COVID-19 (2019 nCo-V)

David Jay Weber, M.D., M.P.H., FSHEA, FIDSA, FRSM (London)
Professor of Medicine, Pediatrics, Epidemiology
Associate Chief Medical Officer, UNC Hospitals
Medical Director, Hospital Epidemiology
University of North Carolina at Chapel Hill

Disclosures: Consultant to PDI, Germitec, Lumagenics, Pfizer; Past Consultant, Merck

nCo-V, WHAT WE KNOW

- nCo-V is a novel coronavirus with ~70% 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 greatly surpasses SARS; number of deaths now surpasses SARS
- Person-to-person transmission documented including in the US to close contacts
- 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; 454 of 3,600 {13% 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 superspreader)
- Mortality: early data; Imperial College of London*, Report #4, 10 February (95% CI)
  - Asymptomatic & symptomatic, 1% (0.5-4%); Hubei Province ~18% (11-81%)%, outside China 1.2-5.6%
  - China data: Nationwide = 2.1%, Wuhan = 4.9%, Hubei = 3.1%, other provinces, 0.16%; admitted to hospital, 15%

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

nCo-V, WHAT WE KNOW

- 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
- 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)

nCo-V: OFFICIAL RESPONSES

- China
  - ~60 million restricted in their movements
  - China's health system running out of beds and supplies in the hardest hit locations
  - 1,000 bed new hospital constructed in Wuhan in 10 days (additional hospitals constructed)
- Travel advisories
  - CDC Warnings: Level 3 (avoid all non-essential travel) to China
  - CDC has issued mandatory quarantine for returnees from Wuhan (first time in >50 years)
  - U.S. State Dept: Level 4 (do not travel) for all of China; Level 2 (exercise increased caution) for Hong Kong & Macau
  - WHO: nCo-V represents a "Global Emergency" (but opposed to travel restrictions; limit relief supplies)
- Travel to and from China
  - Most international airlines have already cancelled all flights to China (US airlines extended cancellation till end of April)
  - US (also Australia and New Zealand) will NOT allow foreign nationals who have traveled from or transited through China to enter (citizens may return but will be quarantined for 14 days)
- US to begin screening for COVID-19 persons in 5 US cities with URIs

nCo-V, WHAT WE DO NOT KNOW

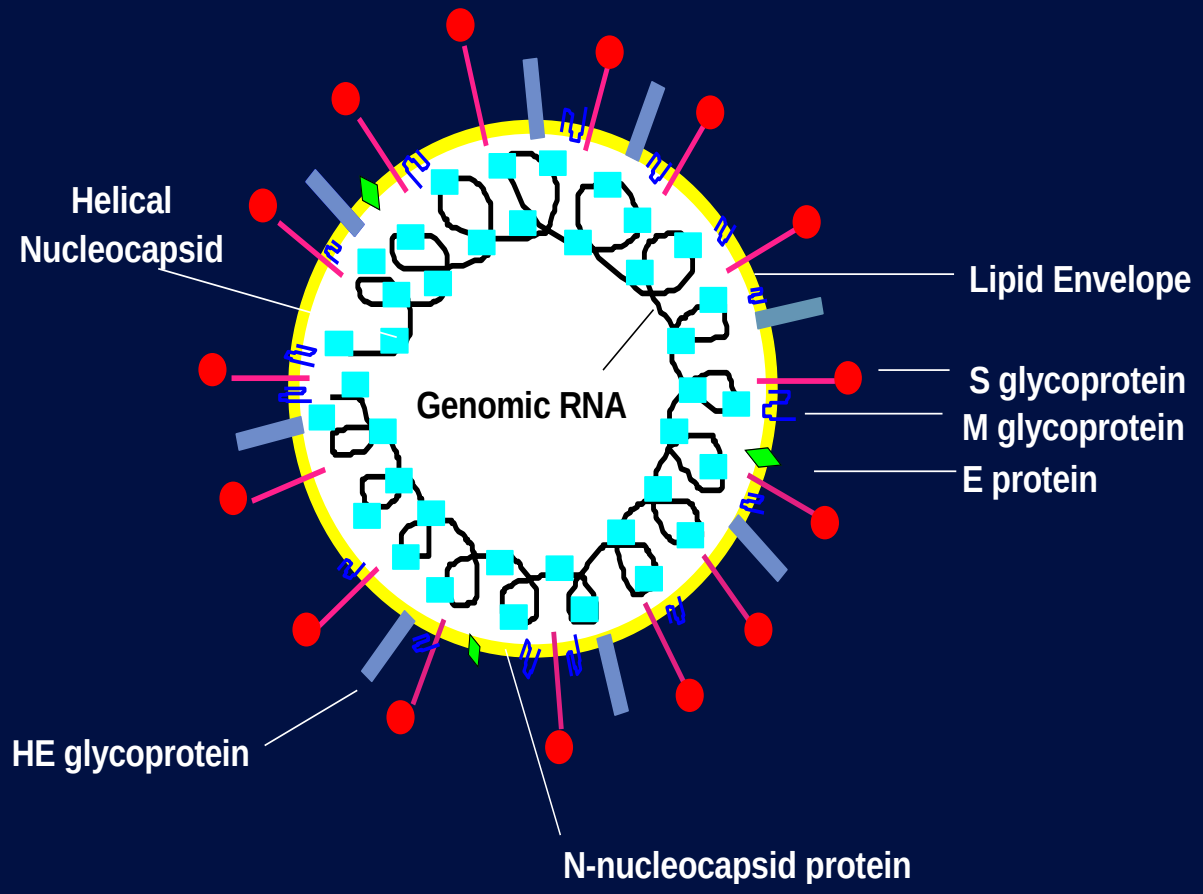
- Transmission: Unknown whether virus can be transmitted by the airborne route (i.e., >6 feet) or by indirect contact (likely based on SARS –CoV and MERS-CoV)
- Sensitivity and specificity of nCo-V tests being used in China (https://www.caixinglobal.com/2020-02-08/key-diagnostic-test-might-be-missing-many-coronavirus-cases-101513176.html)
- When to expand epidemiological (travel) parameters for screening possible cases: Wuhan city ➔ Hubei Provence ➔ mainland China ➔ Asia?
  - Outbreak in France resulted from traveler who acquired infection in Singapore (i.e., no travel to China)
- 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)
- Possibility of spread by fecal material (nCo-V has been isolated from stool and some patients have diarrhea)
- Frequency of super-spreaders

nCo-V, WHAT WE DO NOT KNOW

- When the outbreak will peak and number of countries that will be affected
- Impact of the outbreak and travel curtailment on goods and supplies from China: High likelihood of shortages of drugs/ PPE
- 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
- Possibility of transmission by contact or aerosolization of feces: nCo-V detected in stool, patients may have nausea and vomiting (SARS Co-V likely to have been transmitted via plumbing)

CORONAVIRUSES

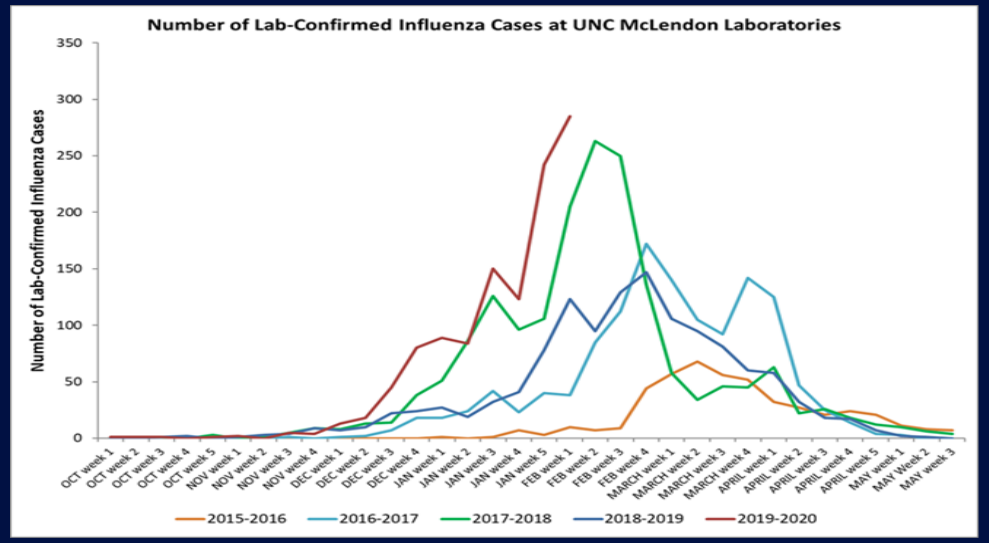
- Size and shape: 120-160 nm, pleomorphic
- Genome: Single-stranded, linear, positive-sense RNA
- Enveloped: Yes
- Reservoirs: Humans, multiple animal species
- Syndromes
  - Common colds: Account for up to 50% of upper respiratory tract infections
  - Gastroenteritis
  - SARS, MERS, SARI (nCo-V)

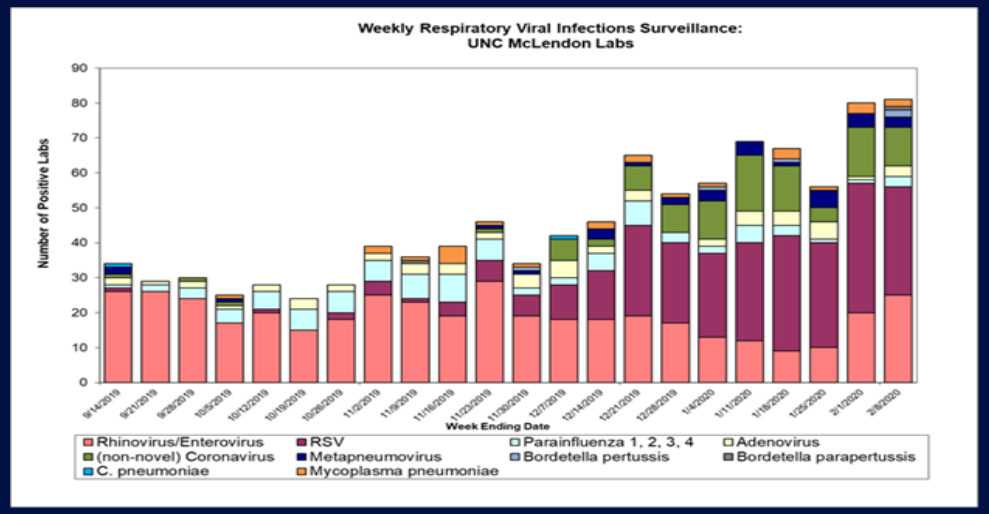


NON-EPIDEMIC, HUMAN CO-Vs: EPIDEMIOLOGY

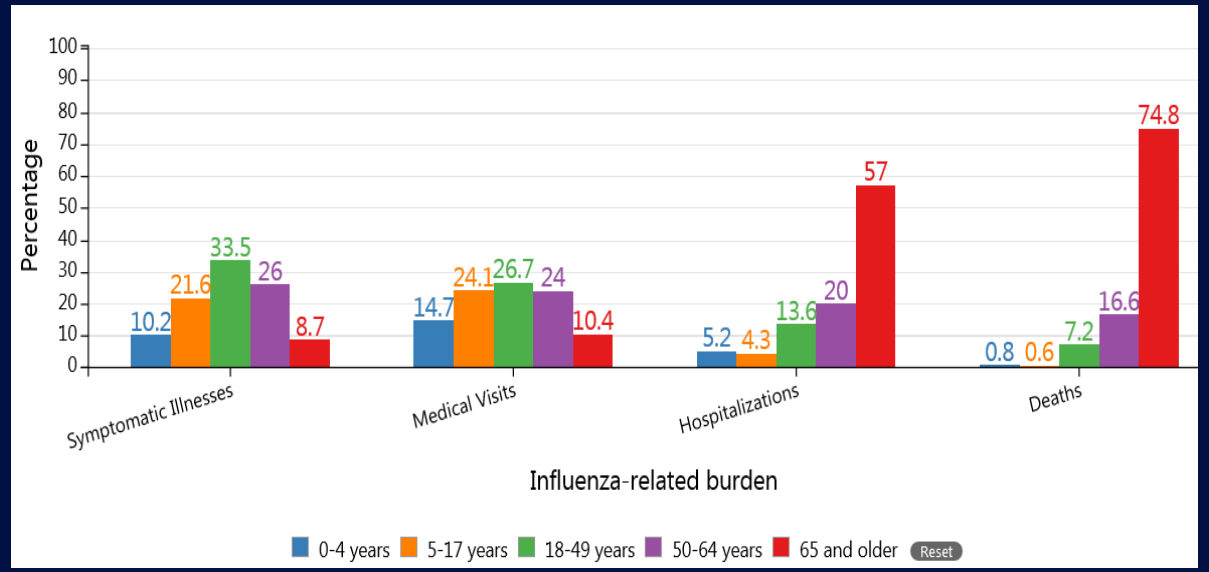
- Epidemiology
  - Worldwide; winter and spring in temperate climates
  - Exposure common in early childhood
  - Droplet, contact, and indirect contact
  - Symptoms and viral loads high first few days of illness
  - Incubation period 2–5 days
- Symptoms
  - Most often associated with upper respiratory tract infections in children
  - Lower tract infections in immunocompromised individuals and older adults
  - May play a role in exacerbations of underlying respiratory diseases

THE RISK OF INFLUENZA AND OTHER VIRAL RESPIRATORY PATHOGENS





- Burden of influenza, US, 2018-19
  - 35,000,000 illnesses; 16,500,000 medical visits; 490,000 hospitalizations; 34,200 deaths
- Burden of influenza, US, 2019-20
  - 22,000,000 illnesses; 210,000 hospitalizations; 12,000 deaths



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	~29 countries (~230 cases)
No. of cases (mortality)	8,096 (9.6%)	2,494 (~34%)	>70,000 (N ~1,775)*; 6,500 critical
No. of cases U.S.	8	2 (2014)	15 (7 states)
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%	2.2, 2.8; 80% in one study
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

* Cases and deaths in mainland China (additional cases and deaths outside of China = ~814 and 3)

^PAPR for cough-inducing procedures

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

Coronavirus Cases:

71,449

view by country

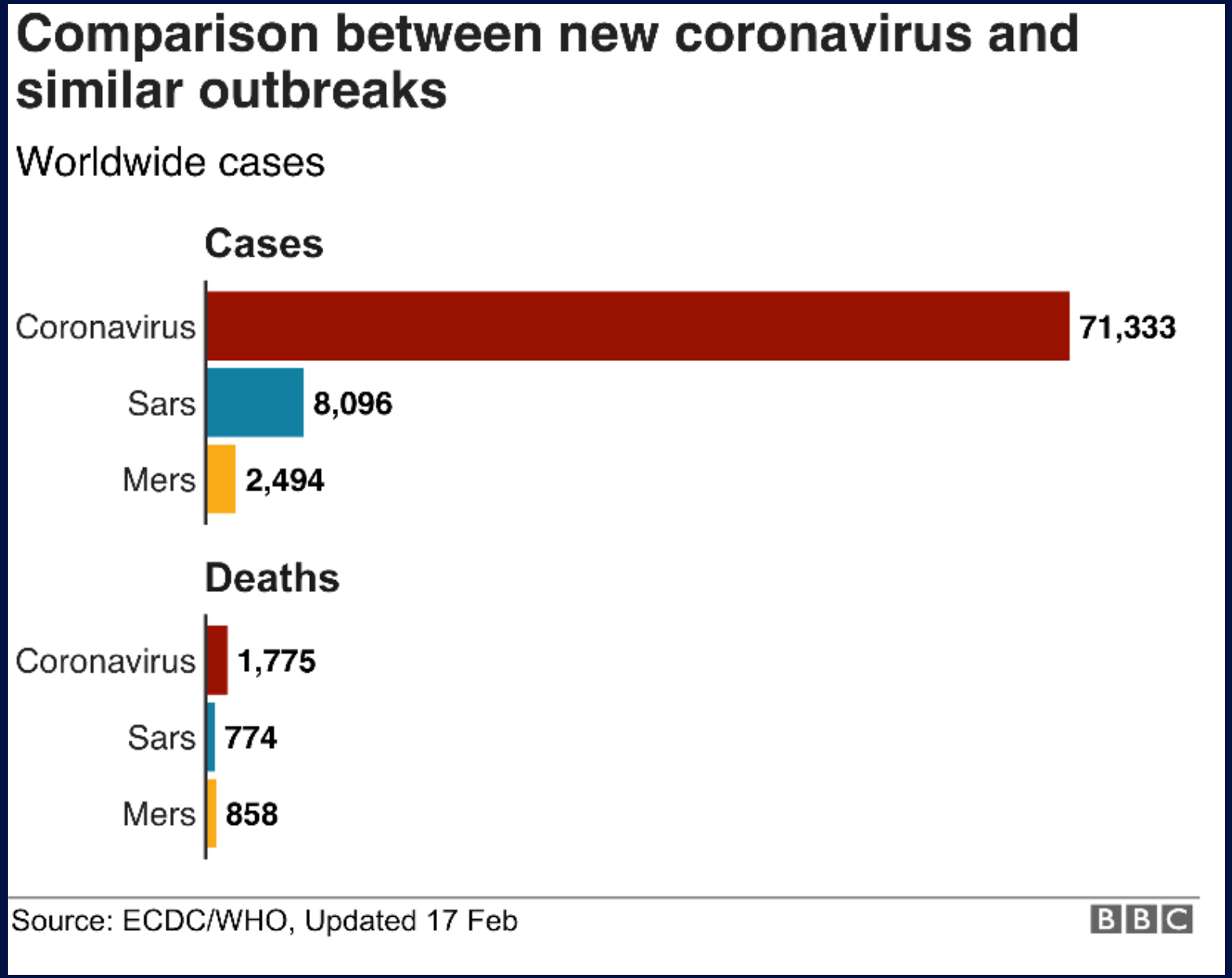
Deaths:

1,776

Recovered:

11,425

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



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

PHYLOGENEATIC ANALYSIS OF 2019-nCo-V AND OTHER CORONAVIRUSES

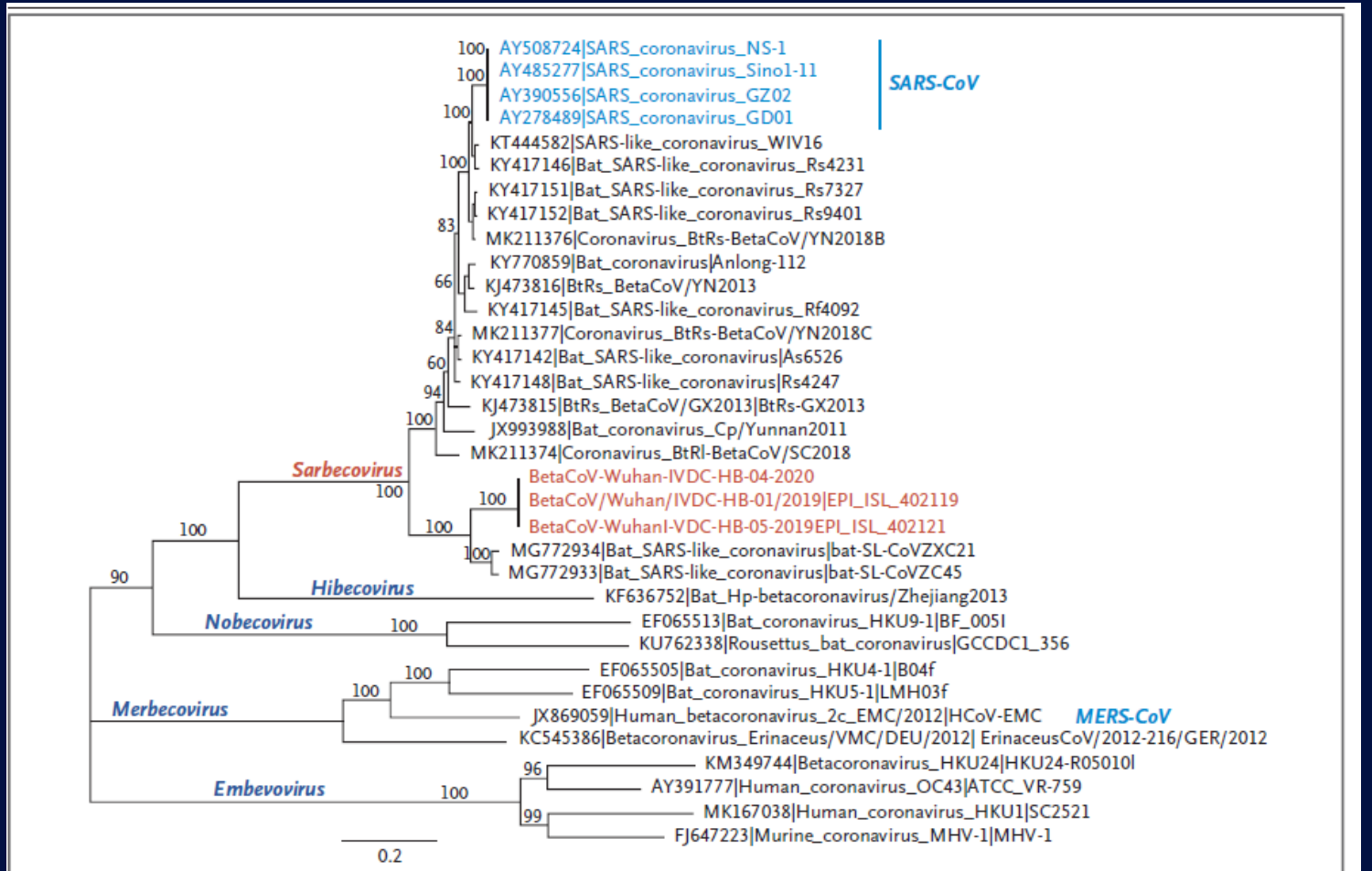
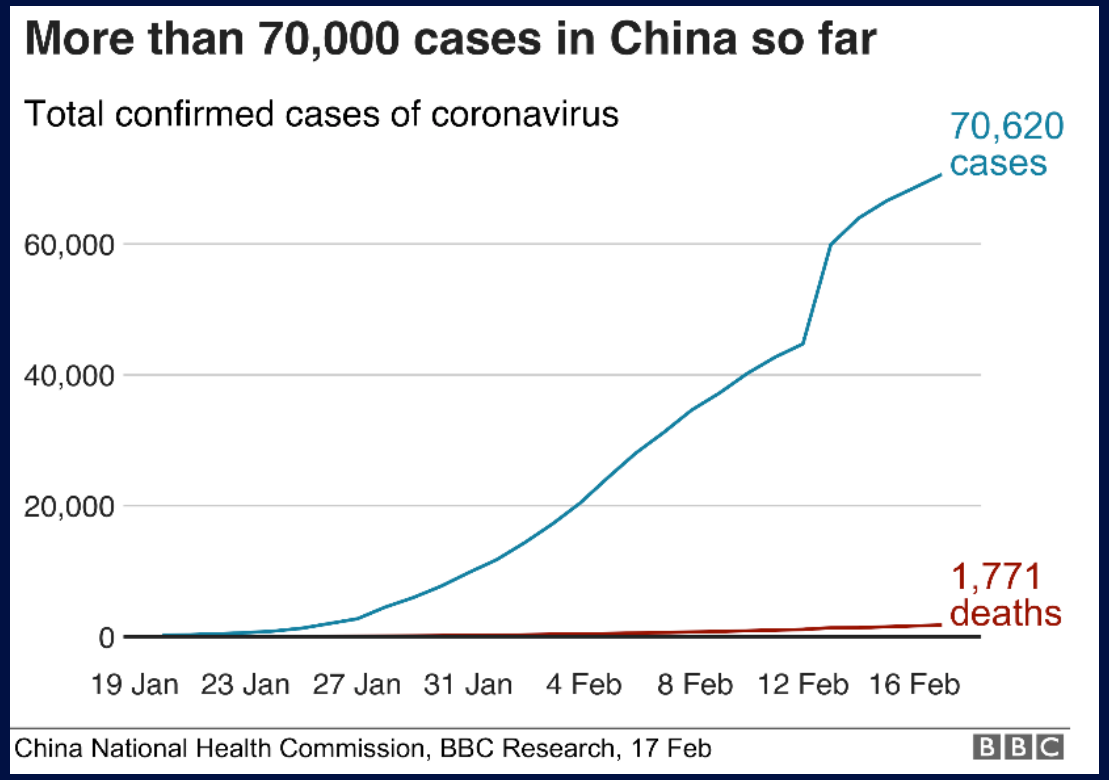
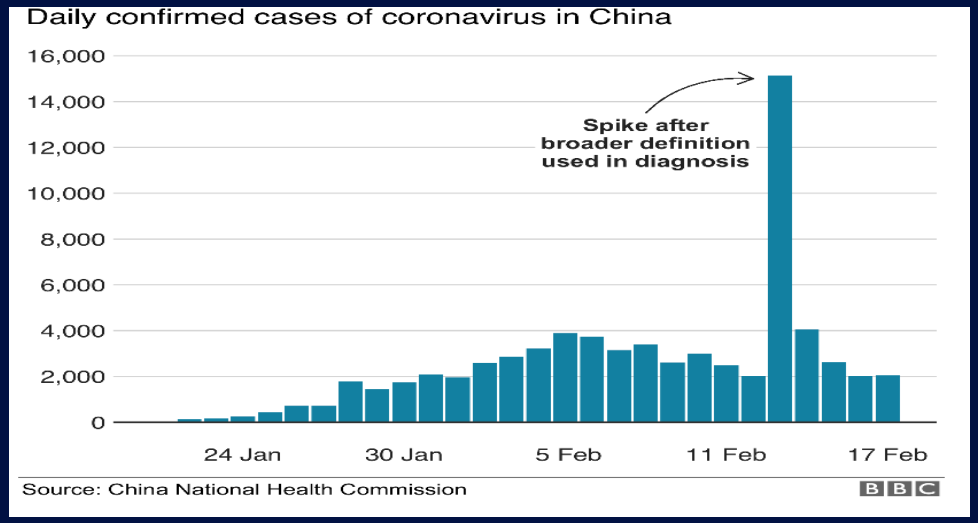
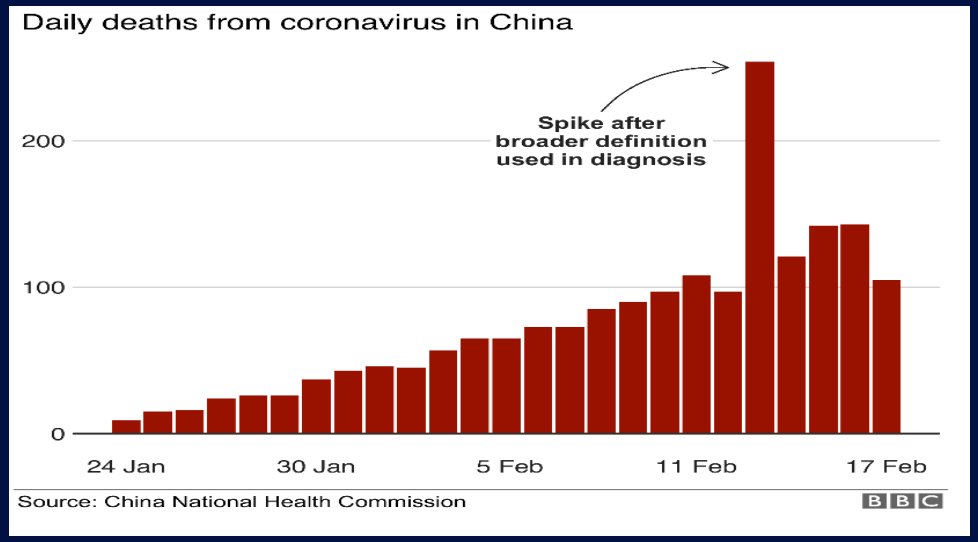


