Mystery outbreak's global reach grows

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The mysterious and deadly pneumonia that has alarmed global health authorities appeared to spread to additional countries Monday and scientists at the Centers for Disease Control and Prevention and the World Health Organization ramped up research into possible causes.

New suspected cases were identified Monday in Australia, England, France, Israel, Slovenia and Switzerland.

In Germany, two women were hospitalized, bringing the total of suspected cases there to four. On Saturday, a Singaporean doctor who treated one of the earliest cases of the illness was taken off an airplane in Frankfurt along with his pregnant wife and mother after he developed symptoms. On Monday, authorities said the wife was ill as well.

Hong Kong health authorities said confirmed cases there have doubled, reaching 95, most of them medical workers.

The World Health Organization said 167 cases of "Severe Acute Respiratory Syndrome" have been identified worldwide, with four deaths known to have been caused by the unfamiliar disease.

In southern California, state health officials identified a possible case and sent samples to the CDC for testing.

ANAT GIVON / Associated Press

Travelers wear masks to ward off Asia's mystery illness at Hong Kong's Chek Lap Kok airport on Monday.

Internationally, tensions eased slightly after the government of China said it will provide information to the global health agency about a

➤ Please see ILLNESS, A12

INSIDE

➤ Chinese government asks the World Health Organization to help identify the cause of a pneumonia outbreak four months ago. A12

From Corona to Corona

SARS then- nCoV now

Annelies Wilder-Smith

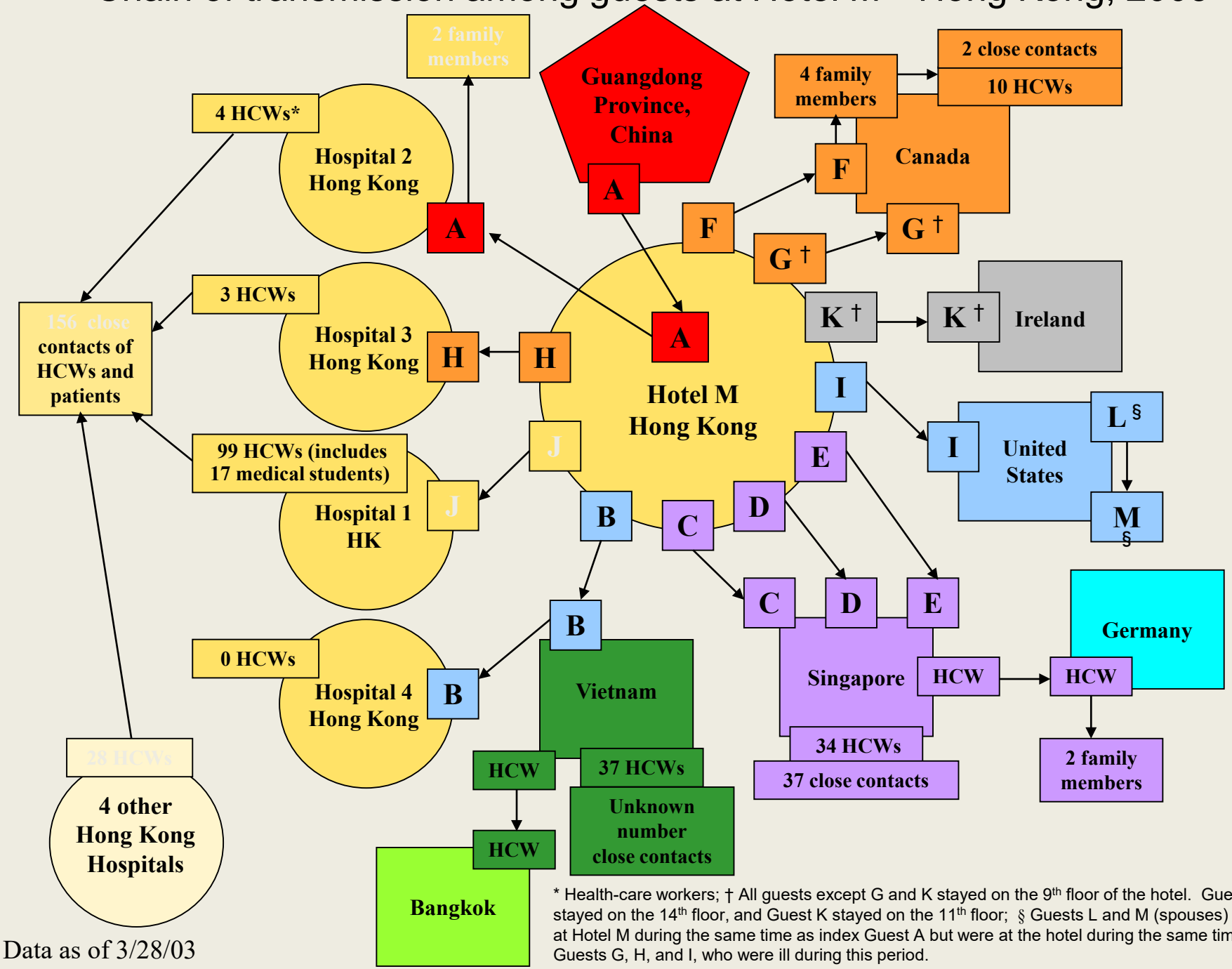
Professor of Emerging Infectious Diseases, London School of Hygiene and Tropical Medicine

