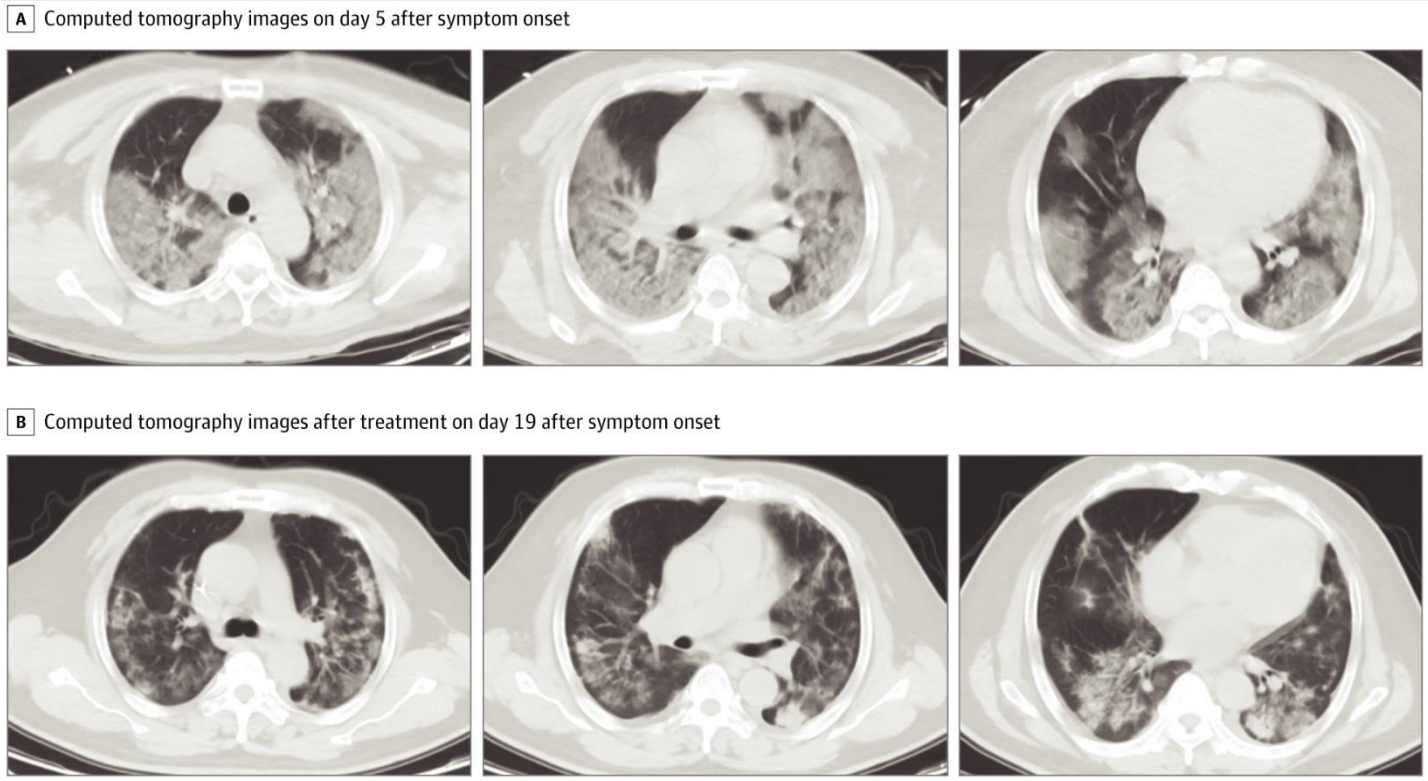



Figure Legend:

Chest Computed Tomographic Images of a 52-Year-Old Patient Infected With 2019 Novel Coronavirus (2019-nCoV)A, Chest computed tomographic images obtained on January 7, 2020, show ground glass opacity in both lungs on day 5 after symptom onset. B, Images taken on January 21, 2020, show the absorption of bilateral ground glass opacity after the treatment of extracorporeal membrane oxygenation from January 7 to 12 in the intensive care unit.

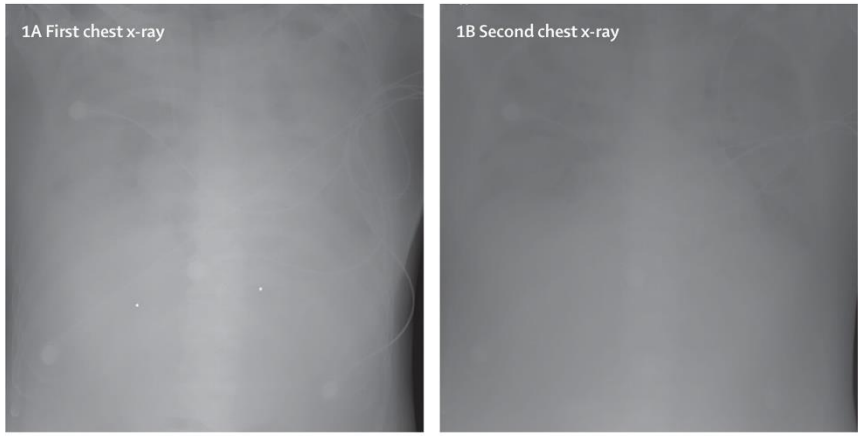
# *Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study*

*Prof Nanshan Chen, MD, Prof Min Zhou, MD, Xuan Dong, PhD, Prof Jieming Qu, MD, Fengyun Gong, MD, Yang Han, PhD, Prof Yang Qiu, PhD, Jingli Wang, MD, Ying Liu, MD, Yuan Wei, MD, Jia'an Xia, MD, Ting Yu, MD, Prof Xinxin Zhang, MD, Prof Li Zhang, MD*

