COVID-19 (2019 nCo-V)

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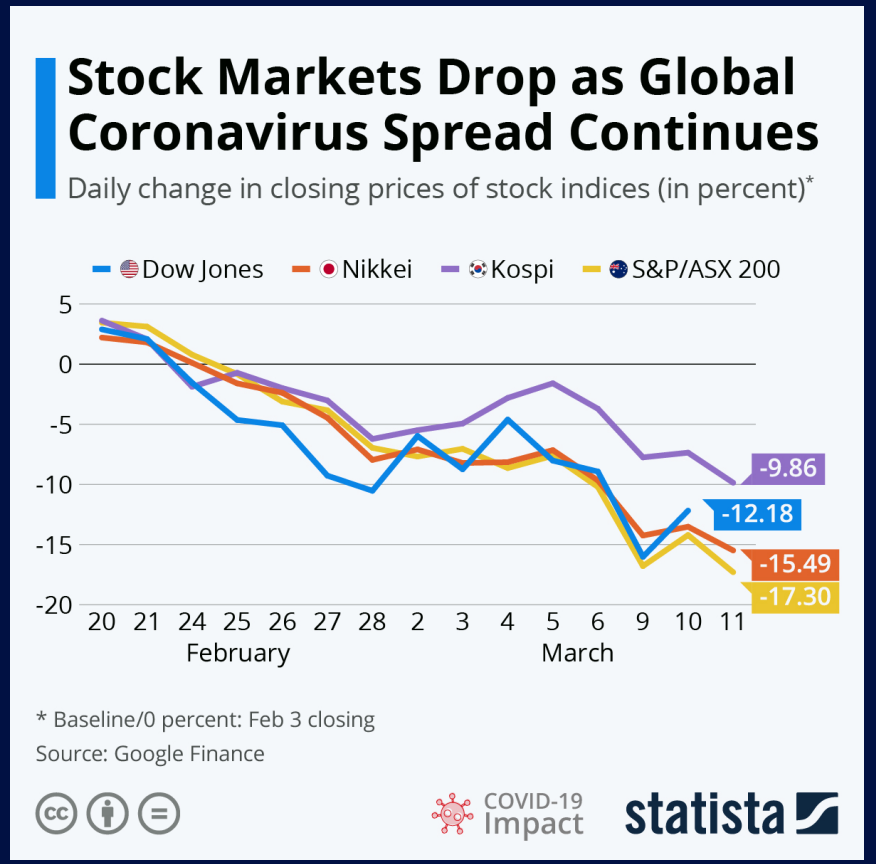
COVID-19: SITUATION UPDATE

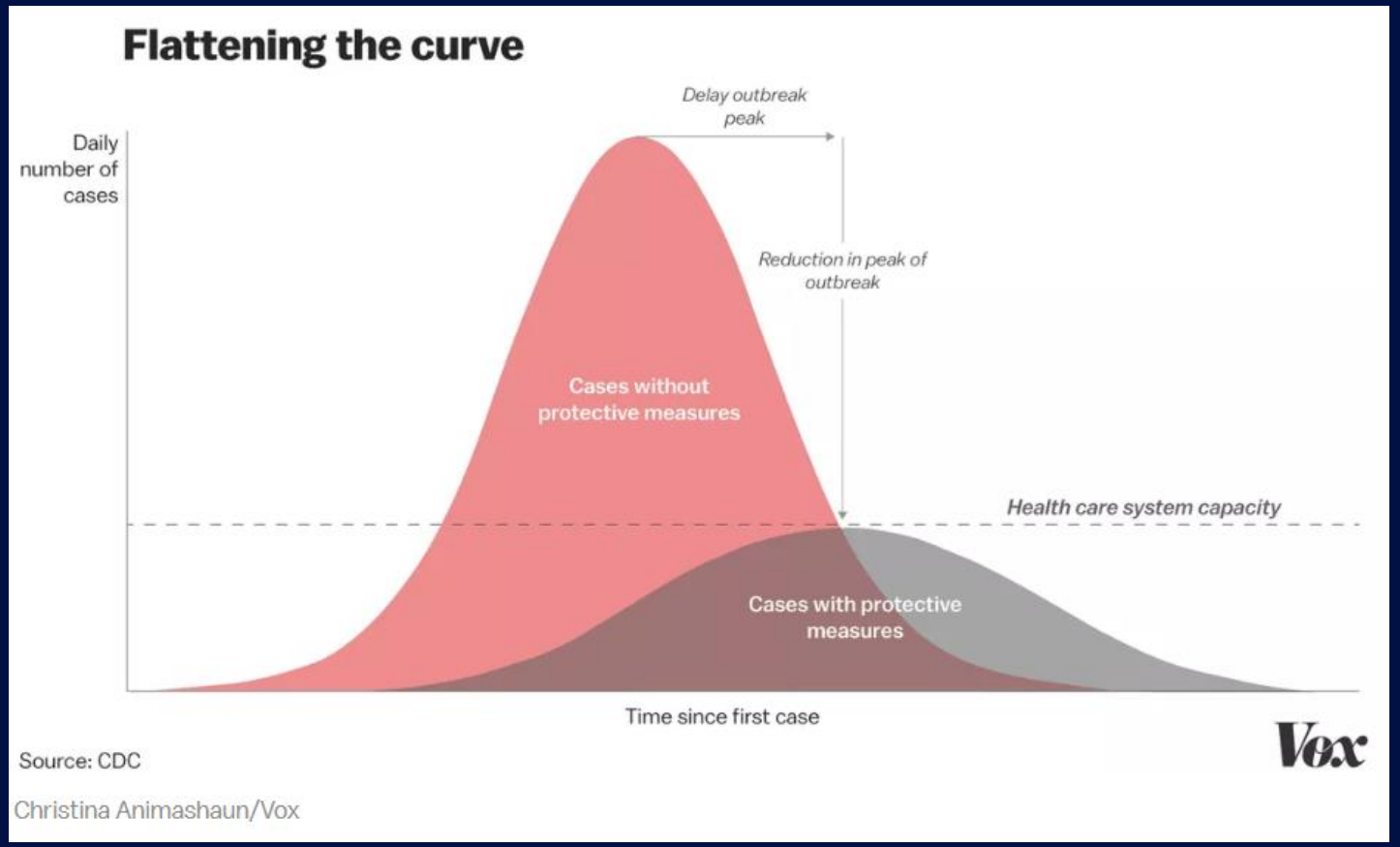
- Cases: Global: >114,400 (>4,000 deaths), >100 countries with cases
  - China: ~80,000 (>2,500 deaths); number of cases/day decreasing
  - Outside China: Rapidly increasing prevalence and geographical spread; Cases (deaths): Italy, >12,500 (827 deaths); South Korea, 7,900 (66); Iran, ~10,000 (429); France, 2,281 (48); Spain, 2,277 (55), Germany, 1,966 (3)
  - US: 1,336 (38 deaths): 44 states have cases; community acquisition in multiple states; outbreaks in nursing home, cruise ship (off SF), hotel (Biogen, Boston); synagogue (NYC), multiple universities have moved to virtual learning
  - NC (n=12): Multiple cases in the triangle area, all have known source of acquisition?
- No evidence for airborne transmission or intrauterine transmission; concern for transmission from asymptomatic persons and/or from aerosolization of feces (neither yet substantiated)
- Transmission rate, ~3; Super-spreaders reported (i.e., transmission from a case to >10 person)
- Mortality rate: ~1-2% of all infected persons; case-fatality rate if hospitalized, ~15%
- CDC Warnings: Level 3 (avoid all non-essential travel), China, Iran, South Korea, Italy; Level 2 (practice enhanced precautions), Japan; Level 1 (practice usual precautions), Hong Kong – Largely irrelevant at present, since CDC not updating CDC warnings
- U.S. State Dept: Level 4 (do not travel) for all of China, Iran; Level 3 (reconsider travel) for South Korea, Italy; Level 2 (exercise increased caution) for Hong Kong, Macau, Japan

COVID-19: SITUATION UPDATE

- Worldwide
  - WHO declared COVID-19 a pandemic (i.e., sustained transmission in >1 continent)
  - Dramatic increases of cases in Europe
- US
  - US outbreak curve similar to European countries with ~2 week lag
  - Stock market has plunged
  - Ban on flights from Europe for 30 days beginning Friday
  - NBA season cancelled as one played has developed COVID
- NC
  - Increasing numbers of case
  - Governor has declared State of Emergency
  - UNC has extended Spring Break – likely to move to distance learning
- UNC Hospitals
  - Task forces working on ambulatory and inpatient plans
  - Maintaining staffing



GOAL OF SOCIAL DISTANCING



KEY CONSIDERATIONS IN ASSESSING AND MANAGING THE THREAT OF AN EMERGING INFECTIOUS DISEASE

- Pathogen
  - Taxonomy (provides clues regarding transmission routes, environmental stability, germicide susceptibility)
  - Hosts
- Epidemiology
  - Locations of endemicity (i.e., locations in the world where sources or reservoirs reside)
  - Incubation period
  - Transmission routes
  - Infectivity (i.e., communicability)
  - Duration of infectivity
- Clinical
  - Symptoms
  - Signs
  - Risk factors for acquisition of infection
  - Morbidity
  - Mortality
  - Risk factors for morbidity and mortality
  - Diagnostic methods (sensitivity, specificity, biosafety)
  - Therapy (availability, efficacy, safety)

Weber DJ, et al. Am J Infect Control 2016;44:e91-100

KEY CONSIDERATIONS IN ASSESSING AND MANAGING THE THREAT OF AN EMERGING INFECTIOUS DISEASE

- Infection control
  - Environmental survival
  - Germicide susceptibility
  - UV susceptibility
  - Isolation recommendations
  - Recommended personal protective equipment
  - Pre-exposure prophylaxis (availability, efficacy, safety)
  - Post-exposure prophylaxis (availability, efficacy, safety)
  - Recommended biosafety level in the laboratory
  - Recommended waste disposal (liquids and solids)

Weber DJ, et al. Am J Infect Control 2016;44:e91-100

nCo-V, WHAT WE KNOW

- nCo-V is a novel coronavirus with ~75% homology by sequencing to SARS-CoV
- Initial cases likely represented animal-to-human transmission (likely reservoir is bats)
- Rapidly increasing prevalence and geographical spread: Number of cases and deaths has greatly surpassed SARS
- Transmission droplet/contact (therefore being ultra-cautious use airborne and contact precautions plus eye protection)
  - Infectivity 2.2-2.8 (i.e., each person with nCo-V, on average infects 2.2 to 2.8 other people)
  - High attack rate in confined quarters (e.g., cruise ship in Japan; 696 of 3,600 {19% AR} passengers and crew)
- Super-spreaders reported (i.e., transmission from a case to >10 persons)
  - A UK citizen who acquired nCo-V in Singapore transmitted infection to >10 persons (i.e., a super-spreader)
- Substantial numbers of healthcare personnel (HCP) infected: 1,700 infected in China
  - Of 139 hospitalized patients in Wuhan, 57 (41.3%) presumed infected in a hospital, including 17 patients (12.3%) already hospitalized for other reasons and 40 HCP (29%) (Wang D, et al. JAMA 2020 {In press})
- Based on other coronaviruses: Any FDA-approved antiseptic will inactivate nCo-V and any EPA-registered disinfectant with a coronavirus claim will inactivate nCo-V

*https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/news--wuhan-coronavirus/

nCo-V, WHAT WE KNOW

- Symptoms are typical of a respiratory tract infection: Fever, cough, shortness of breath (fever may be absent)
  - 80% mild disease, 20% more severe disease requiring hospitalization
  - Older adults and person with co-morbidities may be at higher risk for severe disease
  - nCo-V can cause severe disease (~20% of hospitalized patients with require mechanical ventilation)
  - Some patients may present with GI symptoms (i.e., nausea, vomiting and diarrhea)
- CDC sent out defective diagnostic test kits to >25 countries and US health departments
- Economic consequences include a shortage of PPE (masks), increases price of basic commodities (e.g., food) in hardest hit areas of China, and closure of some factories outside of China that use Chinese parts); drop in the price of oil

nCo-V, WHAT WE DO NOT KNOW

- Transmission: Unknown whether virus can be transmitted by the airborne route (i.e., >6 feet) or by indirect contact (likely based on SARS –CoV and MERS-CoV)
- What parameters to use to assess risk of travel in the US
- Morbidity and mortality (biases could result in under or over estimates)
- CDC states “Asymptomatic infection with 2019-nCoV has been reported, but it is not yet known what role asymptomatic infection plays in transmission. Similarly, the role of pre-symptomatic transmission (infection detection during the incubation period prior to illness onset) is unknown” (https://www.cdc.gov/coronavirus/2019-ncov/hcp/faq.html)
- Frequency of super-spreaders
- When the outbreak will peak and number of countries that will be affected
- Impact of the outbreak and travel curtailment on supply chain of goods and supplies
- Method of acquisition by HCP: (1) in community, (2) failure to promptly identify and isolate cases in the healthcare facility, (3) adequate PPE, (4) improper donning and doffing of PPE, or (5) failure of properly donned and doffed PPE

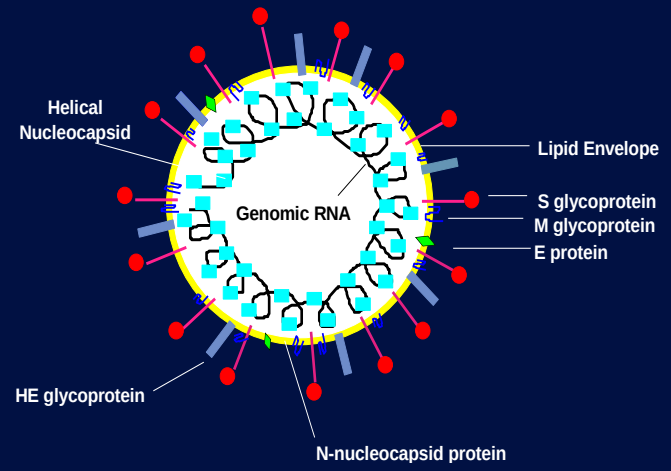
POSSIBLE TRANSMISSION OF COVID-19 FROM ASYMPTOMATIC OR PRE-SYMPTOMATIC PATIENTS

- A 10 year old male tested positive for COVID-19 but had no symptoms: patient had visible changes in lung imaging and blood markers of disease. (Chan JF-W. Lancet 2020; 24 January)
- A patient in Wuhan is said to have infected 14 HCP prior to fever onset. (China National Health Commission)
- A medical expert exhibited conjunctivitis of the his left eye before appearance of catarrhal symptoms and fever "suggesting that having the patient wear a mask might not prevent transmission." (South China Morning Post)
- A patient who travelled from Shanghai to attend a meeting in Germany was subclinical until on the flight back to China. However, two of this patient's close contacts and another two patients attending the meeting without close contact were found to be infected with COVID-19 (Rothe C, et al. NEJM 2002; 30 Jan)
- Conclusion: The reports are suggestive but not definitive for transmission from asymptomatic or pre-symptomatic patients.

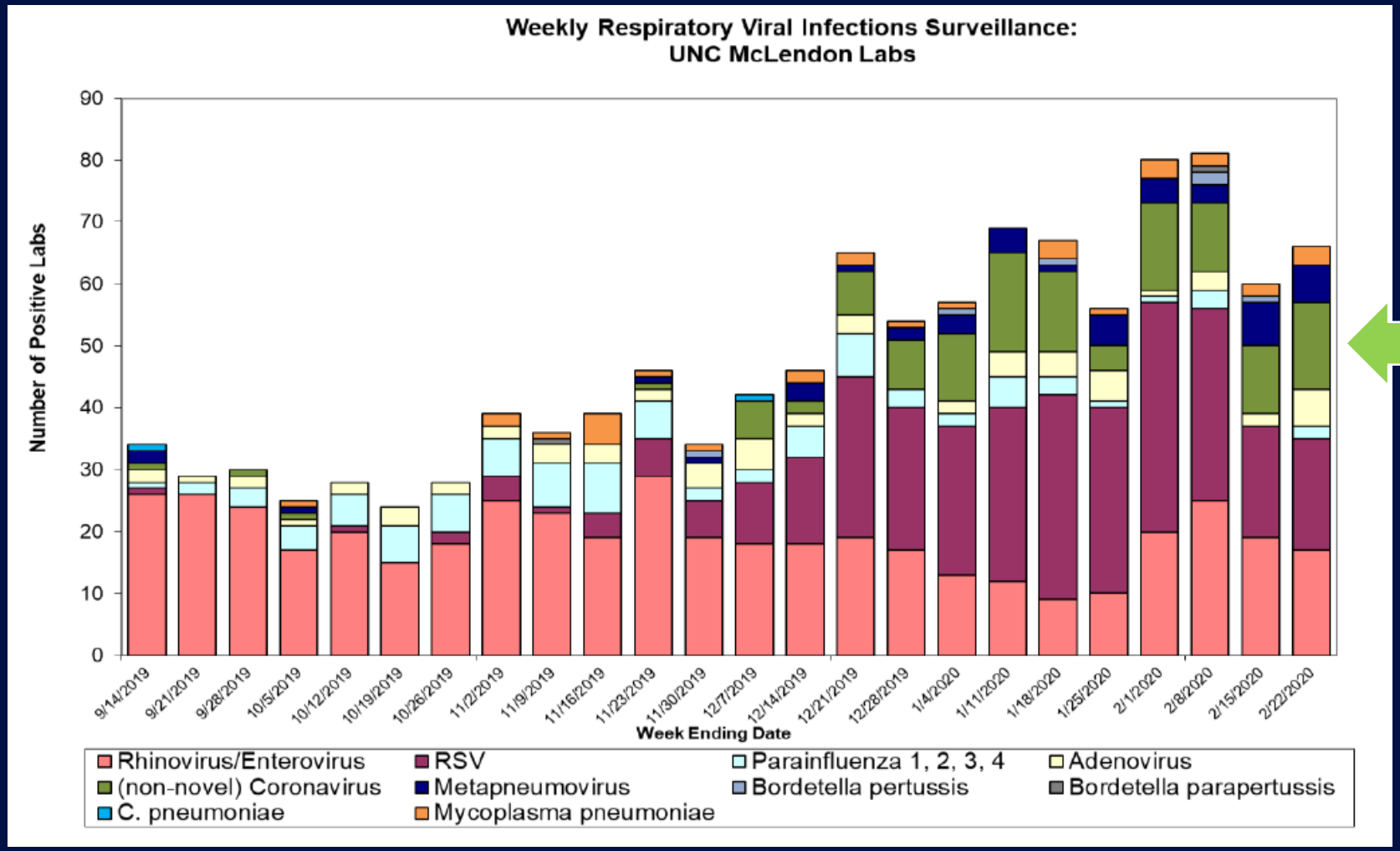
De Chang, et al. Lancet Respir Med 2020;13 February

CORONAVIRUSES

- Single-stranded, linear, positive-sense RNA, enveloped virus, 120-160 nm
- Reservoirs: Humans, multiple animal species, bats
- Epidemiology: Worldwide; winter and spring in temperate climate
- Syndromes
  - Common colds: Account cause of upper respiratory tract infections
  - Lower tract infections in immunocompromised individuals and older adults
  - Gastroenteritis
  - Epidemic coronaviruses: SARS, MERS, COVID-19 (nCo-V-19)