Consultant, WHO- Immunization and Vaccines

Initial Signs of a Worldwide Outbreak

- February 10, 2003
  - A report posted on ProMed describes a problem of pneumonia in China's Guangdong province
- February 11
  - China reports to WHO that an outbreak of highly infectious pneumonia of unknown etiology has resulted in 300 cases and 5 deaths in Guangdong province since November 16, 2002
- February 23
  - Singapore receives a 23 year old traveller who had stayed at the Metropole Hotel, Hong Kong. She deteriorates rapidly.
- February 26
  - ID doctors institute infection control. Managing doctor departs for an ID conference in New York…..the rest is history.

Chain of transmission among guests at Hotel M—Hong Kong, 2003



Data as of 3/28/03

* Health-care workers; † All guests except G and K stayed on the 9th floor of the hotel. Guest G stayed on the 14th floor, and Guest K stayed on the 11th floor; § Guests L and M (spouses) were not at Hotel M during the same time as index Guest A but were at the hotel during the same times as Guests G, H, and I, who were ill during this period.

CHAIN EFFECT

How one person infected more than 120 people.
SALMA KHALIK traces the links.

SUPER SPREADER 1

Esther* was in ward 5A before she was isolated at Tan Tock Seng Hospital

**Esther Mok and two other women who stayed at Metropole Hotel in Hongkong where they got the virus from a Guangdong professor, who has since died.*

Note: Esther was among seven people who were infected overseas. But she was the only one who was so highly infectious.

Mother of Esther Mok: Died on April 7 | Pastor Simon Loh: Died on March 26 | Joseph Mok, father: Died on March 25 | Hospital staff | **SUPER SPREADER 2** Nurse worked in ward 5A; warded in ward 8A (Discharged) | Friend | Friend | Friend | Her father | Hospital staff | Hospital staff | Friend | Mother | Sister | Daughter | Son | Patient in same ward | Patient in same ward | Esther's grandma | Esther's uncle, in intensive care | Hospital staff | Hospital staff | Patient | Hospital staff | Hospital staff | Hospital staff | Hospital staff | Patient in same ward | Hospital staff | Hospital staff | Seah Kuay Chee infected while patient at TTSH. Was discharged. Admitted to NUH. Sent to TTSH where she died on April 3 | Friend | Her daughter | Patient in same ward | Her son | Dr Leong Hoe Nam (Frankfurt): Looked after Esther in ward | SIA stewardess on his flight from New York to Frankfurt on April 3 | Doctor's pregnant wife | Mother-in-law | Indonesian maid who was looking after elderly woman at intensive care in TTSH | Hospital staff

Husband of Super Infector 2 | Patient X in ward 8A | X's sister who visited her in the ward. Later warded at CGH before transfer to TTSH | CGH nurse | CGH nurse | X's daughter who visited her in the ward | Hospital staff | **SUPER SPREADER 3** Madam Painah Abdullah. Patient in same ward as Super Infector 2. Died on March 29 | Hospital staff | Hospital staff | Hospital staff | His god-sister | Visitor of X | Hospital staff of ward 8A | **Mother of three, in intensive care** | Son (Junior College student) | Boy, 5, from Pat's Schoolhouse | Visitor of X: Died on March 8 | **SUPER SPREADER 4** Hospital staff or patient at SGH | Hospital staff | Hospital staff at ward 8A | Patient in same ward | Hospital staff | Hospital staff | Hospital staff | Hospital staff | Hospital staff in ward 8A | Patient in ward 8A | His mother, in intensive care