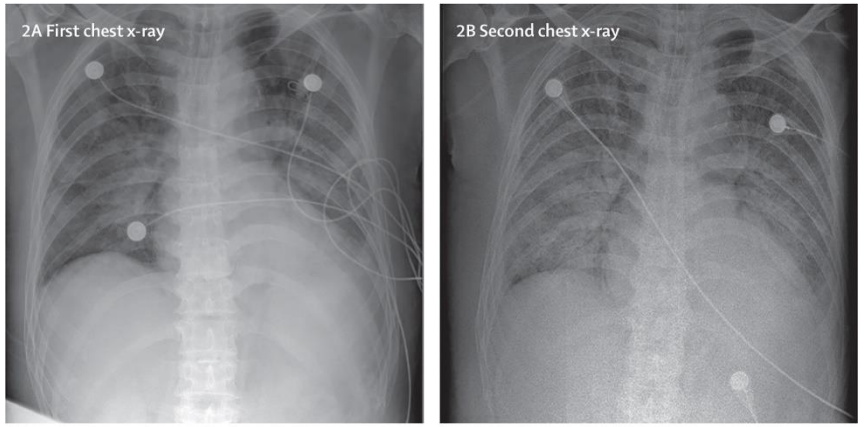
*The Lancet*

DOI: 10.1016/S0140-6736(20)30211-7

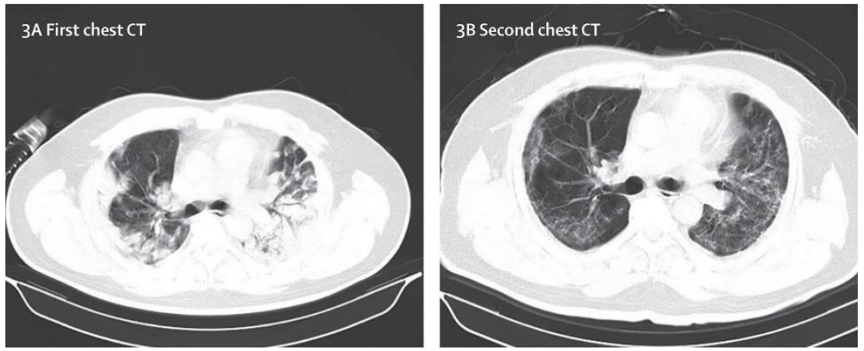
Case 1




Case 2




Case 3



# Course of Disease

- In hospitalized patients (Wuhan)
  - ~50% develop hypoxemia by day 8
  - ARDS 17-29%
  - For all ICU patients
    - Non-invasive ventilation 42%
    - Mechanical ventilation 47%
    - High-flow $O_2$ 11%
    - ECMO 2-5%
  - Most deaths from ARDS/complications of ARDS

JAMA Network™

From: **Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China**

JAMA. Published online February 07, 2020. doi:10.1001/jama.2020.1585

**Table 4. Complications and Treatments of Patients Infected With 2019-nCoV**

| | No. (%) | | | |
|---|---|---|---|---|
| | Total (N = 138) | ICU (n = 36) | Non-ICU (n = 102) | *P* Value[a] |
| **Complications** | | | | |
| Shock | 12 (8.7) | 11 (30.6) | 1 (1.0) | <.001 |
| Acute cardiac injury | 10 (7.2) | 8 (22.2) | 2 (2.0) | <.001 |
| Arrhythmia | 23 (16.7) | 16 (44.4) | 7 (6.9) | <.001 |
| ARDS | 27 (19.6) | 22 (61.1) | 5 (4.9) | <.001 |
| AKI | 5 (3.6) | 3 (8.3) | 2 (2.0) | .11 |
| **Treatment** | | | | |
| Antiviral therapy | 124 (89.9) | 34 (94.4) | 90 (88.2) | .36 |
| Glucocorticoid therapy | 62 (44.9) | 26 (72.2) | 36 (35.3) | <.001 |
| CKRT | 2 (1.45) | 2 (5.56) | 0 | >.99 |
| Oxygen inhalation | 106 (76.81) | 4 (11.11) | 102 (100) | <.001 |
| NIV | 15 (10.9) | 15 (41.7) | 0 | <.001 |
| IMV | 17 (12.32) | 17 (47.22) | 0 | <.001 |
| ECMO | 4 (2.9) | 4 (11.1) | 0 | .004 |

Abbreviations: AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; CKRT, continuous kidney replacement therapy; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IMV, invasive mechanical ventilation; NIV, noninvasive ventilation; 2019-nCoV, 2019 novel coronavirus.

[a] *P* values indicate differences between ICU and non-ICU patients. *P* < .05 was considered statistically significant.

From: **Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China**

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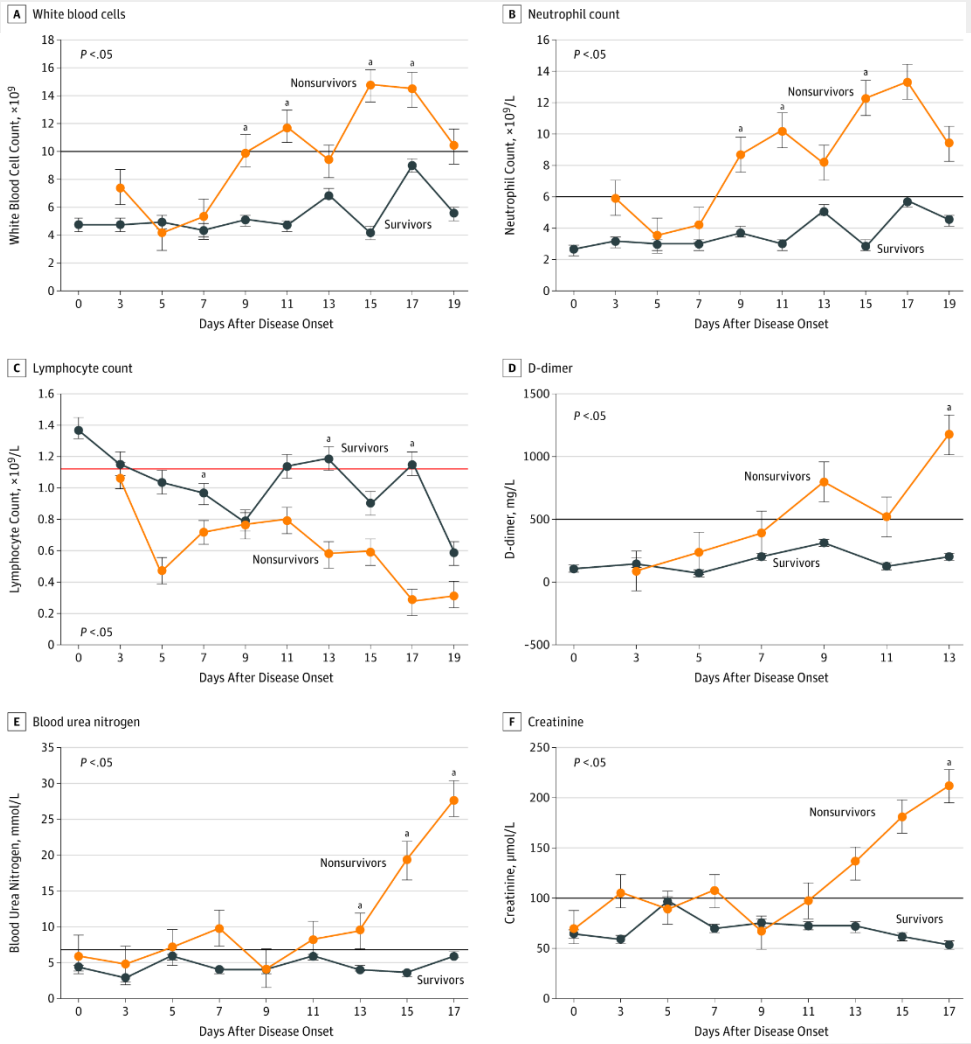



Dynamic Profile of Laboratory Parameters in 33 Patients With Novel Coronavirus–Infected Pneumonia (NCIP)Timeline charts illustrate the laboratory parameters in 33 patients with NCIP (5 nonsurvivors and 28 survivors) every other day based on the days after the onset of illness. The solid lines in black show the upper normal limit of each parameter, and the solid line in red shows the lower normal limit of lymphocyte count.