NON-NOVEL CORONAVIRUSES AS A CAUSE OF RESPIRATORY TRACT INFECTIONS



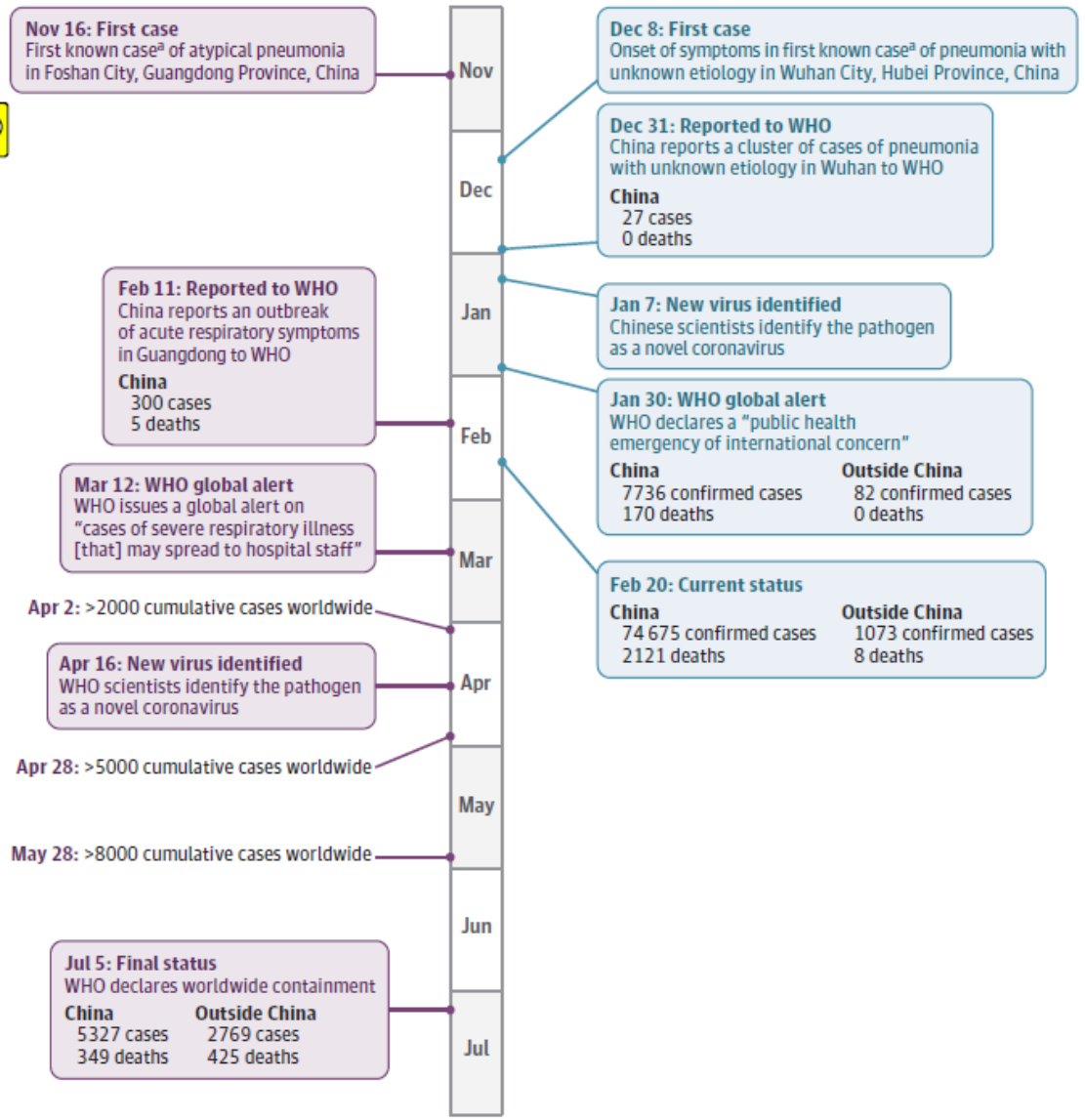
UPDATE ON NEWLY DISCOVERED CORONAVIRUS

	SARS CoV	MERS CoV	2019 nCo-V (COVID-19)
Virion Structure	Enveloped RNA virus	Enveloped RNA virus	Enveloped RNA virus
Outbreak period	2003-2004	2012-present	2019-present
Initial site of isolation	Guangdong province, China	Saudi Arabia	Wuhan, China
No. of countries with cases	29	27	>100 countries
No. of cases (mortality)	8,096 (9.6%)	2,494 (~34%)	>114,000 (>4,000)
No. of cases U.S. (deaths)	8	2 (2014)	>500 (~25)
Reservoir (intermediate host)	Bats (palm civet)	Bats (dromedary camels)	Unknown (likely a zoonosis)
Incubation period	2-7 days (range, 2-21)	2-7 (range, 2-14 days)	2-7 days (range, 2-14 days)
Infectivity, rho; attack rate	2.2-3.7 (range, 0.3-4.1); 10-60%	0.3-1.3; 4-20%	Average, 3.28; median, 2.79
Super spreaders	Yes	Yes (uncommon)	Yes (? frequency)
Asymptomatic/Pre-sx	No	Rare	Perhaps yes
Transmission (including to HCP)	Droplet/Direct, Airborne/Indirect?	Droplet/Direct, Airborne/Indirect?	Droplet/Direct; Airborne/Indirect?
Treatment (PEP)	Supportive (none)	Supportive (none)	Supportive (none)
Infection Prevention*	Airborne, contact, face shield	Airborne, contact, face shield	Airborne, contact, face shield

*PAPR or N95 respirator for cough-inducing procedures;

Weber DJ, et al. Am J Infect Control 2016;44:e91-100

Figure 2. Timeline Comparing the Severe Acute Respiratory Syndrome (SARS) and Coronavirus Disease 2019 (COVID-19) Outbreaks



The timeline of events for the SARS outbreak (left) from first case to final worldwide containment. The timeline of events for the COVID-19 outbreak (right) from the onset of symptoms for the first case on December 8, 2019, to status on February 20, 2020. Over the course of the first 2 months, more than 70 000 cases have been confirmed and many more are suspected. WHO indicates World Health Organization.

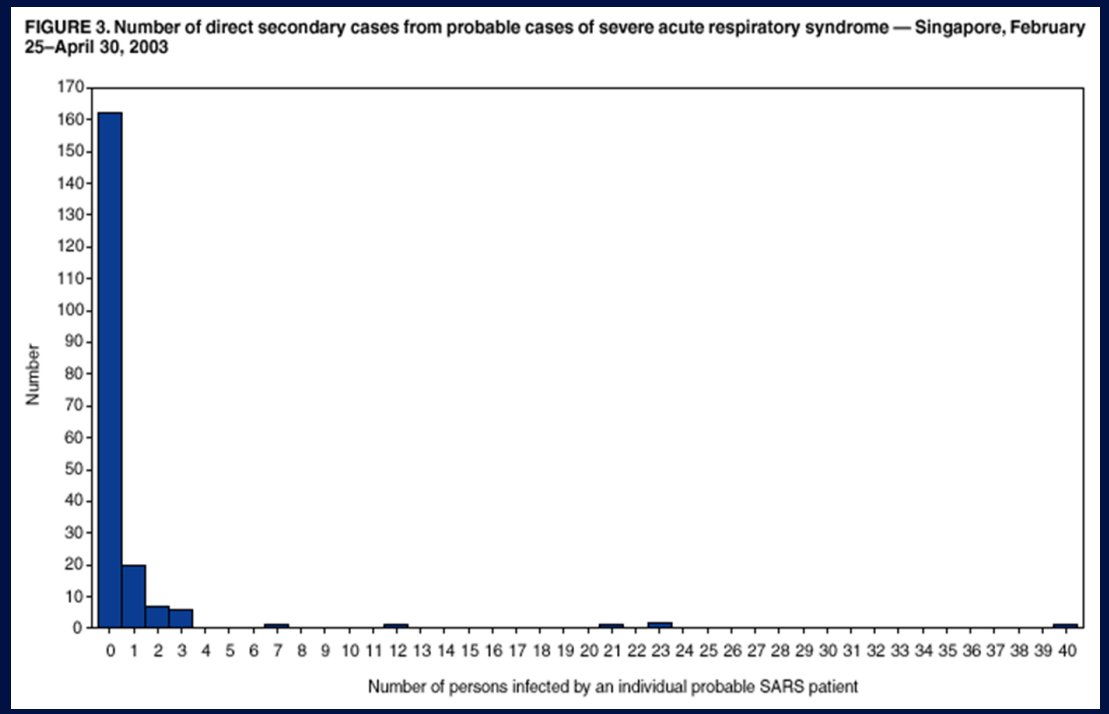
[a] Identified later retrospectively.

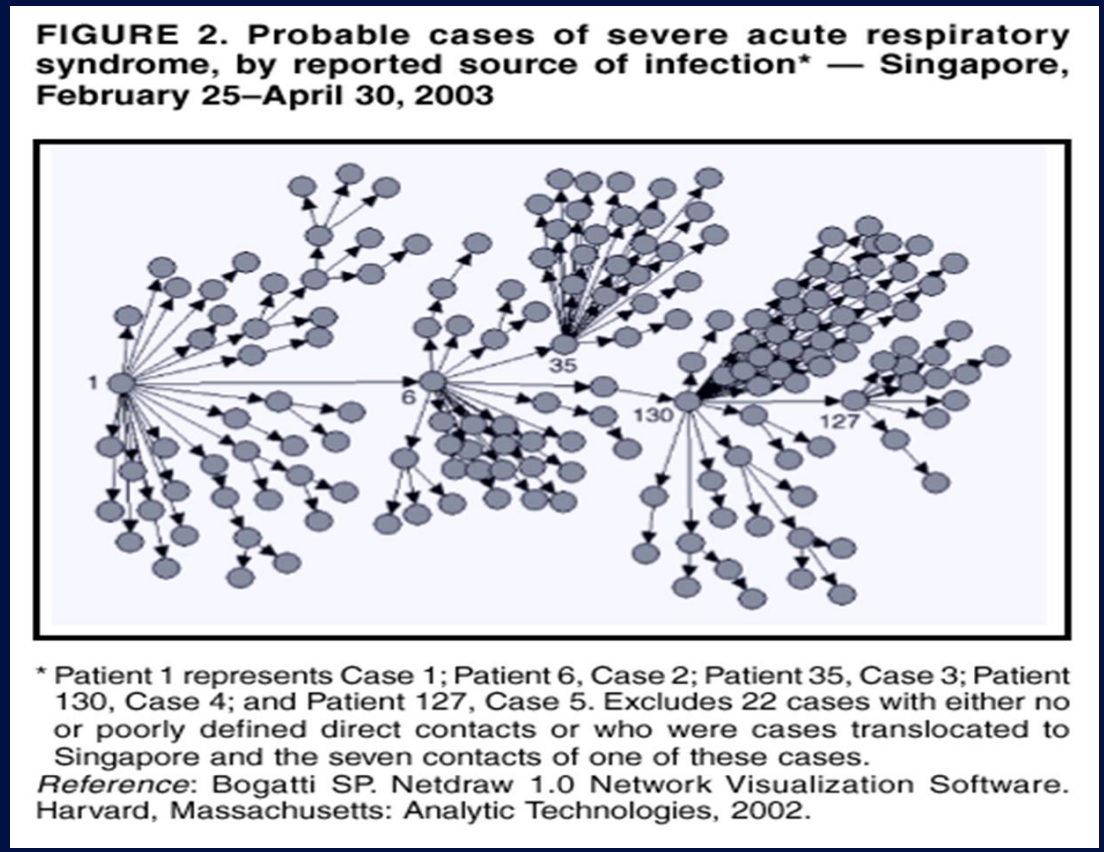
Wu Z, McGoogan JM
JAMA 2020;24 February

LESSONS LEARNED FROM SARS

- Initial detection via the astute observer (not via a surveillance system)
- A new or emerging infectious disease can involve multiple countries
- Continued threat from zoonotic agents jumping species boundaries
- Healthcare personnel at high risk with highly communicable diseases (~20% of cases and deaths)
- Diagnostic methods key to control
- Epidemics can be contained using quarantine and infection control methods
- Need to nestle response to a highly communicable disease in hospital disaster plan
- Inadequate supplies of personal protective equipment (PPE)
- Inadequate outpatient facilities to handle large numbers highly communicable diseases
- Need to screen for travel to endemic area at entry to hospital or clinic

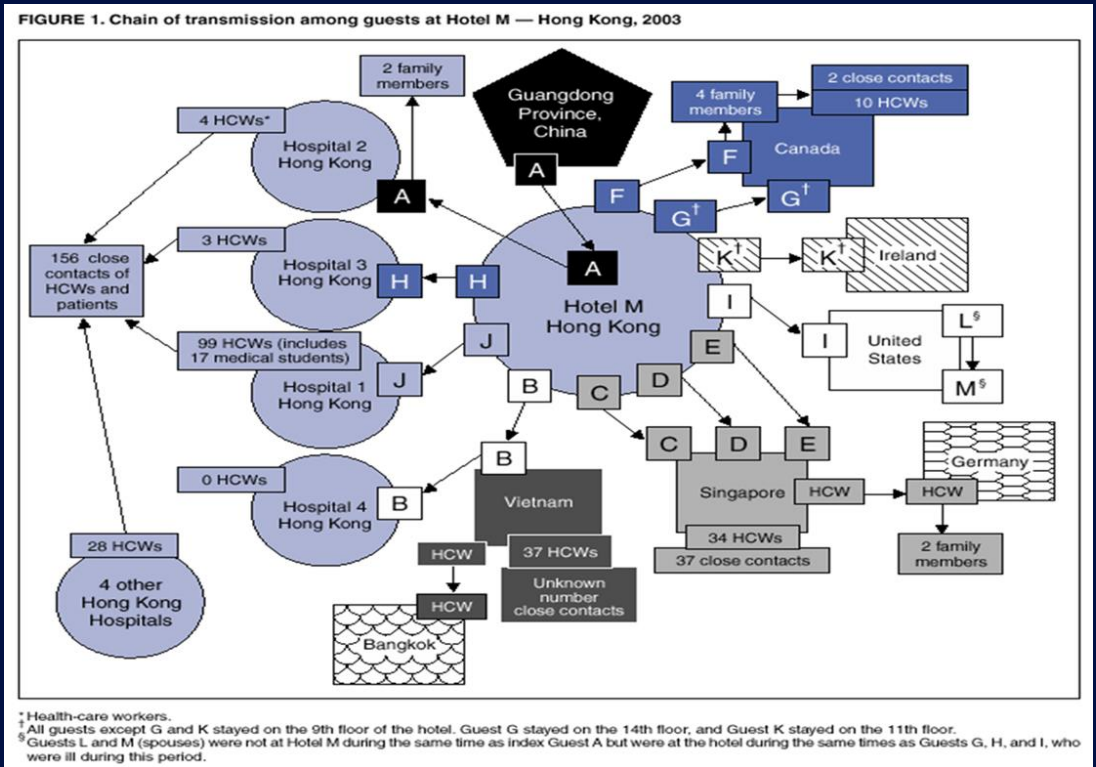
WHAT IS A SUPERSPREADER?
(A person with transmits infection to >10 persons)

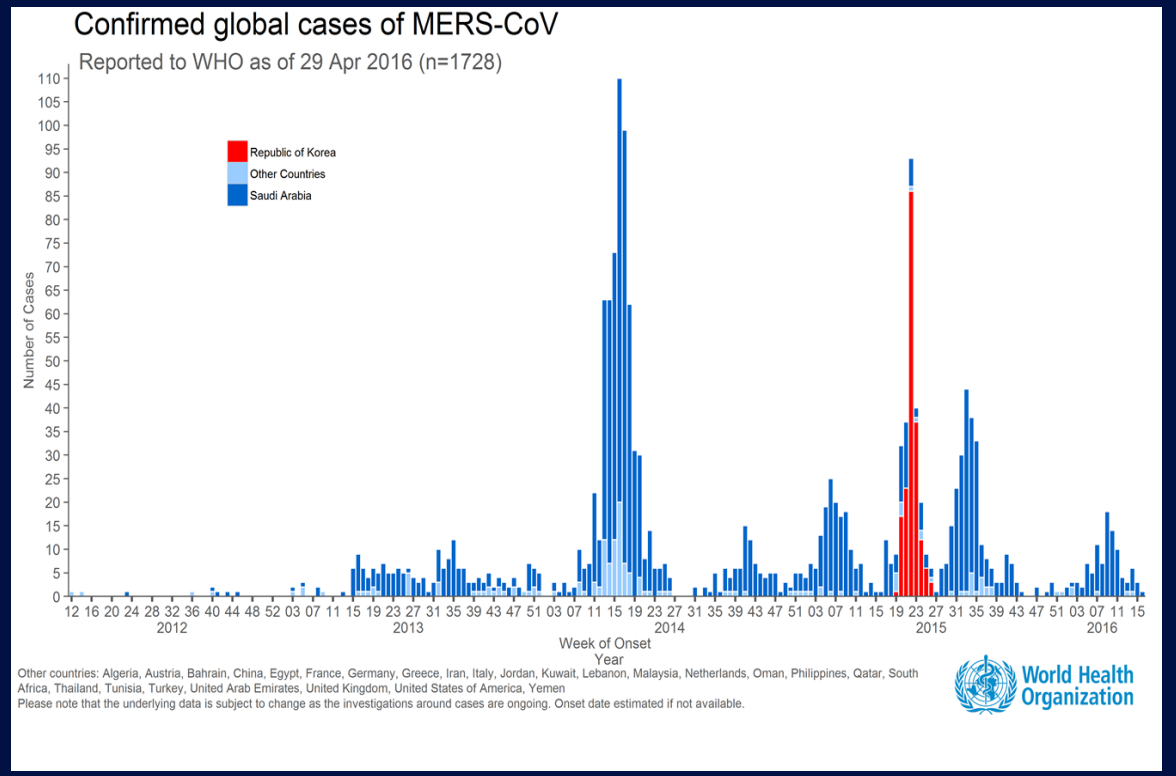




Infectivity of SARS and demonstration of superspreaders

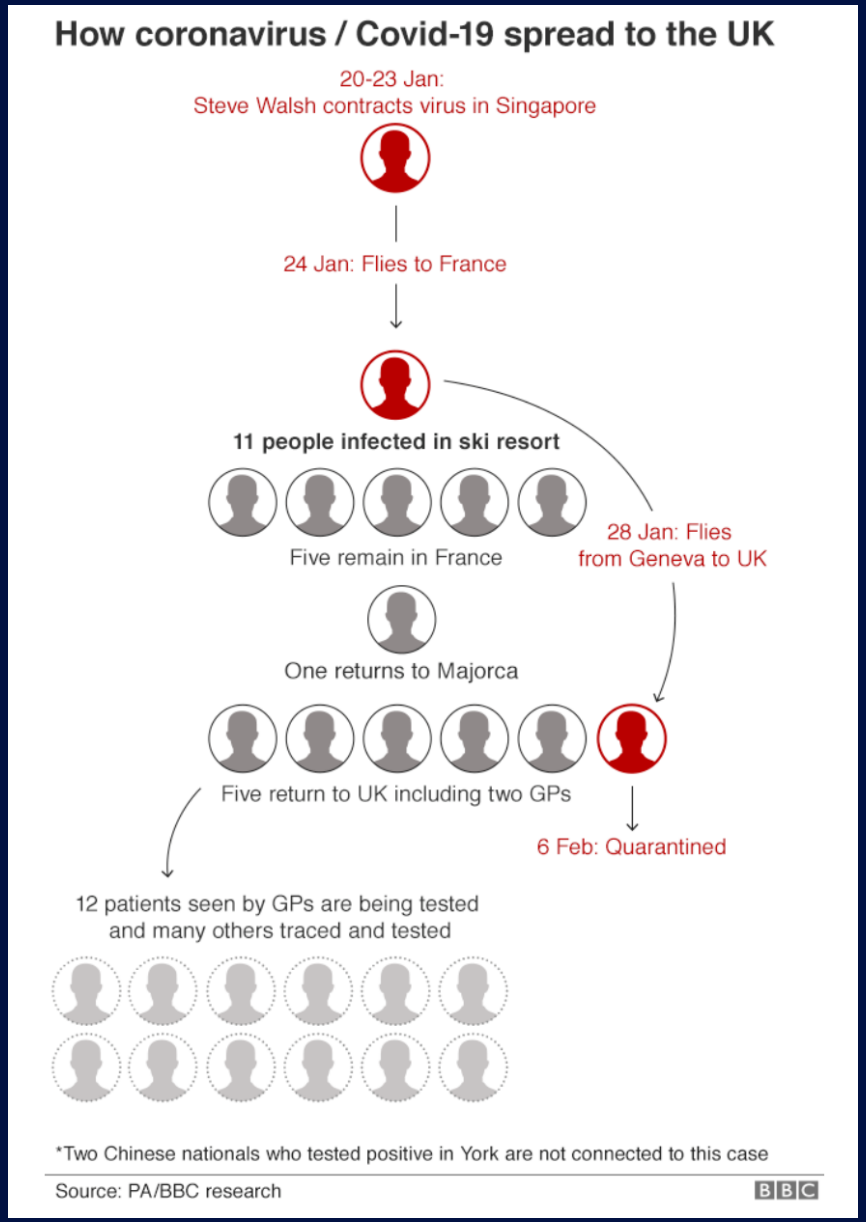
IMPACT OF A SINGLE SUPERSPEADER





A single infected physician who traveled to Hong Kong led to worldwide transmission of SARS