Figure 4. Phylogenetic Analysis of 2019-nCoV and Other Betacoronavirus Genomes in the Orthocoronavirinae Subfamily.

OUTBREAK CURVES, nCo-V

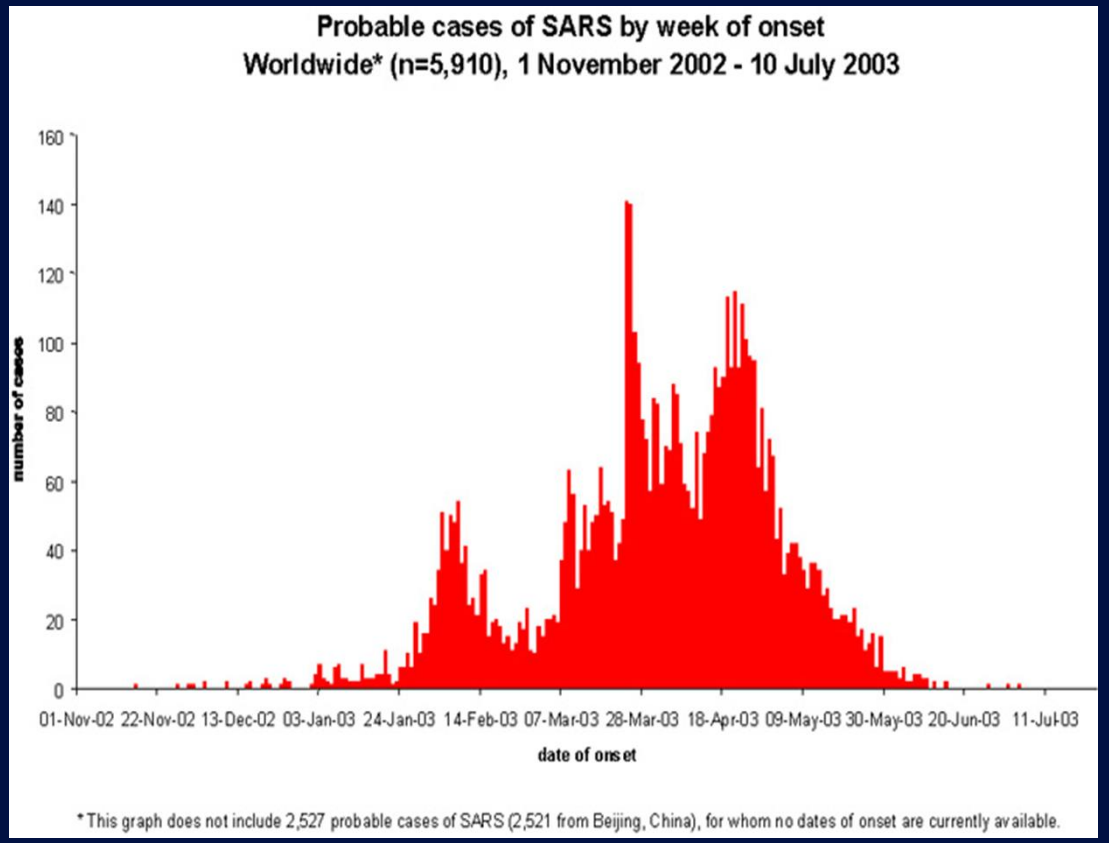


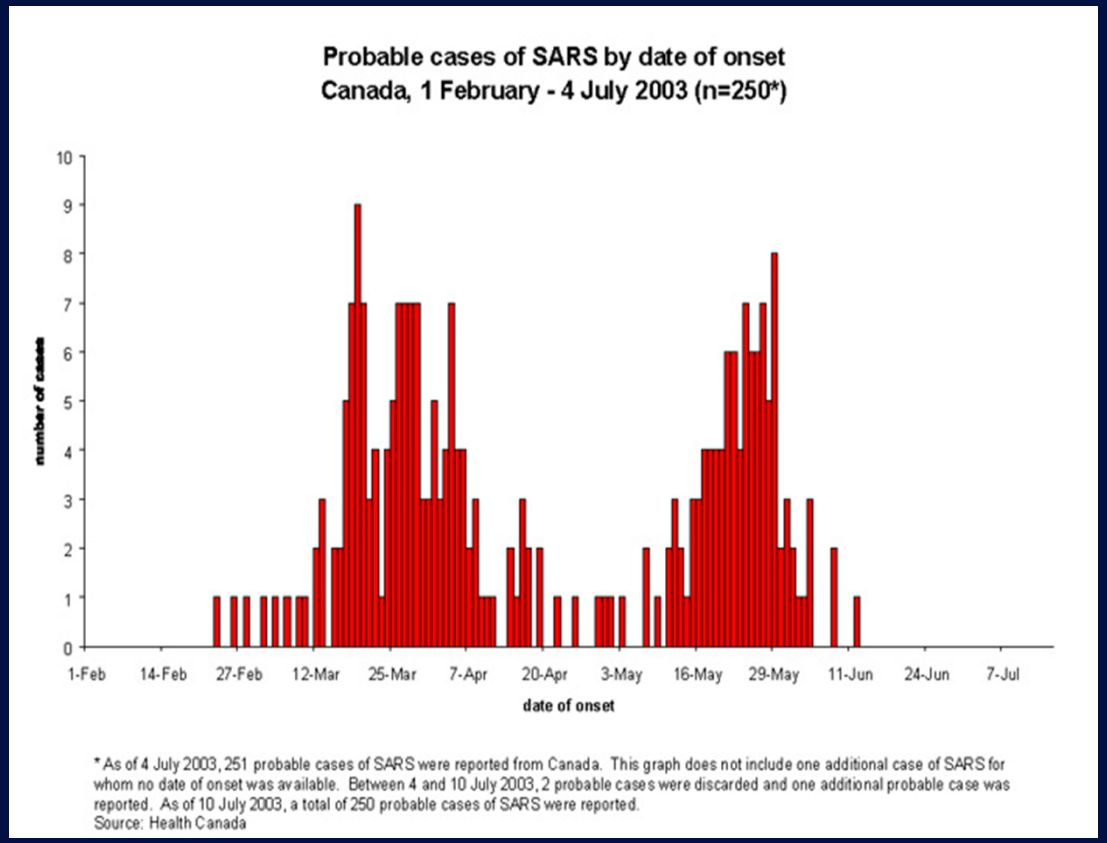


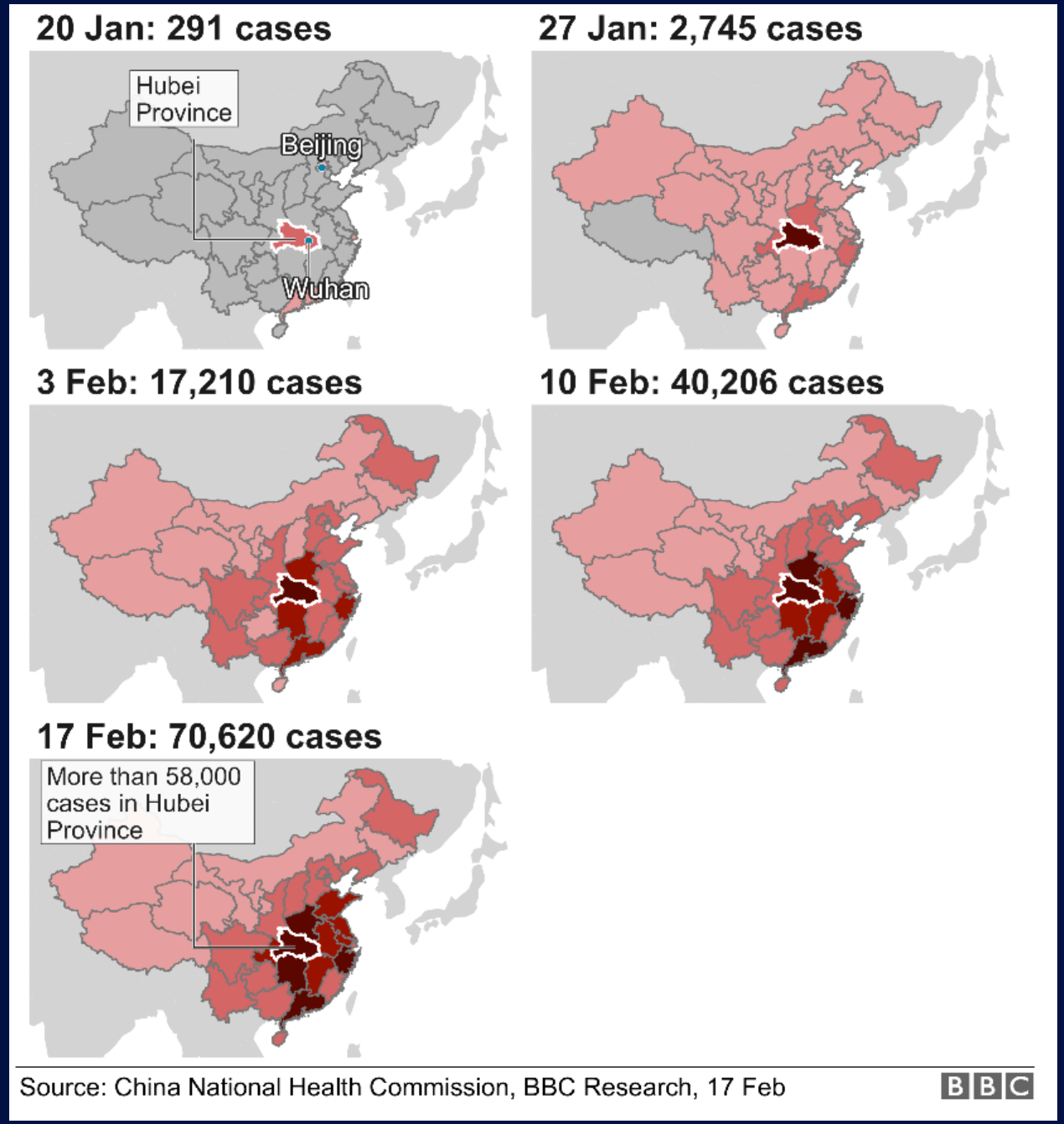


China has added a clinical definition (sx plus abn CxR/CT) to positive nCo-V tests for case counting
https://www.bbc.com/news/world-51235105

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







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

nCo-V COMPARED TO OTHER EMERGING VIRUSES

Table 1. Pathogenicity and Transmissibility Characteristics of Recently Emerged Viruses in Relation to Outbreak Containment.

Virus	Case Fatality Rate (%)	Pandemic	Contained	Remarks
2019-nCoV	Unknown*	Unknown	No, efforts ongoing	
pH1N1	0.02–0.4	Yes	No, postpandemic circulation and establishment in human population	
H7N9	39	No	No, eradication efforts in poultry reservoir ongoing	
NL63	Unknown	Unknown	No, endemic in human population	
SARS-CoV	9.5	Yes	Yes, eradicated from intermediate animal reservoir	58% of cases result from nosocomial transmission
MERS-CoV	34.4	No	No, continuous circulation in animal reservoir and zoonotic spillover	70% of cases result from nosocomial transmission
Ebola virus (West Africa)	63	No	Yes	

* Number will most likely continue to change until all infected persons recover.

Munster VJ, et al. NEJM 2020;Jan 24 (epub)

COMPARISON OF nCo-V TO OTHER OUTBREAKS

Wuhan coronavirus compared to other major viruses

VIRUS	YEAR IDENTIFIED	CASES	DEATHS	FATALITY RATE	NUMBER OF COUNTRIES
Ebola**	1976	33,577	13,562	40.4%	9
Nipah	1998	513	398	77.6%	2
SARS	2002	8,096	774	9.6%	29
MERS*	2012	2,494	858	34.4%	28
Wuhan**	2020	914	26	2.8%	10

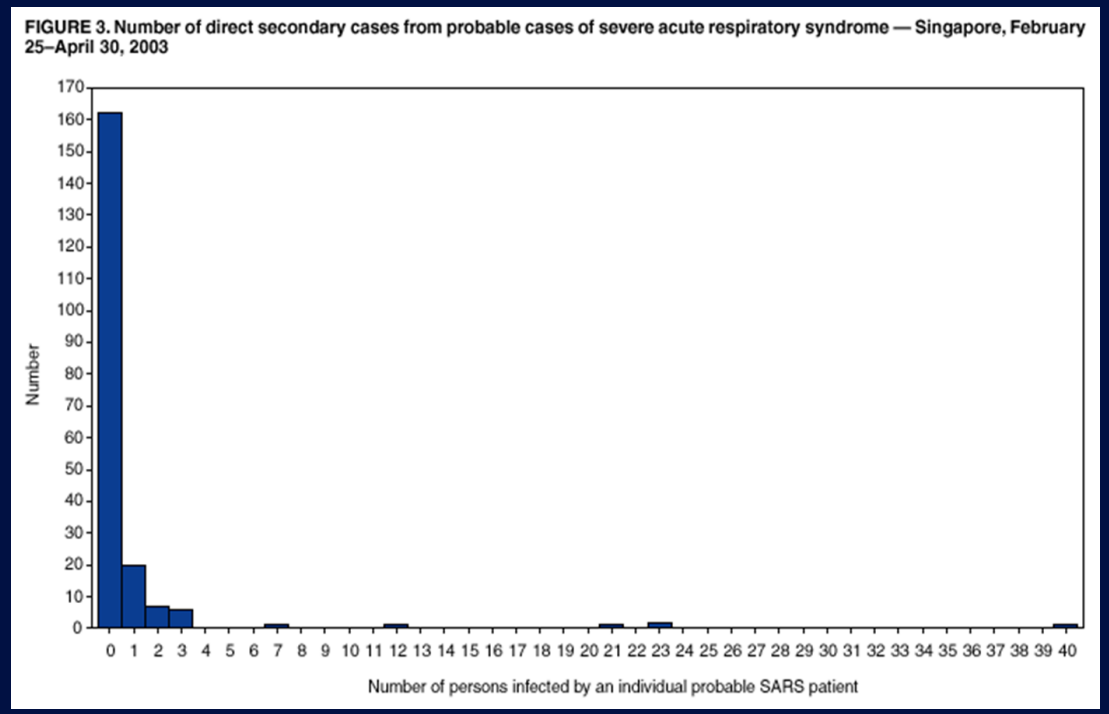
Sources: CDC; World Health Organization; New England Journal of Medicine; Malaysian Journal of Pathology

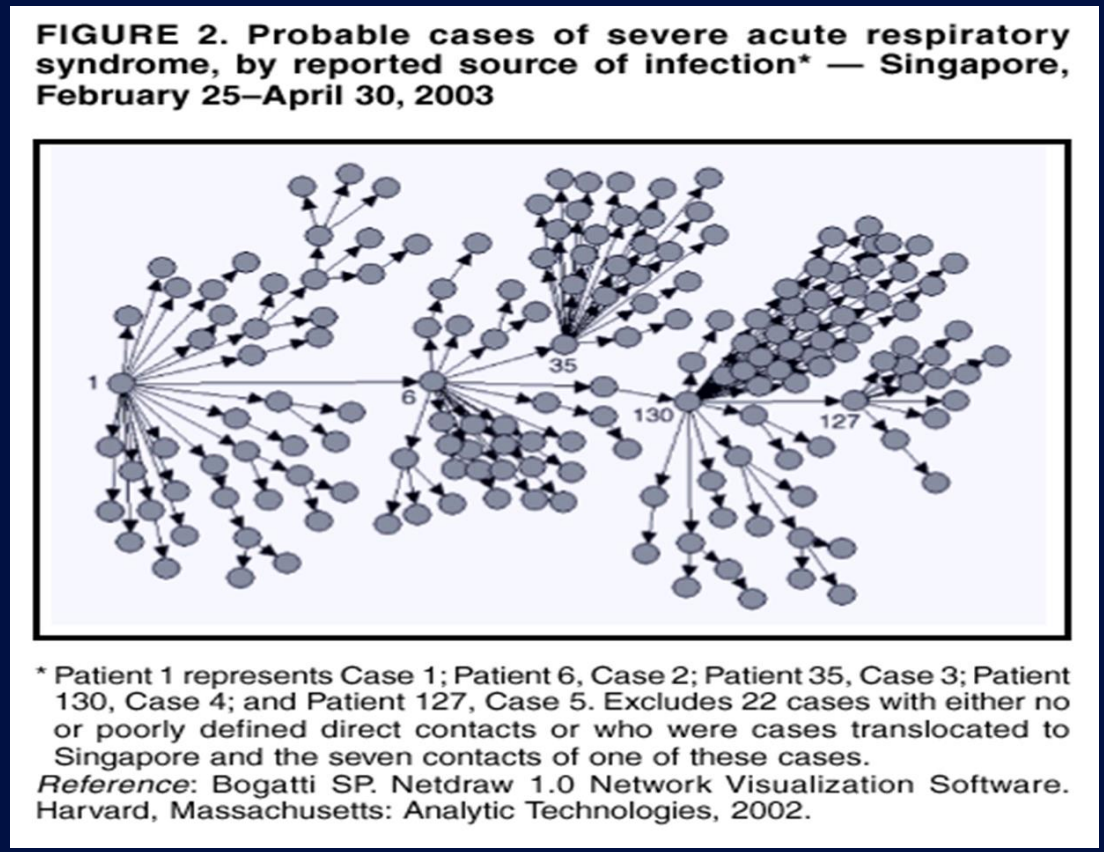
*As of November 2019 **As of January 24, 2020

BUSINESS INSIDER

https://www.businessinsider.com/china-virus-everything-we-know-deadly-2019-ncov-wuhan-spread-2020-1#but-there-are-still-ways-to-protect-yourself-travelers-should-avoid-touching-their-eyes-nose-or-mouth-with-unwashed-hands-7

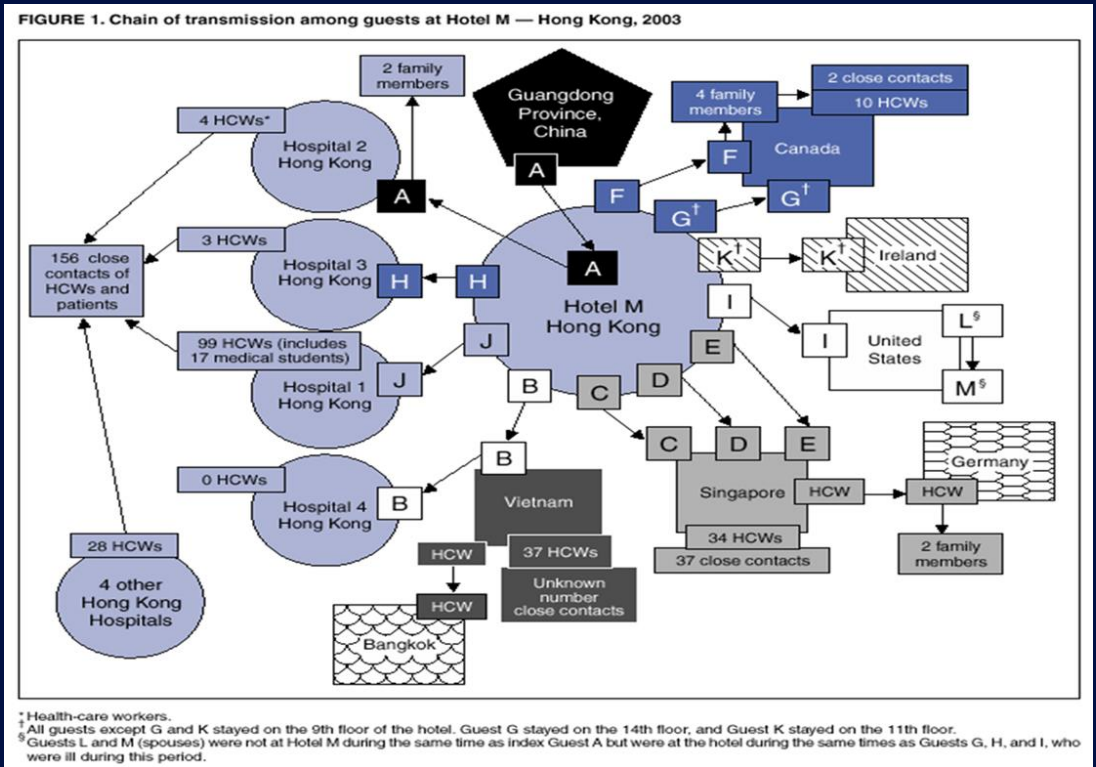
WHAT IS A SUPERSPREADER?
(A person with transmits infection to >10 persons)