[a]P < .05 for nonsurvivors vs survivors.

Figure Legend:

# Outcomes

**Table 3. Complications, Treatments, and Clinical Outcomes.**

| Variable | All Patients (N=1099) | Disease Severity | | Presence of Composite Primary End Point | |
|---|---|---|---|---|---|
| | | Nonsevere (N=926) | Severe (N=173) | Yes (N=67) | No (N=1032) |
| **Complications** | | | | | |
| Septic shock — no. (%) | 12 (1.1) | 1 (0.1) | 11 (6.4) | 9 (13.4) | 3 (0.3) |
| Acute respiratory distress syndrome — no. (%) | 37 (3.4) | 10 (1.1) | 27 (15.6) | 27 (40.3) | 10 (1.0) |
| Acute kidney injury — no. (%) | 6 (0.5) | 1 (0.1) | 5 (2.9) | 4 (6.0) | 2 (0.2) |
| Disseminated intravascular coagulation — no. (%) | 1 (0.1) | 0 | 1 (0.6) | 1 (1.5) | 0 |
| Rhabdomyolysis — no. (%) | 2 (0.2) | 2 (0.2) | 0 | 0 | 2 (0.2) |
| Physician-diagnosed pneumonia — no./total no. (%) | 972/1067 (91.1) | 800/894 (89.5) | 172/173 (99.4) | 63/66 (95.5) | 909/1001 (90.8) |
| Median time until development of pneumonia (IQR) — days* | | | | | |
| After initial Covid-19 diagnosis | 0.0 (0.0–1.0) | 0.0 (0.0–1.0) | 0.0 (0.0–2.0) | 0.0 (0.0–3.5) | 0.0 (0.0–1.0) |
| After onset of Covid-19 symptoms | 3.0 (1.0–6.0) | 3.0 (1.0–6.0) | 5.0 (2.0–7.0) | 4.0 (0.0–7.0) | 3.0 (1.0–6.0) |
| **Treatments** | | | | | |
| Intravenous antibiotics — no. (%) | 637 (58.0) | 498 (53.8) | 139 (80.3) | 60 (89.6) | 577 (55.9) |
| Oseltamivir — no. (%) | 393 (35.8) | 313 (33.8) | 80 (46.2) | 36 (53.7) | 357 (34.6) |
| Antifungal medication — no. (%) | 31 (2.8) | 18 (1.9) | 13 (7.5) | 8 (11.9) | 23 (2.2) |
| Systemic glucocorticoids — no. (%) | 204 (18.6) | 127 (13.7) | 77 (44.5) | 35 (52.2) | 169 (16.4) |
| Oxygen therapy — no. (%) | 454 (41.3) | 331 (35.7) | 123 (71.1) | 59 (88.1) | 395 (38.3) |
| Mechanical ventilation — no. (%) | 67 (6.1) | 0 | 67 (38.7) | 40 (59.7) | 27 (2.6) |
| Invasive | 25 (2.3) | 0 | 25 (14.5) | 25 (37.3) | 0 |
| Noninvasive | 56 (5.1) | 0 | 56 (32.4) | 29 (43.3) | 27 (2.6) |
| Use of extracorporeal membrane oxygenation — no. (%) | 5 (0.5) | 0 | 5 (2.9) | 5 (7.5) | 0 |
| Use of continuous renal-replacement therapy — no. (%) | 9 (0.8) | 0 | 9 (5.2) | 8 (11.9) | 1 (0.1) |
| Use of intravenous immune globulin — no. (%) | 144 (13.1) | 86 (9.3) | 58 (33.5) | 27 (40.3) | 117 (11.3) |
| Admission to intensive care unit — no. (%) | 55 (5.0) | 22 (2.4) | 33 (19.1) | 55 (82.1) | 0 |
| Median length of hospital stay (IQR) — days† | 12.0 (10.0–14.0) | 11.0 10.0–13.0) | 13.0 (11.5–17.0) | 14.5 (11.0–19.0) | 12.0 (10.0–13.0) |
| **Clinical outcomes at data cutoff — no. (%)** | | | | | |
| Discharge from hospital | 55 (5.0) | 50 (5.4) | 5 (2.9) | 1 (1.5) | 54 (5.2) |
| Death | 15 (1.4) | 1 (0.1) | 14 (8.1) | 15 (22.4) | 0 |
| Recovery | 9 (0.8) | 7 (0.8) | 2 (1.2) | 0 | 9 (0.9) |
| Hospitalization | 1029 (93.6) | 875 (94.5) | 154 (89.0) | 51 (76.1) | 978 (94.8) |

* For the development of pneumonia, data were missing for 347 patients (31.6%) regarding the time since the initial diagnosis and for 161 patients (14.6%) regarding the time since symptom onset.
† Data regarding the median length of hospital stay were missing for 136 patients (12.4%).