A single traveler to Republic of Korea led to an outbreak in that country



COVID-19 SUPERSPREADER

https://www.bbc.com/news/world-51235105

LATEST ESTIMATES FOR Ro

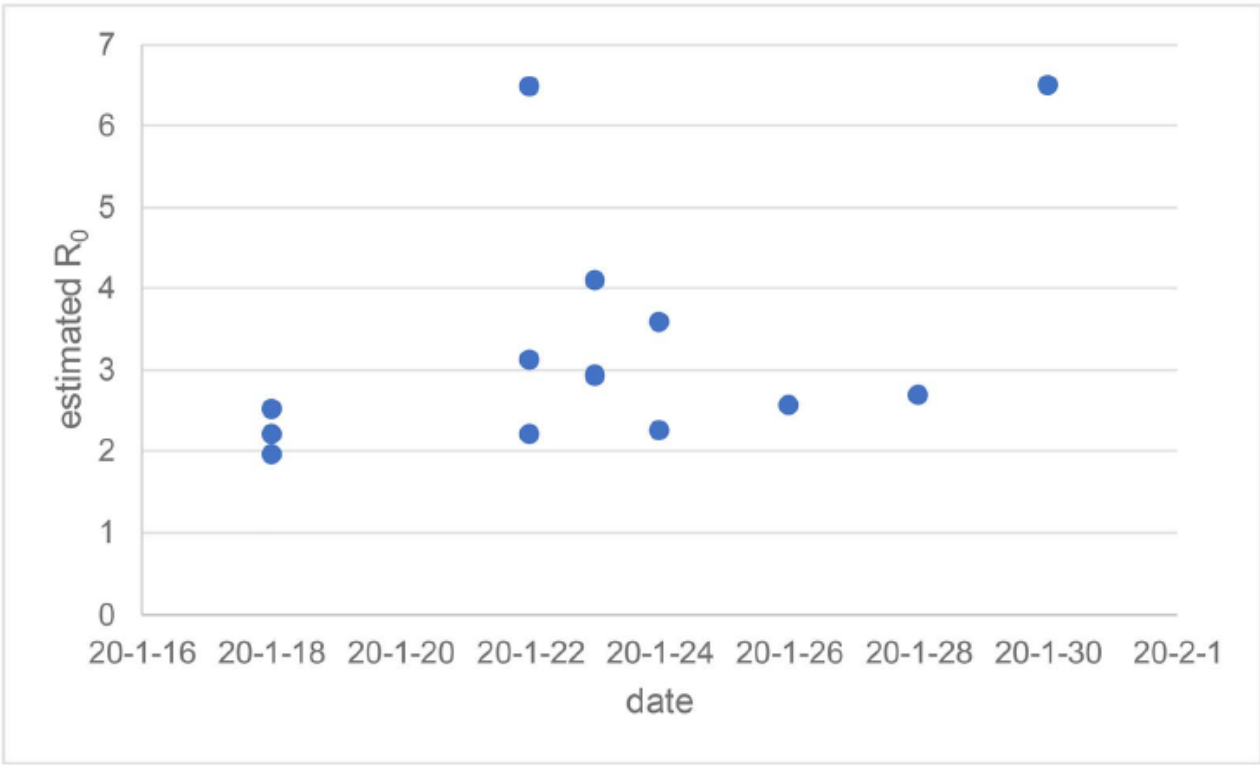


Figure 1. Timeline of the R_0 estimates for the 2019-nCoV virus in China

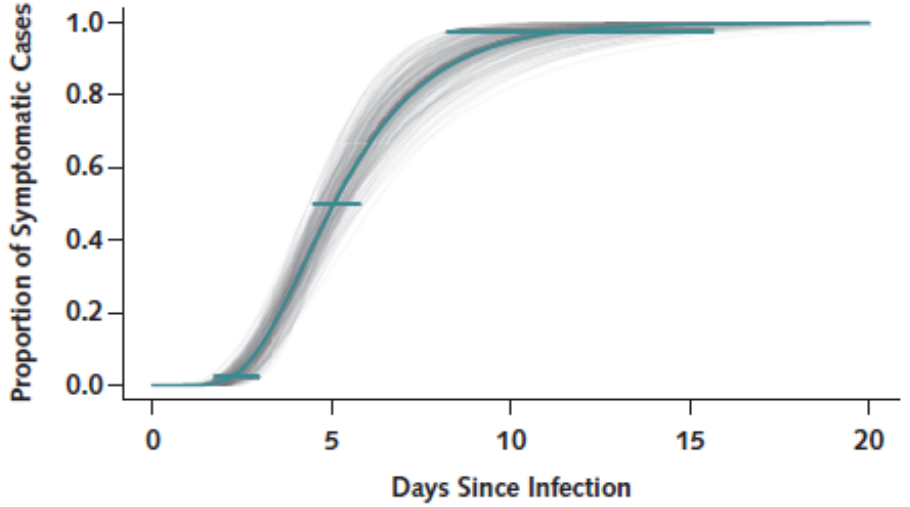
Liu Y, et al. J Travel Med 2020;1-4 (Epub)

COVID-19 INCUBATION PERIOD

- Goal: Estimate incubation period
- Date: 181 cases; obtained from news reports and press releases
- Results:
  - Median = 5.1 days (95% CI, 4.5-5.8)
  - 97.5% within 11.5 days
  - ~1% after 14 days
- Comments
  - Modeling used to estimate some parameters
  - Data not based on actual observations
  - Model assumes constant risk for infection

Lauer S, et al. Ann Intern Med 2020

Figure 2. Cumulative distribution function of the COVID-19 incubation period estimate from the log-normal model.



The estimated median incubation period of COVID-19 was 5.1 days (CI, 4.5 to 5.8 days). We estimated that fewer than 2.5% of infected persons will display symptoms within 2.2 days (CI, 1.8 to 2.9 days) of exposure, whereas symptom onset will occur within 11.5 days (CI, 8.2 to 15.6 days) for 97.5% of infected persons. Horizontal bars represent the 95% CIs of the 2.5th, 50th, and 97.5th percentiles of the incubation period distribution. The estimate of the dispersion parameter is 1.52 (CI, 1.32 to 1.72). COVID-19 = coronavirus disease 2019.

COVID-19: SUMMARY

Coronavirus Cases:

127,810

view by country

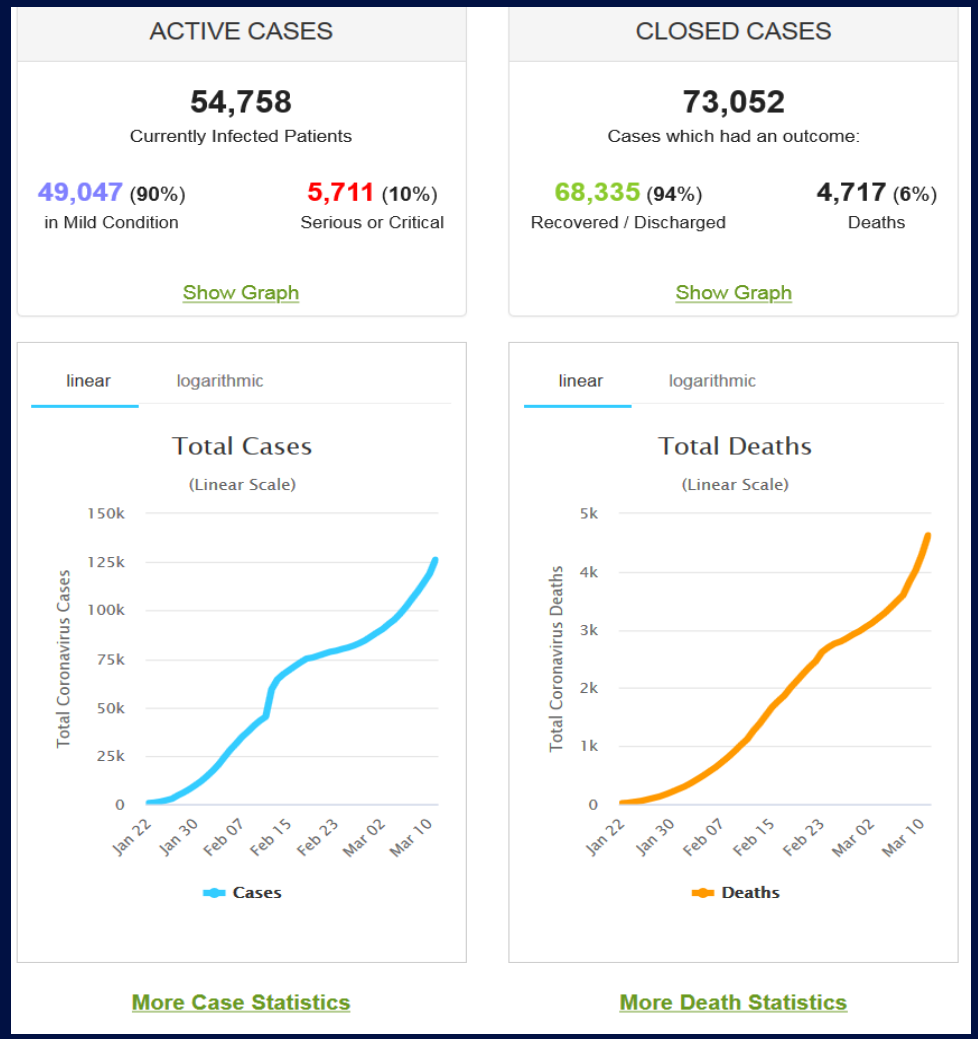
Deaths:

4,717

Recovered:

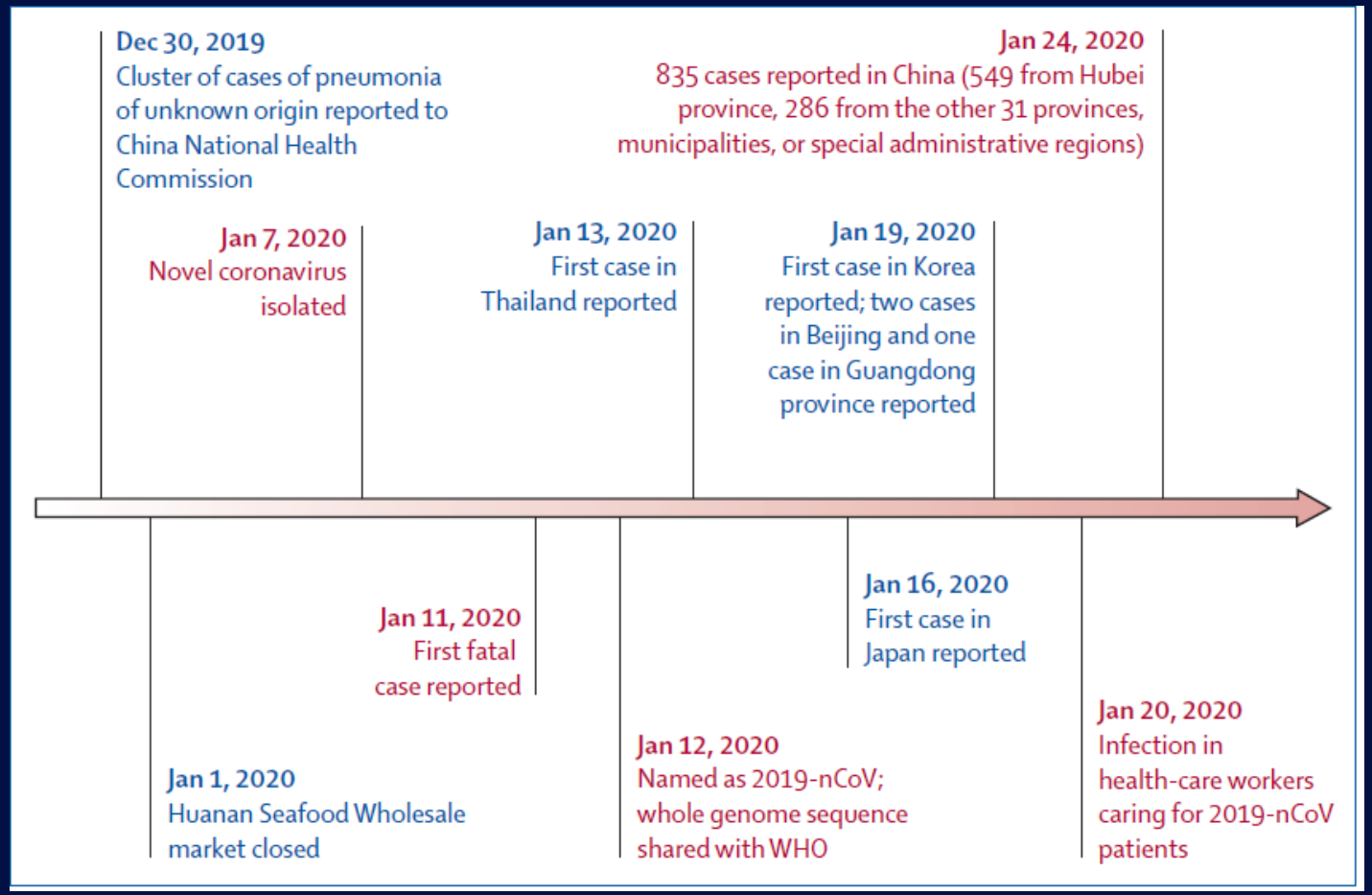
68,335

https://www.worldometers.info/coronavirus/



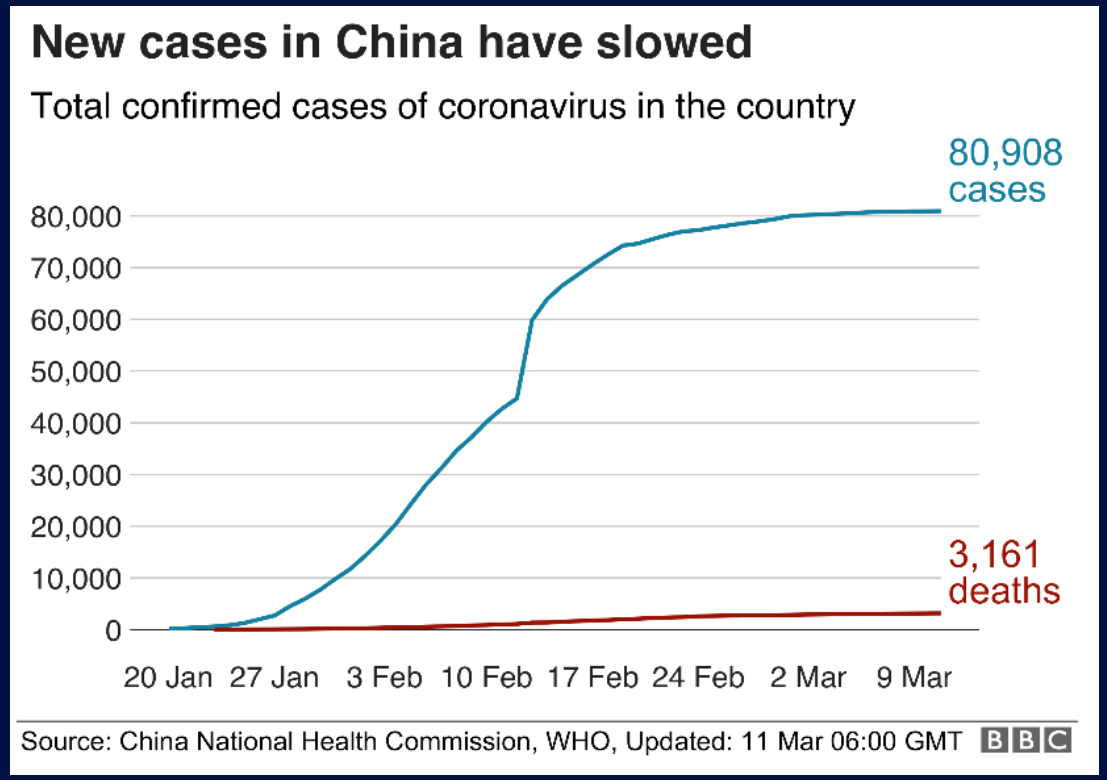

Wuhan Tianhe International Airport

TIMELINE OF EARLY STAGES OF 2019-nCo-V OUTBREAK

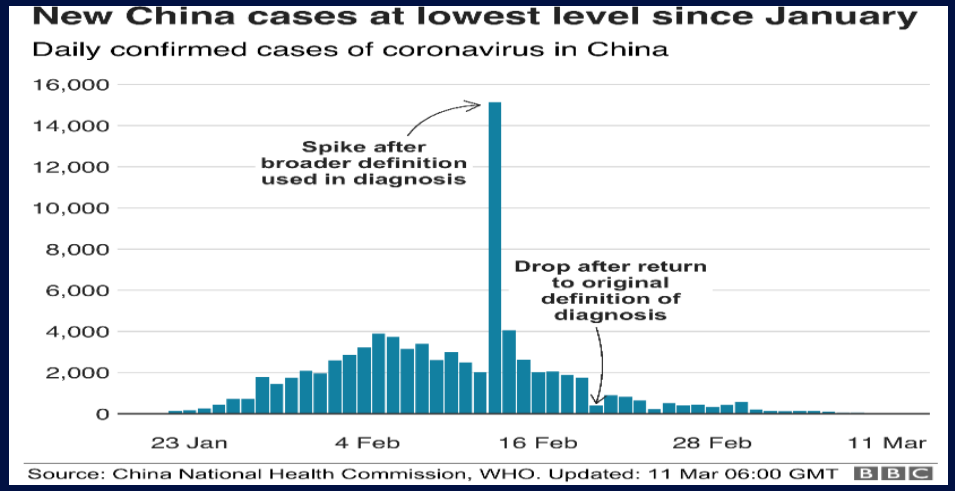


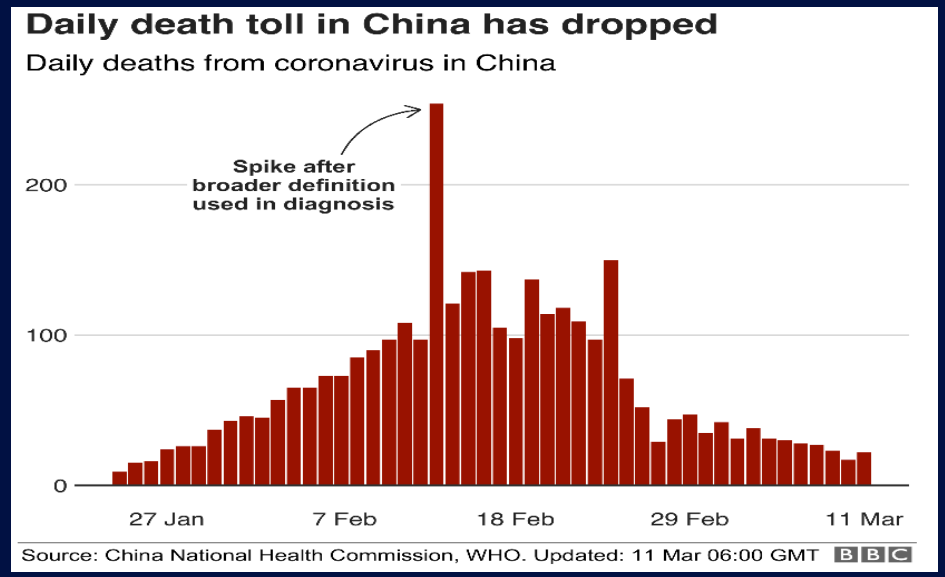
Wang C, et al
Lancet 2020; 24 Jan
(Epub ahead of print)