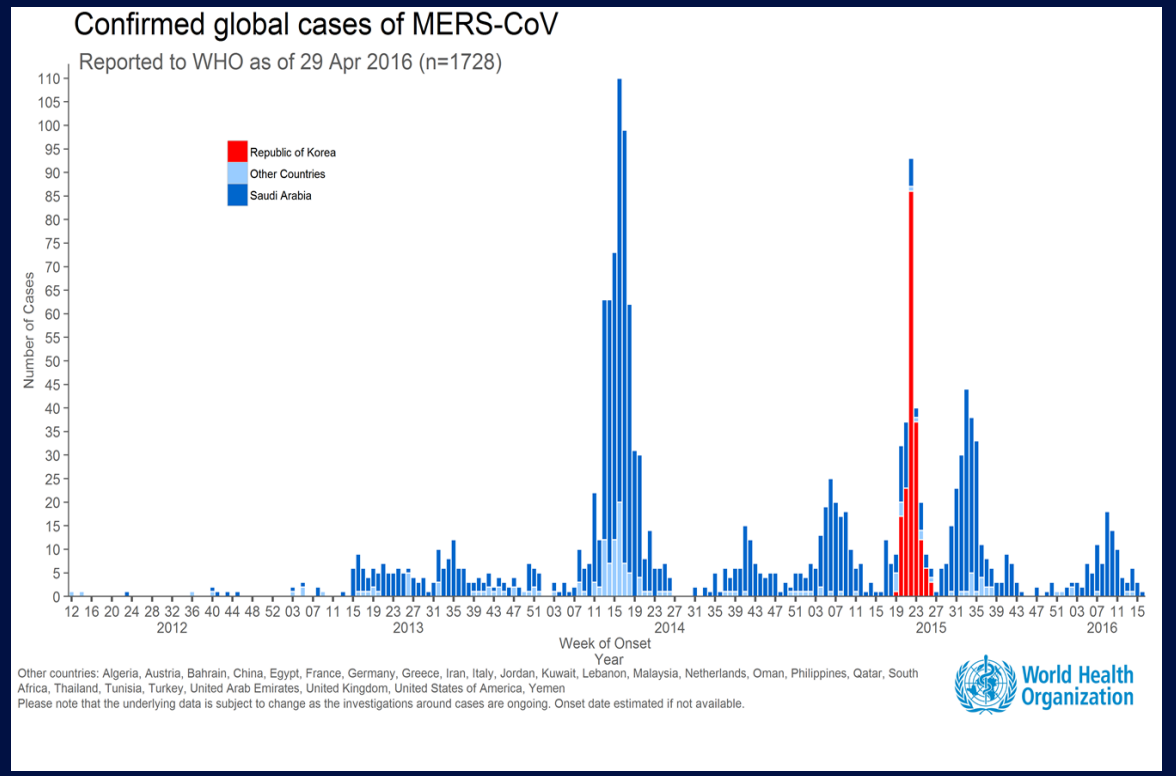




Infectivity of SARS and demonstration of superspreaders

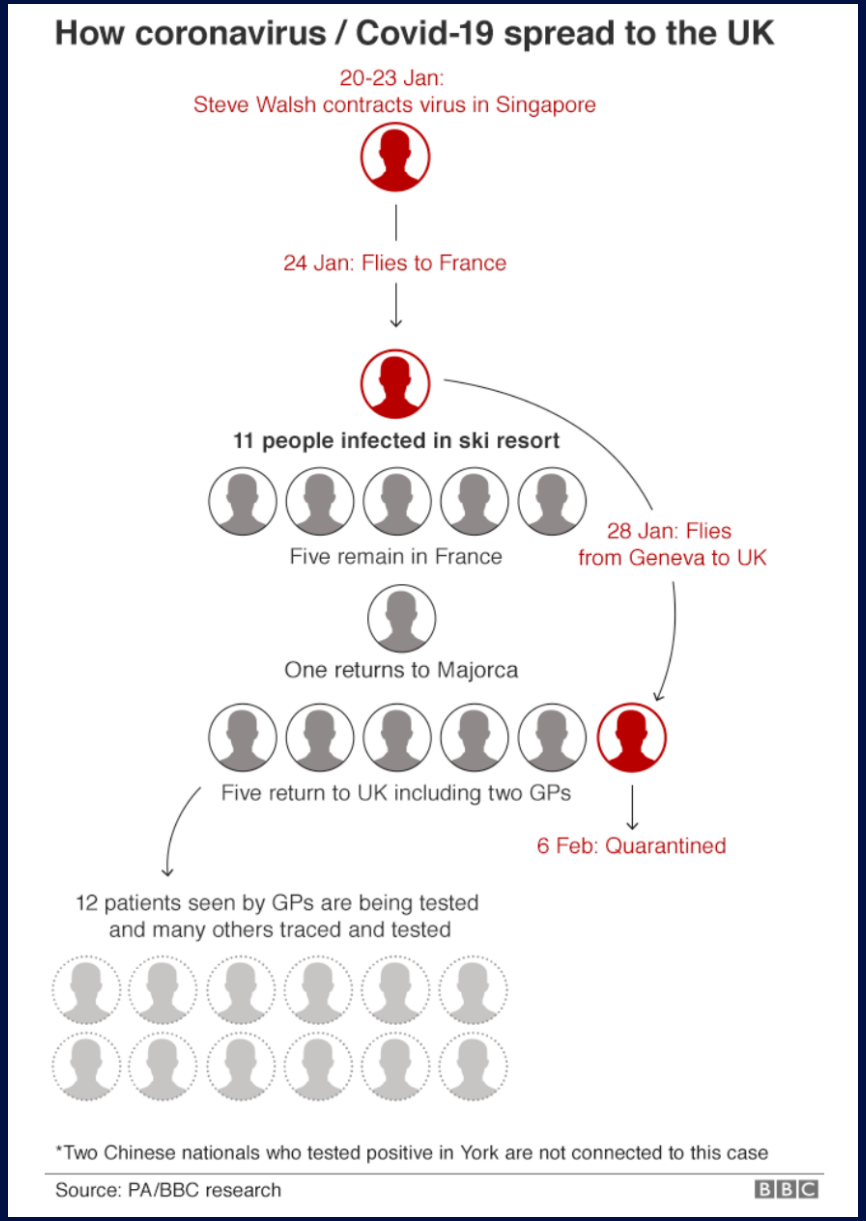
IMPACT OF A SINGLE SUPERSPEADER





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

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

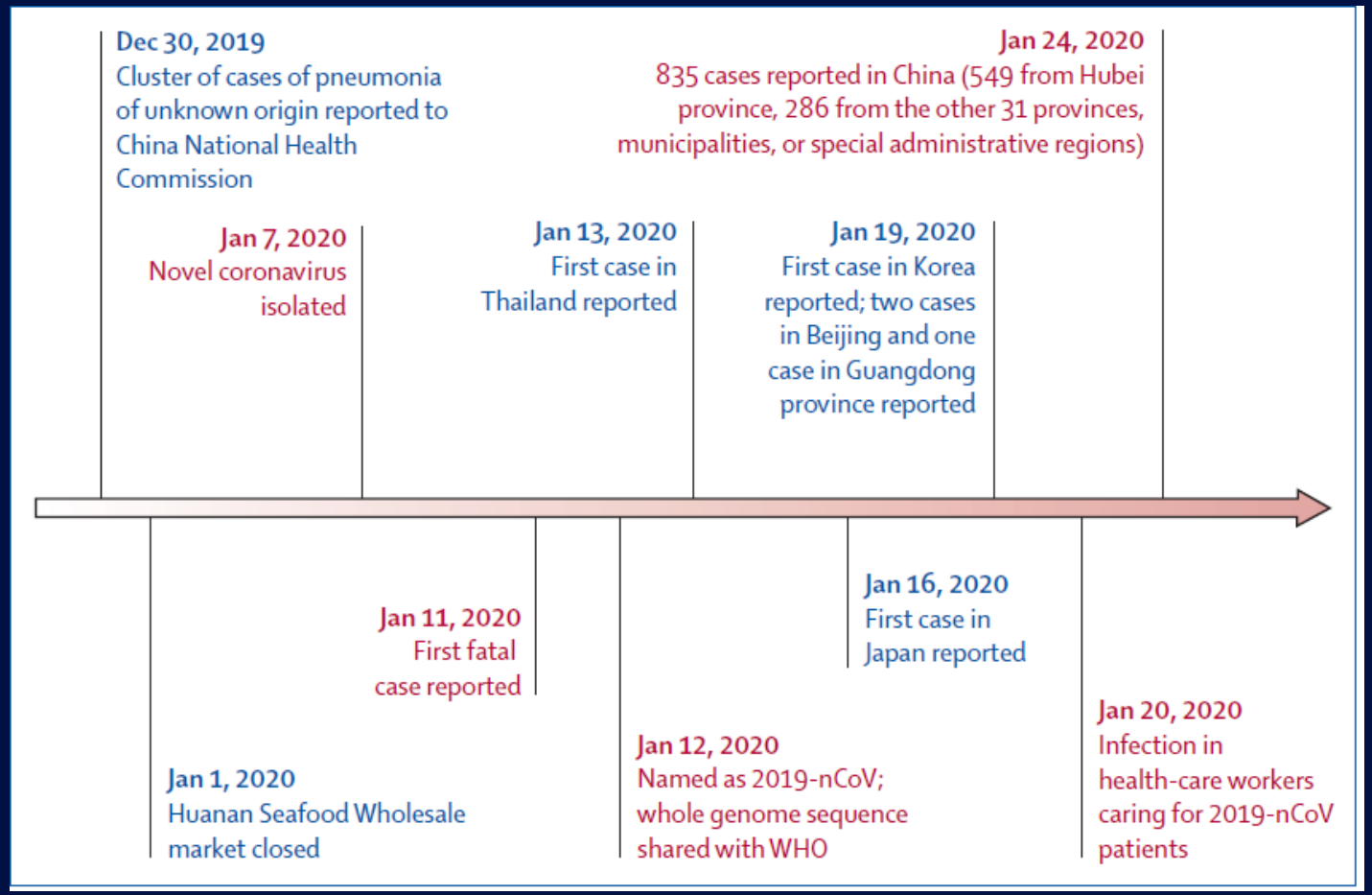
LESSONS LEARNED FROM SARS

- 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 personnal 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

CURRENT OUTBREAK OF nCo-V

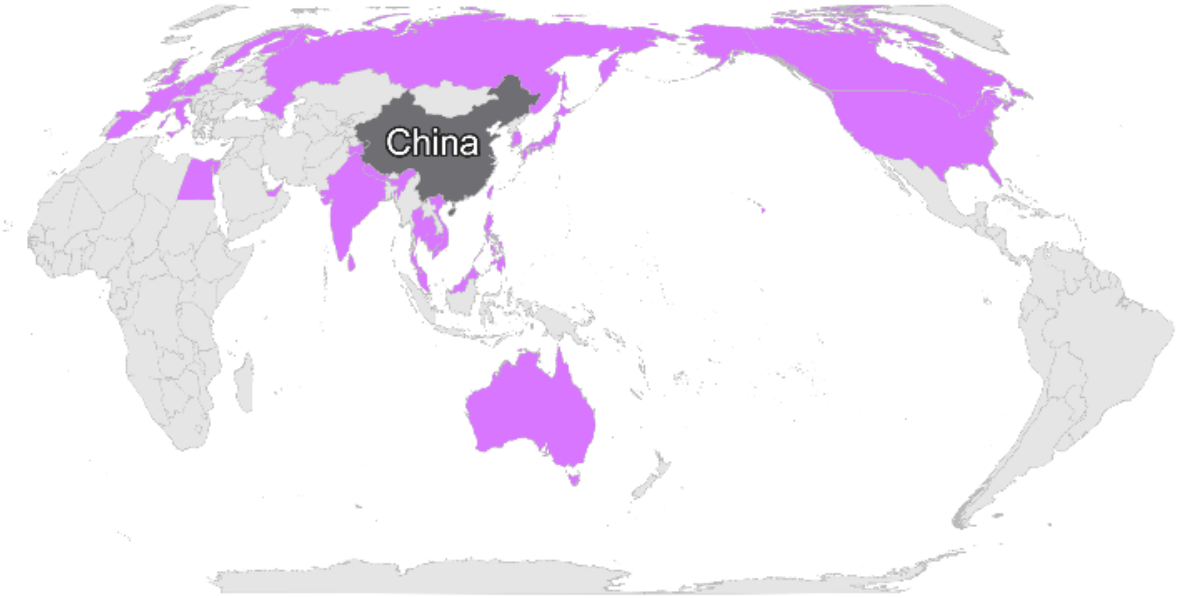

Wuhan Tianhe International Airport

TIMELINE OF EARLY STAGES OF 2019-nCo-V OUTBREAK



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

Cases of coronavirus outside China



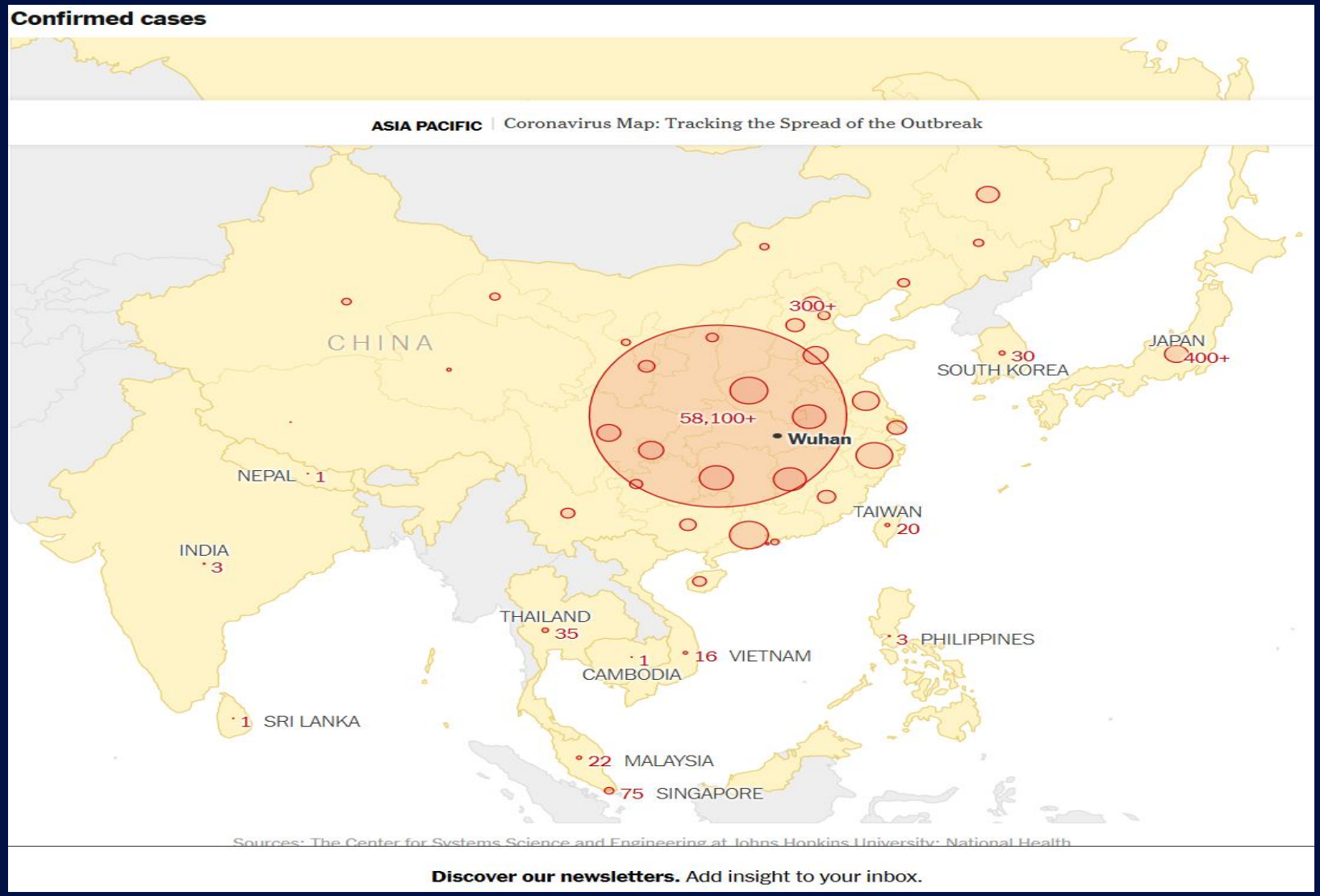
Japan*	513	Vietnam	16	India	3	Nepal	1
Singapore	75	Australia	15	Philippines	3	Sri Lanka	1
Thailand	34	US	15	Italy	3	Sweden	1
South Korea	30	France	12	Russia	2	Belgium	1
Malaysia	22	UK	9	Spain	2	Egypt	1
Taiwan	20	UAE	9	Cambodia	1		
Germany	16	Canada	8	Finland	1		

*figure includes 454 cases on board a cruise ship

Source: ECDP and Japanese Ministry of Health. Updated: 17 Feb

BBC

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

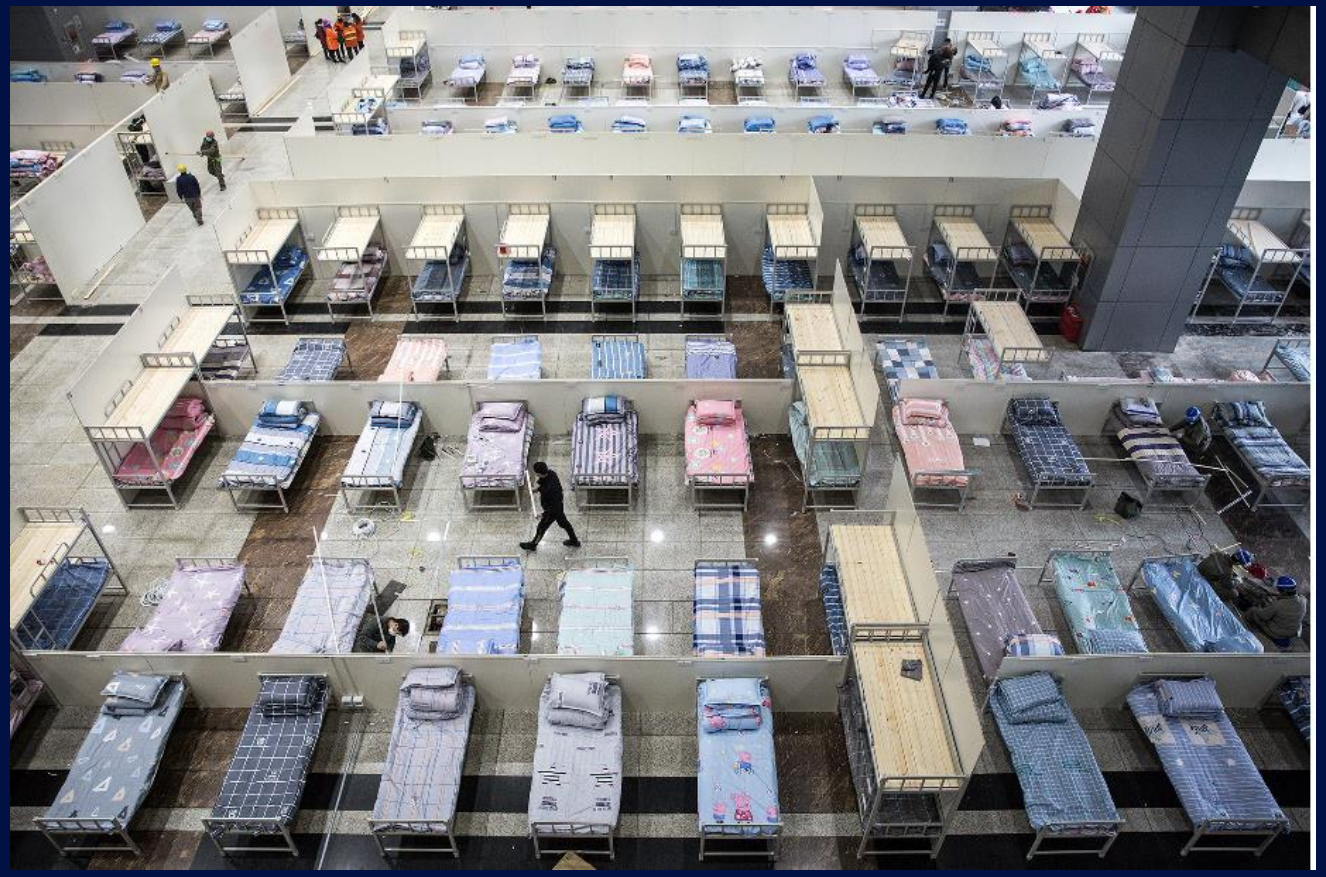


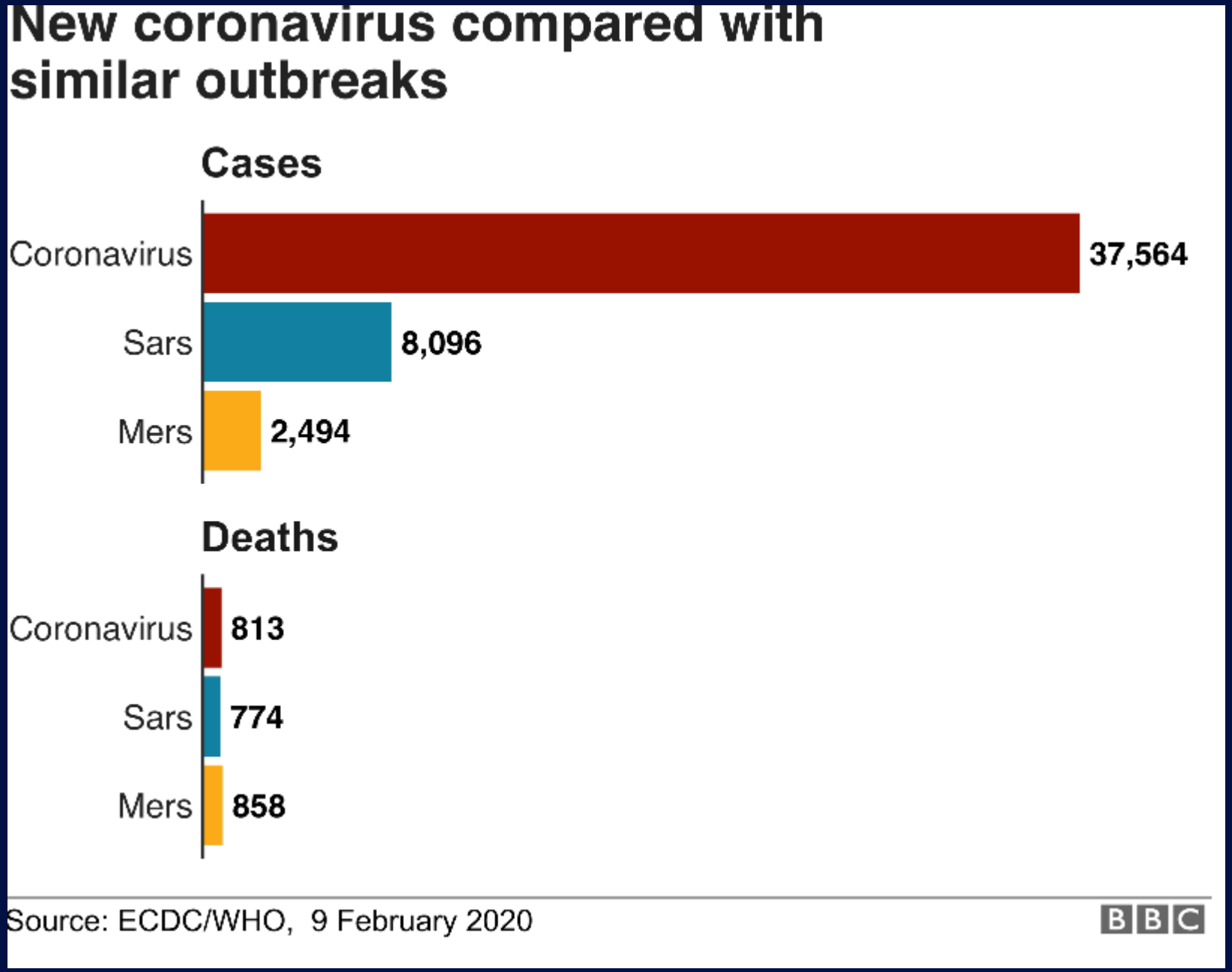
https://www.nytimes.com/interactive/2020/world/asia/china-wuhan-coronavirus-maps.html