# Outcomes

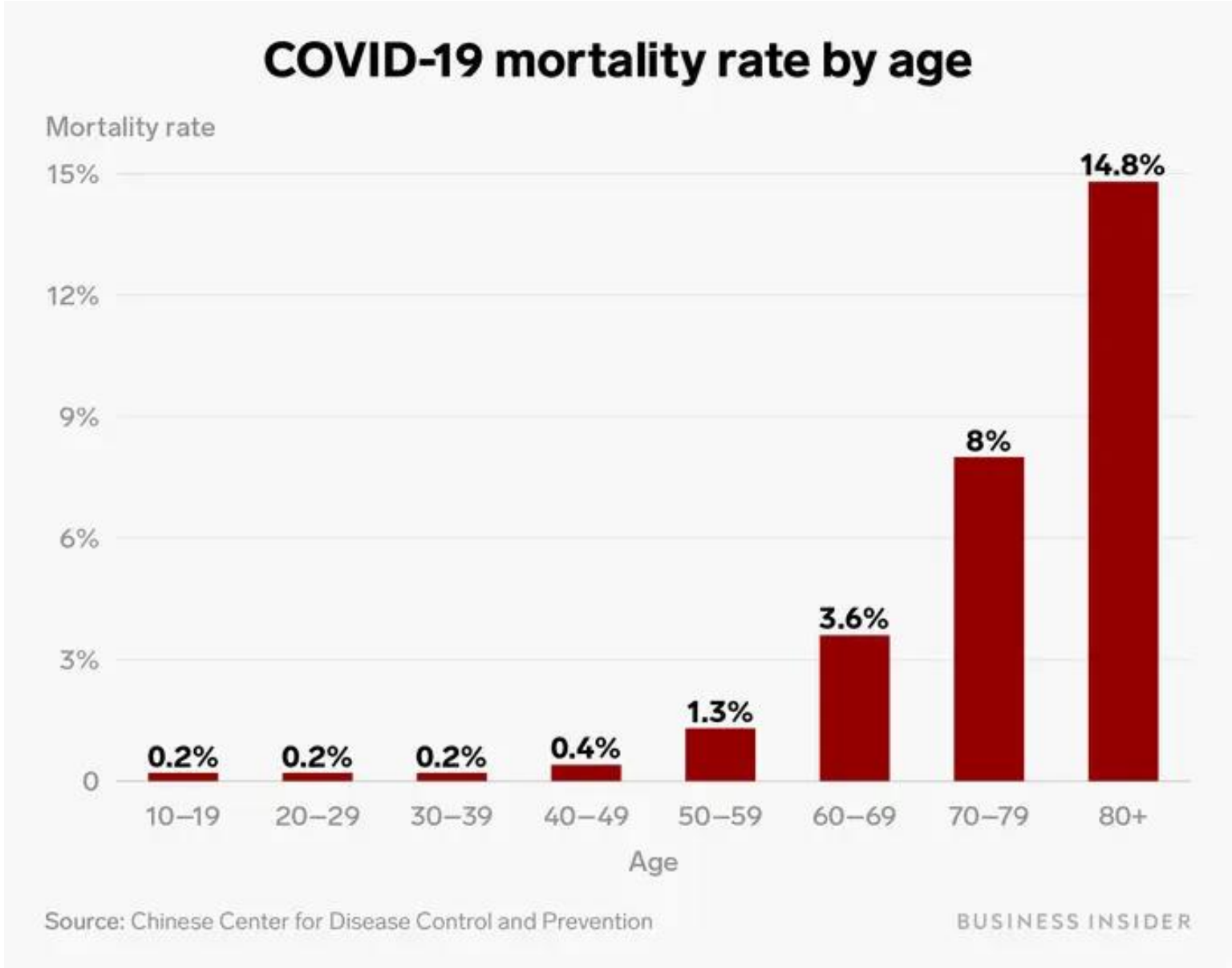
Deaths 1.4%

Current death rate
excluding “top ten”= 0.6%

**Table 3. Complications, Treatments, and Clinical Outcomes.**

| Variable | All Patients (N=1099) | Disease Severity | | Presence of Composite Primary End Point | |
|---|---|---|---|---|---|
| | | Nonsevere (N=926) | Severe (N=173) | Yes (N=67) | No (N=1032) |
| **Complications** | | | | | |
| Septic shock — no. (%) | 12 (1.1) | 1 (0.1) | 11 (6.4) | 9 (13.4) | 3 (0.3) |
| Acute respiratory distress syndrome — no. (%) | 37 (3.4) | 10 (1.1) | 27 (15.6) | 27 (40.3) | 10 (1.0) |
| Acute kidney injury — no. (%) | 6 (0.5) | 1 (0.1) | 5 (2.9) | 4 (6.0) | 2 (0.2) |
| Disseminated intravascular coagulation — no. (%) | 1 (0.1) | 0 | 1 (0.6) | 1 (1.5) | 0 |
| Rhabdomyolysis — no. (%) | 2 (0.2) | 2 (0.2) | 0 | 0 | 2 (0.2) |
| Physician-diagnosed pneumonia — no./total no. (%) | 972/1067 (91.1) | 800/894 (89.5) | 172/173 (99.4) | 63/66 (95.5) | 909/1001 (90.8) |
| Median time until development of pneumonia (IQR) — days* | | | | | |
| After initial Covid-19 diagnosis | 0.0 (0.0–1.0) | 0.0 (0.0–1.0) | 0.0 (0.0–2.0) | 0.0 (0.0–3.5) | 0.0 (0.0–1.0) |
| After onset of Covid-19 symptoms | 3.0 (1.0–6.0) | 3.0 (1.0–6.0) | 5.0 (2.0–7.0) | 4.0 (0.0–7.0) | 3.0 (1.0–6.0) |
| **Treatments** | | | | | |
| Intravenous antibiotics — no. (%) | 637 (58.0) | 498 (53.8) | 139 (80.3) | 60 (89.6) | 577 (55.9) |
| Oseltamivir — no. (%) | 393 (35.8) | 313 (33.8) | 80 (46.2) | 36 (53.7) | 357 (34.6) |
| Antifungal medication — no. (%) | 31 (2.8) | 18 (1.9) | 13 (7.5) | 8 (11.9) | 23 (2.2) |
| Systemic glucocorticoids — no. (%) | 204 (18.6) | 127 (13.7) | 77 (44.5) | 35 (52.2) | 169 (16.4) |
| Oxygen therapy — no. (%) | 454 (41.3) | 331 (35.7) | 123 (71.1) | 59 (88.1) | 395 (38.3) |
| Mechanical ventilation — no. (%) | 67 (6.1) | 0 | 67 (38.7) | 40 (59.7) | 27 (2.6) |
| Invasive | 25 (2.3) | 0 | 25 (14.5) | 25 (37.3) | 0 |
| Noninvasive | 56 (5.1) | 0 | 56 (32.4) | 29 (43.3) | 27 (2.6) |
| Use of extracorporeal membrane oxygenation — no. (%) | 5 (0.5) | 0 | 5 (2.9) | 5 (7.5) | 0 |
| Use of continuous renal-replacement therapy — no. (%) | 9 (0.8) | 0 | 9 (5.2) | 8 (11.9) | 1 (0.1) |
| Use of intravenous immune globulin — no. (%) | 144 (13.1) | 86 (9.3) | 58 (33.5) | 27 (40.3) | 117 (11.3) |
| Admission to intensive care unit — no. (%) | 55 (5.0) | 22 (2.4) | 33 (19.1) | 55 (82.1) | 0 |
| Median length of hospital stay (IQR) — days† | 12.0 (10.0–14.0) | 11.0 10.0–13.0) | 13.0 (11.5–17.0) | 14.5 (11.0–19.0) | 12.0 (10.0–13.0) |
| **Clinical outcomes at data cutoff — no. (%)** | | | | | |
| Discharge from hospital | 55 (5.0) | 50 (5.4) | 5 (2.9) | 1 (1.5) | 54 (5.2) |
| Death | 15 (1.4) | 1 (0.1) | 14 (8.1) | 15 (22.4) | 0 |
| Recovery | 9 (0.8) | 7 (0.8) | 2 (1.2) | 0 | 9 (0.9) |
| Hospitalization | 1029 (93.6) | 875 (94.5) | 154 (89.0) | 51 (76.1) | 978 (94.8) |

* For the development of pneumonia, data were missing for 347 patients (31.6%) regarding the time since the initial diagnosis and for 161 patients (14.6%) regarding the time since symptom onset.
† Data regarding the median length of hospital stay were missing for 136 patients (12.4%).