COVID-19, OUTBREAK CURVES, CHINA

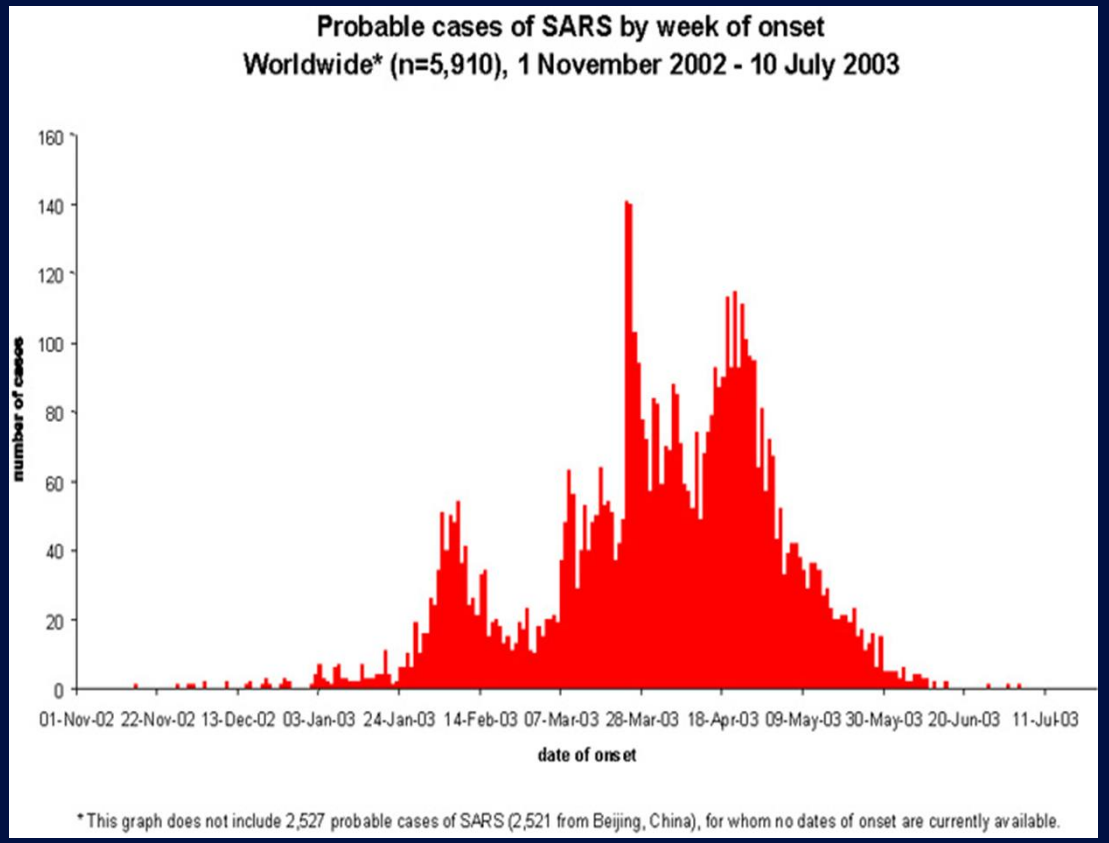


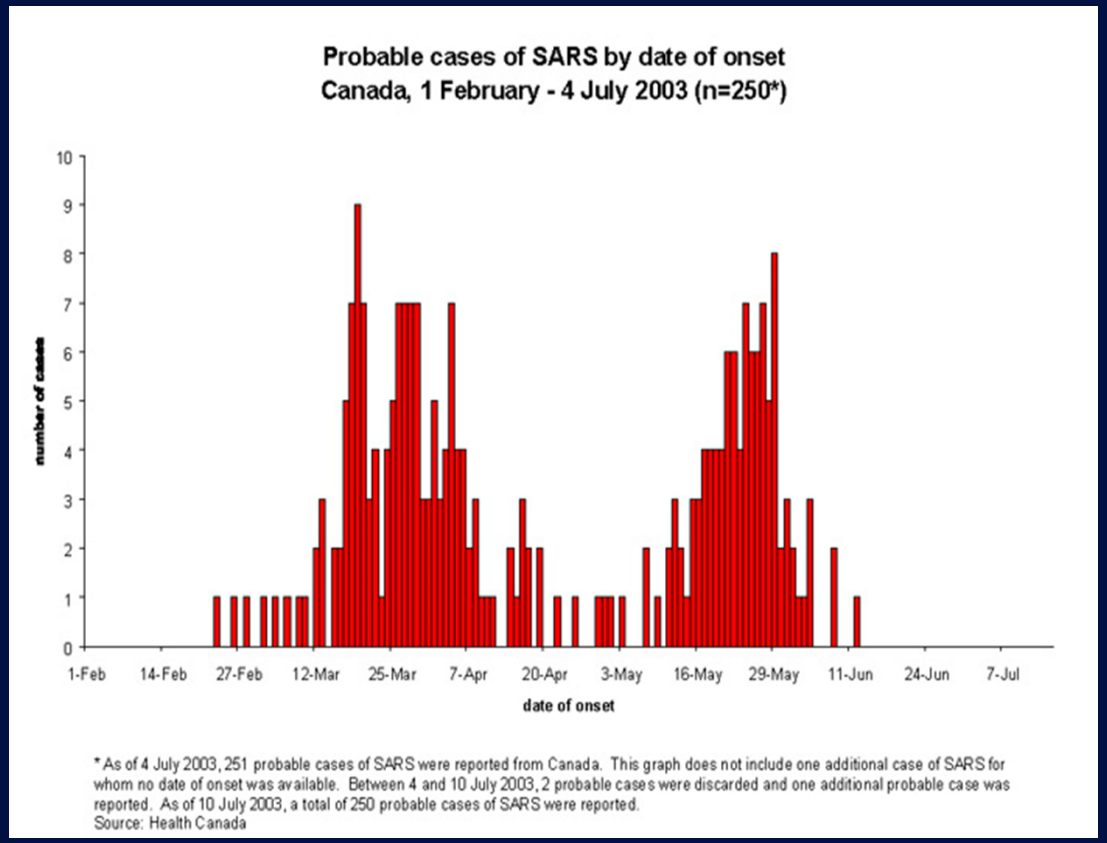
China has changed COVID definitions twice (see chart)
https://www.bbc.com/news/world-51235105



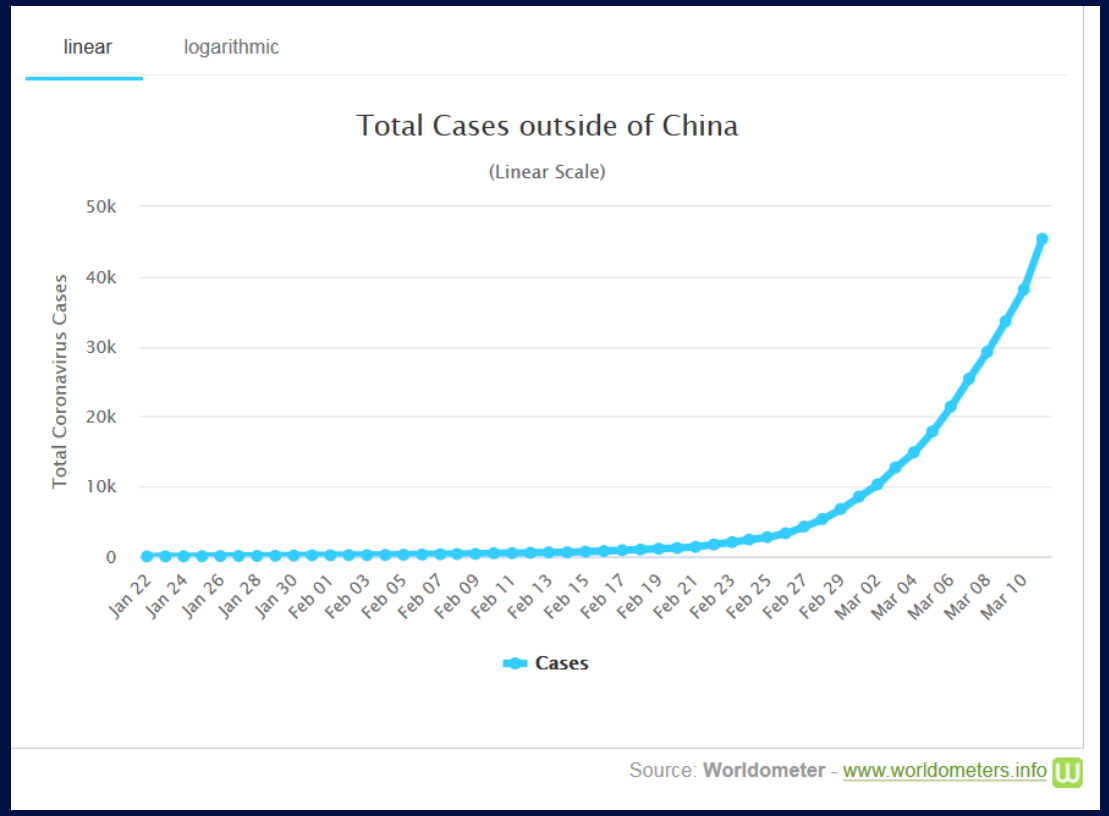


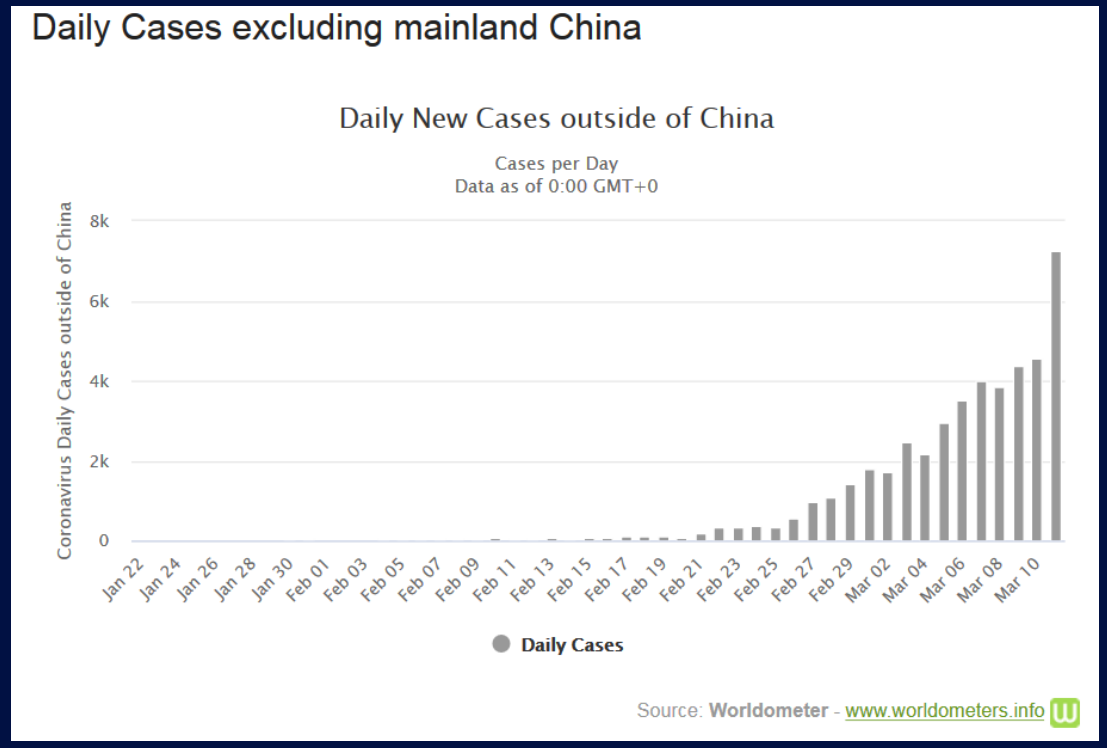
RESULTS OF ENDING PUBLIC HEALTH INTERVENTIONS TOO EARLY: A SECOND PEAK OF INFECTIONS





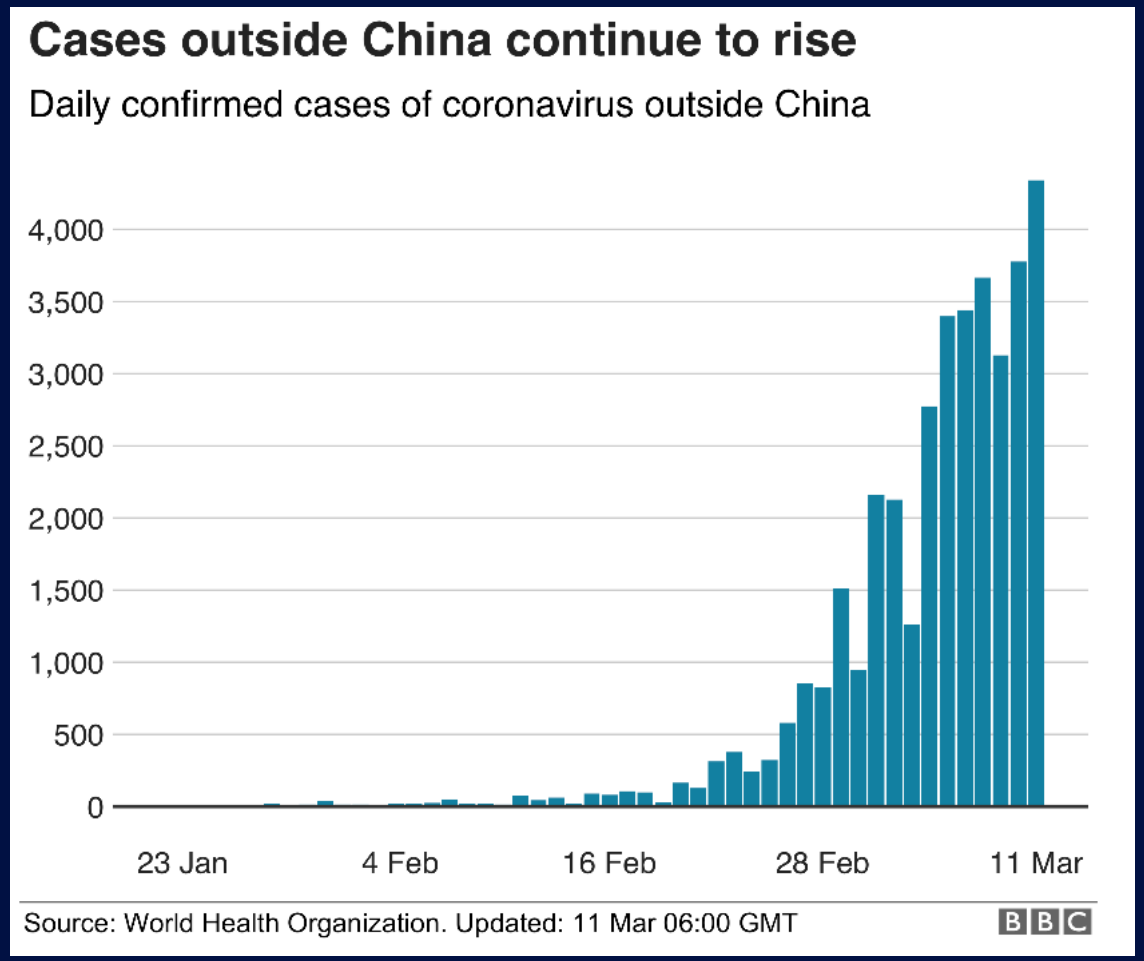
COVID-19 OUTSIDE OF CHINA



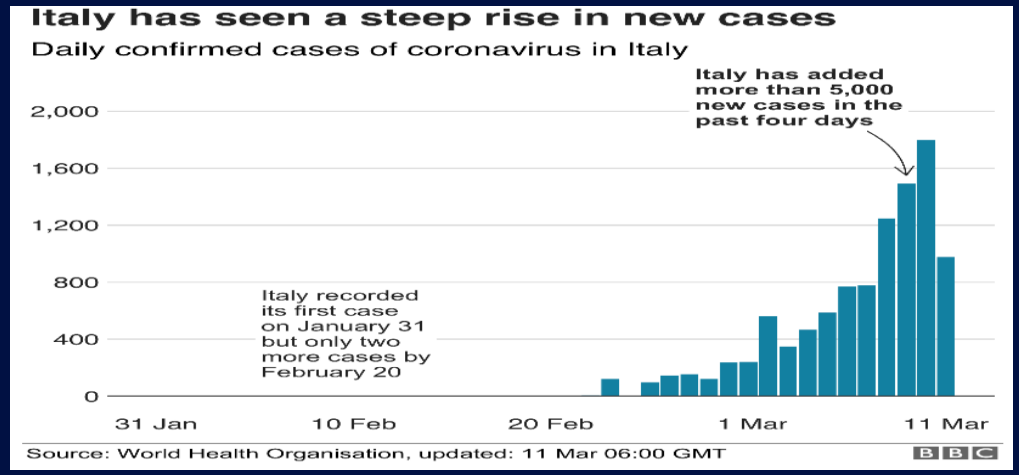


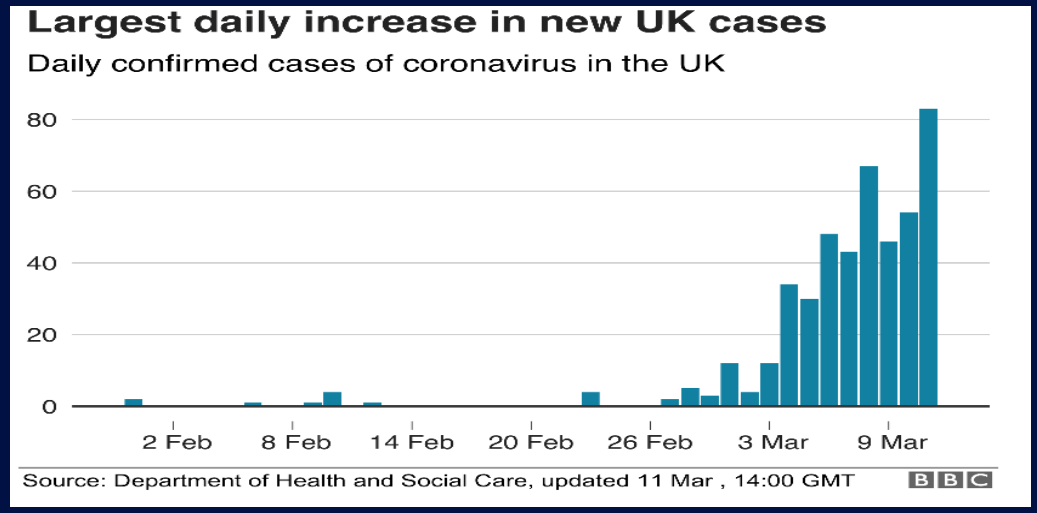
https://www.worldometers.info/coronavirus/coronavirus-cases/#case-tot-outchina

COVID-19 OUTSIDE OF CHINA



https://www.bbc.com/news/world-51235105





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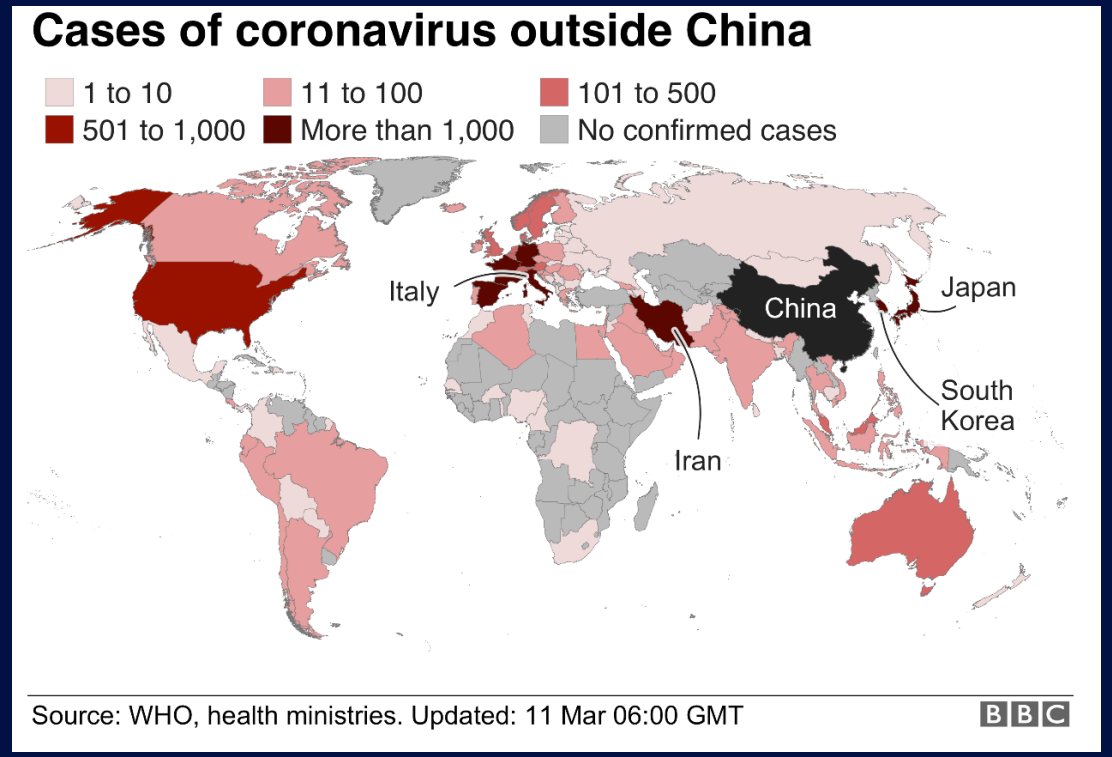