THE SGH CLUSTER

Hospital staff | Hospital staff | Hospital staff | Hospital staff | Hospital staff | Patient, in intensive care | Hospital staff | Hospital staff | Hospital staff | Patient | Visitor, in intensive care | Hospital staff | Hospital staff | Hospital staff | Hospital staff | Hospital staff | Hospital staff | Patient | Patient | Visitor | Visitor

Dr Lim Ing Haan TTSH registrar | Hospital staff | Hospital staff | Hospital staff | **Dr Ong Hoi Sin**: medical officer in the cardiac unit: Died on April 7 | His mother, in intensive care | Hospital staff | Mdm Painah's sister | Hospital staff | **Hospital staff** | Her friend | Hospital staff | Mdm Painah's brother | Mdm Painah's sister | Hospital staff | **Mdm Painah's sister** | Probable link | Mdm Painah's mother, in ICU | **Jamaliah Mat Saad**: Visitor to TTSH; may have been infected by visitor to Mdm Painah. She was admitted to NUH when she fell ill. Died on March 31 | Hospital staff | Hospital staff | Hospital staff | Hospital staff | Hospital staff | Hospital staff in Intensive Care Unit 6A | Hospital staff | Hospital staff | Hospital staff

Mohd Fairuz Abu, her son | Dr Lee Kang Hoe NUH doctor in intensive care | TTSH staff working at Ang Mo Kio Community Hospital. Was in NUH with relative

UNCONFIRMED CASE

Orange Valley Nursing Home

TTSH patient discharged. Went to Orange Valley Nursing Home. Sick, sent to CGH on March 25. Died of pneumonia on March 30. Unable to confirm if she was a Sars patient.

- Male nurse at the nursing home → His girlfriend, also a nurse at the nursing home
- Her daughter-in-law, a MediaCorp employee, in intensive care → Her friend

LEGEND

- Sars patients who have been discharged
- Sars patients infected outside Tan Tock Seng Hospital
- Sars patients still in Tan Tock Seng
- Sars patients who infect many others
- Sars patients who died

SGH: Singapore General Hospital
CGH: Changi General Hospital

Source: HEALTHMINISTRY, TAN TOCK SENG HOSPITAL, OTHER SOURCES.

Graphics: G. CHANDRADAS

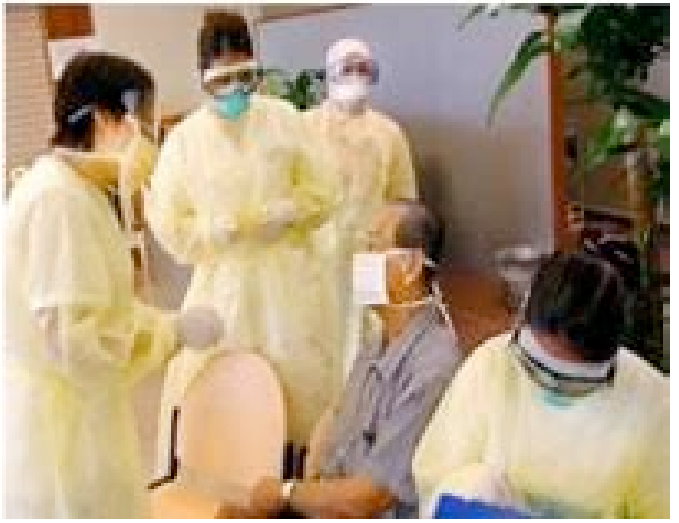
Strict Adherence

Airborne Precautions

- use of N95 masks

Contact and Droplet Precautions

- hand hygiene, gloves
- gowns
- eye protection



Public Health Tools: Definitions

- ***Isolation****

  Restriction of movement / separation of **sick** infected person(s) with contagious disease;
  - usually in a hospital setting, but can also be at home or in a dedicated isolation facility

- ***Quarantine****

  Restriction of movement / separation of **well** person(s) presumed exposed to a contagious disease;
  - usually at home, but can also be in a dedicated quarantine facility
  - individual(s) or community/population level