COVID-19 mortality rate by age
Mortality rate
15%
12%
9%
6%
3%
0
0.2%
0.2%
0.2%
0.4%
1.3%
3.6%
8%
14.8%
10–19
20–29
30–39
40–49
50–59
60–69
70–79
80+
Age
Source: Chinese Center for Disease Control and Prevention
BUSINESS INSIDER

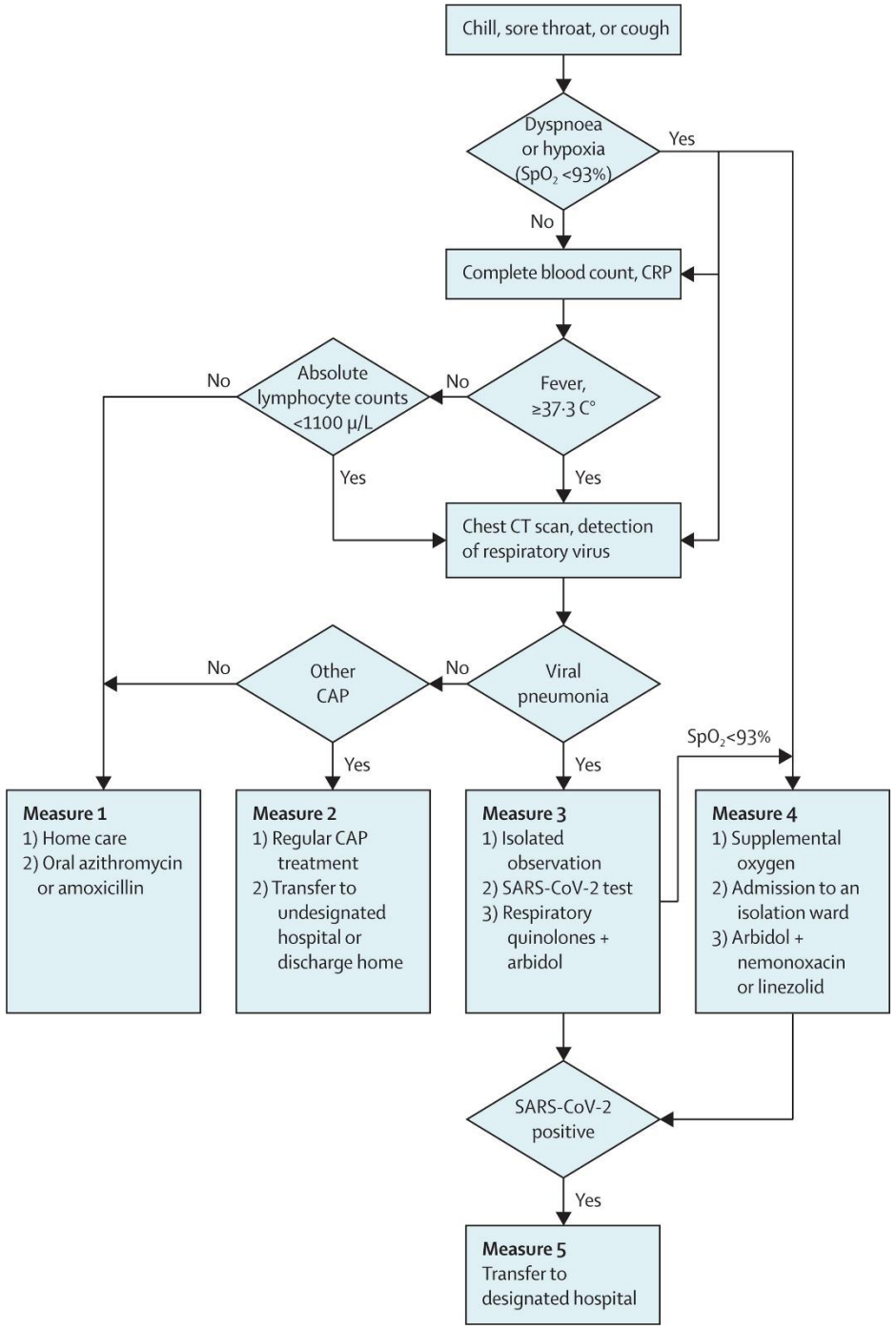
# Observations from Treating Physicians in Wuhan

- “There’s no data showing that an incubation period longer than 14 days ever existed”
- Underlying diseases like hypertension and diabetes, the prolonged used of non-invasive ventilation and high doses of corticosteroids over a long period of time were major factors in deaths of younger patients
- “would have been more aggressive in using invasive mechanical ventilation in all patients who showed hypoxemia”

# More Observations from China

- Majority of cases resulted from close contacts
- Transmission driven by family clusters (75-85% of clusters)
- Health care facilities, prisons and other closed systems not a driver of the epidemic in China (maybe they don’t have SNFs?)
- Was not in schools (perhaps due to being shut down)
- Many examples of superspreaders

# Triage system in Wuhan for COVID-19



# COVID-19 Infection Prevention

To facilitate the early identification of cases of suspected COVID-19 infection, healthcare facilities should:

- encourage HCWs to have a high level of clinical suspicion
- establish a well-equipped triage station at the entrance of health care facility, supported by trained staff
- institute the use of screening questionnaires according to the updated case definition (https://www.who.int/publications-detail/globalsurveillance-for-human-infection-with-novelcoronavirus-(2019-ncov)
- post signs in public areas reminding symptomatic patients to alert HCWs. The promotion of hand hygiene and respiratory hygiene are essential preventive measures.

# Infection Prevention

- Ensure that the following respiratory hygiene measures are used:
  - ensure that all patients cover their nose and mouth with a tissue or elbow when coughing or sneezing;
  - offer a medical mask to patients with suspected COVID-19 infection while they are in waiting/public areas or in cohorting rooms
  - perform hand hygiene after contact with respiratory secretions.