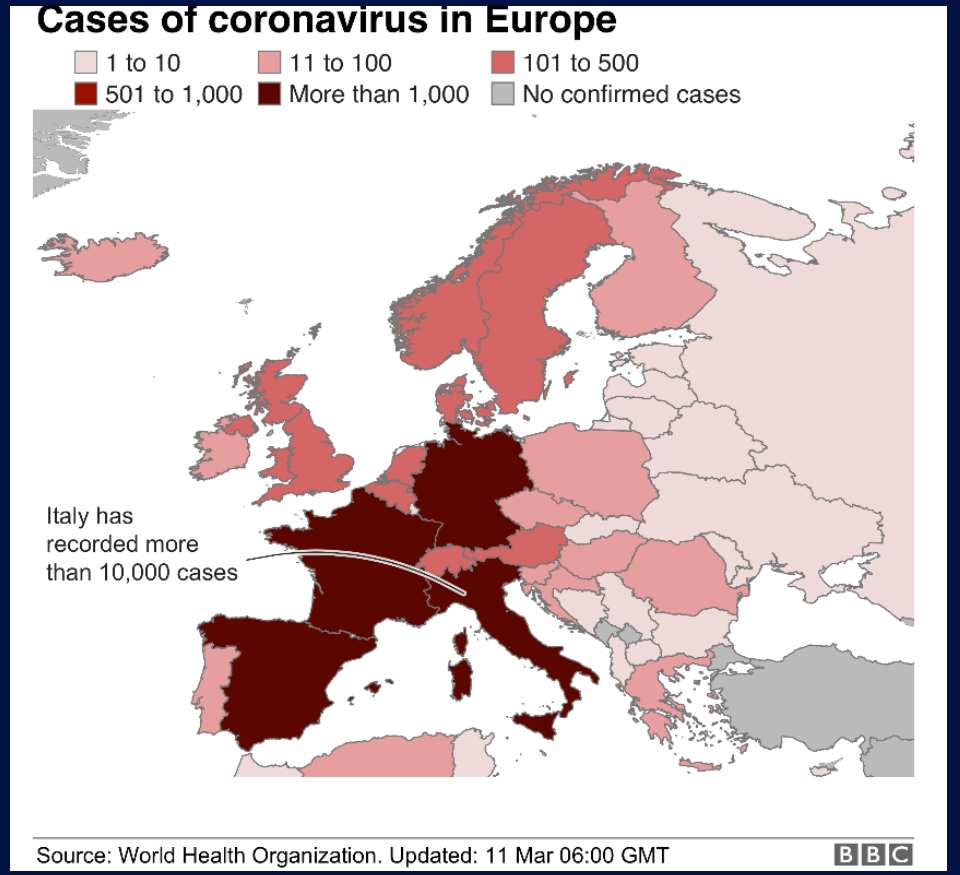

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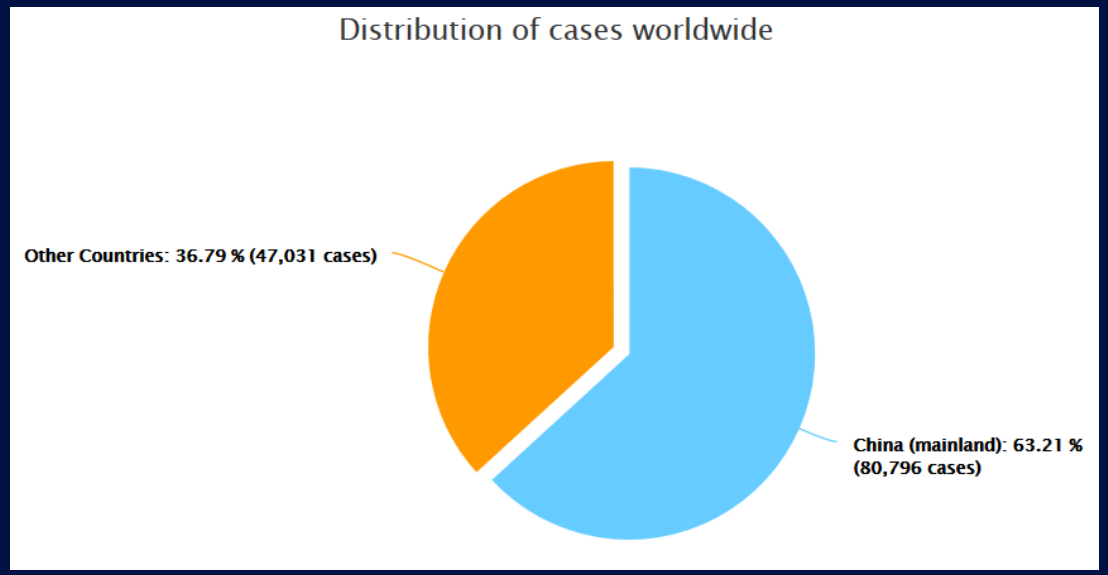
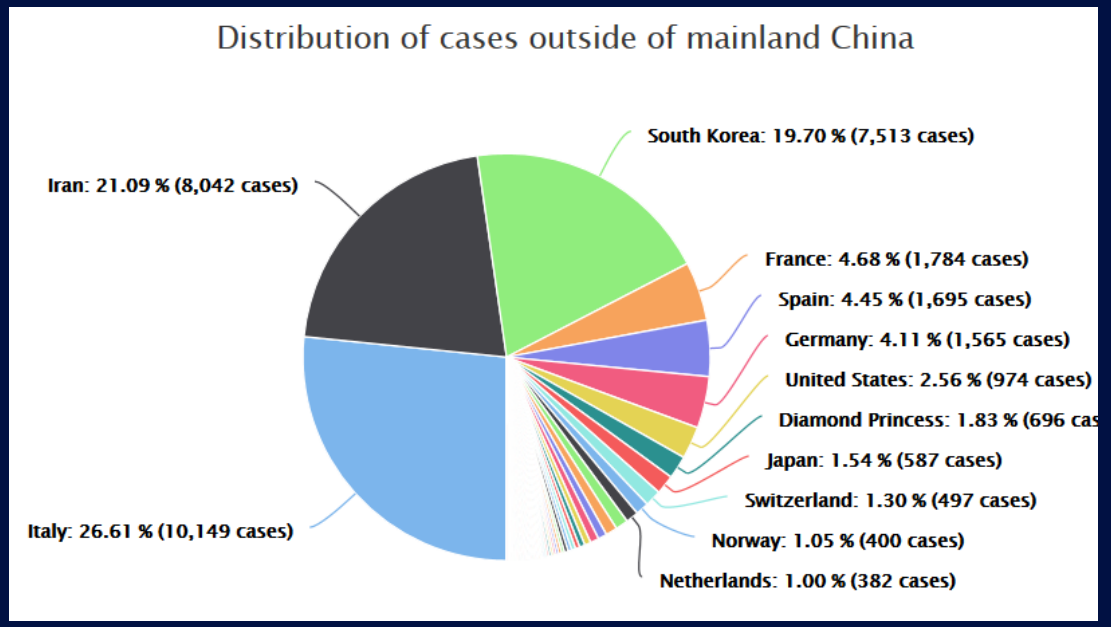
COVID, OUTSIDE OF CHINA





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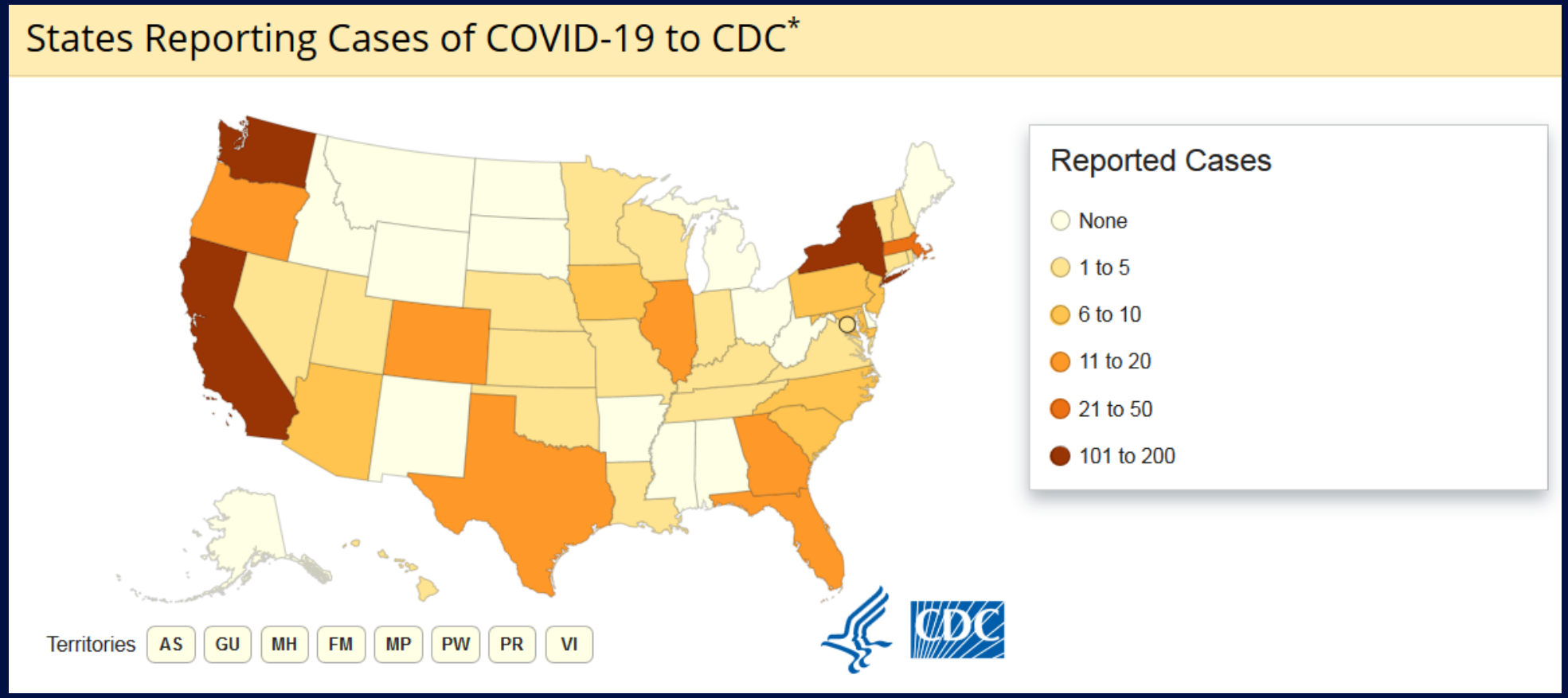
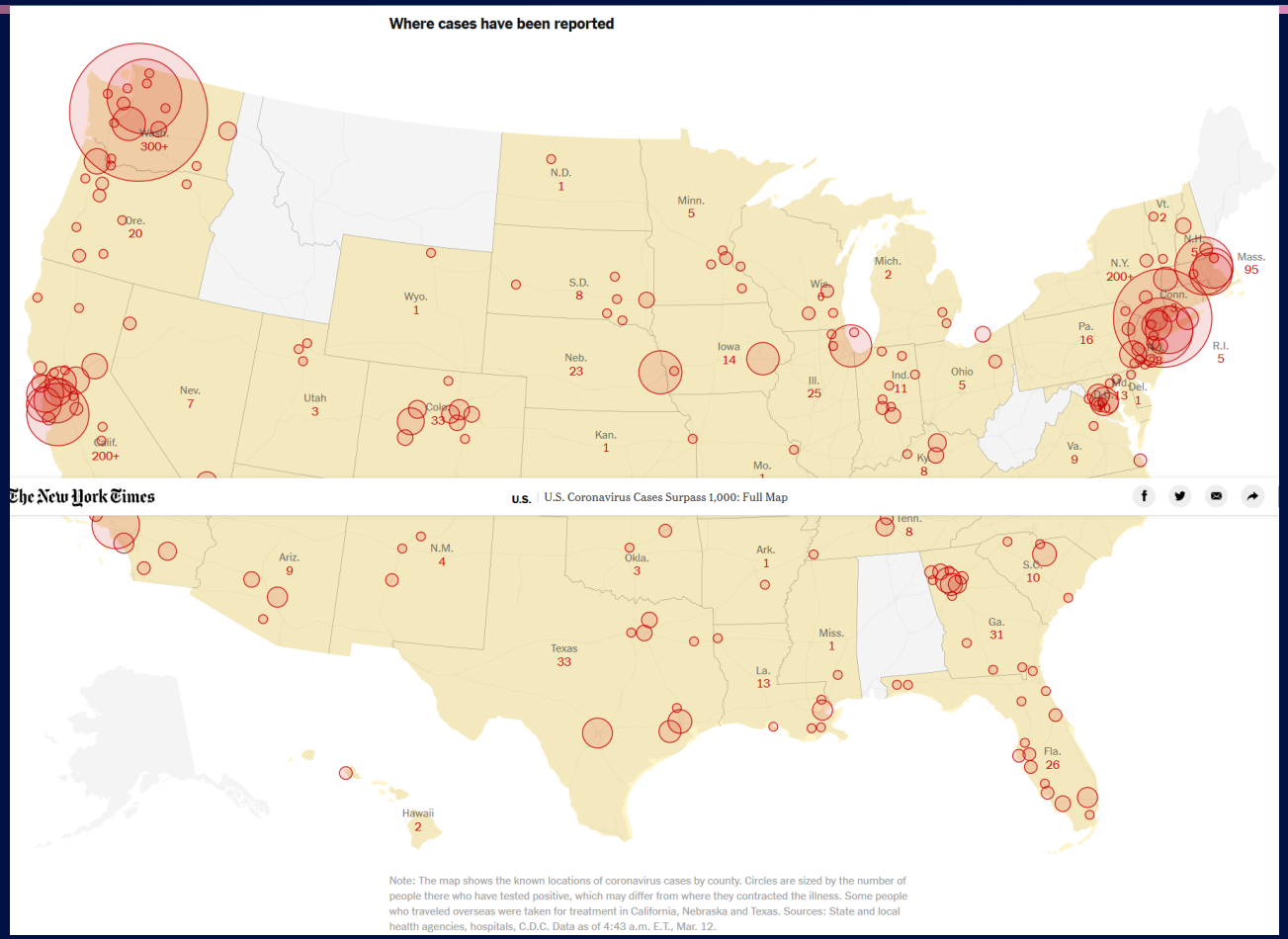
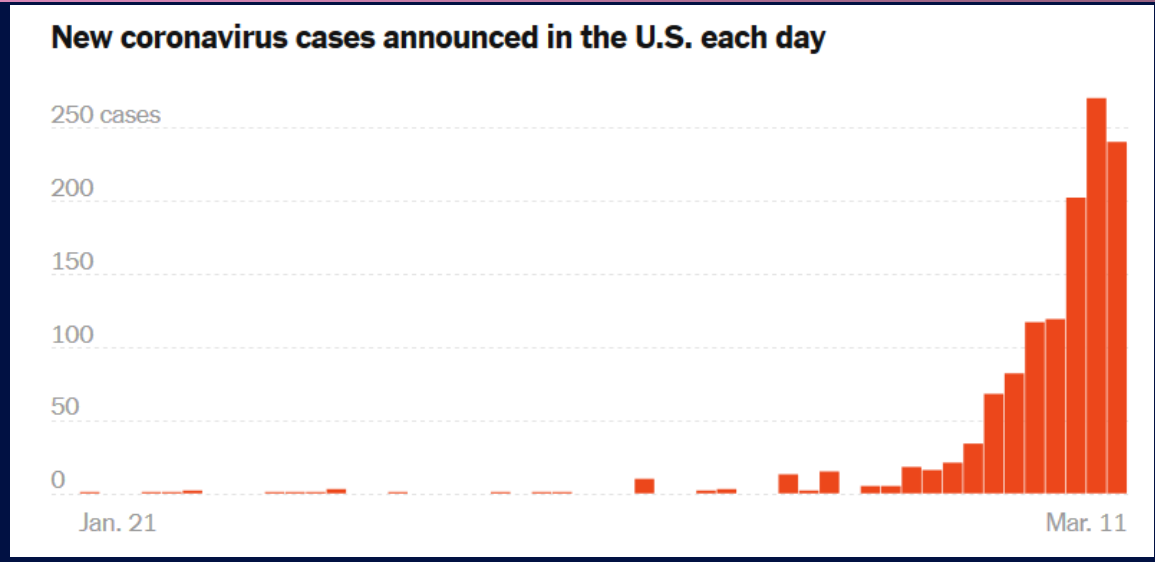
COVID-19, US



https://www.cdc.gov/coronavirus/2019-ncov/cases-in-us.html

COVID-19, US





https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html

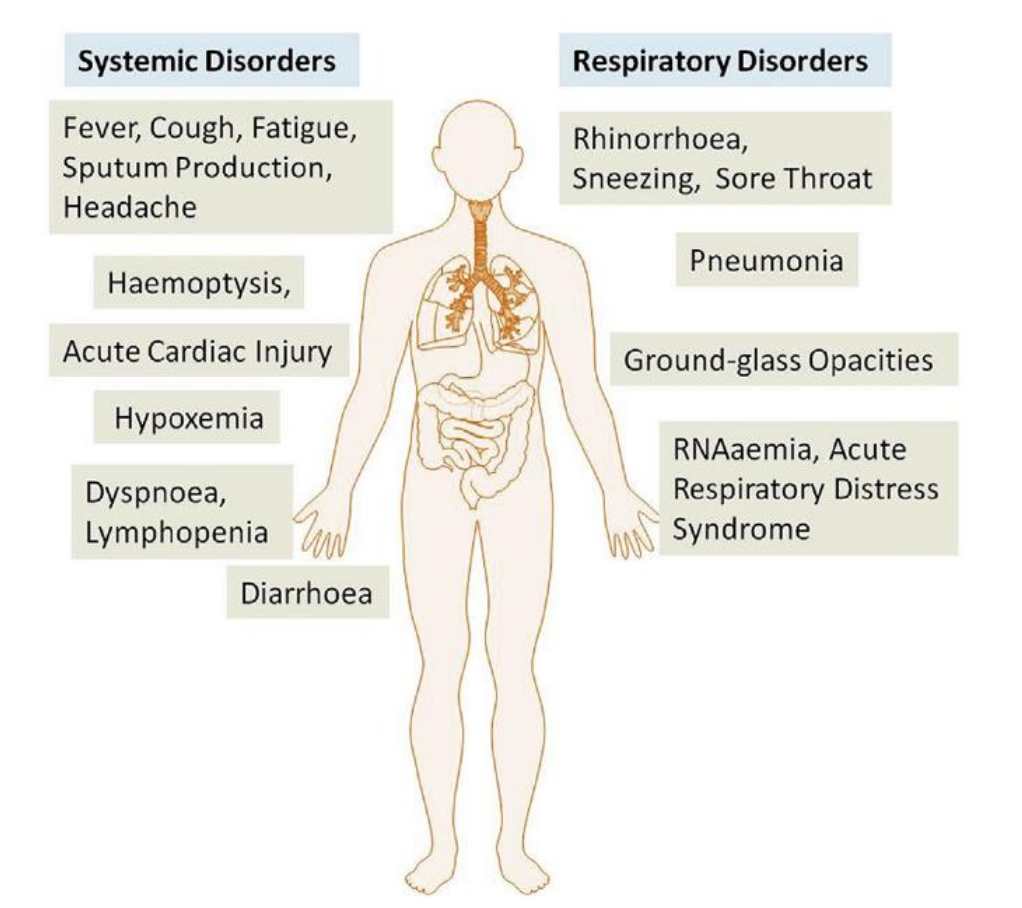
COVID-19, US

HOW VIRUS WAS CONTRACTED	CASES
Cluster connected to a community in New Rochelle, N.Y.	113
Personal contact in U.S.	78
Nursing facility in Kirkland, Wash.	57
Travel overseas	46
Diamond Princess cruise ship	43
Travel in Egypt	40
Travel in Italy	31
Business conference in Boston	29
Travel within the U.S.	29
Grand Princess cruise in February	21
Grand Princess cruise in March	21
Travel in China	15
Hospital in Vacaville, Calif.	3
Connected to Port Everglades in Fort Lauderdale, Fla.	3
Connected to Episcopal church in Washington, D.C.	3
Nursing facility in Stanwood, Wash.	3
Travel in Iran	2
Travel in South Korea	1
Unknown	710

https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html

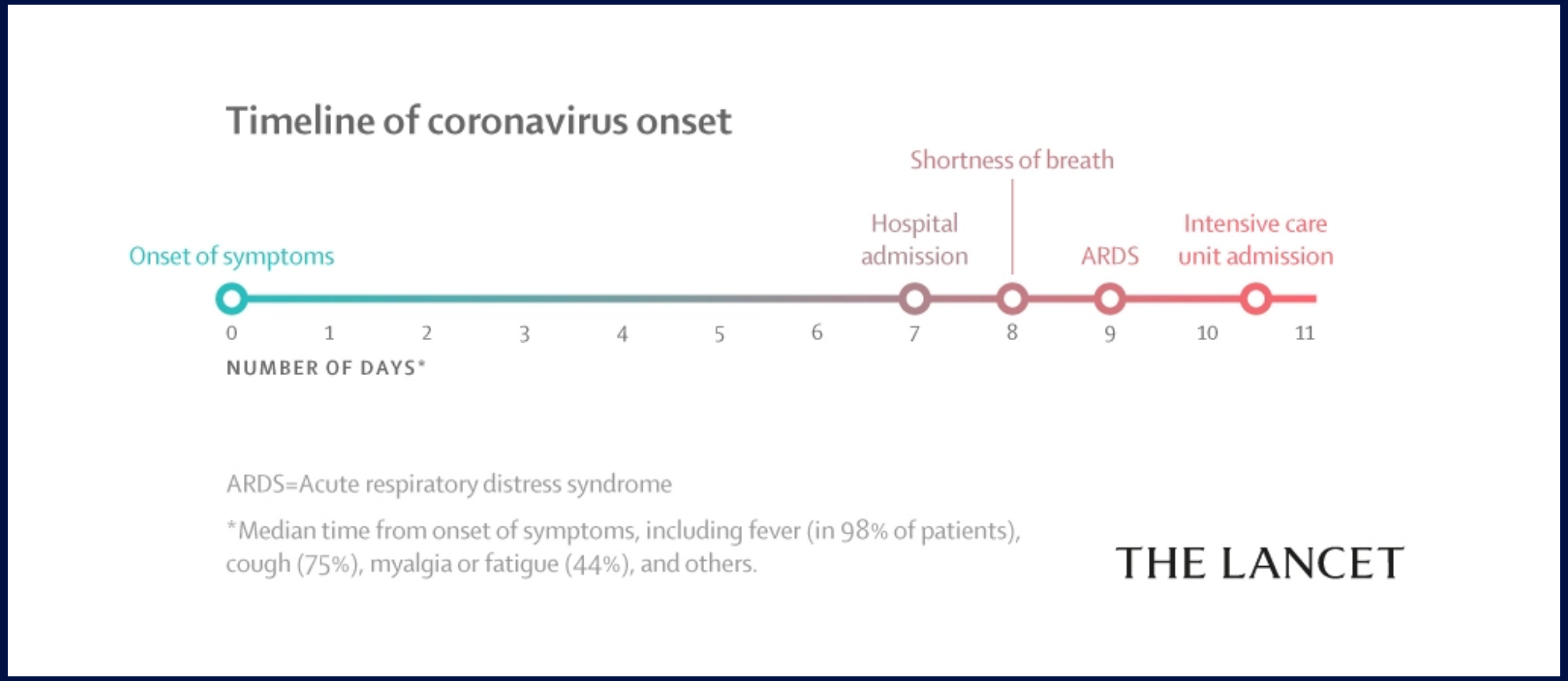
SYMPTOMS of nCo-V

- Uncomplicated upper respiratory infection
  - Fever, cough, sore throat, nasal congestion
  - Malaise, headache, myalgias
  - Shortness of breath
- Most patients have reportedly had mild to severe respiratory illness
- Older and immunocompromised patients may present with atypical symptoms (e.g., no fever)
- Complications for infection
  - Mild to severe pneumonia
  - Acute Respiratory Distress Syndrome
  - Sepsis
  - Septic shock