** Measures usually **voluntary**, but can be **mandatory**; legal quarantine authority covers "isolation" and "quarantine" tools*

CDC
Centers for Disease Control and Prevention

Public health tools

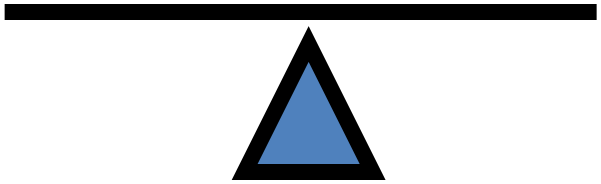
- **Isolate** symptomatic individuals (communicable phase)
  - SARS Hospitals
  - Home
  - Recovery during period of communicability
- **Quarantine** 1^0 asymptomatic contacts (pre-communicable phase)
  - Home vs. Residential facility?
  - Fever surveillance of close contacts
- **Community Measures**: decrease social contacts
  - Cancel public gatherings e.g. schools, workplace, sporting
  - Limit translocation, restrict travel

Hong Kong is the city of masks, Singapore is the city of thermometers

Quarantine

A collective action for the common good

Public good **Individual liberties**



Paramount to meet needs of individuals infected and exposed

Managing public fear and anxiety

Clear information on what we know and what we don`t know
Regular (daily) situational updates
What the public can do/get their help
Complete transparency
Guidelines for workplaces (temperature)

Success of early isolation was based on….