CHINESE HOSPITAL, WUHAN

https://www.nytimes.com/2020/01/24/world/asia/china-coronavirus.html

CONVERSION OF A GYMNASIUM AND EXHIBITION CENTER INTO A CORONAVIRUS HOSOPITAL, WUHAN





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

FORECASTING nCo-V SPREAD

- Forecasting nCo-V spread
- Methods: Data from 12/31/19 to 1/28/20
- Results:
  - Reproductive number, 2.68 (95% CI, 2.47-2.86)
  - Estimate 75,815 people infected
  - Epidemic doubling time, 6.4 days (95% CI, 5.8-7.1)

Wu JT, et al. Lancet; 31 January 2020

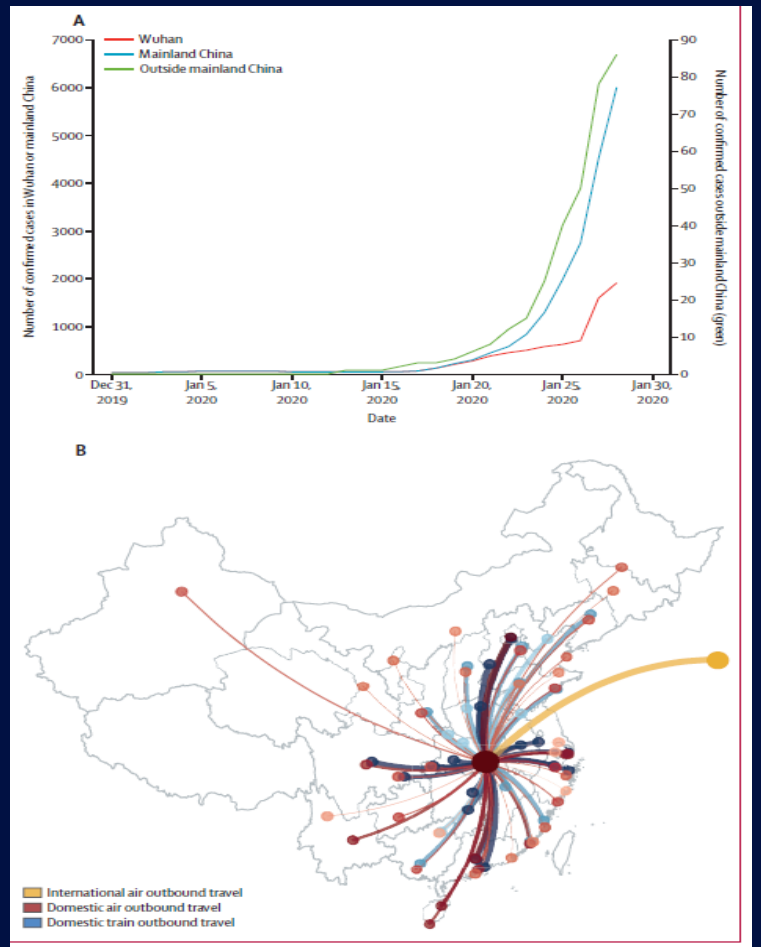


Figure 1: **Risk of spread outside Wuhan**
(A) Cumulative number of confirmed cases of 2019 novel coronavirus as of Jan 28, 2020, in Wuhan, in mainland China (including Wuhan), and outside mainland China. (B) Major routes of outbound air and train travel originating from Wuhan during *chunyun*, 2019. Darker and thicker edges represent greater numbers of passengers. International outbound air travel (yellow) constituted 13·5% of all outbound air travel, and the top 40 domestic (red) outbound air routes constituted 81·3%. Islands in the South China Sea are not shown.

	Number of air passengers per month in 2019
Bangkok	16 202
Hong Kong*	7531
Seoul	5982
Singapore	5661
Tokyo	5269
Taipei	5261
Kota Kinabalu	4531
Phuket	4411
Macau	3731
Ho Chi Minh City	3256
Kaohsiung	2718
Osaka	2636
Sydney	2504
Denpasar-Bali	2432
Phnom Penh	2000
London	1924
Kuala Lumpur	1902
Melbourne	1898
Chiang Mai	1816
Dubai	1799

Data were obtained from the Official Airline Group. *Due to the ongoing social unrest since June, 2019, we used actual flight volume based on local estimates in the models.

Table 2: **Cities outside of mainland China to which Wuhan had the greatest volume of outbound air travel in January–February, 2019**

	SARS-CoV	MERS-CoV	Commonly circulating human CoVs (229E, NL63, OC43, HKU1)
Basic reproductive number, mean (95% CI), or prevalence of infection (for commonly circulating human CoVs)	Beijing: 1·88 overall,[1] 0·94 after generation 1 (excluding SSE).[1] Hong Kong: 1·70 (0·44–2·29)* overall,[2] 2·7 (2·2–3·7) in the early phase (excluding SSE),[3] range 0·14–1 in the later phase (excluding SSE).[3] Singapore: 1·63 overall[1] or 1·83 (0·47–2·47)* overall,[2] range 2·2–3·6 in the early phase (including SSE).[4] Toronto 0·86 (0·24–1·18)* overall.[2] Worldwide: 0·95 (0·67–1·23) overall.[5]	Middle East: 0·47 (0·29–0·80) overall.[6] Saudi Arabia: 0·45 (0·33–0·58) overall.[7] Middle East and South Korea: 0·91 (0·36–1·44) overall.[5] South Korea: range 2·0–8·1 in early phase (including SSE).[8]	229E and OC43 in USA:[9] annual infection attack rates of 2·8% to 26·0% in prospective cohorts. Guangzhou, China:[10] CoVs detected in 2·25% of adults and children with fever and upper respiratory infection symptoms, among which 60% were OC43, 17% were 229E, 15% were NL63, and 7·8% were HKU1. UK:[11] CoVs detected in all age groups, most frequently in children aged 7–12 months (4·86%)
Incubation period, days, mean (SD) or mean (95% CI)	Hong Kong:[12] 4·6 (3·8–5·8). Hong Kong:[13] 4·4 (4·6). Beijing:[13] 5·7 (9·7). Taiwan:[13] 6·9 (6·1)	Saudi Arabia:[14] 5·0 (4·0–6·6). South Korea:[14] 6·9 (6·3–7·5).	OC43 and other common human CoVs:[15] range 2–4. common human CoVs:[16] range 2–5. Common human CoVs:[17] range 3–4.
Serial interval, days, mean (SD)	Singapore:[4] 8·4 (3·8).	Saudi Arabia:[7] 6·8 (4·1). South Korea:[18] 12·4 (2·8).	..
Seroprevalence among non-cases	Hong Kong, among close contacts:[19] around 0%.	Qatar:[20] 0·21% (10 of 4719) among healthy blood donors, 0·74% (1 of 135) among individuals who are close contacts of cases but not sick. Arabian Peninsula:[21] 0·15% (15 of 10 365) among general population, 6·2% (68 of 1090) among individuals exposed to camels.	OC43 and 229E:[22] 86–100%. HKU1, S-protein-based ELISA:[23] 0% in children aged <10 years, to a plateau of 21·6% in adults aged 31–40 years.
Case-hospitalisation probability, mean (95% CI)	Around 100%.[12]	South Korea:[24] around 100%.	OC43 in Canada:[25] 12·6% among older and disabled adults in a long-term care facility. 229E and OC43 in USA:[9] prevalence of 3·3–11·1% in a hospitalised cohort. Brazil:[26] 11% among children aged <3 years attending the paediatric emergency room with acute lower respiratory infection and hospitalised.
Case-fatality proportion	Worldwide (WHO): 9·6% among probable cases. mainland China:[27] 6·4% among probable cases. Hong Kong:[12] 17% among laboratory-confirmed cases.	Worldwide (WHO): 34·5% among laboratory-confirmed cases. South Korea:[24] 20·4% among laboratory-confirmed cases.	..

CoV=coronavirus. SARS=severe acute respiratory syndrome. MERS=Middle East respiratory syndrome. SSE=superspreading event. *Data are mean (IQR).

Table 1: **Epidemiological characteristics of human CoVs**

Wu JT, et al. Lancet; 31 January 2020

2019 nCo-V, US

Persons Under Investigation (PUI) in the United States*†

Positive	15
Negative	347
Pending§	81
Total	443

*Cumulative since January 21, 2020.
†Numbers closed out at 4 p.m. the day before reporting.
§Includes specimens received and awaiting testing, as well as specimens en route to CDC.

Number of states and territories with PUI: 42

https://www.nytimes.com/interactive/2020/world/asia/china-wuhan-coronavirus-maps.html
www.cdc.gov/coronavirus/2019-ncov/cases-in-us.html

FAMILY CLUSTER DEMONSTRATING PERSON-TO-PERSON TRANSMISSION AND ASYMPTOMATIC INFECTION

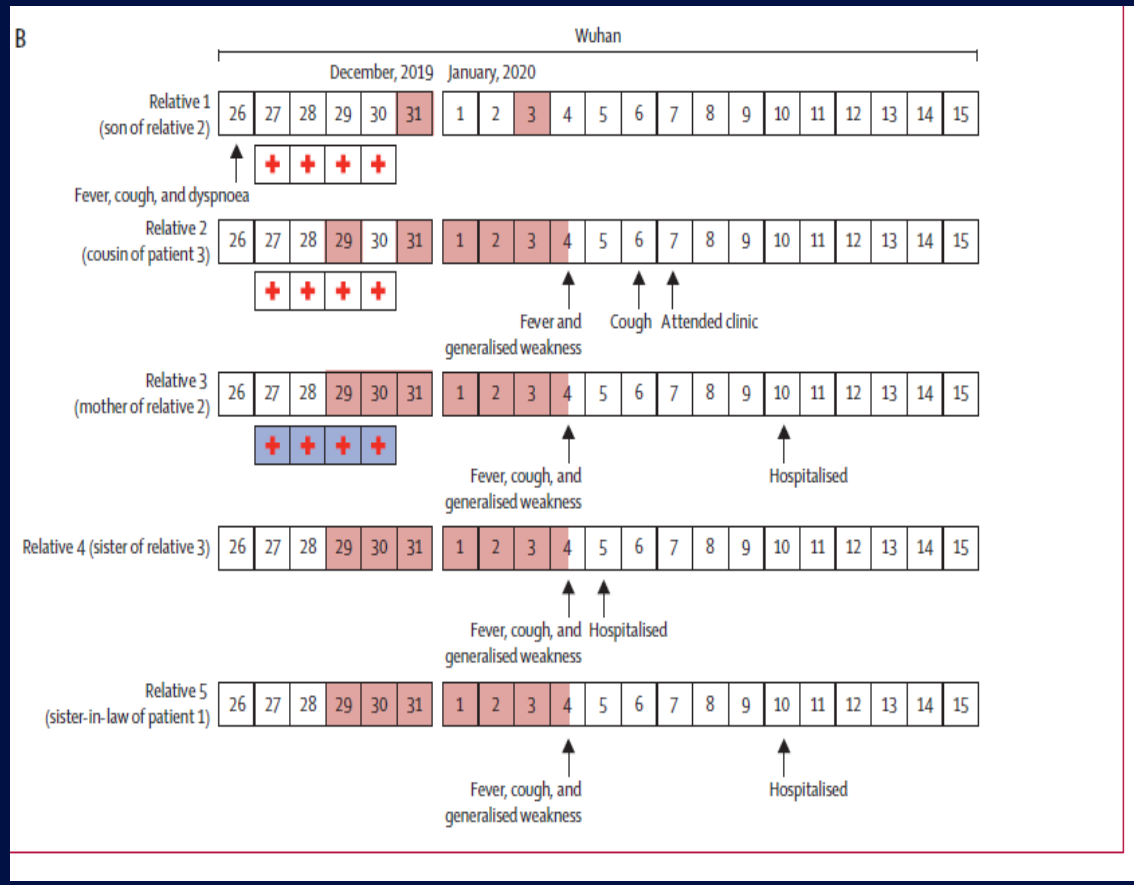


Figure 1: **Chronology of symptom onset of the Shenzhen family cluster and their contacts in Wuhan**
Dates filled in red are the dates on which patients 1–6 had close contacts with their relatives (relatives 1–5).
Dates filled in yellow are the dates on which patients 3–6 stayed with patient 7.
The boxes with an internal red cross are the dates on which patients 1 and 3 or relatives 1, 2, and 3 had stayed overnight (white boxes) at or had visited (blue boxes) the hospital in which relative 1 was admitted for febrile pneumonia.
The information of relatives 1–5 was provided by patient 3. No virological data were available.

Fuk-Woo Chan, J et al. Lancet (epub ahead of print)

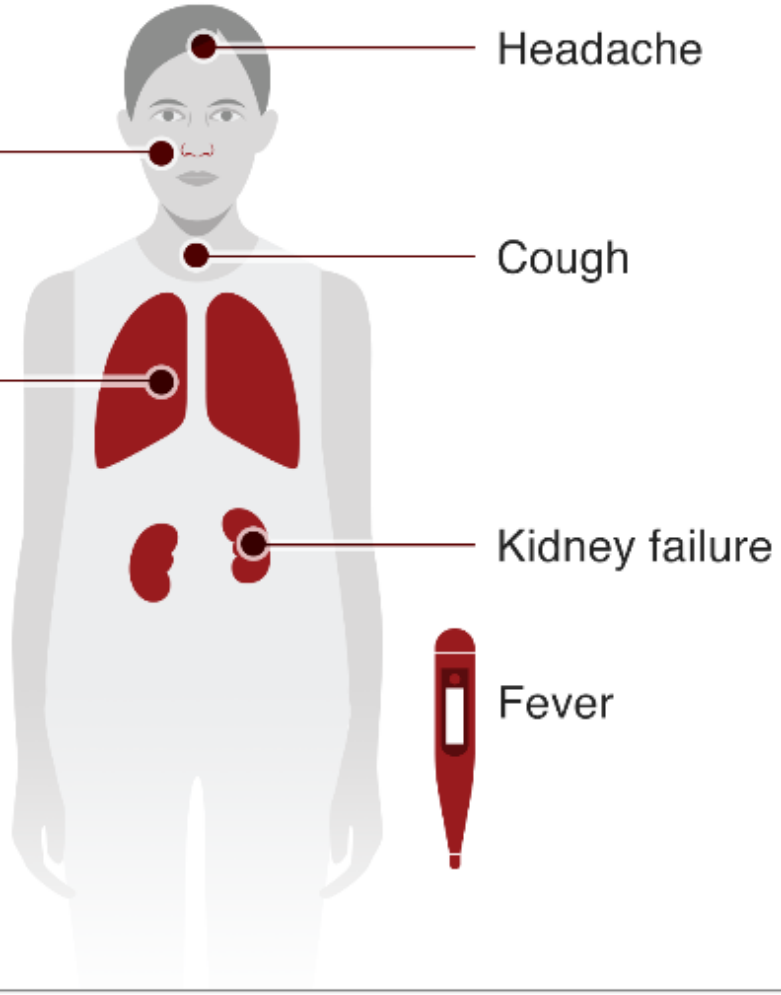
SYMPTOMS of nCo-V

- 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

Symptoms of China coronavirus



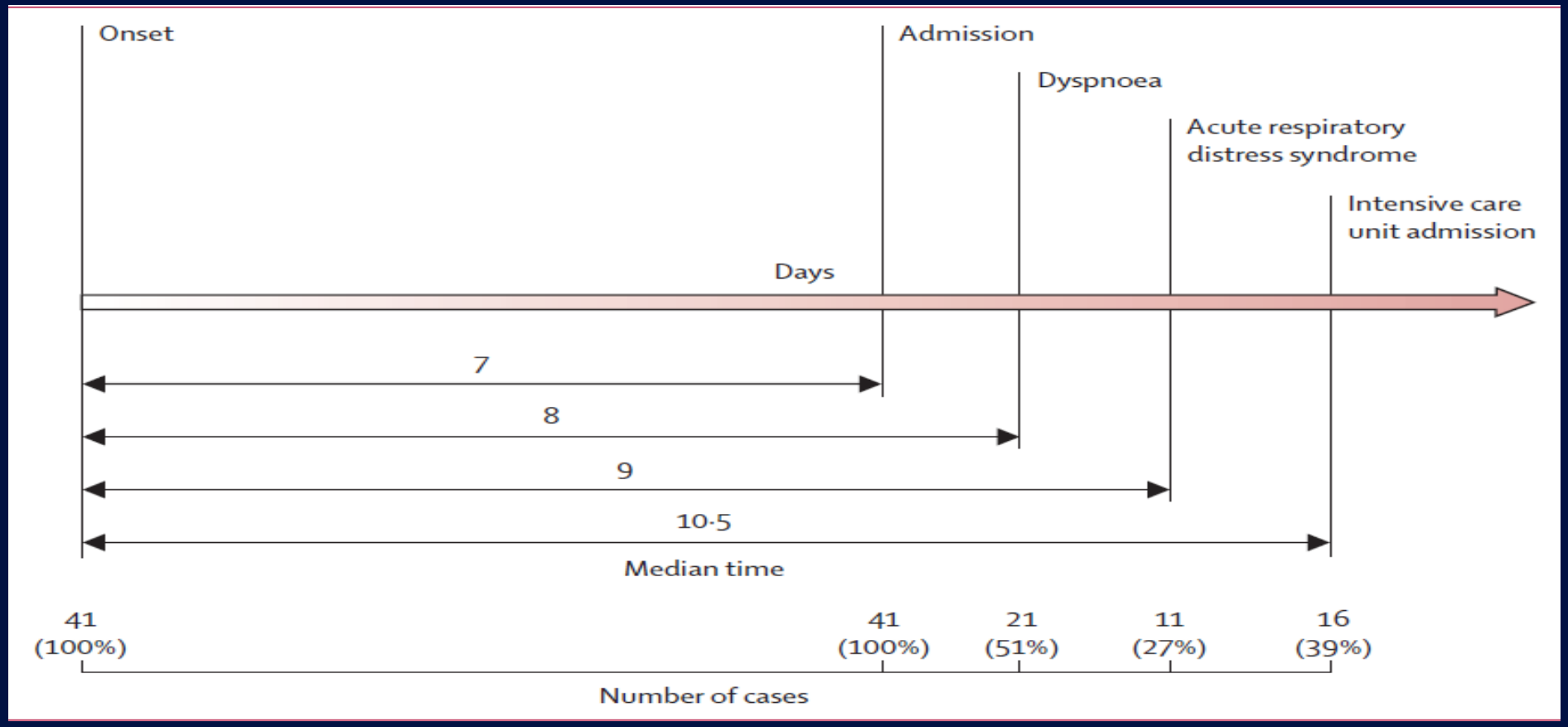
Virus seems to start with a **fever**, followed by a **dry cough** and then, after a week, leads to **shortness of breath** and some patients needing hospital treatment

Source: WHO

BBC

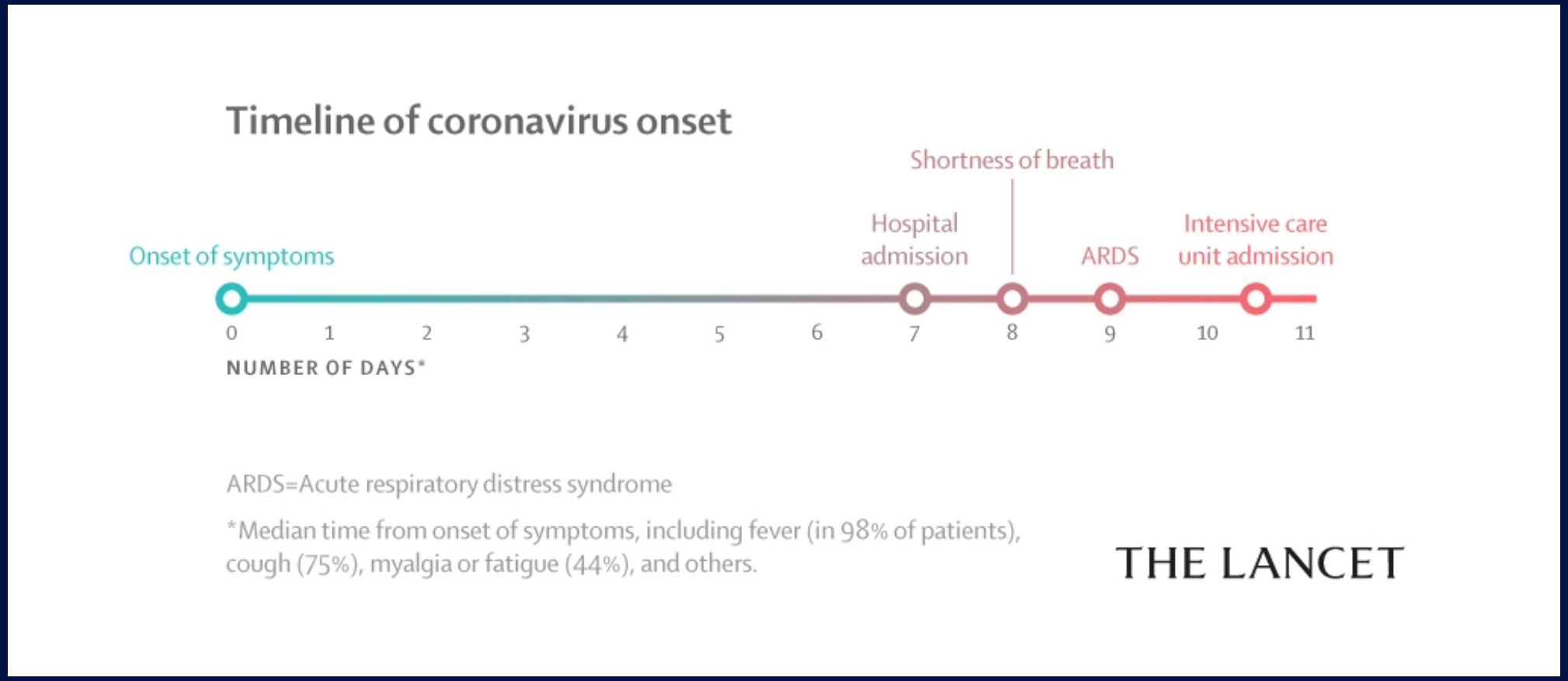
https://www.bbc.com/news/world-51235105

TIMELINE OF 2019 nCo-V CASES AFTER ONSET OF ILLNESS



Huang C, et al. Lancet 2020;Jan 24 (Epub ahead of print)T

TIMELINE OF 2019 nCo-V CASES AFTER ONSET OF ILLNESS



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

CHARACTERISTICS OF PATIENTS WHO HAVE BEEN INFECTED WITH 2019-nCo-V, MERS-CoV, and SARS-CoV

	2019-nCoV*	MERS-CoV	SARS-CoV
Demographic			
Date	December, 2019	June, 2012	November, 2002
Location	Wuhan, China	Jeddah, Saudi Arabia	Guangdong, China
Age, years (range)	49 (21–76)	56 (14–94)	39·9 (1–91)
Male:female sex ratio	2·7:1	3·3:1	1:1·25
Confirmed cases	835†	2494	8096
Mortality	25† (2·9%)	858 (37%)	744 (10%)
Health-care workers	16‡	9·8%	23·1%
Symptoms			
Fever	40 (98%)	98%	99–100%
Dry cough	31 (76%)	47%	29–75%
Dyspnoea	22 (55%)	72%	40–42%
Diarrhoea	1 (3%)	26%	20–25%
Sore throat	0	21%	13–25%
Ventilatory support	9·8%	80%	14–20%

Data are n, age (range), or n (%) unless otherwise stated. 2019-nCoV=2019 novel coronavirus. MERS-CoV=Middle East respiratory syndrome coronavirus. SARS-CoV=severe acute respiratory syndrome coronavirus. *Demographics and symptoms for 2019-nCoV infection are based on data from the first 41 patients reported by Chaolin Huang and colleagues (admitted before Jan 2, 2020).[8] Case numbers and mortalities are updated up to Jan 21, 2020) as disclosed by the Chinese Health Commission. †Data as of Jan 23, 2020. ‡Data as of Jan 21, 2020.[9]

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

DEMOGRAPHIC AND BASELINE CHARACTERISTICS OF PATIENTS (N=99) INFECTED WITH COVID-19

	Patients (n=99)
Age, years	
Mean (SD)	55·5 (13·1)
Range	21–82
≤39	10 (10%)
40–49	22 (22%)
50–59	30 (30%)
60–69	22 (22%)
≥70	15 (15%)
Sex	
Female	32 (32%)
Male	67 (68%)
Occupation	
Agricultural worker	2 (2%)
Self-employed	63 (64%)
Employee	15 (15%)
Retired	19 (19%)
Exposure to Huanan seafood market*	49 (49%)
Long-term exposure history	47 (47%)
Short-term exposure history	2 (2%)
Chronic medical illness	50 (51%)
Cardiovascular and cerebrovascular diseases	40 (40%)
Digestive system disease	11 (11%)
Endocrine system disease†	13 (13%)
Malignant tumour	1 (1%)
Nervous system disease	1 (1%)
Respiratory system disease	1 (1%)
Admission to intensive care unit	23 (23%)
Clinical outcome	
Remained in hospital	57 (58%)
Discharged	31 (31%)
Died	11 (11%)

Data are n (%) unless specified otherwise. 2019-nCoV=2019 novel coronavirus. *Long-term exposure is having worked at or lived in or around Huanan seafood market, whereas short-term exposure is having been to Huanan seafood market occasionally. †12 were diabetic.