WHO. https://www.who.int/internal-publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected. 24 January; Rothan HA, Byrareddy SN. J Autoimmunity (In press)

TIMELINE OF 2019 nCo-V CASES AFTER ONSET OF ILLNESS



https://www.thelancet.com/infographics/coronavirus

KEY FINDINGS FROM CHINESE CDC

72 314 Cases (as of February 11, 2020)
- Confirmed cases: 44 672 (62%)
- Suspected cases: 16 186 (22%)
- Diagnosed cases: 10 567 (15%)
- Asymptomatic cases: 889 (1%)

Age distribution (N = 44 672)
- ≥80 years: 3% (1408 cases)
- 30-79 years: 87% (38 680 cases)
- 20-29 years: 8% (3619 cases)
- 10-19 years: 1% (549 cases)
- <10 years: 1% (416 cases)

Spectrum of disease (N = 44 415)
- Mild: 81% (36 160 cases)
- Severe: 14% (6168 cases)
- Critical: 5% (2087 cases)

Case-fatality rate
- 2.3% (1023 of 44 672 confirmed cases)
- 14.8% in patients aged ≥80 years (208 of 1408)
- 8.0% in patients aged 70-79 years (312 of 3918)
- 49.0% in critical cases (1023 of 2087)

Health care personnel infected
- 3.8% (1716 of 44 672)
- 63% in Wuhan (1080 of 1716)
- 14.8% cases classified as severe or critical (247 of 1668)
- 5 deaths

Wu Z, McGoogan JM. JAMA 2020; 24 Feb

DEMOGRAPHIC AND BASELINE CHARACTERISTICS OF PATIENTS (N=138) INFECTED WITH COVID-19

Table 1. Baseline Characteristics of Patients Infected With 2019-nCoV

	No. (%)			
	Total (N = 138)	ICU (n = 36)	Non-ICU (n = 102)	*P* Value[a]
Age, median (IQR), y	56 (42-68)	66 (57-78)	51 (37-62)	<.001
Sex				
Female	63 (45.7)	14 (38.9)	51 (37-62)	.34
Male	75 (54.3)	22 (61.1)	53 (52.0)	
Huanan Seafood Wholesale Market exposure	12 (8.7)	5 (13.9)	7 (6.9)	.30
Infected				
Hospitalized patients	17 (12.3)	9 (25.0)	8 (7.8)	.02
Medical staff	40 (29)	1 (2.8)	39 (38.2)	<.001
Comorbidities	64 (46.4)	26 (72.2)	38 (37.3)	<.001
Hypertension	43 (31.2)	21 (58.3)	22 (21.6)	<.001
Cardiovascular disease	20 (14.5)	9 (25.0)	11 (10.8)	.04
Diabetes	14 (10.1)	8 (22.2)	6 (5.9)	.009
Malignancy	10 (7.2)	4 (11.1)	6 (5.9)	.29
Cerebrovascular disease	7 (5.1)	6 (16.7)	1 (1.0)	.001
COPD	4 (2.9)	3 (8.3)	1 (1.0)	.054
Chronic kidney disease	4 (2.9)	2 (5.6)	2 (2.0)	.28
Chronic liver disease	4 (2.9)	0	4 (3.9)	.57
HIV infection	2 (1.4)	0	2 (2.0)	>.99
Signs and symptoms				
Fever	136 (98.6)	36 (100)	100 (98.0)	>.99
Fatigue	96 (69.6)	29 (80.6)	67 (65.7)	.10
Dry cough	82 (59.4)	21 (58.3)	61 (59.8)	.88
Anorexia	55 (39.9)	24 (66.7)	31 (30.4)	<.001
Myalgia	48 (34.8)	12 (33.3)	36 (35.3)	.83
Dyspnea	43 (31.2)	23 (63.9)	20 (19.6)	<.001
Expectoration	37 (26.8)	8 (22.2)	29 (28.4)	.35
Pharyngalgia	24 (17.4)	12 (33.3)	12 (11.8)	.003
Diarrhea	14 (10.1)	6 (16.7)	8 (7.8)	.20
Nausea	14 (10.1)	4 (11.1)	10 (9.8)	>.99
Dizziness	13 (9.4)	8 (22.2)	5 (4.9)	.007
Headache	9 (6.5)	3 (8.3)	6 (5.9)	.70
Vomiting	5 (3.6)	3 (8.3)	2 (2.0)	.13
Abdominal pain	3 (2.2)	3 (8.3)	0 (0)	.02
Onset of symptom to, median (IQR), d				
Hospital admission	7.0 (4.0-8.0)	8.0 (4.5-10.0)	6.0 (3.0-7.0)	.009
Dyspnea	5.0 (1.0-10.0)	6.5 (3.0-10.8)	2.5 (0.0-7.3)	.02
ARDS	8.0 (6.0-12.0)	8.0 (6.0-12.0)	8.0 (6.3-11.3)	.97
Heart rate, median (IQR), bpm	88 (78-97)	89 (81-101)	86 (77-96)	.14
Respiratory rate, median (IQR)	20 (19-21)	20 (16-25)	20 (19-21)	.57
Mean arterial pressure, median (IQR), mm Hg	90 (84-97)	91 (78-96)	90 (85-98)	.33

Wang D, et al. JAMA, February 7, 2020

LAB FINDINGS AND COMPLICATIONS OF PATIENTS INFECTED WITH COVID-19

Table 2. Laboratory Findings of Patients Infected With 2019-nCoV on Admission to Hospital

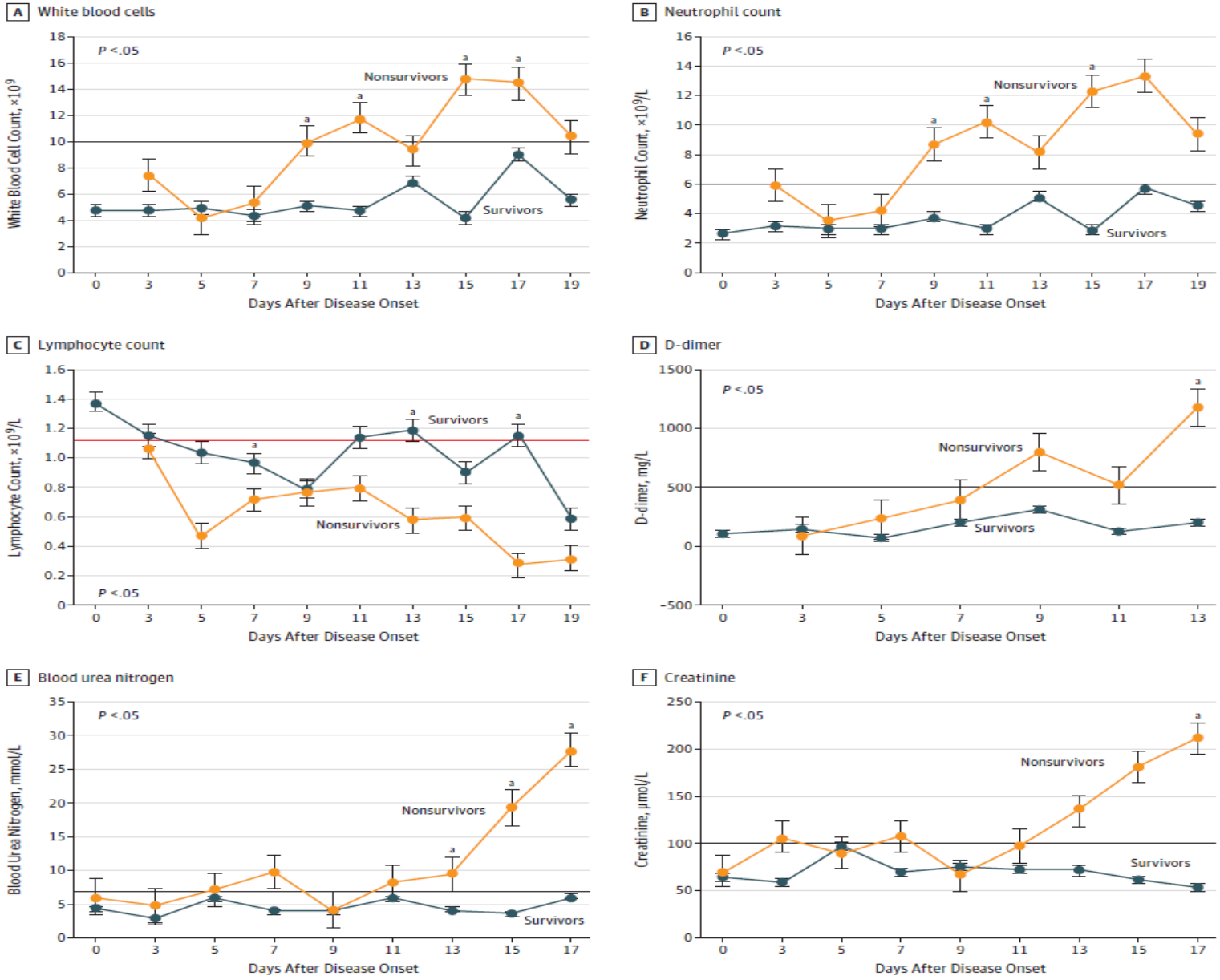
		Median (IQR)			
	Normal Range	Total (N = 138)	ICU (n = 36)	Non-ICU (n = 102)	*P* Value[a]
White blood cell count, $\times 10^9$/L	3.5-9.5	4.5 (3.3-6.2)	6.6 (3.6-9.8)	4.3 (3.3-5.4)	.003
Neutrophil count, $\times 10^9$/L	1.8-6.3	3.0 (2.0-4.9)	4.6 (2.6-7.9)	2.7 (1.9-3.9)	<.001
Lymphocyte count, $\times 10^9$/L	1.1-3.2	0.8 (0.6-1.1)	0.8 (0.5-0.9)	0.9 (0.6-1.2)	.03
Monocyte count, $\times 10^9$/L	0.1-0.6	0.4 (0.3-0.5)	0.4 (0.3-0.5)	0.4 (0.3-0.5)	.96
Platelet count, $\times 10^9$/L	125-350	163 (123-191)	142 (119-202)	165 (125-188)	.78
Prothrombin time, s	9.4-12.5	13.0 (12.3-13.7)	13.2 (12.3-14.5)	12.9 (12.3-13.4)	.37
Activated partial thromboplastin time, s	25.1-36.5	31.4 (29.4-33.5)	30.4 (28.0-33.5)	31.7 (29.6-33.5)	.09
D-dimer, mg/L	0-500	203 (121-403)	414 (191-1324)	166 (101-285)	<.001
Creatine kinase, U/L	<171	92 (56-130)	102 (62-252)	87 (54-121)	.08
Creatine kinase-MB, U/L	<25	14 (10-18)	18 (12-35)	13 (10-14)	<.001
Lactate dehydrogenase, U/L	125-243	261 (182-403)	435 (302-596)	212 (171-291)	<.001
Alanine aminotransferase, U/L	9-50	24 (16-40)	35 (19-57)	23 (15-36)	.007
Aspartate aminotransferase, U/L	15-40	31 (24-51)	52 (30-70)	29 (21-38)	<.001
Total bilirubin, mmol/L	5-21	9.8 (8.4-14.1)	11.5 (9.6-18.6)	9.3 (8.2-12.8)	.02
Blood urea nitrogen, mmol/L	2.8-7.6	4.4 (3.4-5.8)	5.9 (4.3-9.6)	4.0 (3.1-5.1)	<.001
Creatinine, μmol/L	64-104	72 (60-87)	80 (66-106)	71 (58-84)	.04
Hypersensitive troponin I, pg/mL	<26.2	6.4 (2.8-18.5)	11.0 (5.6-26.4)	5.1 (2.1-9.8)	.004
Procalcitonin, ng/mL					
≥0.05, No. (%)	<0.05	49 (35.5)	27 (75.0)	22 (21.6)	<.001
Bilateral distribution of patchy shadows or ground glass opacity, No. (%)	NA	138 (100)	36 (100)	102 (100)	>.99

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

Wang D, et al. JAMA, February 7, 2020

Figure 2. 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.

Wang D, et al. JAMA, February 7, 2020

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)

Data = 1,099 patients,
552 hospitals, 30 provinces
Through 29 January

Median age = 47

Fever present in only 44% on admission; 89% during Hospitalization
Cough, 68%

Median incubation = 4d

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)

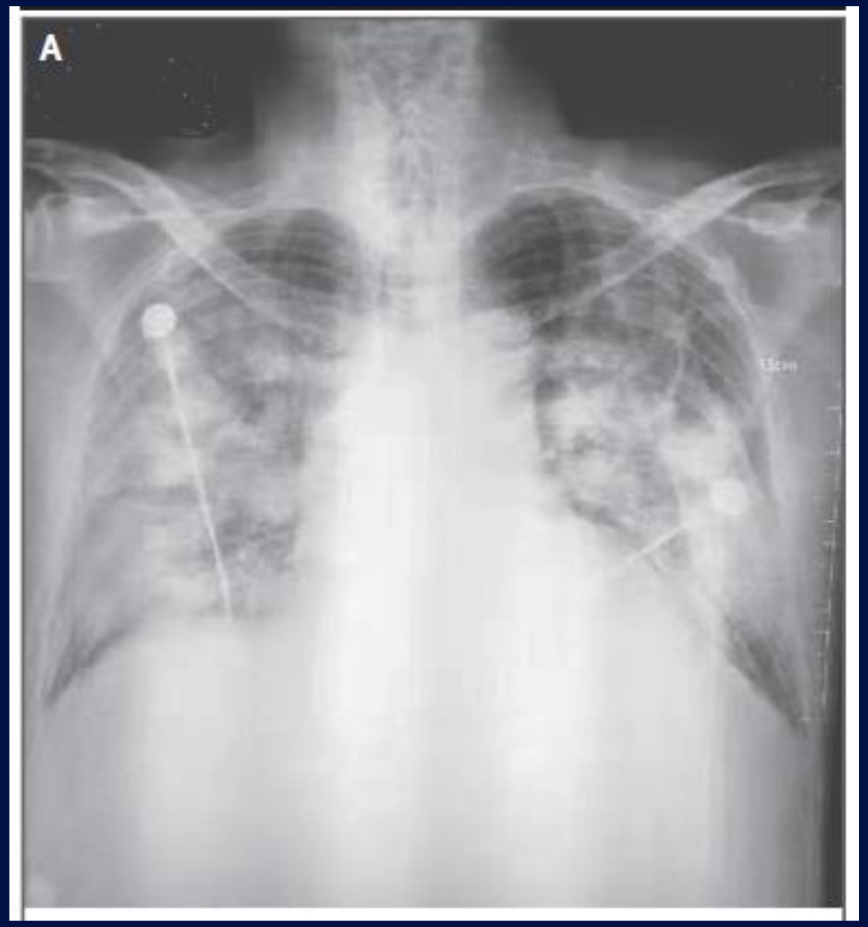
* The denominators of patients who were included in the analysis are provided if they differed from the overall numbers in the group. Percentages may not total 100 because of rounding. Covid-19 denotes coronavirus disease 2019, and IQR interquartile range.
† The primary composite end point was admission 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.

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%).

CHEST RADIOGRAPHS, nCo-V CASE



Shown are chest radiographs from Patient 2 on days 8 and 11 after the onset of illness. The trachea was intubated and mechanical ventilation instituted in the period between the acquisition of the two images. Bilateral fluffy opacities are present in both images but are increased in density, profusion, and confluence in the second image; these changes are most marked in the lower lung fields. Changes consistent with the accumulation of pleural liquid are also visible in the second image.

Zhu N, et al.
NEJM 2020;Jan 24 (Epub)

Table 1. Risk Categories for Exposures Associated with International Travel or Identified during Contact Investigations of Laboratory-confirmed Cases

Risk Level	Geographic (Travel-associated) Exposures*	Exposures Identified through Contact Investigation
High	Travel from Hubei Province, China	Living in the same household as, being an intimate partner of, or providing care in a nonhealthcare setting (such as a home) for a person with symptomatic laboratory-confirmed COVID-19 infection ***without using recommended precautions*** for home care and home isolation
Medium (assumes no exposures in the high-risk category)	• Travel from mainland China outside Hubei Province or Iran • Travel from a country with widespread sustained transmission, other than China or Iran • Travel from a country with sustained community transmission	• Close contact with a person with symptomatic laboratory-confirmed COVID-19 • 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 • Living in the same household as, an intimate partner of, or caring for a person in a nonhealthcare setting (such as a home) to a person with symptomatic laboratory-confirmed COVID-19 infection ***while consistently using recommended precautions*** for home care and home isolation
Low (assumes no exposures in the high-risk category)	Travel from any other country	Being in the same indoor environment (e.g., a classroom, a hospital waiting room) as a person with symptomatic laboratory-confirmed COVID-19 for a prolonged period of time but not meeting the definition of close contact
No identifiable risk	Not applicable	Interactions with a person with symptomatic laboratory-confirmed COVID-19 infection that do not meet any of the high-, medium- or low-risk conditions above, such as walking by the person or being briefly in the same room.

*In general, geographic exposure categories do not apply to travelers who only transit through an airport.

https://www.cdc.gov/coronavirus/2019-ncov/php/risk-assessment.html

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
Prolonged close contact with a COVID-19 patient who was not wearing a facemask (i.e., no 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[b]	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

https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html

COVID-19 DIAGNOSTIC TESTING

- Testing options (turnaround time)
  - NC Health Department (1 day), LabCorp or Quest (3-4 days); UNC Medical Center working on a test (4-24 hours)
  - Point of care tests which are not FDA approved should not be used
- Test procedures
  - Use synthetic fiber swabs with plastic or metal shafts (do NOT use calcium alginate)
  - Upper respiratory tract - Nasopharyngeal swab (see: http://www.youtube.com/watch?v=DVJNWefmHjE) PLUS throat
  - Lower respiratory tract – Bronchoalveolar lavage or wash; mini-BAL
  - Should be performed in an airborne isolation room; healthcare should wear gowns, gloves, face shield/goggles, PAPR or N95 respirator (need to have had medical clearance and fit testing)
  - All persons undergoing tests are considered Persons Under Investigation (PUI) and must be reported to the NC Health Dept.

NC HEALTH DEPARTMENT CRITERIA FOR COVID TESTING, 10 MARCH

- Case investigation and testing
  - Clinicians should use their judgment to determine if a patient has signs and symptoms compatible with COVID-19 and whether the patient should be tested. Decisions on which patients receive testing should be based on the local epidemiology of COVID-19, as well as the clinical course of illness. Most patients with confirmed COVID-19 have developed fever1 and/or symptoms of acute respiratory illness (e.g., cough, difficulty breathing). Clinicians are strongly encouraged to test for other causes of respiratory illness, including infections such as influenza.
  - Epidemiologic factors that may help guide decisions on whether to test include: any persons, including HCP, who have had close contact with a laboratory-confirmed COVID-19 patient within 14 days of symptom onset, or a history of travel from affected geographic areas5 (see below) within 14 days of symptom onset.
- NC Health Department criteria for a Person Under Investigation (PUI) who would be considered for investigation
  - Fever (>100.0 oF) OR signs/symptoms of lower respiratory illness (e.g., cough, shortness of breath) in any person, including HCP, who has had close contact with a laboratory-confirmed COVID-19 patient within 14 days of symptom onset.
  - Fever AND signs/symptoms of lower respiratory illness (e.g., cough, shortness of breath) AND negative influenza test (rapid or PCR) and no other more likely diagnosis.