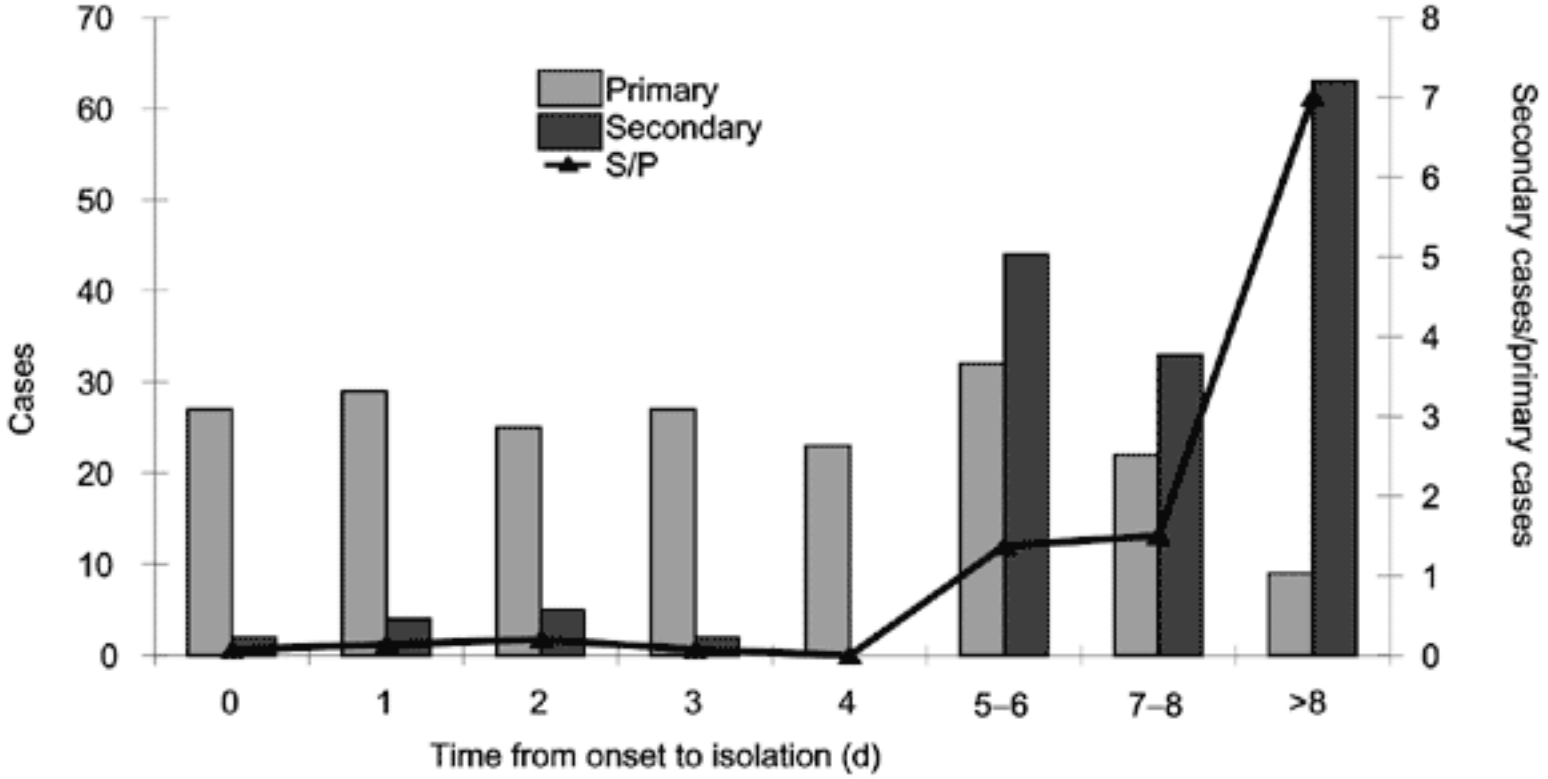
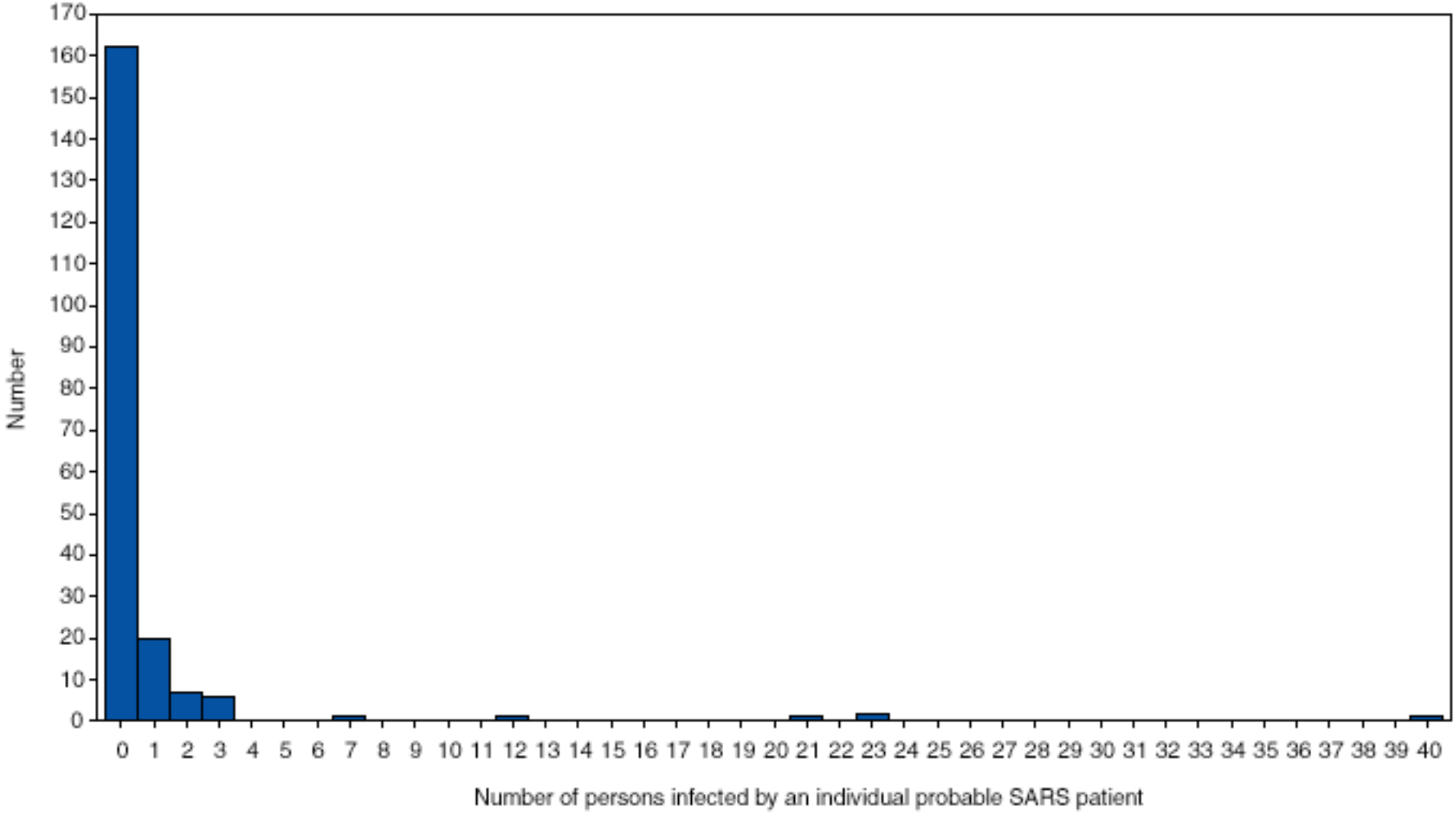