# Surface Disinfection

- Human coronaviruses can persist on inanimate surfaces for up to 9 days
- Efficiently inactivated by 62-71% ethanol, 0.5% hydrogen peroxide or 0.1% sodium hypochlorite within 1 minute
- Other agents such as 0.05-0.2% benzalkonium chloride or 0.02% chlorhexidine digluconate are less effective

J Hosp Infect. 2020 Feb 6. pii: S0195-6701(20)30046-3. doi: 10.1016/j.jhin.2020.01.022. [Epub ahead of print

# Case Definition PUI CDC 2/28

| Clinical Features | | Epidemiologic Risk |
|---|---|---|
| Fever[1] **or** signs/symptoms of lower respiratory illness (e.g., cough or shortness of breath) | **AND** | Any person, including healthcare personnel[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[5], within 14 days of symptom onset |
| Fever[1] with severe acute lower respiratory illness (e.g., pneumonia, ARDS (acute respiratory distress syndrome) requiring hospitalization and without an alternative explanatory diagnosis (e.g., influenza).[6] | **AND** | No identified source of exposure |

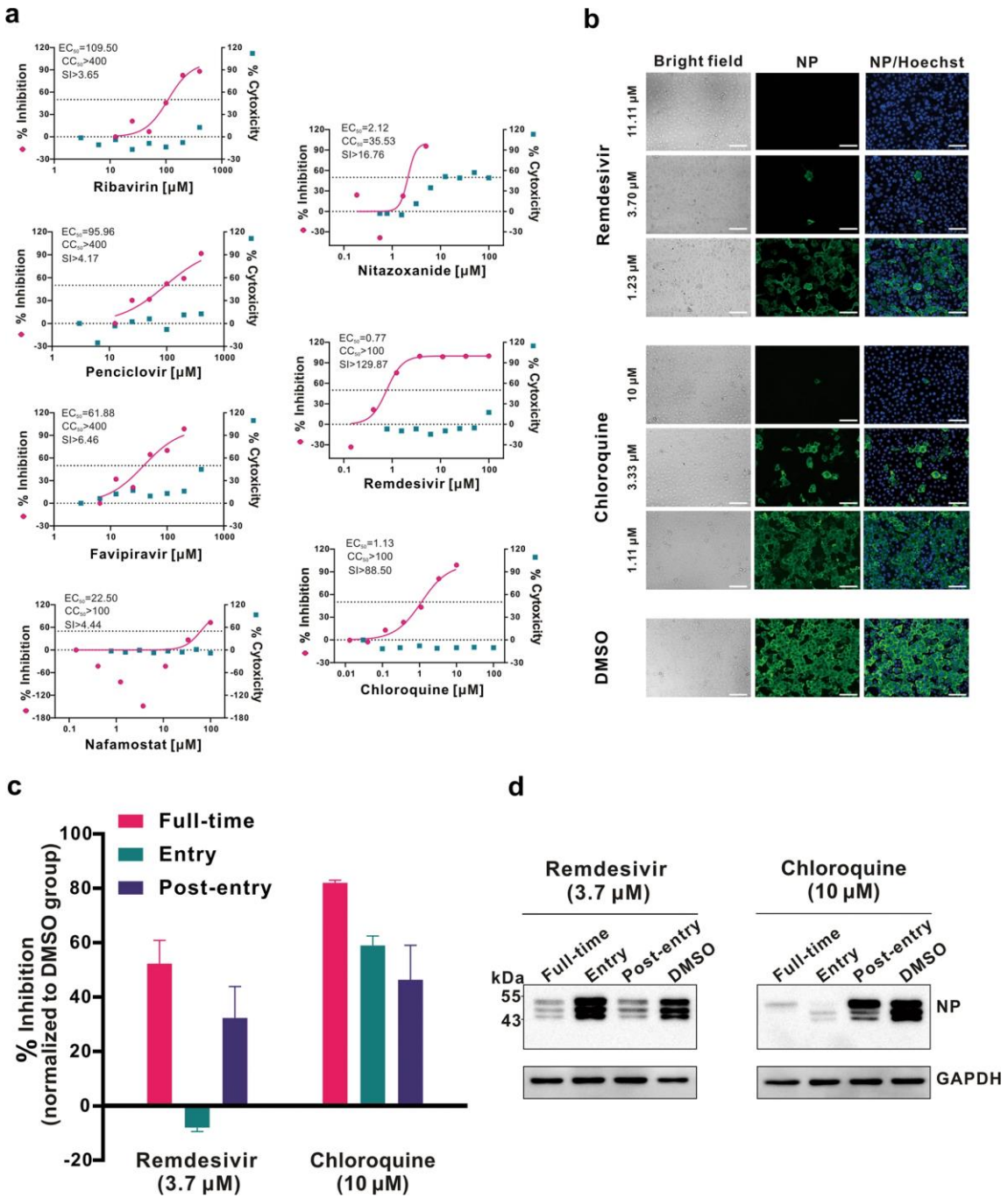
# Managing HCP Exposures – CDC Guidance 3/4/20

| Epidemiologic risk factors | Exposure category | Recommended Monitoring for COVID-19 *(until 14 days after last potential exposure)* | Work Restrictions for Asymptomatic HCP |
|---|---|---|---|
| **Prolonged close contact with a COVID-19 patient who was wearing a facemask (i.e., source control)** | | | |
| HCP PPE: None | Medium | Active | Exclude from work for 14 days after last exposure |
| HCP PPE: Not wearing a facemask or respirator | Medium | Active | Exclude from work for 14 days after last exposure |
| HCP PPE: Not wearing eye protection | Low | Self with delegated supervision | None |
| HCP PPE: Not wearing gown or gloves[a] | Low | Self with delegated supervision | None |
| HCP PPE: Wearing all recommended PPE (except wearing a facemask instead of a respirator) | Low | Self with delegated supervision | None |

# HCP Exposure – CDC Guidance 3/4/20

| Prolonged close contact with a COVID-19 patient who was not wearing a facemask (i.e., source control) | | | |
|---|---|---|---|
| HCP PPE: None | High | Active | Exclude from work for 14 days after last exposure |
| HCP PPE: Not wearing a facemask or respirator | High | Active | Exclude from work for 14 days after last exposure |
| HCP PPE: Not wearing eye protection[a] | Medium | Active | Exclude from work for 14 days after last exposure |
| HCP PPE: Not wearing gown or gloves[a,b] | Low | Self with delegated supervision | None |
| HCP PPE: Wearing all recommended PPE (except wearing a facemask instead of a respirator) [b] | Low | Self with delegated supervision | None |