WHO TREATMENT GUIDELINES, 28 JANUARY

- Give supplemental oxygen therapy immediately to patients with COVID-19 and respiratory distress, hypoxaemia, or shock
- Use conservative fluid management in patients with COVID-19 when there is no evidence of shock.
- Give empiric antimicrobials to treat all likely pathogens causing COVID-19. Give antimicrobials within one hour of initial patient assessment for patients with sepsis.
- Do not routinely give systemic corticosteroids for treatment of viral pneumonia or ARDS outside of clinical trials unless they are indicated for another reason.
- Closely monitor patients with COVID-19 for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis, and apply supportive care interventions immediately.
- Understand the patient's co-morbid condition(s) to tailor the management of critical illness and appreciate the prognosis. Communicate early with patient and family.

POTENTIAL THERAPIES FOR COVID-19

Table 1. Antivirals included in the Guidelines (version 6) for treatment of COVID-19

Drug	Dosage	Method of administration	Duration of treatment
IFN-α	5 million U or equivalent dose each time, 2 times/day	Vapor inhalation	No more than 10 days
Lopinavir/ritonavir	200 mg/50 mg/capsule, 2 capsules each time, 2 times/day	Oral	No more than 10 days
Ribavirin	500 mg each time, 2 to 3 times/day in combination with IFN-α or lopinavir/ritonavir	Intravenous infusion	No more than 10 days
Chloroquine phosphate	500 mg (300 mg for chloroquine) each time, 2 times/day	Oral	No more than 10 days
Arbidol	200 mg each time, 3 times/day	Oral	No more than 10 days

Other potential therapies discussed in text: remdesivir, faviparivir, darunavir; 30 total agents demonstrated to have activity in screening tests

Dong L, et al. Drug Discoveries & Therapeutics 2020;14:58-60

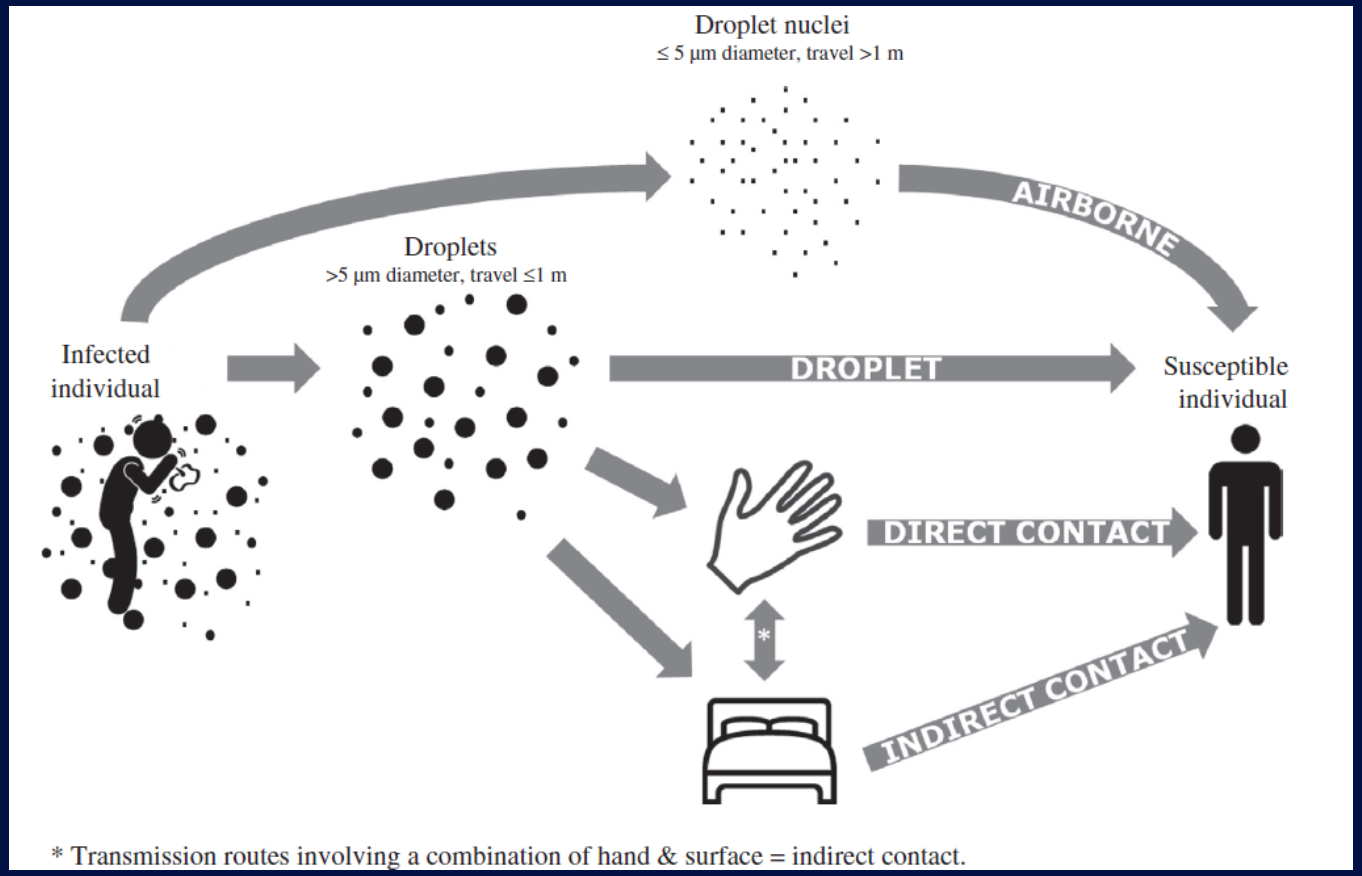
POTENTIAL THERAPIES FOR COVID-19

- Currently there is NO proven effective therapy for SARS or MERS (and by extension nCo-V) – only supportive therapy is available
- Lopinavir/ritonavir +/- interferon-bata-1b (Momattin H, et al. Travel Med Infect Dis 2019;30:9-18)
  - The combination of lopinavir/ritonavir and interferon-beta- 1b showed excellent results in common marmosets and currently is in a randomized control trial.
  - Ribavirin and interferon were the most widely used combination and experience comes from a number of observational studies. Although, the data are heterogenous, this combination might be of potential benefit and deserve further investigation.
  - RDV and IFNb had superior antiviral activity to PPV/RTV in vitro and in vivo (mouse model)(Sheehan T, et al. Nature Communications;2020 - https://www.nature.com/articles/s41467-019-13940-6)
- Convalescent plasma (Chen L, et al. Lancet 2020;27 February)
  - No data for COVID-19; evidence of efficacy for Ebola, influenza; case reports for SARS and MERS
  - Bottom line = Possible effectiveness (no clinical trial available for coronaviruses)
- Immunoglobulin
  - A fully human polyclonal IgG antibody (SAB-301) was safe and well tolerated in healthy individuals and this agent may deserve further testing for efficacy.

POTENTIAL THERAPIES FOR COVID-19

- Chloroquine (Touret F, de Lamballerie X. Antiviral Res 2020;177:104762)
  - Narrow therapeutic and toxic dose is narrow and chloroquine poisoning has been associated with cardiovascular disorders that can be life-threatening
  - In animal models chloroquine enhances alphavirus replication
  - Chloroquine has not been shown effective for the treatment of any acute viral disease
  - Bottom line = Unlikely to be effective
- Ribavirin
  - Promising results in a MERS-CoV (ribavirin plus IFNalpha-2b) in a rhesus macaque model, conflicting data with patients
  - Ribavirin reduces hemoglobin concentrations, an undesirable side effect in patients with respiratory disorders
- Remdesivir/GS-5734)
  - Remdesivir (RDV), a nucleotide prodrug, currently in clinical development for treatment of Ebola virus disease, can inhibit SARS-CoV and MERS-CoV replication in multiple *in vitro* systems. (Sheahan TP, et al. Sci Transl Med 2017;9,396)
  - Broad spectrum anti-CoV activity in animal models (Martinez MA. AAC 2020;9 March)
  - Efficacy of remdesivir superior to that of LPV/RTV-INFb against MERS in a transgenic humanized mouse model
  - Bottom line = Most likely drug to be successful; multiple clinical trials being conducted

LIKELY TRANSMISSION ROUTES FOR nCo-V



Otter JA, Donskey C, Yezli S, Douthwaite S, Goldenberg SD, Weber DJ. J Hosp Infect 2016;92:235-50

HUMAN CORONAVIRUSES: ENVIRONMENTAL CONTAMINATION

Human coronavirus							
Booth *et al.*[63]	2005	Hospitals in Toronto, Canada	19 rooms in SARS units and 'control' areas not housing SARS patients	Moistened swabs; PCR for viral RNA and viral culture	85	3 (3.5)	Positive sites were a bed table, a television remote control and a refrigerator handle in a nurses' medication station. All swabs were culture negative. Two (5%) of 40 air-slit samples were positive for SARS-CoV.
Dowell *et al.*[44]	2004	Hospitals in Bangkok, Thailand and Taipei, Taiwan	SARS-infected patient areas (patient rooms, nursing stations, emergency department)	Moistened swabs; PCR for viral RNA and viral culture	63	24 (38.1)	All swabs were culture negative.
			Public areas		31	2 (6.4)	
Memish *et al.*[64]	2014	Jeddah airport, Saudi Arabia	Various frequently touched items in public areas	Moistened swabs; PCR panel for viral culture	40	3 (7.5)	Human coronavirus (OC43/HKU1) RNA was identified from surfaces. Influenza B virus RNA was identified from 1/18 air samples, but was not identified on surfaces.

SARS-CoV, severe acute respiratory syndrome coronavirus; PCR, polymerase chain reaction.

Otter JA, Donskey C, Yezli S, Douthwaite S, Goldenberg SD, Weber DJ. J Hosp Infect 2016;92:235-50

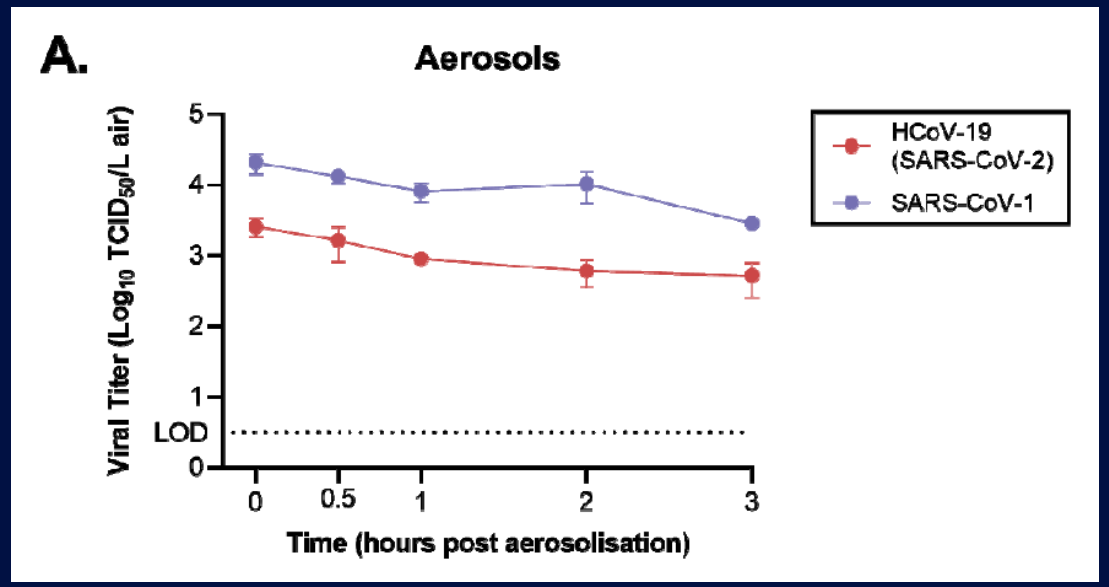
HUMAN CORONAVIRUSES: ENVIRONMENTAL SURVIVAL

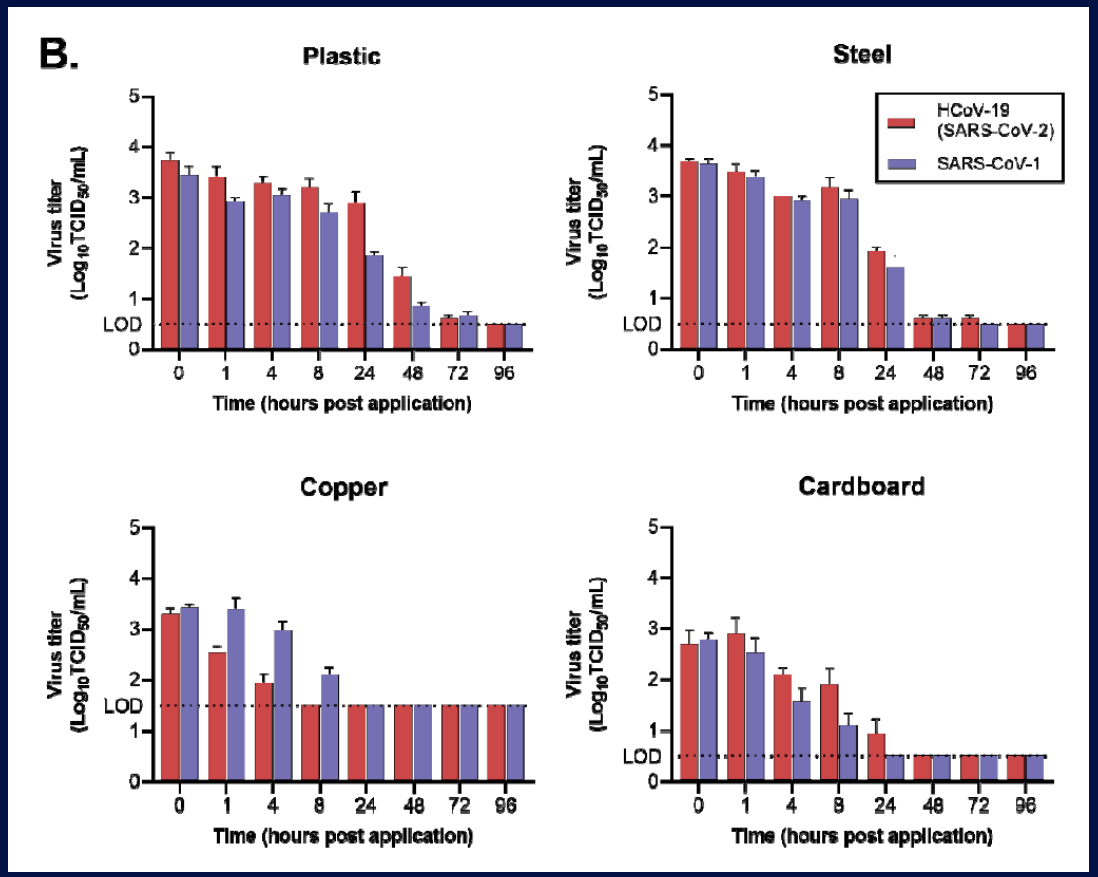
Survival of SARS-CoV, MERS-CoV, and surrogates on dry surfaces

Study	Year	Location	Test virus	Load applied	Substrate(s)	Suspending medium	Volume applied (μL)	Temperature (°C)/RH (%)	Drying time (min) for time 0 sample	Results
van Doremalen *et al.*[16]	2013	USA	MERS-CoV	10^5	Steel and plastic	Cell culture medium only	100	Variable	10	Viable virus detected after 48 h at 20°C/40% RH. Less survival at 30°C/80% RH (8 h) and 30°C/30% RH (24 h). Half-life ranged from ~0.5 to 1 h.
Chan *et al.*[17]	2011	Hong Kong	SARS-CoV	10^5	Plastic	Cell culture medium only	10	Variable	Until visibly dry	SARS-CoV survived for 5 days with <10-fold reduction in titre at room temperature and humidity, and was viable for >20 days. The virus was more stable at lower temperatures (28 vs 38°C) and lower humidity (80–89% vs >95%). The reduction in viral titre was similar in suspension compared with virus dried on surfaces.
Casanova *et al.*[26]	2010	USA	TGEV	$>10^3$	Latex/nitrile gloves, N95 respirator, hospital scrubs, isolation gowns	Cell culture medium only	10	20/50	0	TGEV survived with $<10^2$ reduction on all items after 4 h and was detected on some items after 24 h
Casanova *et al.*[19]	2009	USA	TGEV, MHV	10^5	Stainless steel discs	Cell culture medium only	10	Variable	Until visibly dry	Both TGEV and MHV could survive in excess of 28 days under some conditions, with lower temperature and relative humidity resulting in improved survival. TGEV and MHV did not differ significantly in their survival properties.
Muller *et al.*[27]	2008	Germany	HCoV-NL63, human metapneumovirus	Not specified	Latex gloves, thermometer caps, stethoscopes, plastic table	Cell culture medium only	Not specified	Ambient	Not specified	Viable virus not detected after drying; viral RNA detectable for up to 7 days
Rabenau *et al.*[28]	2005	Germany	SARS-CoV, HCoV-229E, herpes simplex virus, adenovirus	10^6–10^7	Polystyrene Petri dish	Cell culture medium ±20% fetal calf serum	500	Ambient	Until visibly dry	SARS-CoV, adenovirus and herpes simplex virus survived >6 days. HCoV-229E survived for <72 h. The addition of FCS made little impact on survival times.

Otter JA, Donskey C, Yezli S, Douthwaite S, Goldenberg SD, Weber DJ.
J Hosp Infect 2016;92:235-50

AEROSOL AND ENVIRONMENTAL SURVIVAL OF nCo-V-2019





Van Doremalen N, et al.
NEJM 2020 (epub)

INFECTION PREVENTION: SUMMARY (Identify, Isolate, Inform)

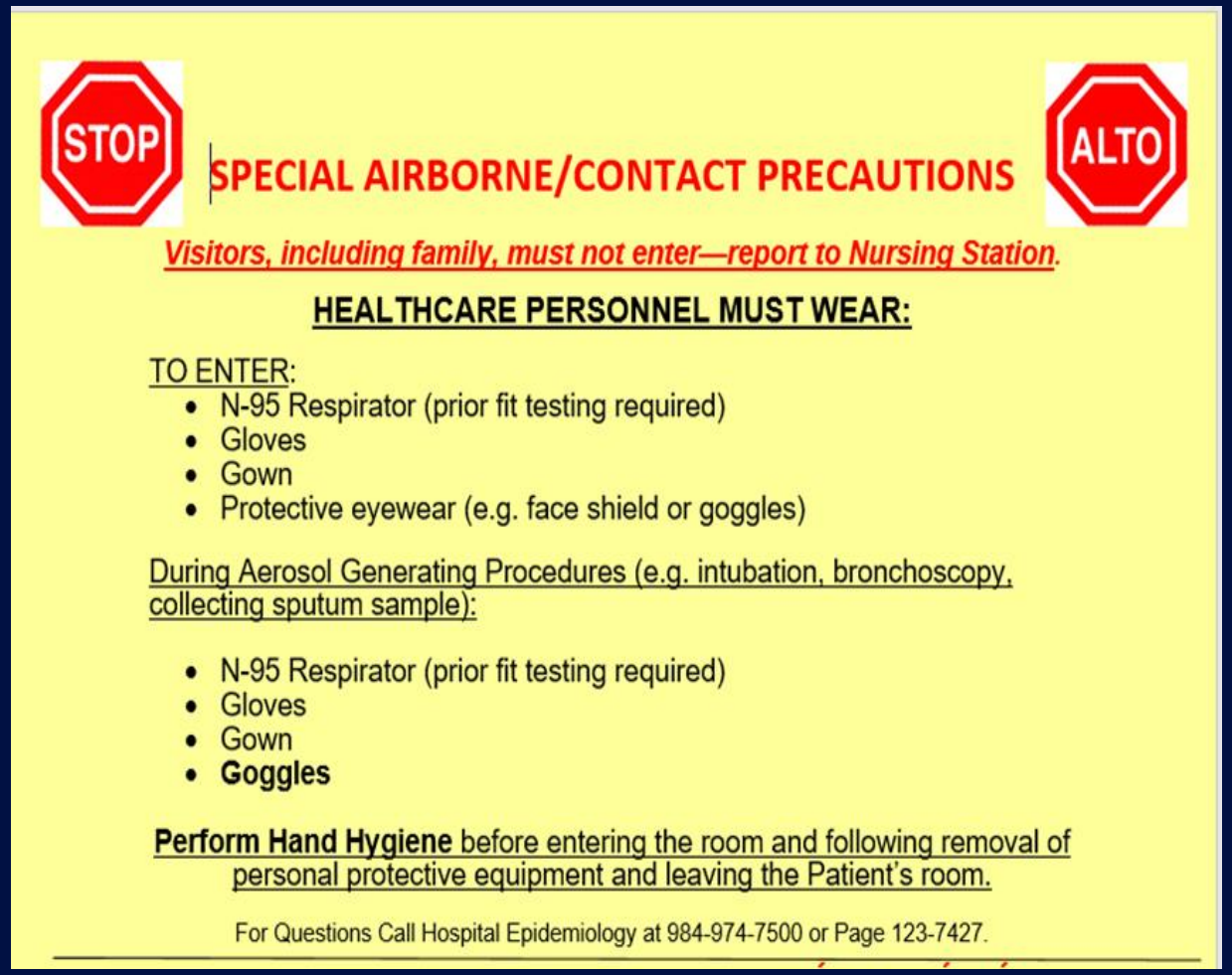
- Outpatients (Identify, Isolate, Inform: Assess all patients at healthcare facility entry for nCo-V (symptoms and travel screen) – now built into UNC Epic
  - Recommended immediate placement of patient with known or suspected nCo-V (outpatient): Private room (preferably an airborne isolation room, if available). Have patient wear a surgical mask covering mouth and nose (however, even if patient masked, HCP need to wear proper PPE; gloves, gowns, surgical mask, eye protection). Transfer to location with AII room for cough inducing procedures (e.g., NP swab)
- Inpatients: Recommended placement of patient with known or suspected nCo-V: Airborne isolation room
  - Recommended personal protective equipment (PPE) for healthcare personnel (HCP): Gloves, gown, mask (properly fit tested N95 respirator or PAPR if in AII), and eye protection (face shield or goggles) – follow CDC donning and doffing protocol
  - Limitation on visitors and non-essential personnel (per CDC) – screen all visitors for nCo-V symptoms
  - Log of all persons entering room (Self-monitoring for symptoms even if wearing appropriate PPE for 14 days)
- Antisepsis and disinfection:
  - All standard FDA approved hospital hand hygiene agents are effective (e.g., alcohol foam/liquid)
  - All standard EPA registered hospital surface disinfectants are effective (prefer products with a coronavirus claim)
- Call Infection Prevention and public health dept. 24/7 if you are aware of any patient with known or suspected nCo-V

INFECTION PREVENTION, NC HEALTH DEPARTMENT RECOMMENDATIONS, 10 MARCH

- CDC currently recommends a cautious approach to management of known or suspected cases.
  - Standard, contact, and airborne precautions are recommended for management of patients in healthcare settings with known or suspected COVID-19. These include:
    - Use of fit-tested NIOSH-approved N95 or higher-level respirators
    - Use of gowns, gloves and eye protection (e.g., goggles or face shield)
    - Use of negative-pressure airborne infection isolation rooms if available
  - Patients should be asked to wear a surgical mask as soon as they are identified as having symptoms of respiratory illness
  - Isolate patients in a private room with the door closed (use an airborne isolation room, if possible).
  - Patients with known or suspected COVID-19 should continue to wear a mask if placed in a private, non-airborne isolation room or if they must be moved from their room.
- As the situation continues to evolve, please find updated guidance at: https://www.cdc.gov/coronavirus/2019-nCoV/hcp/infection-control.html.