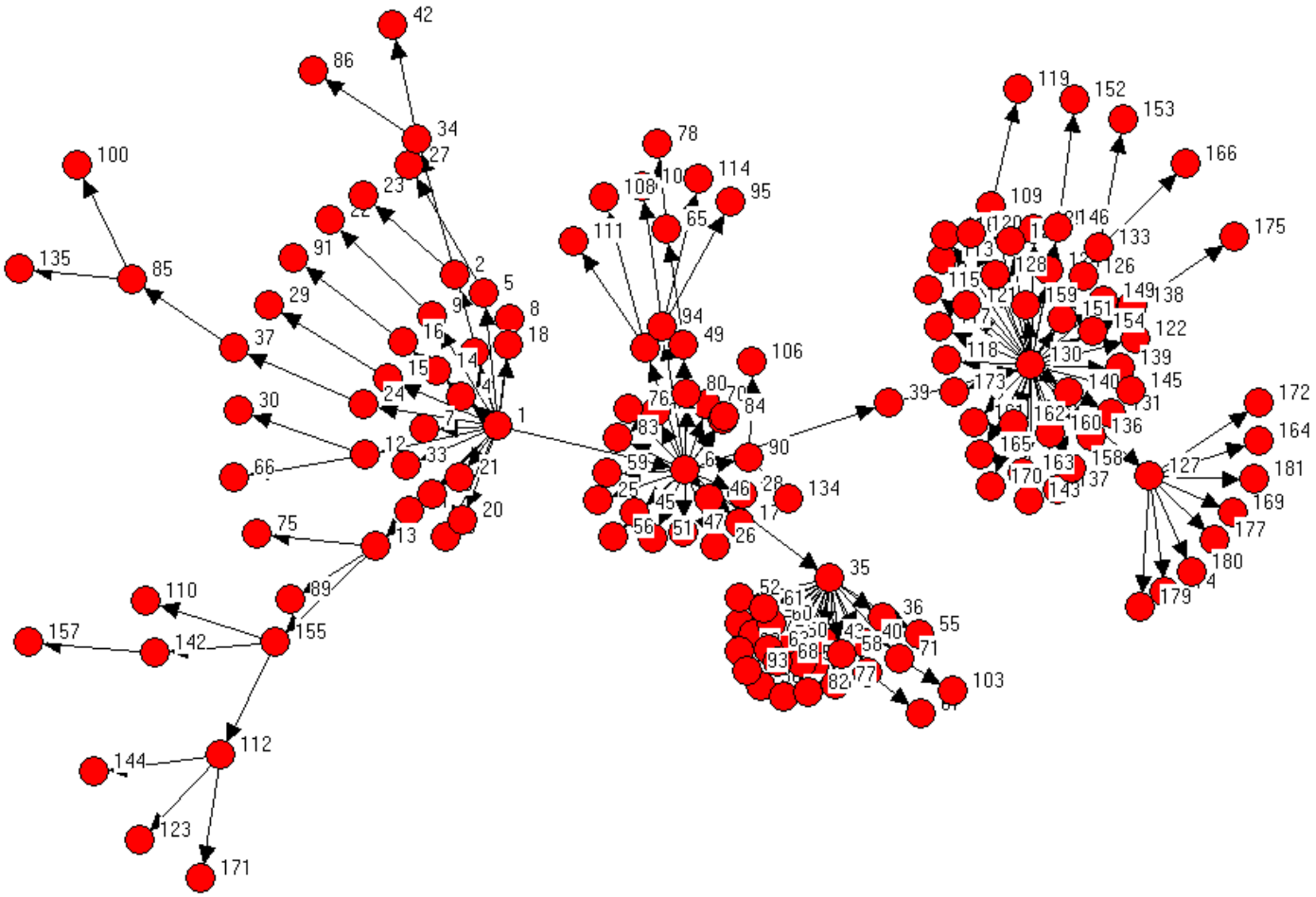