Table 1: **Demographics, baseline characteristics, and clinical outcomes of 99 patients admitted to Wuhan Jinyintan Hospital (Jan 1–20, 2020)**

Chen N, et al Lancet 2020;395:507-13 (29 Jan)

DEMOGRAPHIC AND BASELINE CHARACTERISTICS OF PATIENTS (N=99) INFECTED WITH COVID-19

	Patients (n=99)
Signs and symptoms at admission	
Fever	82 (83%)
Cough	81 (82%)
Shortness of breath	31 (31%)
Muscle ache	11 (11%)
Confusion	9 (9%)
Headache	8 (8%)
Sore throat	5 (5%)
Rhinorrhoea	4 (4%)
Chest pain	2 (2%)
Diarrhoea	2 (2%)
Nausea and vomiting	1 (1%)
More than one sign or symptom	89 (90%)
Fever, cough, and shortness of breath	15 (15%)
Comorbid conditions	
Any	33 (33%)
ARDS	17 (17%)
Acute renal injury	3 (3%)
Acute respiratory injury	8 (8%)
Septic shock	4 (4%)
Ventilator-associated pneumonia	1 (1%)
Chest x-ray and CT findings	
Unilateral pneumonia	25 (25%)
Bilateral pneumonia	74 (75%)
Multiple mottling and ground-glass opacity	14 (14%)
Treatment	
Oxygen therapy	75 (76%)
Mechanical ventilation	
Non-invasive (ie, face mask)	13 (13%)
Invasive	4 (4%)
CRRT	9 (9%)
ECMO	3 (3%)
Antibiotic treatment	70 (71%)
Antifungal treatment	15 (15%)
Antiviral treatment	75 (76%)
Glucocorticoids	19 (19%)
Intravenous immunoglobulin therapy	27 (27%)

2019-nCoV=2019 novel coronavirus. ARDS=acute respiratory distress syndrome. ECMO=extracorporeal membrane oxygenation. CRRT=continuous renal replacement therapy.

Chen N, et al Lancet 2020; 395:507-13 (29 Jan)

LABORATORY FINDINGS OF PATIENTS (N=99) INFECTED WITH COVID-19

	Patients (n=99)
Blood routine	
Leucocytes (×10⁹ per L; normal range 3·5–9·5)	7·5 (3·6)
Increased	24 (24%)
Decreased	9 (9%)
Neutrophils (×10⁹ per L; normal range 1·8–6·3)	5·0 (3·3–8·1)
Increased	38 (38%)
Lymphocytes (×10⁹ per L; normal range 1·1–3·2)	0·9 (0·5)
Decreased	35 (35%)
Platelets (×10⁹ per L; normal range 125·0–350·0)	213·5 (79·1)
Increased	4 (4%)
Decreased	12 (12%)
Haemoglobin (g/L; normal range 130·0–175·0)	129·8 (14·8)
Decreased	50 (51%)
Coagulation function	
Activated partial thromboplastin time (s; normal range 21·0–37·0)	27·3 (10·2)
Increased	6 (6%)
Decreased	16 (16%)
Prothrombin time (s; normal range 10·5–13·5)	11·3 (1·9)
Increased	5 (5%)
Decreased	30 (30%)
D-dimer (μg/L; normal range 0·0–1·5)	0·9 (0·5–2·8)
Increased	36 (36%)

Blood biochemistry	
Albumin (g/L; normal range 40·0–55·0)	31·6 (4·0)
Decreased	97 (98%)
Alanine aminotransferase (U/L; normal range 9·0–50·0)	39·0 (22·0–53·0)
Increased	28 (28%)
Aspartate aminotransferase (U/L; normal range 15·0–40·0)	34·0 (26·0–48·0)
Increased	35 (35%)
Total bilirubin (μmol/L; normal range 0·0–21·0)	15·1 (7·3)
Increased	18 (18%)
Blood urea nitrogen (mmol/L; normal range 3·6–9·5)	5·9 (2·6)
Increased	6 (6%)
Decreased	17 (17%)
Serum creatinine (μmol/L; normal range 57·0–111·0)	75·6 (25·0)
Increased	3 (3%)
Decreased	21 (21%)
Creatine kinase (U/L; normal range 50·0–310·0)	85·0 (51·0–184·0)
Increased	13 (13%)
Decreased	23 (23%)
Lactate dehydrogenase (U/L; normal range 120·0–250·0)	336·0 (260·0–447·0)
Increased	75 (76%)
Myoglobin (ng/mL; normal range 0·0–146·9)	49·5 (32·2–99·8)
Increased	15 (15%)
Glucose (mmol/L; normal range 3·9–6·1)	7·4 (3·4)
Increased	51 (52%)
Decreased	1 (1%)

Chen N, et al Lancet 2020; 395:507-13 (29 Jan)

LAB FINDINGS OF PATIENTS INFECTED WITH 2019 nCo-V

	All patients (n=41)	ICU care (n=13)	No ICU care (n=28)	p value
White blood cell count, x 10⁹/L	6·2 (4·1–10·5)	11·3 (5·8–12·1)	5·7 (3·1–7·6)	0·011
<4	10/40 (25%)	1/13 (8%)	9/27 (33%)	0·041
4–10	18/40 (45%)	5/13 (38%)	13/27 (48%)	..
>10	12/40 (30%)	7/13 (54%)	5/27 (19%)	..
Neutrophil count, x 10⁹/L	5·0 (3·3–8·9)	10·6 (5·0–11·8)	4·4 (2·0–6·1)	0·00069
Lymphocyte count, x 10⁹/L	0·8 (0·6–1·1)	0·4 (0·2–0·8)	1·0 (0·7–1·1)	0·0041
<1·0	26/41 (63%)	11/13 (85%)	15/28 (54%)	0·045
≥1·0	15/41 (37%)	2/13 (15%)	13/28 (46%)	..
Haemoglobin, g/L	126·0 (118·0–140·0)	122·0 (111·0–128·0)	130·5 (120·0–140·0)	0·20
Platelet count, x 10⁹/L	164·5 (131·5–263·0)	196·0 (165·0–263·0)	149·0 (131·0–263·0)	0·45
<100	2/40 (5%)	1/13 (8%)	1/27 (4%)	0·45
≥100	38/40 (95%)	12/13 (92%)	26/27 (96%)	..
Prothrombin time, s	11·1 (10·1–12·4)	12·2 (11·2–13·4)	10·7 (9·8–12·1)	0·012
Activated partial thromboplastin time, s	27·0 (24·2–34·1)	26·2 (22·5–33·9)	27·7 (24·8–34·1)	0·57
D-dimer, mg/L	0·5 (0·3–1·3)	2·4 (0·6–14·4)	0·5 (0·3–0·8)	0·0042
Albumin, g/L	31·4 (28·9–36·0)	27·9 (26·3–30·9)	34·7 (30·2–36·5)	0·0066
Alanine aminotransferase, U/L	32·0 (21·0–50·0)	49·0 (29·0–115·0)	27·0 (19·5–40·0)	0·038
Aspartate aminotransferase, U/L	34·0 (26·0–48·0)	44·0 (30·0–70·0)	34·0 (24·0–40·5)	0·10
≤40	26/41 (63%)	5/13 (38%)	21/28 (75%)	0·025
>40	15/41 (37%)	8/13 (62%)	7/28 (25%)	..
Total bilirubin, mmol/L	11·7 (9·5–13·9)	14·0 (11·9–32·9)	10·8 (9·4–12·3)	0·011
Potassium, mmol/L	4·2 (3·8–4·8)	4·6 (4·0–5·0)	4·1 (3·8–4·6)	0·27
Sodium, mmol/L	139·0 (137·0–140·0)	138·0 (137·0–139·0)	139·0 (137·5–140·5)	0·26
Creatinine, μmol/L	74·2 (57·5–85·7)	79·0 (53·1–92·7)	73·3 (57·5–84·7)	0·84
≤133	37/41 (90%)	11/13 (85%)	26/28 (93%)	0·42
>133	4/41 (10%)	2/13 (15%)	2/28 (7%)	..
Creatine kinase, U/L	132·5 (62·0–219·0)	132·0 (82·0–493·0)	133·0 (61·0–189·0)	0·31
≤185	27/40 (68%)	7/13 (54%)	20/27 (74%)	0·21
>185	13/40 (33%)	6/13 (46%)	7/27 (26%)	..
Lactate dehydrogenase, U/L	286·0 (242·0–408·0)	400·0 (323·0–578·0)	281·0 (233·0–357·0)	0·0044
≤245	11/40 (28%)	1/13 (8%)	10/27 (37%)	0·036
>245	29/40 (73%)	12/13 (92%)	17/27 (63%)	..
Hypersensitive troponin I, pg/mL	3·4 (1·1–9·1)	3·3 (3·0–163·0)	3·5 (0·7–5·4)	0·08
>28 (99th percentile)	5/41 (12%)	4/13 (31%)	1/28 (4%)	0·017
Procalcitonin, ng/mL	0·1 (0·1–0·1)	0·1 (0·1–0·4)	0·1 (0·1–0·1)	0·031
<0·1	27/39 (69%)	6/12 (50%)	21/27 (78%)	0·0029
≥0·1 to <0·25	7/39 (18%)	3/12 (25%)	4/27 (15%)	..
≥0·25 to <0·5	2/39 (5%)	0/12	2/27 (7%)	..
≥0·5	3/39 (8%)	3/12 (25%)*	0/27	..
Bilateral involvement of chest radiographs	40/41 (98%)	13/13 (100%)	27/28 (96%)	0·68
Cycle threshold of respiratory tract	32·2 (31·0–34·5)	31·1 (30·0–33·5)	32·2 (31·1–34·7)	0·39

Data are median (IQR) or n/N (%), where N is the total number of patients with available data. p values comparing ICU care and no ICU care are from χ^2, Fisher's exact test, or Mann-Whitney U test. 2019-nCoV=2019 novel coronavirus. ICU=intensive care unit. *Complicated typical secondary infection during the first hospitalisation.

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

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

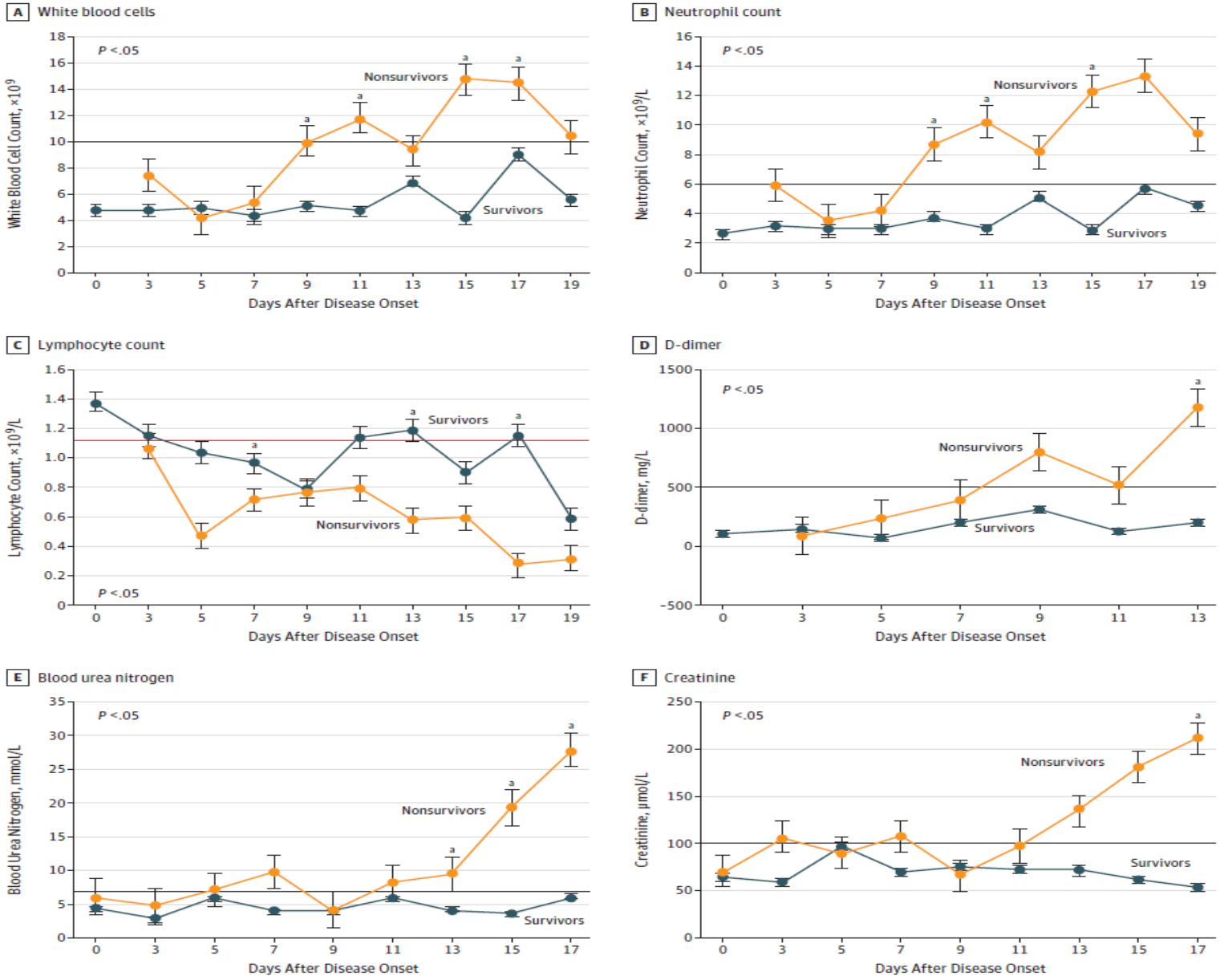
		Median (IQR)			
	Normal Range	Total (N = 138)	ICU (n = 36)	Non-ICU (n = 102)	*P* Value[a]
White blood cell count, $\times 10^9$/L	3.5-9.5	4.5 (3.3-6.2)	6.6 (3.6-9.8)	4.3 (3.3-5.4)	.003
Neutrophil count, $\times 10^9$/L	1.8-6.3	3.0 (2.0-4.9)	4.6 (2.6-7.9)	2.7 (1.9-3.9)	<.001
Lymphocyte count, $\times 10^9$/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)

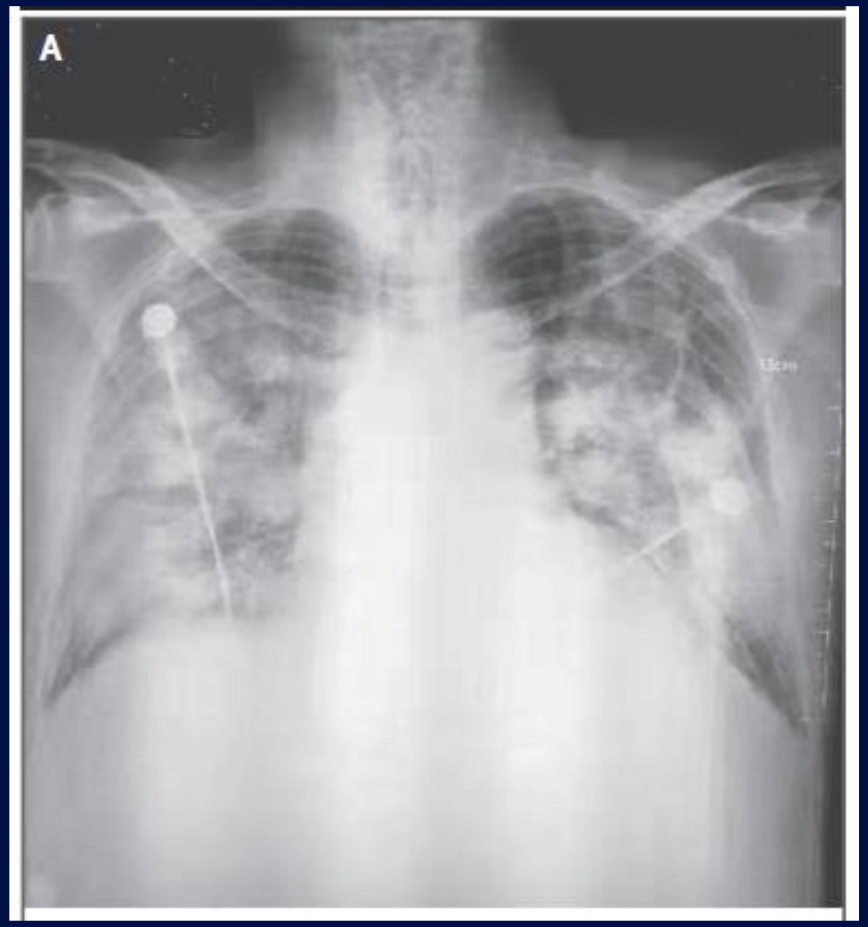


Timeline charts illustrate the laboratory parameters in 33 patients with NCIP (5 nonsurvivors and 28 survivors) every other day based on the days after the onset of illness. The solid lines in black show the upper normal limit of each parameter, and the solid line in red shows the lower normal limit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

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

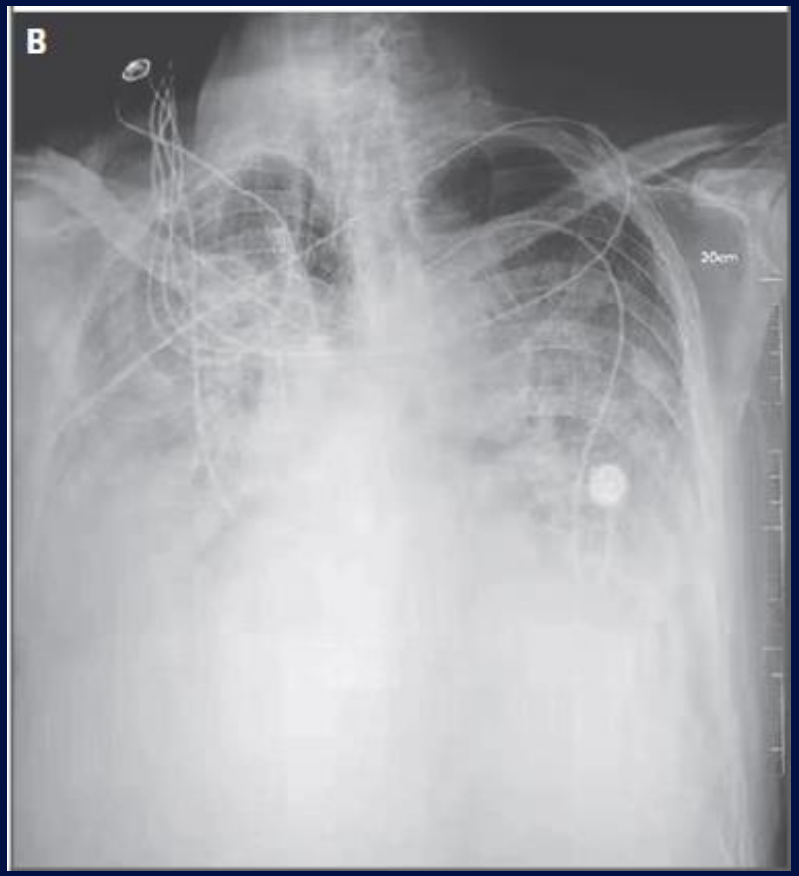
Wang D, et al. JAMA, February 7, 2020

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)



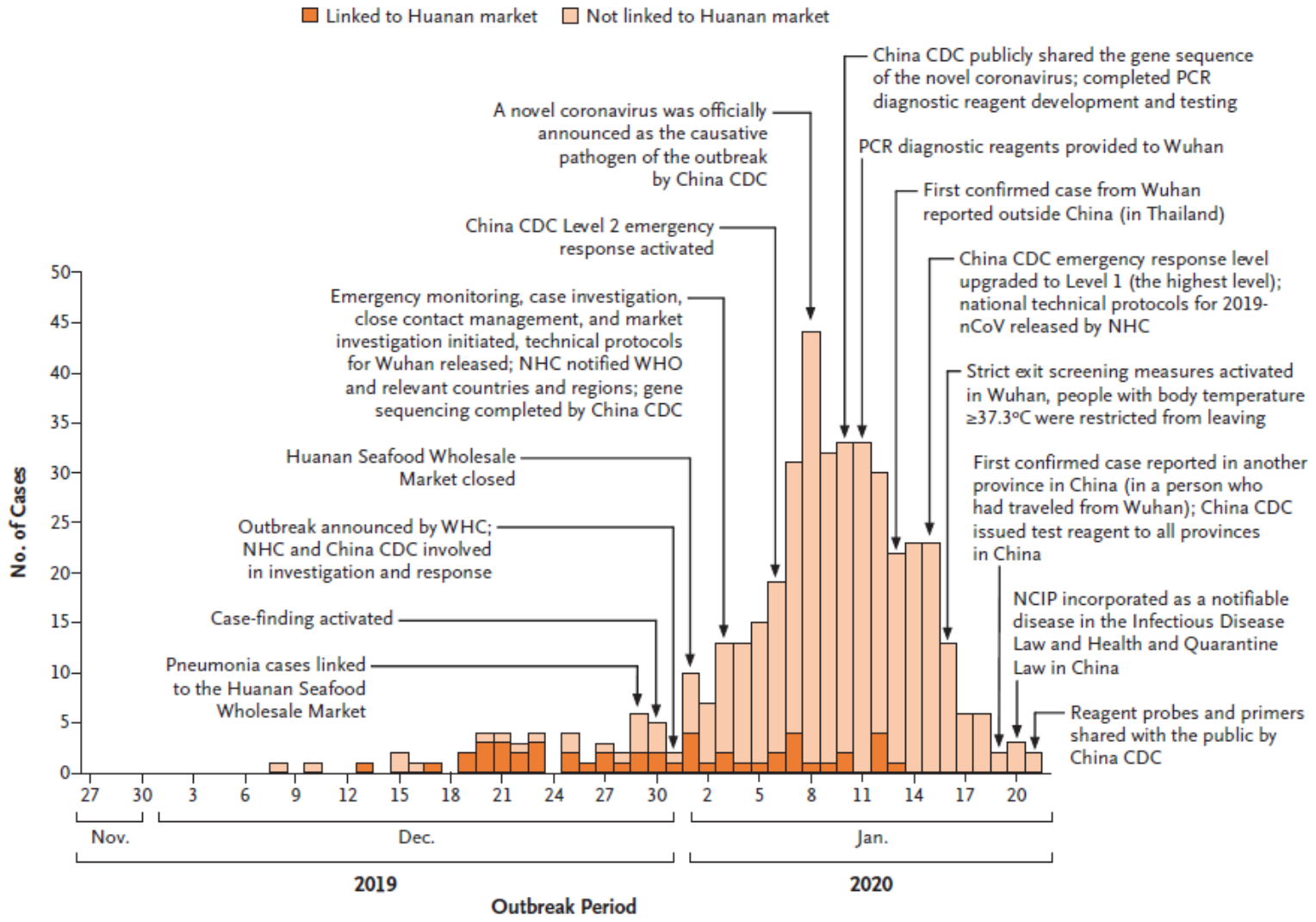


Figure 1. Onset of Illness among the First 425 Confirmed Cases of Novel Coronavirus (2019-nCoV)–Infected Pneumonia (NCIP) in Wuhan, China.