# Potential Treatments for COVID-19

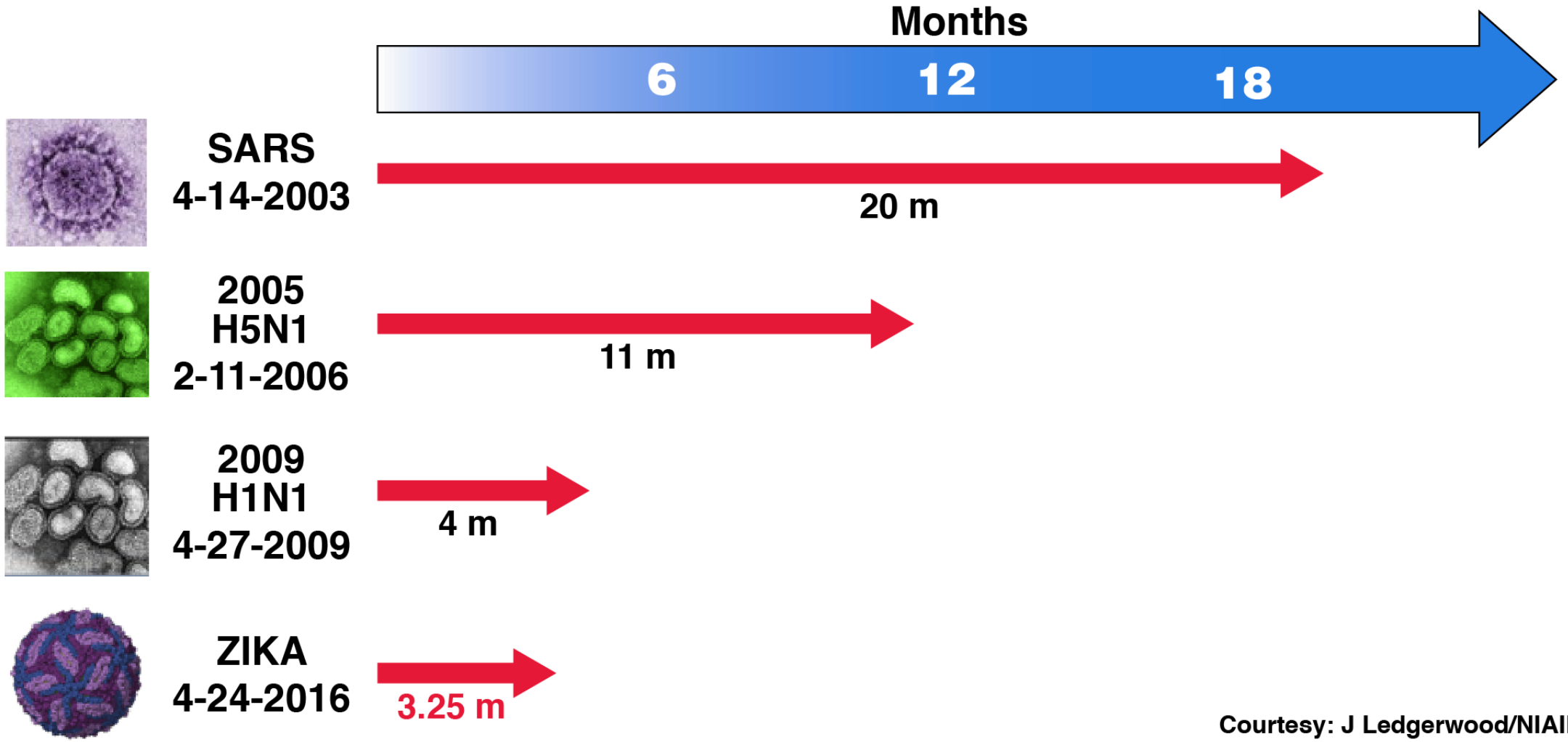


# Therapeutics for 2019 Novel Coronavirus (2019-nCoV)

- Antivirals and monoclonal antibodies (mAbs) are being tested
  - **Remdesivir**, which has shown promise against coronaviruses in animal models
  - **Kaletra (lopinavir/ritonavir)** and **interferon-beta** which have been used investigationally for other coronaviruses
  - Other **broad-spectrum antivirals**
  - **Drug screening and targeted drug design**
  - **Monoclonal antibodies being isolated and tested**

# VRC DNA Vaccines for Emerging Infections

## Sequence Selection to 1st Human Injection




Courtesy: J Ledgerwood/NIAID VRC

# No Joking Matter?

- Best to avoid “joking” with our colleagues of Asian descent
  - “Hey, did you bring coronavirus with you”
  - “Don’t get me sick”
  - Etc.

# Summary

- What do we know about COVID-2019?
  - We are likely to see cases in our facility
  - Healthcare workers at risk
  - Sick leave policy for staff may require temporary amendment
  - Superspreaders appear to play a role; unclear how large
  - Close contact key to spread
  - Focal geographic distribution so far
  - Notable that severity/CFR is seemingly significantly greater in some settings than others