COVID-19, INFECTION PREVENTION

- Patients with COVID-19 will be cared for in Airborne Isolation rooms (i.e., >10 air exchanges per hour, direct out exhausted air, negative pressure)
- PPE is listed on the sign
- We will follow CDC Guideline for assessing any HCP exposed without proper PPE



USE OF ROOMS THAT CONTAINED A PATIENT WITH TB/MEASLES (per CDC reasonable to use with COVID-19)

TABLE 1. Air changes per hour (ACH) and time required for removal efficiencies of 99% and 99.9% of airborne contaminants*

	Minutes required for removal efficiency†	
ACH	99%	99.9%
2	138	207
4	69	104
6	46	69
12	23	35
15	18	28
20	14	21
50	6	8
400	<1	1

* This table can be used to estimate the time necessary to clear the air of airborne *Mycobacterium tuberculosis* after the source patient leaves the area or when aerosol-producing procedures are complete.
† Time in minutes to reduce the airborne concentration by 99% or 99.9%.

- Ideally, a large room (e.g., ED waiting room) a patient with TB/measles needs to remain unused by another patient for at least 2 hours (if not possible, have persons in the room wear a surgical mask)
- If the air exchange rate is known, use table to determine time to 99.9% clearance
- If the air exchange rate is not known (e.g., clinic, ED or inpatient room) leave door closed and do not use the room for 3.5 hours

MMWR 2005;54(RR-17):page 20
https://www.cdc.gov/infectioncontrol/guidelines/environmental/appendix/air.html#tableb1

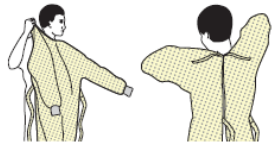
CDC, DONNING AND DOFFING PPE

SEQUENCE FOR PUTTING ON PERSONAL PROTECTIVE EQUIPMENT (PPE)

The type of PPE used will vary based on the level of precautions required, such as standard and contact, droplet or airborne infection isolation precautions. The procedure for putting on and removing PPE should be tailored to the specific type of PPE.

1. GOWN

- Fully cover torso from neck to knees, arms to end of wrists, and wrap around the back
- Fasten in back of neck and waist



2. MASK OR RESPIRATOR

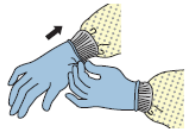
- Secure ties or elastic bands at middle of head and neck
- Fit flexible band to nose bridge
- Fit snug to face and below chin
- Fit-check respirator

3. GOGGLES OR FACE SHIELD

- Place over face and eyes and adjust to fit

4. GLOVES

- Extend to cover wrist of isolation gown



USE SAFE WORK PRACTICES TO PROTECT YOURSELF AND LIMIT THE SPREAD OF CONTAMINATION

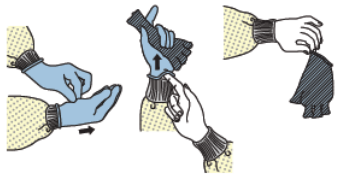
- Keep hands away from face
- Limit surfaces touched
- Change gloves when torn or heavily contaminated
- Perform hand hygiene

HOW TO SAFELY REMOVE PERSONAL PROTECTIVE EQUIPMENT (PPE) EXAMPLE 1

There are a variety of ways to safely remove PPE without contaminating your clothing, skin, or mucous membranes with potentially infectious materials. Here is one example. **Remove all PPE before exiting the patient room** except a respirator, if worn. Remove the respirator **after** leaving the patient room and closing the door. Remove PPE in the following sequence:

1. GLOVES

- Outside of gloves are contaminated!
- If your hands get contaminated during glove removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Using a gloved hand, grasp the palm area of the other gloved hand and peel off first glove
- Hold removed glove in gloved hand
- Slide fingers of ungloved hand under remaining glove at wrist and peel off second glove over first glove
- Discard gloves in a waste container

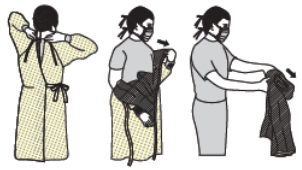


2. GOGGLES OR FACE SHIELD

- Outside of goggles or face shield are contaminated!
- If your hands get contaminated during goggle or face shield removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Remove goggles or face shield from the back by lifting head band or ear pieces
- If the item is reusable, place in designated receptacle for reprocessing. Otherwise, discard in a waste container

3. GOWN

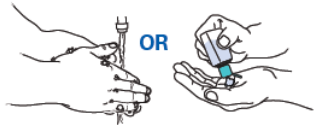
- Gown front and sleeves are contaminated!
- If your hands get contaminated during gown removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Unfasten gown ties, taking care that sleeves don't contact your body when reaching for ties
- Pull gown away from neck and shoulders, touching inside of gown only
- Turn gown inside out
- Fold or roll into a bundle and discard in a waste container



4. MASK OR RESPIRATOR

- Front of mask/respirator is contaminated — DO NOT TOUCH!
- If your hands get contaminated during mask/respirator removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Grasp bottom ties or elastics of the mask/respirator, then the ones at the top, and remove without touching the front
- Discard in a waste container

5. WASH HANDS OR USE AN ALCOHOL-BASED HAND SANITIZER IMMEDIATELY AFTER REMOVING ALL PPE



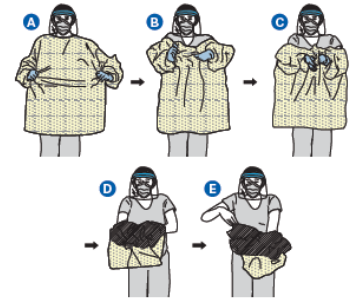
PERFORM HAND HYGIENE BETWEEN STEPS IF HANDS BECOME CONTAMINATED AND IMMEDIATELY AFTER REMOVING ALL PPE

HOW TO SAFELY REMOVE PERSONAL PROTECTIVE EQUIPMENT (PPE) EXAMPLE 2

Here is another way to safely remove PPE without contaminating your clothing, skin, or mucous membranes with potentially infectious materials. **Remove all PPE before exiting the patient room** except a respirator, if worn. Remove the respirator **after** leaving the patient room and closing the door. Remove PPE in the following sequence:

1. GOWN AND GLOVES

- Gown front and sleeves and the outside of gloves are contaminated!
- If your hands get contaminated during gown or glove removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Grasp the gown in the front and pull away from your body so that the ties break, touching outside of gown only with gloved hands
- While removing the gown, fold or roll the gown inside-out into a bundle
- As you are removing the gown, peel off your gloves at the same time, only touching the inside of the gloves and gown with your bare hands. Place the gown and gloves into a waste container



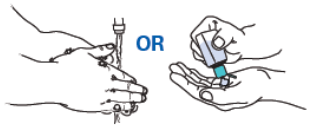
2. GOGGLES OR FACE SHIELD

- Outside of goggles or face shield are contaminated!
- If your hands get contaminated during goggle or face shield removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Remove goggles or face shield from the back by lifting head band and without touching the front of the goggles or face shield
- If the item is reusable, place in designated receptacle for reprocessing. Otherwise, discard in a waste container

3. MASK OR RESPIRATOR

- Front of mask/respirator is contaminated — DO NOT TOUCH!
- If your hands get contaminated during mask/respirator removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Grasp bottom ties or elastics of the mask/respirator, then the ones at the top, and remove without touching the front
- Discard in a waste container

4. WASH HANDS OR USE AN ALCOHOL-BASED HAND SANITIZER IMMEDIATELY AFTER REMOVING ALL PPE



PERFORM HAND HYGIENE BETWEEN STEPS IF HANDS BECOME CONTAMINATED AND IMMEDIATELY AFTER REMOVING ALL PPE

MERS: REASONS FOR HOSPITAL OUTBREAKS (failure to follow infection prevention recommendations)

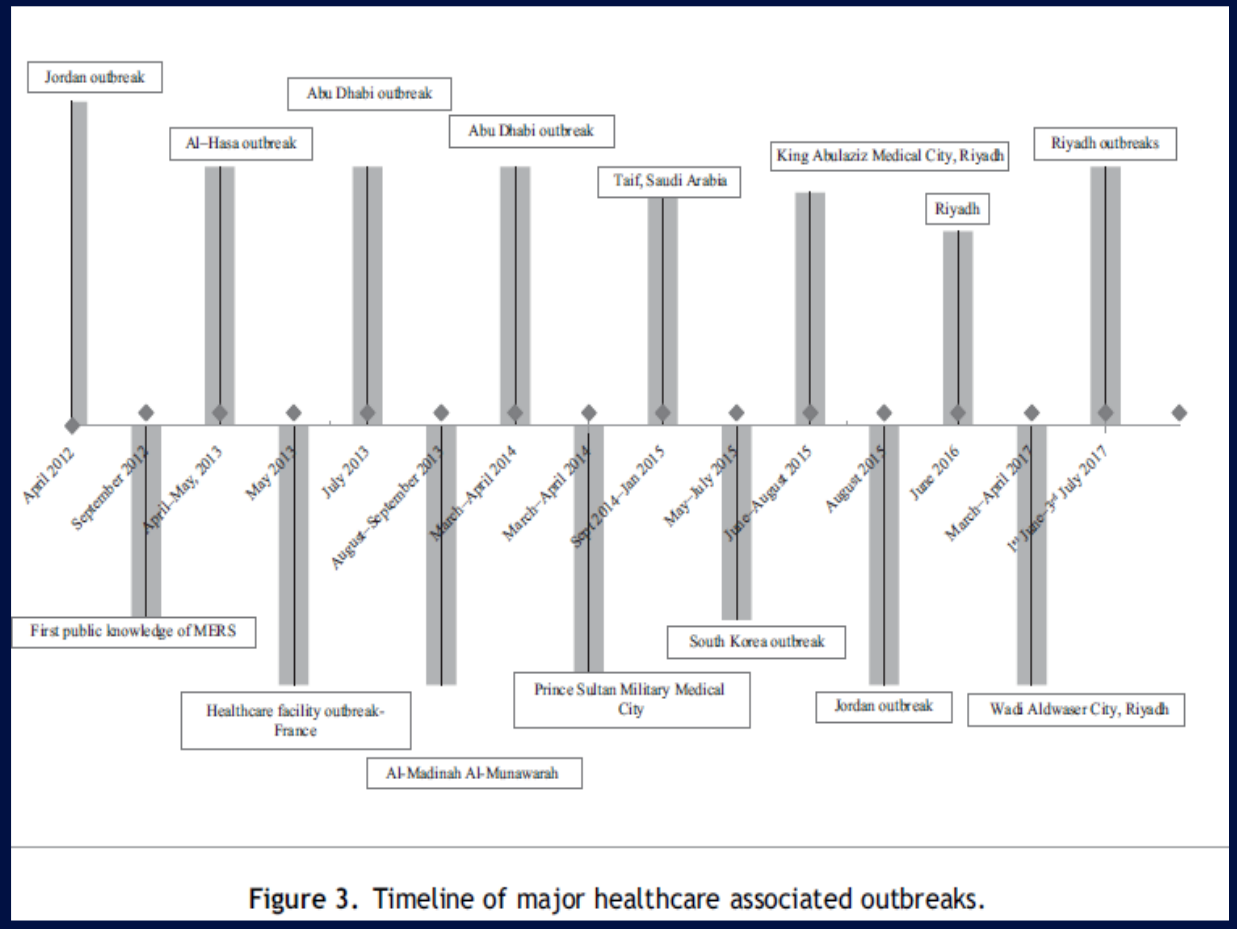


Figure 3. Timeline of major healthcare associated outbreaks.

Factors contributing to hospital outbreaks

Infection control issues	Examples	Number of instances where this was an issue	Involved hospitals	Reference
Hospital design	Absence of physical barriers between different beds, inadequate separation of suspected MERS patients, lack of isolation and negative pressure rooms	3	Jordan, Jeddah, Taif	[5,14,16,27,33,87]
Healthcare workers' adherence	Suboptimal adherence to infection control measures	4	Jordan, Al-Madinah Al-Muwnawarah, Jeddah, Riyadh	[5,14,16,21,23–25,33,87]
	Contacts prior to MERS diagnosis and under-recognition	1	Abu Dhabi	[28]
	Contact without respiratory protection	1	Abu Dhabi	[28]
	Overcrowding	2	South Korea,	[1,14,16,33–36,40–44,87]
Patient flow	No triaging and isolation of patients with respiratory illness, patients remained in the emergency room for many days, use of multi-bed rooms, extensive patients movements,	2	South Korea,	[1,14,16,33–36,40–44,87]
	Unfamiliarity with MERS infection	1	South Korea	[1,34–36,40–44]
	Under-recognition	2	Al-Madinah Al-Muwnawarah	[10,21,49]
Aerosol-generating procedures	Use of CPAP and nebulized medications and the performance of resuscitations	3	South Korea, Al-Hasa	[1,4,10,34–36,40–44]
Patients' characteristics	Contribution of super-spreaders	1	South Korea	[1,34–36,40–44]
Social norms	'Medical shopping', presence of multiple friends and family members with patients	1	South Korea	[1,34–36,40–44]

MERS, Middle East respiratory syndrome; CPAP, continuous positive airways pressure.

A—Tawfiq JA, Auwaerter PG. J Hosp Infect 2019:101:20-29

PPE STEWARDSHIP

- Do not request more PPE supplies than your area's normal usage supports.
- As we manage our increased usage and potential supply constraints, you may see the substitution of familiar PPE items with similar items (e.g., tie surgical masks substituting for ear loop masks).
- Appropriate usage of surgical masks includes only the following instances:
  - Essential healthcare personnel entering a patient room on Droplet Precautions,
  - Staff participating in surgery/procedures that require use of a mask,
  - Patients with coughs that cannot be contained with tissues,
  - Visitors of patients on Droplet Precautions
  - Staff who are appropriate to work (see occupational health policies) who have a cough that needs to be contained.
- Do not use surgical masks for:
  - Sick visitors. Sick visitors should not be allowed to visit and **should not** be given surgical masks unless they must visit due to extenuating circumstances (i.e. end of life visit).
  - 'Worried well' employees, patients or guests.
  - Personal use at home or in the community.

Mar 10, 2020

Governor Cooper Declares State Of Emergency To Respond To Coronavirus COVID-19

Department of Health and Human Services Issues Recommendations to Slow Spread

- State of Emergency includes:
  - Provisions similar to those enacted in a natural disaster
  - Improved access to funding to reduce cost and supply burdens
  - Increased state role in supporting local health departments
- Recommendations from Dr. Mandy Cohen, Secretary of DHHS
  - Implement work from home policy
  - Stagger start/end of shift to reduce mass gatherings
  - High risk and elder populations should avoid mass gatherings
  - Restrict visitors at residential facilities for high risk populations (ie nursing homes and elder care facilities)
  - Schools will remain open at this point as kids are low risk

UNC HEALTH RESPONSE TO STATE OF EMERGENCY

- Actions taken:
  - Distributed a clear Return to Work policy (emailed earlier today)
  - Voluntary visitor restrictions to be implemented
  - Guidance established for large group meetings (>50 people)
- Actions coming soon:
  - Work from home policy
  - Guidance for changes in other operations

AMBULATORY CARE STRATEGY
(Lead = Dr. Ian Buchanan)

- Ambulatory Care Goals
  - Minimize patient contact with other patients and staff
  - Provide rigorous, evidence-based screening of potential patients
  - Provide testing only in locations where physical environment and staff training support both safe testing and accurate results
- Operational Strategy:
  - Patients with respiratory symptoms should be directed to call the UNC COVID Hotline at: 1-888-850-2684. They should NOT go to their provider office or ED (unless acutely ill)
  - The COVID Hotline will triage patients to either 1) home care, 2) ED care, or 3) testing at a designated Respiratory Diagnostic Center (RDC) in each community. RDCs will provide both RPP testing and COVID testing (when available/appropriate).
  - Patients requiring home follow up after testing will receive daily calls from a trained nurse, with escalation to a virtual visit with a primary care physician when clinically indicated

Inpatient/ED Care Strategy – Christian Lawson

Tier 1
Enhanced Operations

- Specialized precautions, workflows & patient treatment areas identified
- Specialized training

Tier 2
Surge Operations

- Stressing capacity outside normal operations
- Designated space established for higher volume of COVID-19 patients
- Identify, train, and activate necessary staff beyond Tier 1 team

Tier 3
Critical Mass

- Volume exceeds Tier 2 operational capacity
- Consider alternate standards of care for COVID-19 patient population (Utilize non-negative pressure rooms, increased staffing ratios)
- Utilize alternate treatment sites (ICU boarding in OR or other procedural areas)

Inpatient/ED Care Strategy with associated triggers and tactics - Christian Lawson

Tier I
Heightened Normal Operations

Actions:
- Emergency Mgmt Executive Council Activated
- Response Teams Formed
- Specialized Acute & IP Workflows
- Tier II & III Plans developed
- Staffing & Travel Notifications generated for situation
- Reserve supplies ordered
- Overall operations normal
- Warning orders issued for Tier II

Triggers:
- Impending/on-going/post natural disaster
- Potential infectious disease outbreak in our service area
- Direction from the leadership, State, or National government

Tier II
Surge Operations

Actions:
- Tier II patient floor and staffing management plan initiated
- Continue Tier I actions
- Critical personnel & resources identified
- PTO and Admin restrictions put in place (can include quarantines)
- Access (visitors) restricted
- Supplies closely monitored and restricted as necessary
- Warning orders for Tier III

Triggers:
- Disease / situation specific patient volume exceeds Tier I capacity
- NC declares State of Emergency
- Direction from the leadership, State, or National government
- Uncontrolled community outbreak of disease

Tier III
Critical Operations Only

Actions:
- Tier III patient floor and staffing management plan initiated
- Continue Tier I & II actions
- Only urgent and emergent surgeries conducted
- Non-essential personnel restricted
- Non-clinical staff re-assigned to support clinical operations
- Non-essential activities halted
- Stand-up additional /excess capacity to support triage / care

Triggers:
- Disease / situation specific patient volume exceeds Tier II capacity
- Direction from the leadership, State, or National government
- Regional / local pandemic
- Mass casualty or acts of war

THANK YOU!!

Wuhan

Italy