The decline in incidence after January 8 is likely to be due to delays in diagnosis and laboratory confirmation. China CDC denotes Chinese Center for Disease Control and Prevention, NHC National Health Commission of the People's Republic of China, PCR polymerase chain reaction, WHC Wuhan Health Commission, and WHO World Health Organization.

Qun L, et al.
NEJM 2020;31 Jan

Table 1. Characteristics of Patients with Novel Coronavirus–Infected Pneumonia in Wuhan as of January 22, 2020.*

Characteristic	Before January 1 (N=47)	January 1 –January 11 (N=248)	January 12 –January 22 (N=130)
Median age (range) — yr	56 (26–82)	60 (21–89)	61 (15–89)
Age group — no./total no. (%)			
<15 yr	0/47	0/248	0/130
15–44 yr	12/47 (26)	39/248 (16)	33/130 (25)
45–64 yr	24/47 (51)	106/248 (43)	49/130 (38)
≥65 yr	11/47 (23)	103/248 (42)	48/130 (37)
Male sex — no./total no. (%)	31/47 (66)	147/248 (59)	62/130 (48)
Exposure history — no./total no. (%)			
Wet market exposure	30/47 (64)	32/196 (16)	5/81 (6)
Huanan Seafood Wholesale Market	26/47 (55)	19/196 (10)	5/81 (6)
Other wet market but not Huanan Seafood Wholesale Market	4/47 (9)	13/196 (7)	0/81
Contact with another person with respiratory symptoms	14/47 (30)	30/196 (15)	21/83 (25)
No exposure to either market or person with respiratory symptoms	12/47 (26)	141/196 (72)	59/81 (73)
Health care worker — no./total no. (%)	0/47	7/248 (3)	8/122 (7)

* Reduced denominators indicate missing data. Percentages may not total 100 because of rounding.

Qun L, et al.
NEJM 2020;31 J

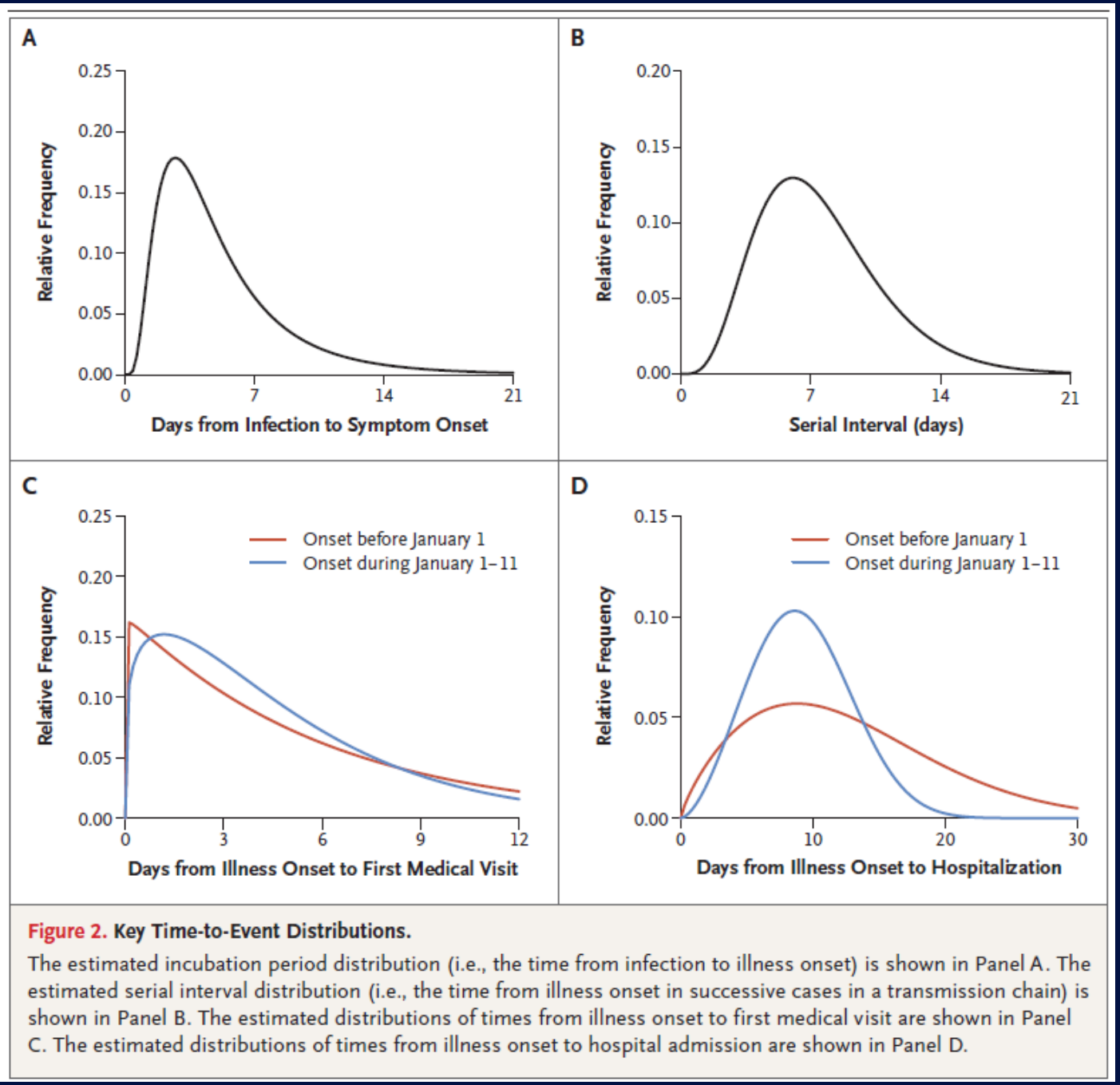


Figure 2. Key Time-to-Event Distributions.

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

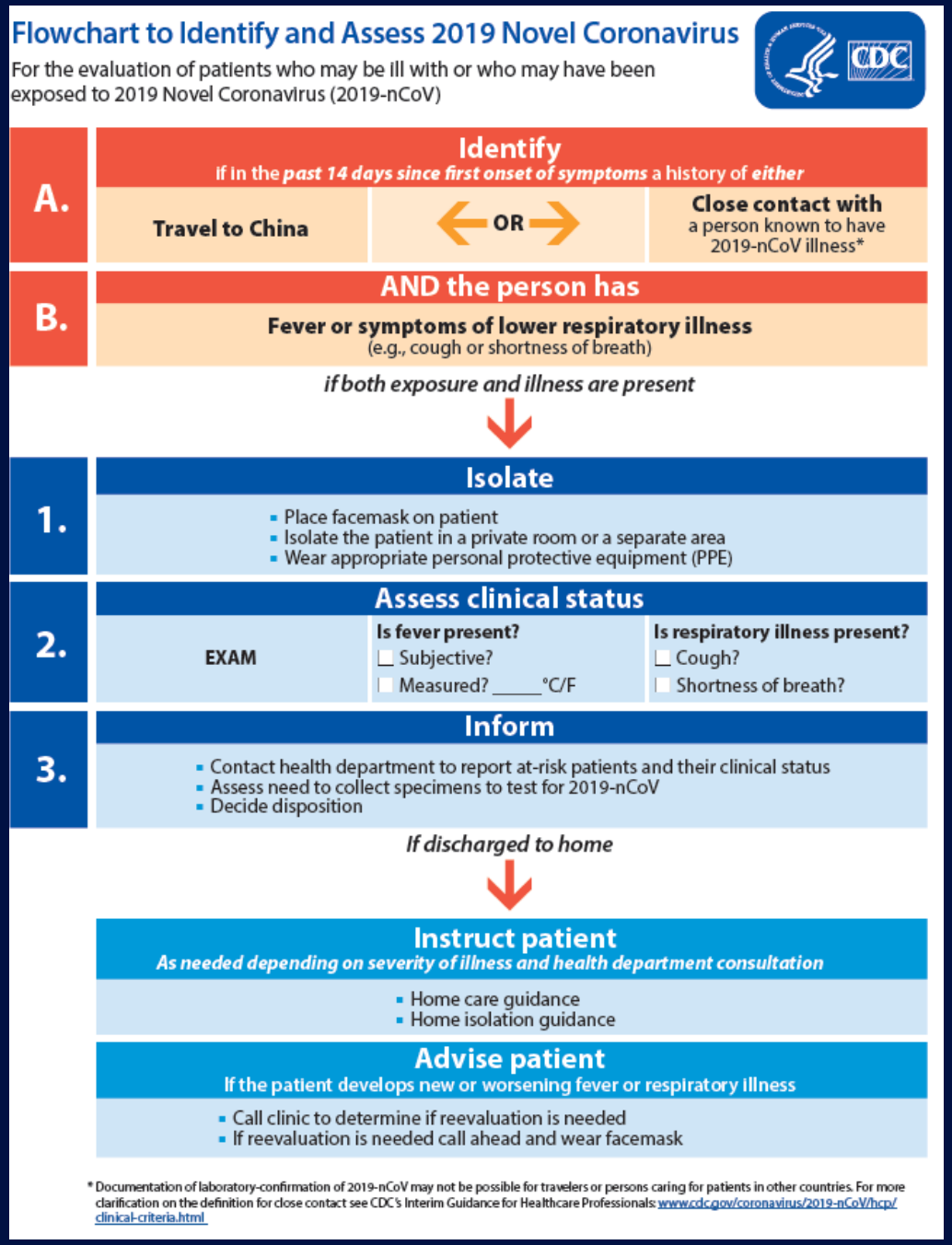
Qun L, et al.
NEJM 2020;31 J

CRITERIA TO GUIDE EVALUATION OF PATIENTS UNDER INVESTIGATION, CDC

Clinical Features	&	Epidemiologic Risk
Fever[1] **or** signs/symptoms of lower respiratory illness (e.g. cough or shortness of breath)	**AND**	Any person, including health care workers, who has had close contact[2] with a laboratory-confirmed[3,4] 2019-nCoV patient within 14 days of symptom onset
Fever[1] **and** signs/symptoms of a lower respiratory illness (e.g., cough or shortness of breath)	**AND**	A history of travel from **Hubei Province**, China 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[4]	**AND**	A history of travel from mainland **China** within 14 days of symptom onset

The criteria are intended to serve as guidance for evaluation. Patients should be evaluated and discussed with public health departments on a case-by-case basis. For severely ill individuals, testing can be considered when exposure history is equivocal (e.g., uncertain travel or exposure, or no known exposure) and another etiology has not been identified.

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



https://www.cdc.gov/coronavirus/2019-ncov/hcp/identify-assess-flowchart.html

RISK ASSESSMENT AND PUBLIC HEALTH MANAGEMENT FOR PERSONS WITH POTENTIAL nCo-V EXPOSURE IN TRAVEL-ASSOCIATED OR COMMUNITY SETTINGS

High Risk

- 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 2019-nCoV infection ***without using recommended precautions*** for home care and home isolation
  - The same risk assessment applies for the above-listed exposures to a person diagnosed clinically with 2019-nCoV infection outside of the United States who did not have laboratory testing.
- Travel from Hubei Province, China

This interim guidance is effective as of February 3, 2020, and does not apply retrospectively to people who have been in China during the previous 14 days and are already in the United States, or those being managed as part of a contact investigation.
CDC will provide separate guidance for healthcare settings.
All exposures apply to the 14 days prior to assessment and recommendations apply until 14 days after the exposure event.

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

RISK ASSESSMENT AND PUBLIC HEALTH MANAGEMENT FOR PERSONS WITH POTENTIAL nCo-V EXPOSURE IN TRAVEL-ASSOCIATED OR COMMUNITY SETTINGS

Medium Risk

- Close contact with a person with symptomatic laboratory-confirmed 2019-nCoV infection, and not having any exposures that meet a high-risk definition.
  - The same risk assessment applies for close contact with a person diagnosed clinically with 2019-nCoV infection outside of the United States who did not have laboratory testing.
  - On an aircraft, being seated within 6 feet (two meters) of a traveler with symptomatic laboratory-confirmed 2019-nCoV infection; this distance correlates approximately with 2 seats in each direction (refer to graphic above)
- 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 2019-nCoV infection ***while consistently using recommended precautions*** for home care and home isolation
- Travel from mainland China outside Hubei Province AND not having any exposures that meet a high-risk definition

RISK ASSESSMENT AND PUBLIC HEALTH MANAGEMENT FOR PERSONS WITH POTENTIAL nCo-V EXPOSURE IN TRAVEL-ASSOCIATED OR COMMUNITY SETTINGS

Low Risk

- Being in the same indoor environment (e.g., a classroom, a hospital waiting room) as a person with symptomatic laboratory-confirmed 2019-nCoV infection for a prolonged period of time but not meeting the definition of close contact
- On an aircraft, being seated within two rows of a traveler with symptomatic laboratory-confirmed 2019-nCoV infection but not within 6 feet (2 meters) (refer to graphic above) AND not having any exposures that meet a medium- or a high-risk definition (refer to graphic above)

No Identifiable Risk

- Interactions with a person with symptomatic laboratory-confirmed 2019-nCoV 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.

SYMPTOMATIC[1]

Risk Category	Movement Restrictions and Public Activities	Medical Evaluation	Travel
High risk	Immediate isolation.	Medical evaluation is recommended; diagnostic testing for 2019-nCoV should be guided by CDC's PUI definition but is recommended for symptomatic people with a known high-risk exposure. If medical evaluation is needed, it should occur with pre-notification to the receiving HCF and EMS, if EMS transport indicated, and with all recommended infection control precautions in place.	Controlled; air travel only via air medical transport. Local travel is only allowed by medical transport (e.g., ambulance) or private vehicle while symptomatic person is wearing a face mask.
Medium risk	Immediate isolation.	Medical evaluation and care should be guided by clinical presentation; diagnostic testing for 2019-nCoV should be guided by CDC's PUI definition If medical evaluation is needed, it should occur with pre-notification to the receiving HCF and EMS, if EMS transport indicated, and with all recommended infection control precautions in place.	Controlled; air travel only via approved air medical transport. Local travel is only allowed by medical transport (e.g., ambulance) or private vehicle while symptomatic person is wearing a face mask.
Low risk	Recommendation to avoid contact with others and public activities while symptomatic	Person should seek health advice to determine if medical evaluation is needed. If sought, medical evaluation and care should be guided by clinical presentation; diagnostic testing for 2019-nCoV should be guided by CDC's PUI definition	Recommendation to not travel on long-distance commercial conveyances or local public transport while symptomatic
No Identifiable Risk[2]	No restriction	Routine medical care	No restriction

ASYMPTOMATIC

Risk Category	Movement Restrictions and Public Activities	Monitoring	Travel
High risk	Remain quarantined (voluntary or under public health orders on a case-by-case basis) in a location to be determined by public health authorities. No public activities.	Daily active monitoring	Controlled
Medium risk	To the extent possible, remain at home or in a comparable setting. Avoid congregate settings, limit public activities, and practice social distancing.	**Travelers from mainland China outside Hubei Province with no known high-risk exposure:** Self-monitoring with public health supervision **All others in this category:** Active monitoring	Recommendation to postpone additional long-distance travel after they reach their final destination. People who intend to travel should be advised that they might not be able to return if they become symptomatic during travel.
Low risk	No restriction	Self-observation	No restriction
No Identifiable Risk	No restriction	None	No restriction

EMS = Emergency medical services
HCF = healthcare facility
PUI = Patient Under Investigation for 2019-nCoV
[1]For the purpose of this document: subjective or measured fever, cough, or difficulty breathing.
[2]No restrictions on travel, movement, or activities due to 2019-nCoV concerns; however, restrictions might be recommended if the person is known or reasonably believed to have another communicable disease that poses a public health threat if others are exposed in community or travel settings.

Epidemiologic Risk Classification1 for Asymptomatic Healthcare Personnel Following Exposure to Patients with 2019 Novel Coronavirus (2019-nCoV) Infection or their Secretions/Excretions in a Healthcare Setting, and their Associated Monitoring and Work Restriction Recommendations

- HCP in any of the risk exposure categories who develop signs or symptoms compatible with 2019-nCoV infection must contact their established point of contact (public health authorities or their facility's occupational health program) for medical evaluation prior to returning to work
- HCP in the high- or medium-risk category should undergo active monitoring, including restriction from work in any healthcare setting until 14 days after their last exposure.
- HCP in the low-risk category should perform self-monitoring with delegated supervision until 14 days after the last potential exposure. Asymptomatic HCP in this category are not restricted from work. They should check their temperature twice daily and remain alert for respiratory symptoms consistent with 2019-nCoV infection infection (e.g., cough, shortness of breath, sore throat)*
- CP in the no identifiable risk category do not require monitoring or restriction from work.

G. HCP using all recommended PPE (i.e., a respirator, eye protection, gloves and a gown) while caring for or having contact with the secretions/excretions of a patient	Low	Self with delegated supervision	None
H. HCP (not using all recommended PPE) who have brief interactions with a or patient regardless of whether patient was wearing a facemask (e.g., brief conversation at a triage desk; briefly entering a patient room but not having direct contact with the patient or their secretions/excretions; entering the patient room immediately after they have been discharged)	Low	Self with delegated supervision	None
I. HCP who walk by a patient or who have no direct contact with the patient or their secretions/excretions and no entry into the patient room	No identifiable risk	None	None

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

Epidemiologic risk factors	Exposure category	Recommended Monitoring for 2019-nCoV *(until 14 days after last potential exposure)*	Work Restrictions for Asymptomatic HCP
A. HCP (with unprotected eyes, nose, or mouth) who perform or are present in the room for a procedure likely to generate higher concentrations of respiratory secretions or aerosols (e.g., cardiopulmonary resuscitation, intubation, extubation, bronchoscopy, nebulizer therapy, sputum induction)	High	Active	Exclude from work for 14 days after last exposure
B. HCP who perform or are present in the room for a procedure likely to generate higher concentrations of respiratory secretions or aerosols (e.g., cardiopulmonary resuscitation, intubation, extubation, bronchoscopy, nebulizer therapy, sputum induction) and not using a gown and gloves. Note: If the HCP's eyes, nose, or mouth were also unprotected they would fall into the high-risk category above.	Medium	Active	Exclude from work for 14 days after last exposure
C. HCP (with unprotected eyes, nose, or mouth) who have prolonged close contact with a patient *who was not wearing a facemask* Note: A respirator confers a higher level of protection than a facemask. However, they are group together in this scenario because (even if a respirator or facemask was worn) the eyes remain uncovered while having prolonged close contact with a patient *who was not wearing a facemask*.	Medium	Active	Exclude from work for 14 days after last exposure
D. HCP (with unprotected eye, nose, and mouth) who have prolonged close contact with a patient *who was wearing a facemask*	Medium	Active	Exclude from work for 14 days after last exposure
E. HCP (not wearing gloves) who have direct contact with the secretions/excretions of a patient and the HCP failed to perform immediate hand hygiene Note: If the HCP performed hand hygiene immediately after contact, this would be considered low risk.	Medium	Active	Exclude from work for 14 days after last exposure

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

DEFINITION OF CLOSE CONTACT

- Being within approximately 6 feet (2 meters), or within the room or care area, of a novel coronavirus case for a prolonged period of time while not wearing recommended personal protective equipment or PPE (e.g., gowns, gloves, NIOSH-certified disposable N95 respirator, eye protection); close contact can include caring for, living with, visiting, or sharing a health care waiting area or room with a novel coronavirus case.

OR

- Having direct contact with infectious secretions of a novel coronavirus case (e.g., being coughed on) while not wearing recommended personal protective equipment.

- Data to inform the definition of close contact are limited. Considerations when assessing close contact include the duration of exposure (e.g., longer exposure time likely increases exposure risk) and the clinical symptoms of the person with novel coronavirus (e.g., coughing likely increases exposure risk as does exposure to a severely ill patient). Special consideration should be given to those exposed in health care settings.