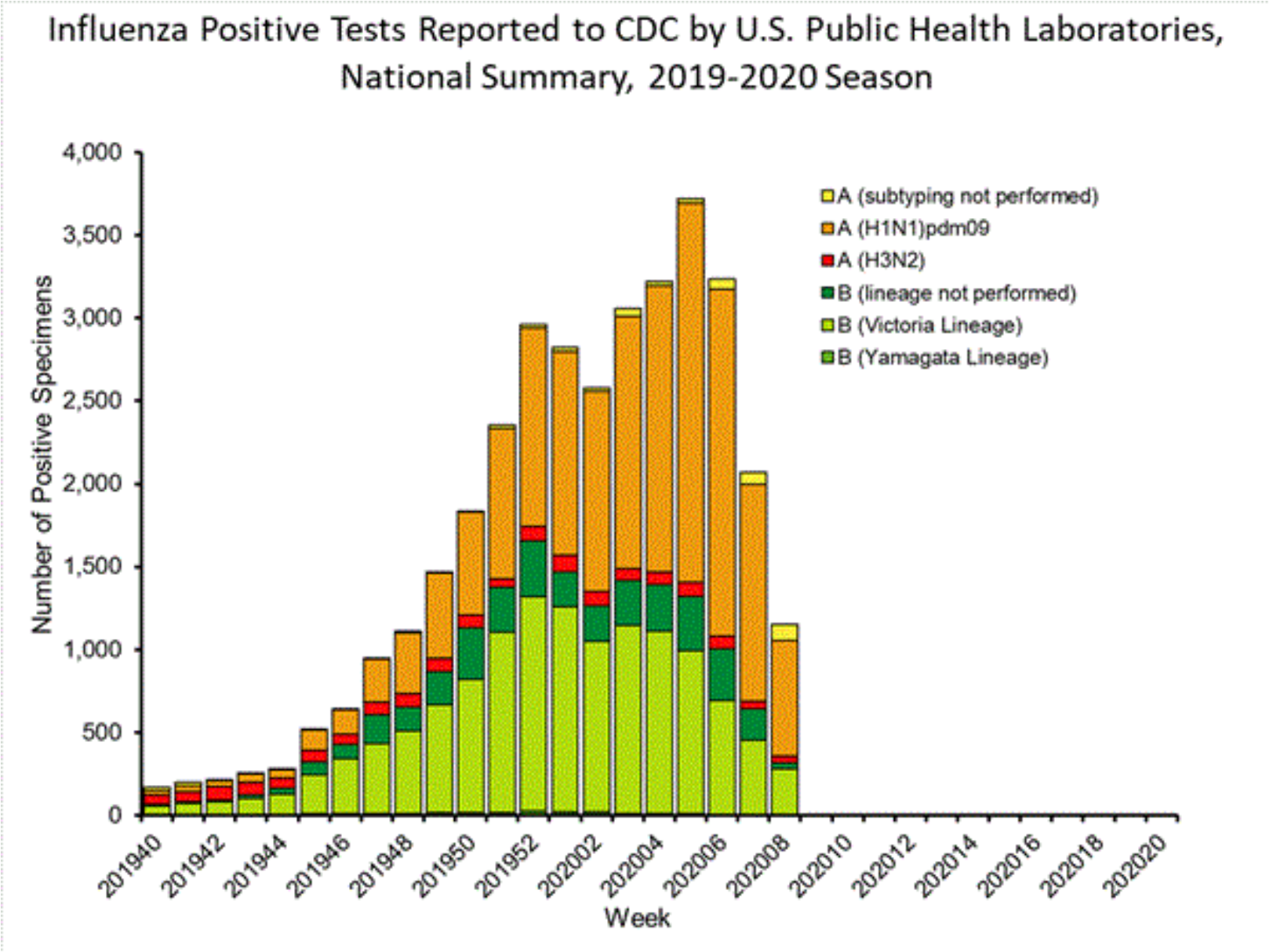
# Summary

- CT imaging important for identifying infiltrates
- Children not ill enough to present for medical care
- Seems plausible that sicker patients are producing greater quantity of virus; if so, exposure to a sicker patient may be more likely to create other sicker patients (speculative)
- Plan for:
  - Many patients with symptoms AND
  - Not enough of anything (lab tests, masks, beds)

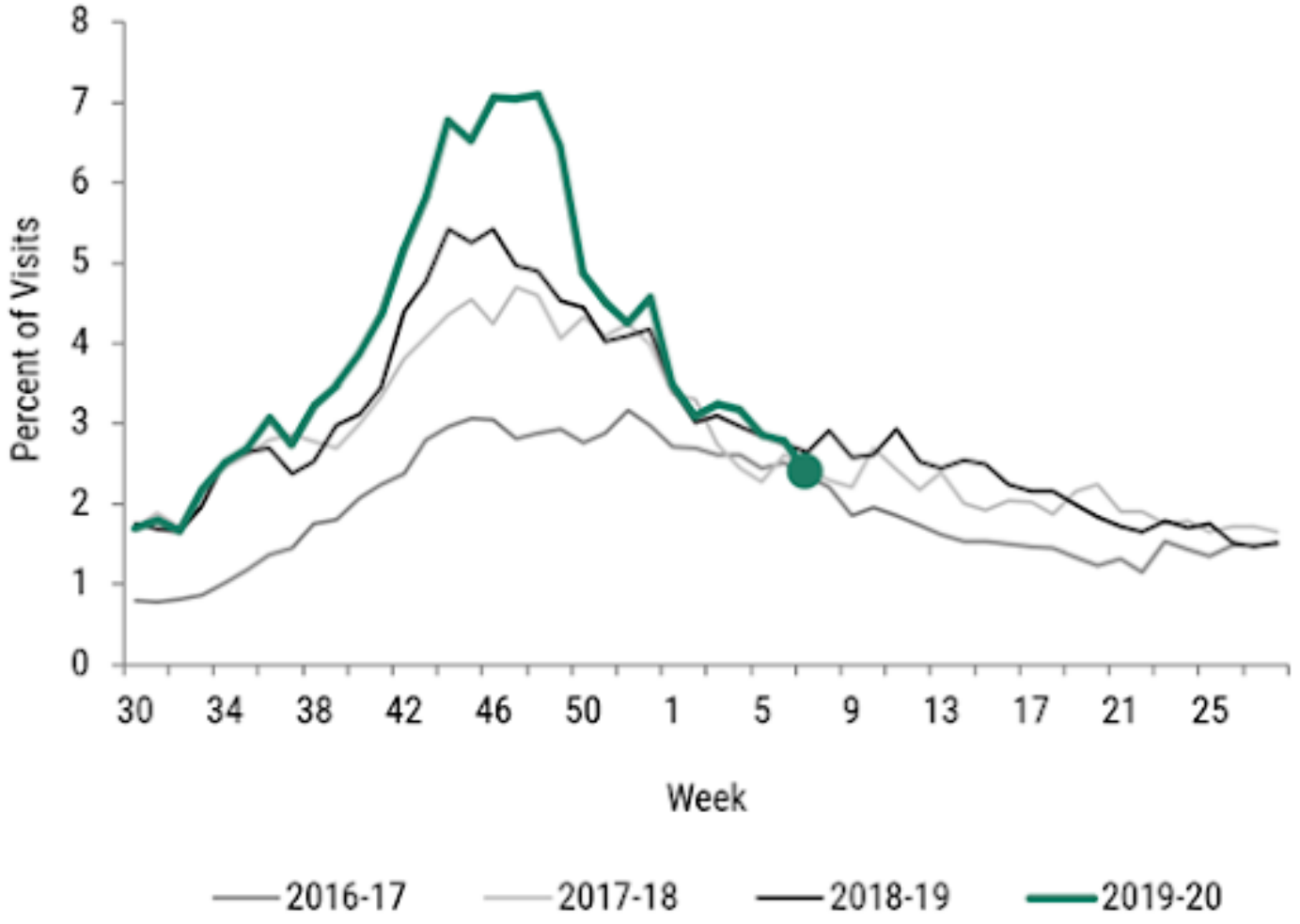
# Thank you!

# Additional Slides

# Flu activity dropping



# RSV activity likely dropping



# Various $R_0$ Comparisons

| Disease | Transmission | $R_0$ |
|---|---|---|
| Measles | Airborne | 12–18 |
| Diphtheria | Droplet/fomite | 6–7 |
| Smallpox | Droplet | 5–7 |
| Polio | Fecal–oral | 5–7 |
| Rubella | Droplet | 5–7 |
| Mumps | Droplet | 4–7 |
| Seasonal Influenza | Droplet | 1.3 |
| HIV/AIDS | Sexual contact | 2–5 |
| SARS | Droplet/airborne | 3 |
| COVID-2019 | Droplet | 2.2 |
| Influenza (1918 pandemic strain) | Droplet | 1.4–2.8 |
| pH1N1 Influenza | Droplet | 1.4–1.6 |
| Chickenpox | Airborne/contact | 5 |