CDC. https://www.cdc.gov/coronavirus/2019-nCoV/clinical-criteria.html; 24 January

DIAGNOSIS

- Diagnostic tests only available in US at CDC
- UNC Hospitals' in process of developing its own test: Likely time frame for availability, mid-February (per Dr. Melissa Miller, Director, UNC Hospitals' Microbiology Laboratory)
- Specimen type and priority: For initial diagnostic testing for 2019-nCoV, CDC recommends collecting and testing upper respiratory (nasopharyngeal AND oropharyngeal swabs), and lower respiratory (sputum, if possible)) for those patients with productive coughs. Induction of sputum is not indicated. Specimens should be collected as soon as possible once a PUI is identified, regardless of the time of symptom onset. Maintain proper infection control when collecting specimens.
- General guidelines: Store specimens at 2-8°C and ship overnight to CDC on ice pack. Label each specimen container with the patient's ID number (e.g., medical record number), unique specimen ID (e.g., laboratory requisition number), specimen type (e.g., serum) and the date the sample was collected. Complete a CDC Form 50.34 for each specimen submitted. In the upper left box of the form, 1) for test requested select "Respiratory virus molecular detection (non-influenza) CDC-10401" and 2) for At CDC, bring to the attention of enter "Stephen Lindstrom: 2019-nCoV PUI".
- NP and OP swabs: Use only synthetic fiber swabs with plastic shafts. Do not use calcium alginate swabs or swabs with wooden shafts, as they may contain substances that inactivate some viruses and inhibit PCR testing. Place swabs immediately into sterile tubes containing 2-3 ml of viral transport media. NP and OP specimens should be kept in separate vials. Refrigerate specimen at 2-8°C and ship overnight to CDC on ice pack.

https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html

POTENTIAL FUTURE THERAPIES

- Currently there is NO proven effective therapy for SARS or MERS (and by extension nCo-V) – only supportive therapy is available
- Research on MERS therapies (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.
  - 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.
- 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)
- 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)

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)

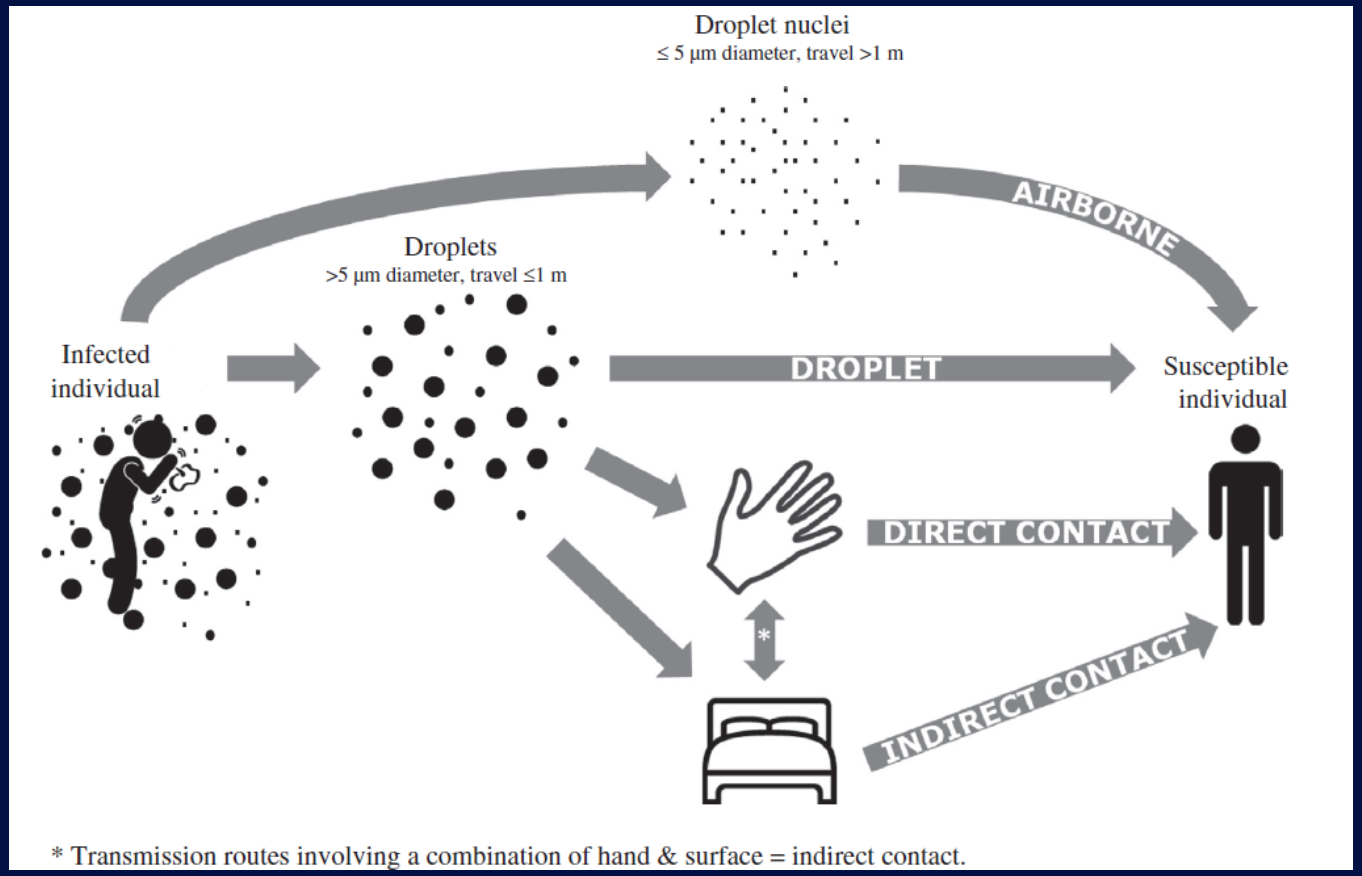
Weber DJ, et al. Am J Infect Control 2016;44:e91-100

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

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

Table I. Persistence of coronaviruses on different types of inanimate surfaces.

Type of surface	Virus	Strain / isolate	Inoculum (viral titer)	Temperature	Persistence	Reference
Steel	MERS-CoV	Isolate HCoV-EMC/2012	10^5	20°C 30°C	48 h 8 – 24 h	[21]
	TGEV	Unknown	10^6	4°C 20°C 40°C	≥ 28 d 3 – 28 d 4 – 96 h	[22]
	MHV	Unknown	10^6	4°C 20°C 40°C	≥ 28 d 4 – 28 d 4 – 96 h	[22]
	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Aluminium	HCoV	Strains 229E and OC43	5×10^3	21°C	2 – 8 h	[24]
Metal	SARS-CoV	Strain P9	10^5	RT	5 d	[25]
Wood	SARS-CoV	Strain P9	10^5	RT	4 d	[25]
Paper	SARS-CoV	Strain P9	10^5	RT	4 – 5 d	[25]
	SARS-CoV	Strain GVU6109	10^6 10^5 10^4	RT	24 h 3 h < 5 min	[26]
Glass	SARS-CoV	Strain P9	10^5	RT	4 d	[25]
	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Plastic	SARS-CoV	Strain HKU39849	10^5	22°-25°C	≤ 5 d	[27]
	MERS-CoV	Isolate HCoV-EMC/2012	10^5	20°C 30°C	48 h 8 – 24 h	[21]
	SARS-CoV	Strain P9	10^5	RT	4 d	[25]
	SARS-CoV	Strain FFM1	10^7	RT	6 – 9 d	[28]
	HCoV	Strain 229E	10^7	RT	2 – 6 d	[28]
PVC	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Silicon rubber	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Surgical glove (latex)	HCoV	Strains 229E and OC43	5×10^3	21°C	≤ 8 h	[24]
Disposable gown	SARS-CoV	Strain GVU6109	10^6 10^5	RT	2 d 24 h	[26]
			10^4		1 h	
Ceramic	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Teflon	HCoV	Strain 229E	10^3	21°C	5 d	[23]

MERS = Middle East Respiratory Syndrome; HCoV = human coronavirus; TGEV = transmissible gastroenteritis virus; MHV = mouse hepatitis virus; SARS = Severe Acute Respiratory Syndrome; RT =

Kampf G, et al. J Hosp Infect 2020;31 January (In press)

Table II. Inactivation of coronaviruses by different types of biocidal agents in suspension tests.

Biocidal agent	Concentration	Virus	Strain / isolate	Exposure time	Reduction of viral infectivity (log_{10})	Reference
Ethanol	95%	SARS-CoV	Isolate FFM-1	30 s	≥ 5.5	[29]
	85%	SARS-CoV	Isolate FFM-1	30 s	≥ 5.5	[29]
	80%	SARS-CoV	Isolate FFM-1	30 s	≥ 4.3	[29]
	80%	MERS-CoV	Strain EMC	30 s	> 4.0	[14]
	78%	SARS-CoV	Isolate FFM-1	30 s	≥ 5.0	[28]
	70%	MHV	Strains MHV-2 and MHV-N	10 min	> 3.9	[30]
	70%	CCV	Strain I-71	10 min	> 3.3	[30]
2-Propanol	100%	SARS-CoV	Isolate FFM-1	30 s	≥ 3.3	[28]
	75%	SARS-CoV	Isolate FFM-1	30 s	≥ 4.0	[14]
	75%	MERS-CoV	Strain EMC	30 s	≥ 4.0	[14]
	70%	SARS-CoV	Isolate FFM-1	30 s	≥ 3.3	[28]
	50%	MHV	Strains MHV-2 and MHV-N	10 min	> 3.7	[30]
	50%	CCV	Strain I-71	10 min	> 3.7	[30]
2-Propanol and 1-propanol	45% and 30%	SARS-CoV	Isolate FFM-1	30 s	≥ 4.3	[29]
		SARS-CoV	Isolate FFM-1	30 s	≥ 2.8	[28]
Benzalkonium chloride	0.2%	HCoV	ATCC VR-759 (strain OC43)	10 min	0.0	[31]
	0.05%	MHV	Strains MHV-2 and MHV-N	10 min	> 3.7	[30]
	0.05%	CCV	Strain I-71	10 min	> 3.7	[30]
	0.00175%	CCV	Strain S378	3 d	3.0	[32]
Didecyldimethyl ammonium chloride	0.0025%	CCV	Strain S378	3 d	> 4.0	[32]
Chlorhexidine digluconate	0.02%	MHV	Strains MHV-2 and MHV-N	10 min	0.7 – 0.8	[30]
	0.02%	CCV	Strain I-71	10 min	0.3	[30]
Sodium hypochlorite	0.21%	MHV	Strain MHV-1	30 s	≥ 4.0	[33]
	0.01%	MHV	Strains MHV-2 and MHV-N	10 min	2.3 – 2.8	[30]
	0.01%	CCV	Strain I-71	10 min	1.1	[30]
	0.001%	MHV	Strains MHV-2 and MHV-N	10 min	0.3 – 0.6	[30]
	0.001%	CCV	Strain I-71	10 min	0.9	[30]
Hydrogen peroxide	0.5%	HCoV	Strain 229E	1 min	> 4.0	[34]
Formaldehyde	1%	SARS-CoV	Isolate FFM-1	2 min	> 3.0	[28]
	0.7%	SARS-CoV	Isolate FFM-1	2 min	> 3.0	[28]
	0.7%	MHV		10 min	> 3.5	[30]
	0.7%	CCV	Strain I-71	10 min	> 3.7	[30]
	0.009%	CCV		24 h	> 4.0	[35]
Glutardialdehyde	2.5%	SARS-CoV	Hanoi strain	5 min	> 4.0	[36]
	0.5%	SARS-CoV	Isolate FFM-1	2 min	> 4.0	[28]
Povidone iodine	7.5%	MERS-CoV	Isolate HCoV-EMC/2012	15 s	4.6	[37]
	4%	MERS-CoV	Isolate HCoV-EMC/2012	15 s	5.0	[37]
	1%	SARS-CoV	Hanoi strain	1 min	> 4.0	[36]
	1%	MERS-CoV	Isolate HCoV-EMC/2012	15 s	4.3	[37]
	0.47%	SARS-CoV	Hanoi strain	1 min	3.8	[36]
	0.25%	SARS-CoV	Hanoi strain	1 min	> 4.0	[36]
	0.23%	SARS-CoV	Hanoi strain	1 min	> 4.0	[36]
	0.23%	SARS-CoV	Isolate FFM-1	15 s	≥ 4.4	[38]
	0.23%	MERS-CoV	Isolate HCoV-EMC/2012	15 s	≥ 4.4	[38]

SARS = Severe Acute Respiratory Syndrome; MERS = Middle East Respiratory Syndrome; MHV = mouse hepatitis virus; CCV = canine coronavirus; HCoV = human coronavirus.

Kampf G, et al. J Hosp Infect 2020;
31 January (In press)

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

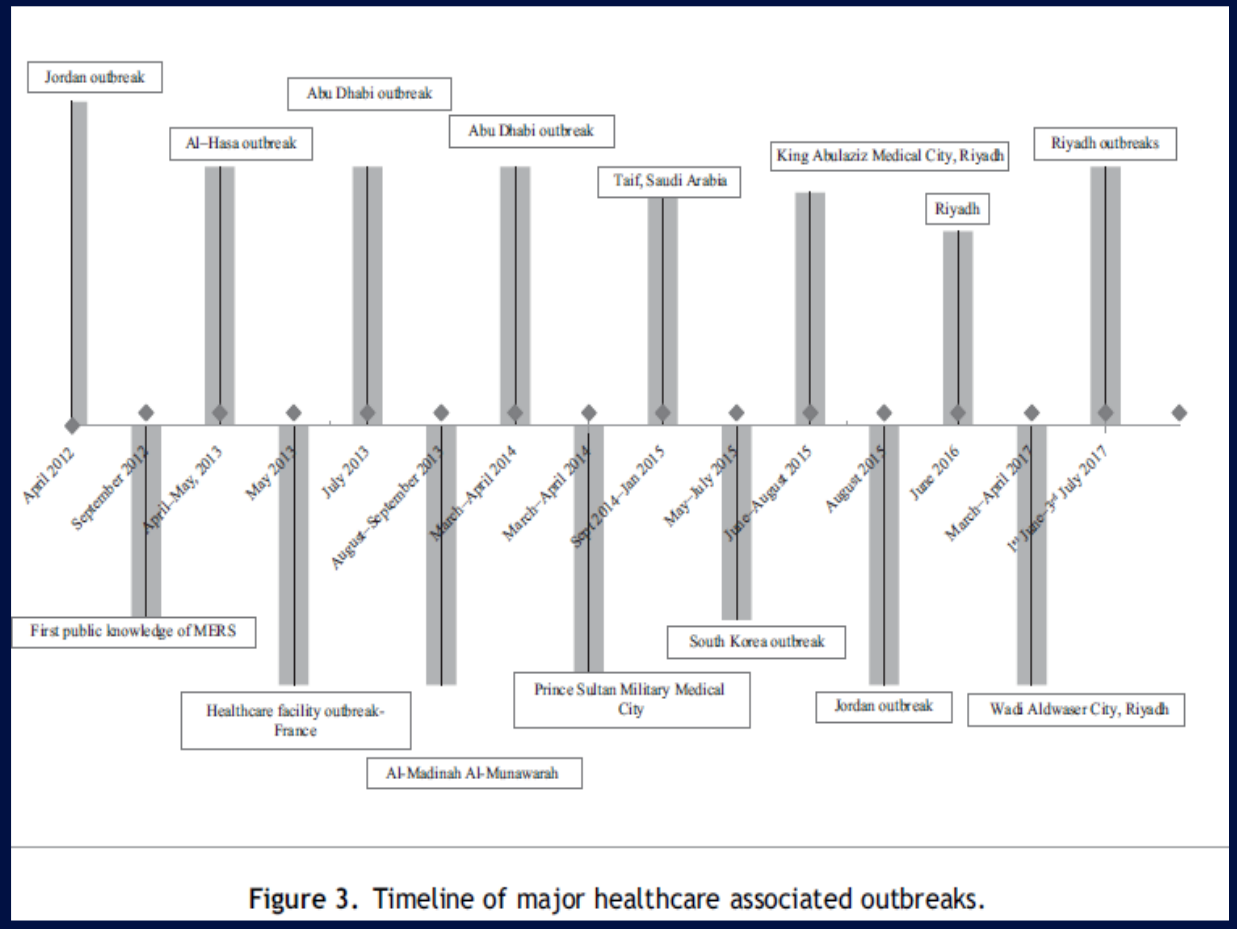


Figure 3. Timeline of major healthcare associated outbreaks.

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

INFECTION PREVENTION: SUMMARY (Identify, Isolate, Inform)

- Assess all patients at healthcare facility entry for nCo-V (symptoms and travel screen) – now built into UNC Epic
- 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
- 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). Transfer to location with AII room for cough inducing procedures (e.g., NP swab)
- Recommended placement of patient with known or suspected nCo-V (inpatient): Airborne isolation room
  - 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
- UNC Hospitals' leaders for nCo-V preparedness: Emily Sickbert-Bennett (Director, Infection Prevention) & Christian Lawson (Clinical Director of Emergency Services)

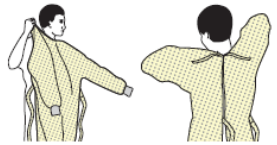
CDC, DONNING AND DOFFING PPE

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

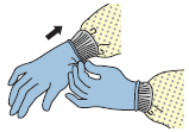
- Secure ties or elastic bands at middle of head and neck
- Fit flexible band to nose bridge
- Fit snug to face and below chin
- Fit-check respirator

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

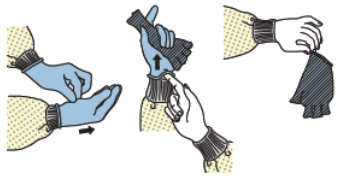
- Keep hands away from face
- Limit surfaces touched
- Change gloves when torn or heavily contaminated
- Perform hand hygiene

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

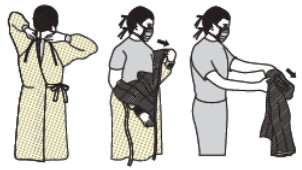


2. GOGGLES OR FACE SHIELD

- 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

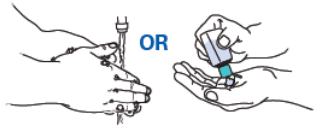
- Gown front and sleeves are contaminated!
- If your hands get contaminated during gown removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Unfasten gown ties, taking care that sleeves don't contact your body when reaching for ties
- Pull gown away from neck and shoulders, touching 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



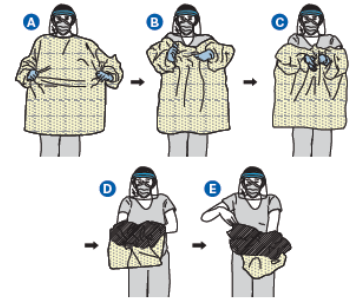
PERFORM HAND HYGIENE BETWEEN STEPS IF HANDS BECOME CONTAMINATED AND IMMEDIATELY AFTER REMOVING ALL PPE

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



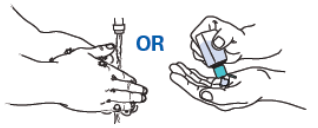
2. GOGGLES OR FACE SHIELD

- 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

INFECTION PREVENTION RECOMMENDATIONS, CDC: 1. MINIMIZE THE CHANCE FOR EXPOSURES

Ensure facility policies and practices are in place to minimize exposures to respiratory pathogens including 2019-nCoV. Measures should be implemented before patient arrival, upon arrival, and throughout the duration of the affected patient's presence in the healthcare setting.

- Before arrival
  - When scheduling appointments, instruct patients and persons who accompany them to call ahead or inform HCP upon arrival if they have symptoms of any respiratory infection (e.g., cough, runny nose, fever1) and to take appropriate preventive actions (e.g., wear a facemask upon entry to contain cough, follow triage procedures).
  - If a patient is arriving via transport by emergency medical services (EMS), the driver should contact the receiving emergency department (ED) or healthcare facility and follow previously agreed upon local or regional transport protocols. This will allow the healthcare facility to prepare for receipt of the patient.

https://www.cdc.gov/coronavirus/2019-nCoV/hcp/infection-control.html

INFECTION PREVENTION RECOMMENDATIONS, CDC: 1. MINIMIZE THE CHANCE FOR EXPOSURES

- Upon arrival and during the visit
  - Take steps to ensure all persons with symptoms of suspected 2019-nCoV or other respiratory infection (e.g., fever, cough) adhere to respiratory hygiene and cough etiquette, hand hygiene, and triage procedures throughout the duration of the visit. Consider posting visual alerts (e.g., signs, posters) at the entrance and in strategic places (e.g., waiting areas, elevators, cafeterias) to provide patients and HCP with instructions (in appropriate languages) about hand hygiene, respiratory hygiene, and cough etiquette. Instructions should include how to use facemasks (See definition of facemask in Appendix) or tissues to cover nose and mouth when coughing or sneezing, to dispose of tissues and contaminated items in waste receptacles, and how and when to perform hand hygiene.
  - Ensure that patients with symptoms of suspected 2019-nCoV or other respiratory infection (e.g., fever, cough) are not allowed to wait among other patients seeking care. Identify a separate, well-ventilated space that allows waiting patients to be separated by 6 or more feet, with easy access to respiratory hygiene supplies. In some settings, patients might opt to wait in a personal vehicle or outside the healthcare facility where they can be contacted by mobile phone when it is their turn to be evaluated.
  - Ensure rapid triage and isolation of patients with symptoms of suspected 2019-nCoV or other respiratory infection (e.g., fever, cough): Identify patients at risk for having 2019-nCoV infection before or immediately upon arrival to the healthcare facility.

INFECTION PREVENTION RECOMMENDATIONS, CDC: 1. MINIMIZE THE CHANCE FOR EXPOSURES

- Upon arrival and during the visit
  - Implement triage procedures to detect patients under investigation (PUI) for 2019-nCoV during or before patient triage or registration (e.g., at the time of patient check-in) and ensure that all patients are asked about the presence of symptoms of a respiratory infection and history of travel to areas experiencing transmission of 2019-nCoV or contact with possible 2019-nCoV patients.
    - Implement respiratory hygiene and cough etiquette (i.e., placing a facemask over the patient's nose and mouth if that has not already been done) and isolate the PUI for 2019-nCoV in an Airborne Infection Isolation Room (AIIR), if available. See recommendations for "Patient Placement" below. Additional guidance for evaluating patients in U.S. for 2019-nCoV infection can be found on the CDC 2019-nCoV website.
    - Inform infection prevention and control services, local and state public health authorities, and other healthcare facility staff as appropriate about the presence of a patient under investigation for 2019-nCoV.
  - Provide supplies for respiratory hygiene and cough etiquette, including 60%-95% alcohol-based hand rub (ABHR), tissues, no touch receptacles for disposal, and facemasks at healthcare facility entrances, waiting rooms, patient check-ins, etc.

INFECTION PREVENTION RECOMMENDATIONS, CDC:
2. ADHERENCE TO STANDARD, CONTACT, AND AIRBORNE PRECAUTIONS

- Patient placement
  - Place a patient with known or suspected 2019-nCoV (i.e., PUI) in an AIIR that has been constructed and maintained in accordance with current guidelines (if available). If an AIIR is not available, the patient should be transferred as soon as is feasible to a facility where an AIIR is available or discharged to home (in consultation with state or local public health authorities) if deemed medically appropriate. Pending transfer, place a facemask on the patient and isolate him/her in an examination room with the door closed. The patient should not be placed in any room where room exhaust is recirculated within the building without HEPA filtration.
  - Limit transport and movement of the patient outside of the AIIR to medically-essential purposes. When not in an AIIR (e.g., during transport or if an AIIR is not available), patients should wear a facemask to contain secretions.
  - Only essential personnel should enter the AIIR. Implement staffing policies to minimize the number of HCP who enter the room. Facilities should consider caring for these patients with dedicated HCP to minimize risk of transmission and exposure to other patients and other HCP.
  - Use dedicated or disposable noncritical patient-care equipment (e.g., blood pressure cuffs). If equipment will be used for more than one patient, clean and disinfect such equipment before use on another patient according to manufacturer's instructions. It is reasonable to apply a similar time period before entering the room without respiratory protection as used for pathogens spread by the airborne route (e.g., measles, tuberculosis)

INFECTION PREVENTION RECOMMENDATIONS, CDC:
2. ADHERENCE TO STANDARD, CONTACT, AND AIRBORNE PRECAUTIONS

- Personal protective equipment (PPE)
  - Gloves: Perform hand hygiene, then put on clean, non-sterile gloves upon entry into the patient room or care area.
  - Gowns: Put on a clean disposable gown upon entry into the patient room or area.
  - Respiratory protection: Use respiratory protection (i.e., a respirator) that is at least as protective as a fit-tested NIOSH-certified disposable N95 filtering facepiece respirator before entry into the patient room or care area.
  - Eye protection: Put on eye protection (e.g., goggles, a disposable face shield that covers the front and sides of the face) upon entry to the patient room or care area.
- Use Caution When Performing Aerosol-Generating Procedures: Some procedures performed on 2019-nCoV patients could generate infectious aerosols. In particular, procedures that are likely to induce coughing; e.g., nasopharyngeal specimen collection, sputum induction, and open suctioning of airways should be performed cautiously and avoided if possible. If performed, these procedures should take place in an AIIR.

INFECTION PREVENTION RECOMMENDATIONS, CDC:

3. Manage Visitor Access and Movement Within the Facility
   - Establish procedures for monitoring, managing and training visitors. Screening visitors for symptoms of acute respiratory illness before entering the healthcare facility.
4. Implement Engineering Controls
5. Monitor and Manage Ill and Exposed Healthcare Personnel
   - Movement and monitoring decisions for HCP with exposure to 2019-nCoV should be made in consultation with public health authorities.
6. Train and Educate Healthcare Personnel
   - Ensure that HCP are educated, trained, and have practiced the appropriate use of PPE prior to caring for a patient, including attention to correct use of PPE and prevention of contamination of clothing, skin, and environment during the process of removing such equipment.

INFECTION PREVENTION RECOMMENDATIONS, CDC: 7. Implement Environmental Infection Control

- Dedicated medical equipment should be used for patient care. All non-dedicated, non-disposable medical equipment used for patient care should be cleaned and disinfected according to manufacturer's instructions and facility policies.
- Routine cleaning and disinfection procedures (e.g., using cleaners and water to pre-clean surfaces prior to applying an EPA-registered, hospital-grade disinfectant to frequently touched surfaces or objects for appropriate contact times as indicated on the product's label) are appropriate for 2019-nCoV in healthcare settings, including those patient-care areas in which aerosol-generating procedures are performed. Products with EPA-approved emerging viral pathogens claims are recommended for use against 2019-nCoV. These products can be identified by the following claim: "[Product name] has demonstrated effectiveness against viruses similar to 2019-nCoV on hard non-porous surfaces. Therefore, this product can be used against 2019-nCoV when used in accordance with the directions for use against [name of supporting virus] on hard, non-porous surfaces." This claim or a similar claim, will be made only through the following communications outlets: technical literature distributed exclusively to health care facilities, physicians, nurses and public health officials, "1-800" consumer information services, social media sites and company websites (non-label related). Specific claims for "2019-nCoV" will not appear on the product or master label. Additional information about EPA-approved emerging viral pathogens claims can be found here: https://www.epa.gov/pesticide-registration/guidance-registrants-process-making-claims-against-emerging-viral-pathogensexternal icon
- If there are no available EPA-registered products that have an approved emerging viral pathogen claim for 2019-nCoV, products with label claims against human coronaviruses should be used according to label instructions.

RESPONDING TO AN OUTBREAK OF A HIGHLY COMMUNICABLE AIRBORNE TRANSMITTED PATHOGEN

- Screening and signage (in English and Spanish)
  - Signs at entrance of all healthcare facilities that include: Epidemiology clues to possible disease exposure (e.g., Wuhan), signs and symptoms of infection (i.e., cough, respiratory symptoms), and who to notify if patient/visitor has both exposure and symptoms (i.e., front desk staff)
  - Inclusion of messaging about signs and symptoms of nCo-V in all telephone contacts with the patient (e.g., appointments)
  - Screening of all patients immediately at time of all health care visits (screening form included in EMR
  - Use of respiratory hygiene (i.e., immediate use of mask and proper disposal of tissues); also appropriate hand hygiene
- Triage
  - Have appropriate PPE available (N95 respiratory, gowns, eye/face shields) immediately available for all HCP (clinics, ED, etc.)
  - Place suspect patients in Airborne isolation room (if available), or private room (ideally with HEPA filter)
- Inpatient care
  - Place patient in Airborne isolation room; limit visitors; care by HCP trained in use of PAPRs and proper donning/doffing
  - Log of HCP providing care; use of only dedicated HCP; HCP to self-monitor for symptoms
- Per NC Health Department – All hospitals can manage patients with nCo-V (transfer only if they cannot provide level of care required)

Weber DJ, et al. Am J Infect Control 2016;44(5 Suppl):e91-e100

SURVEILLANCE PYRAMID AND ITS RELATION TO OUTBREAK CONTAINMENT

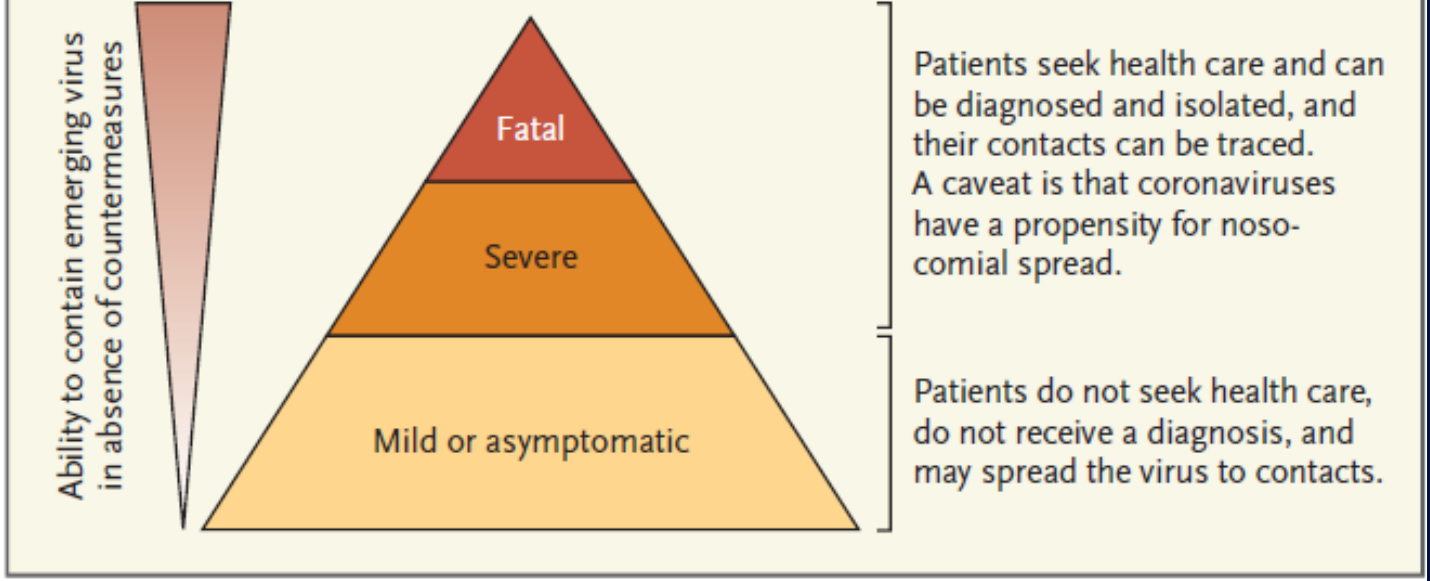


Figure 1. Surveillance Pyramid and Its Relation to Outbreak Containment.

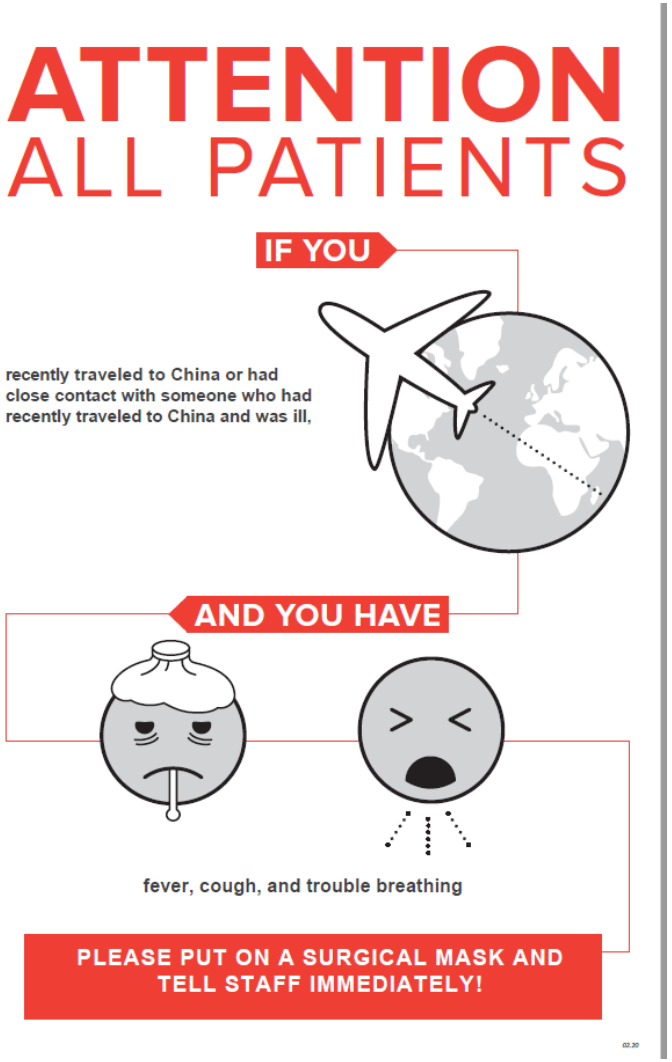
The proportion of mild and asymptomatic cases versus severe and fatal cases is currently unknown for 2019-nCoV — a knowledge gap that hampers realistic assessment of the virus's epidemic potential and complicates the outbreak response.

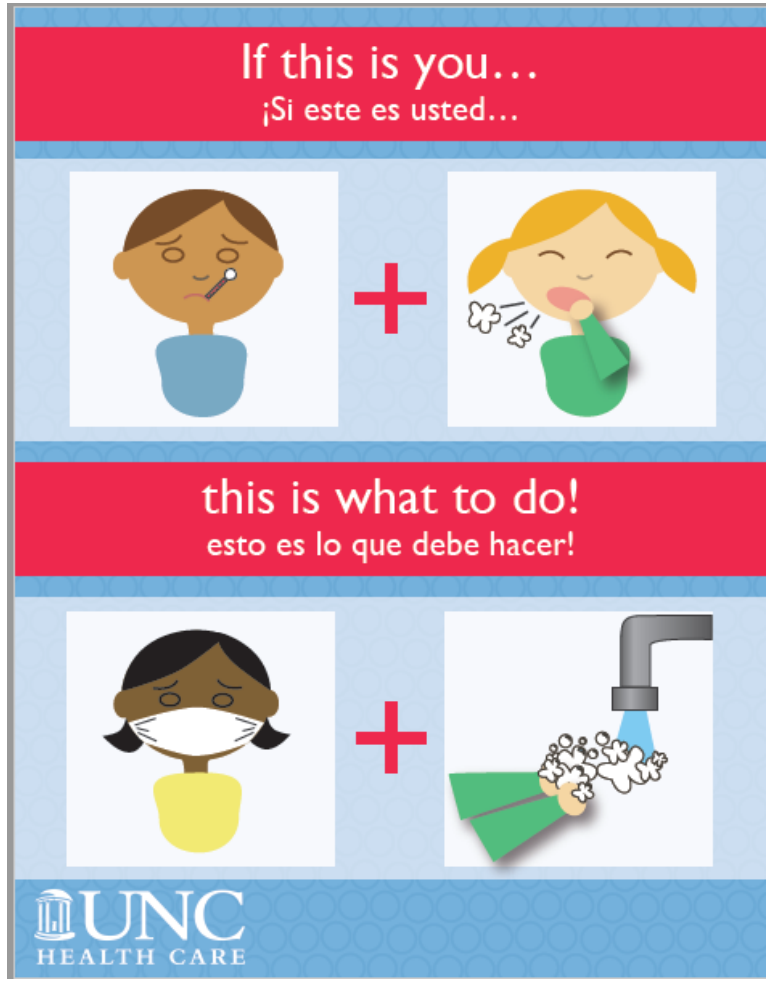
Munster VJ, et al. NEJM 2020;Jan 24 (epub)

UNC Medical Center – What do we need to do?

Identify:

All persons with symptoms of suspected 2019-nCoV or other respiratory infection (e.g., fever, cough) should adhere to respiratory hygiene/cough etiquette and hand hygiene. Signs, masks and hand hygiene should be available in strategic locations.





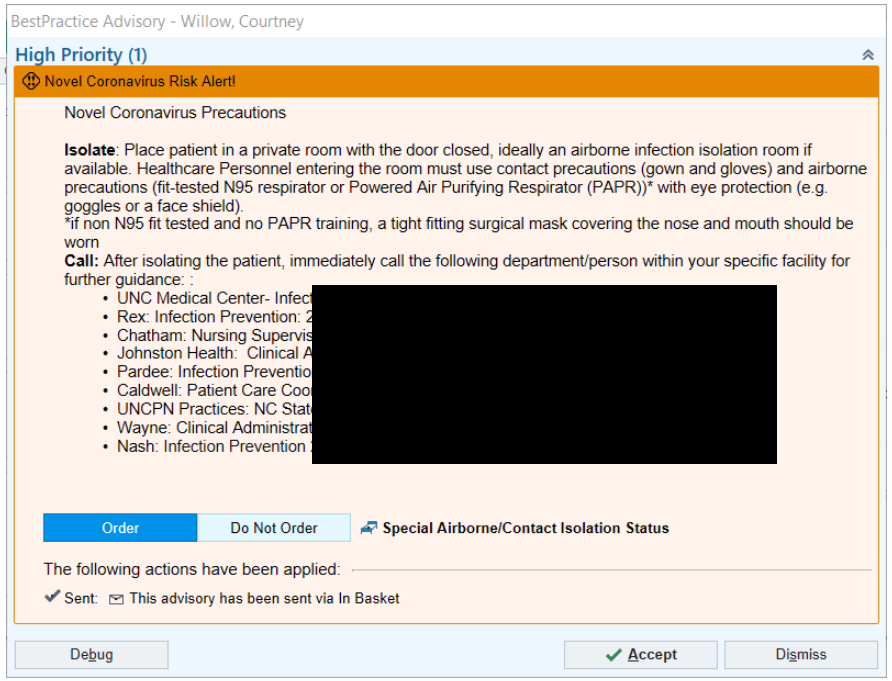
UNC HEALTH CARE

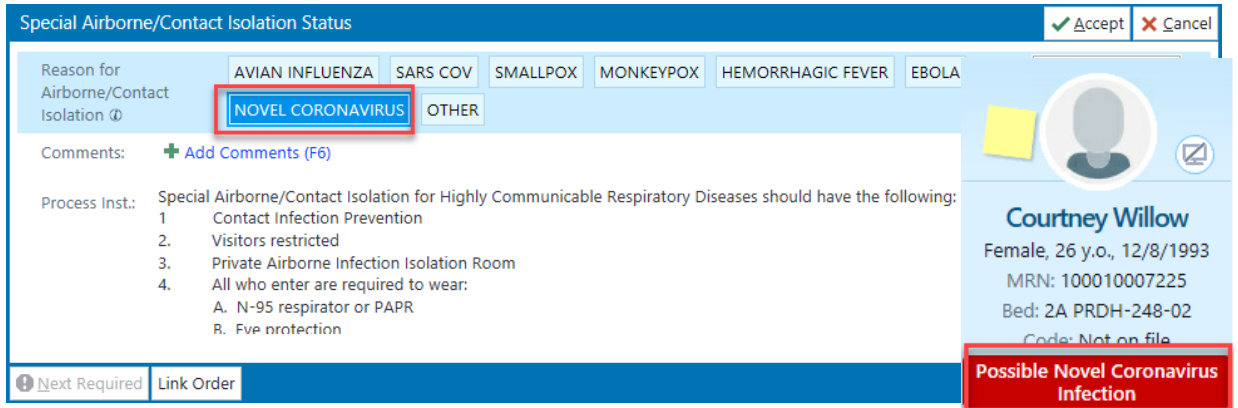
New Epic Screening Tool

1

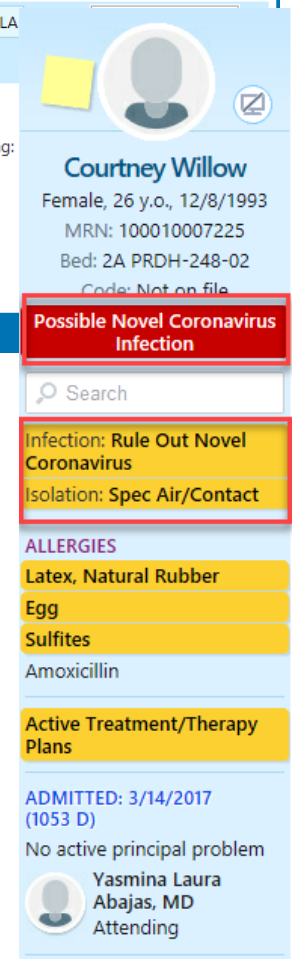
3

2





4



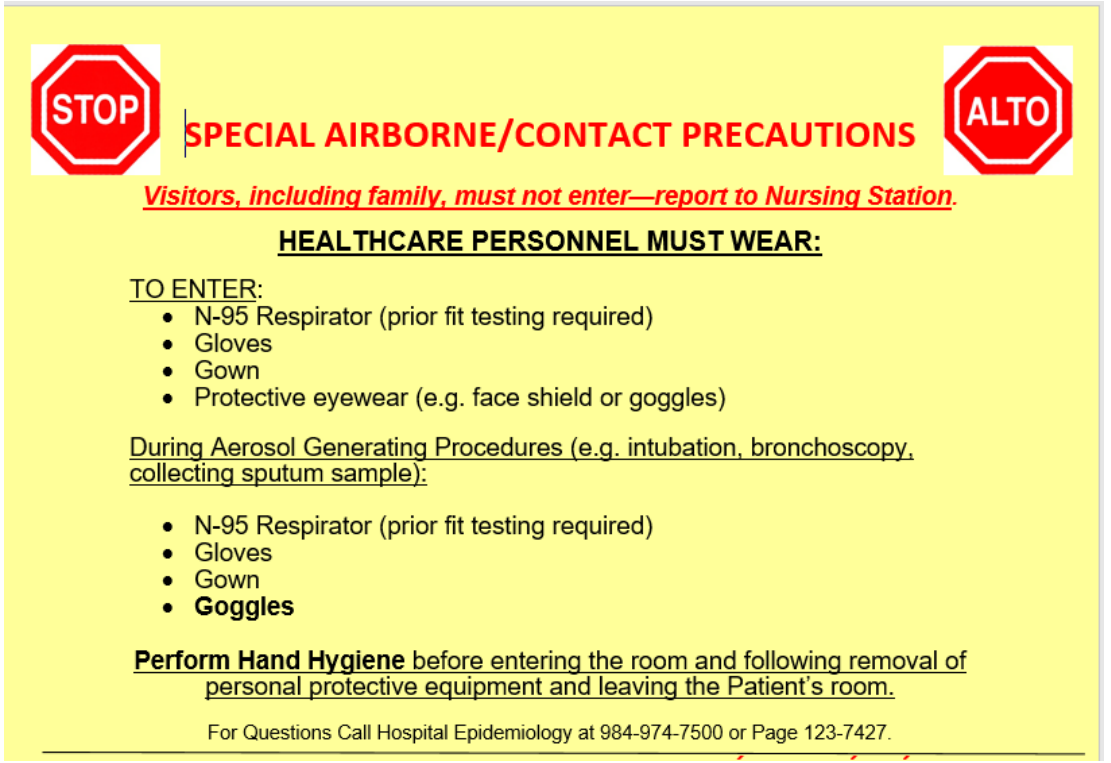
*Tip sheets will be disseminated

UNC HEALTH CARE

UNC Medical Center – What do we need to do?

Isolate:

Patients with symptoms of suspected 2019-nCoV or other respiratory infection (e.g., fever, cough) should be masked and isolated in a private room with the door closed. Healthcare personnel should also wear their PPE.



Special airborne/contact precautions for patients under investigation of novel coronavirus: Patients under investigation for novel coronavirus will be placed in an airborne isolation room as soon as possible. Healthcare personnel entering the room should use contact precautions (gown and gloves) and airborne precautions (N-95 respirators or PAPRs) with eye protection (e.g., goggles or a face shield).

UNC HEALTH CARE

PREVENTION FOR THE GENERAL PUBLIC, CDC

Recommendations to prevent transmission of ALL viral respiratory pathogens

- Wash your hands often with soap and water for at least 20 seconds. Use an alcohol-based hand sanitizer that contains at least 60% alcohol if soap and water are not available.
- Avoid touching your eyes, nose, and mouth with unwashed hands.
- Avoid close contact with people who are sick.
- Stay home when you are sick.
- Cover your cough or sneeze with a tissue, then throw the tissue in the trash.
- Clean and disinfect frequently touched objects and surfaces.

https://www.cdc.gov/coronavirus/2019-ncov/about/prevention-treatment.html

What can travelers do to protect themselves and others, CDC

- CDC recommends avoiding nonessential travel to China; if you travel you should:
  - Avoid contact with sick people.
  - Discuss travel to China with your healthcare provider. Older adults and travelers with underlying health issues may be at risk for more severe disease.
  - Avoid animals (alive or dead), animal markets, and products that come from animals (such as uncooked meat).
  - Wash hands often with soap and water for at least 20 seconds. Use an alcohol-based hand sanitizer if soap and water are not available.
- If you were in China in the last 14 days and feel sick with fever, cough, or difficulty breathing you should:
- Seek medical care right away. Before you go to a doctor's office or emergency room, call ahead and tell them about your recent travel and your symptoms.
  - Avoid contact with others and not travel while sick.
  - Cover your mouth and nose with a tissue or your sleeve (not your hands) when coughing or sneezing.
  - Wash hands often with soap and water for at least 20 seconds. Use an alcohol-based hand sanitizer if soap and water are not available.

https://wwwnc.cdc.gov/travel/notices/warning/novel-coronavirus-china

WHO, INFOGRAPHICS

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

REFERENCES

- Weber DJ, Sickbert-Bennett EE, Kanamori H, Rutala WA. New and emerging infectious diseases (Ebola, Middle Eastern respiratory syndrome coronavirus, carbapenem-resistant Enterobacteriaceae, Candida auris): Focus on environmental survival and germicide susceptibility. Am J Infect Control. 2019 Jun;47S:A29-A38.
- Weber DJ, Rutala WA, Fischer WA, Kanamori H, Sickbert-Bennett EE. Emerging infectious diseases: Focus on infection control issues for novel coronaviruses (Severe Acute Respiratory Syndrome-CoV and Middle East Respiratory Syndrome-CoV), hemorrhagic fever viruses (Lassa and Ebola), and highly pathogenic avian influenza viruses, A(H5N1) and A(H7N9). Am J Infect Control. 2016 May 2;44(5 Suppl):e91-e100.
- Otter JA, Donskey C, Yezli S, Douthwaite S, Goldenberg SD, Weber DJ. Transmission of SARS and MERS coronaviruses and influenza virus in healthcare settings: the possible role of dry surface contamination. J Hosp Infect. 2016 Mar;92(3):235-50.
- Hulkower RL, Casanova LM, Rutala WA, Weber DJ, Sobsey MD. Inactivation of surrogate coronaviruses on hard surfaces by health care germicides. Am J Infect Control. 2011 Jun;39(5):401-407.
- Casanova L, Rutala WA, Weber DJ, Sobsey MD. Coronavirus survival on healthcare personal protective equipment. Infect Control Hosp Epidemiol. 2010 May;31(5):560-1.
- Casanova LM, Jeon S, Rutala WA, Weber DJ, Sobsey MD. Effects of air temperature and relative humidity on coronavirus survival on surfaces. Appl Environ Microbiol. 2010 May;76(9):2712-7.
- Casanova L, Rutala WA, Weber DJ, Sobsey MD. Survival of surrogate coronaviruses in water. Water Res. 2009 Apr;43(7):1893-8