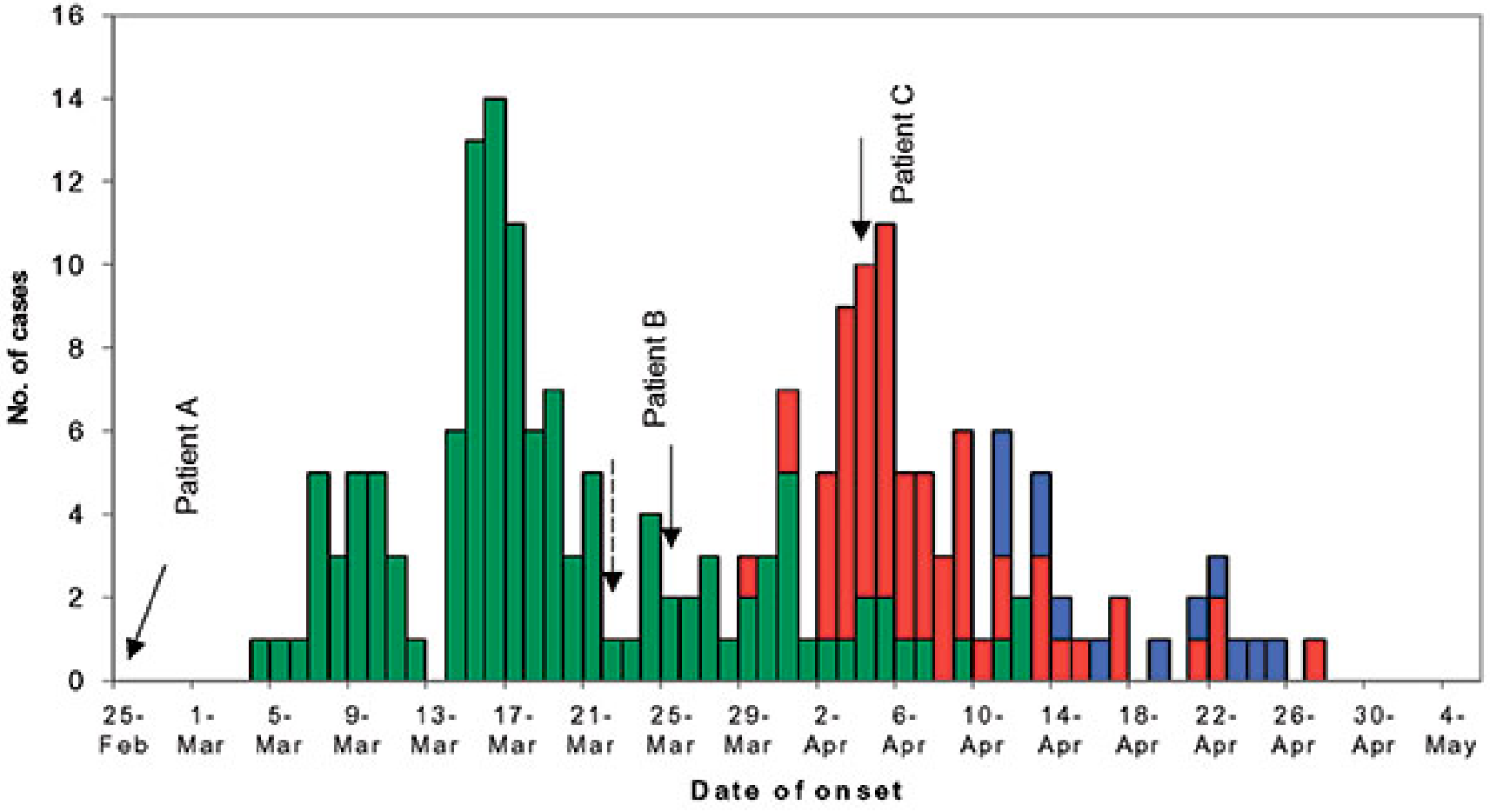
FIGURE 3. Number of direct secondary cases from probable cases of severe acute respiratory syndrome — Singapore, February 25–April 30, 2003



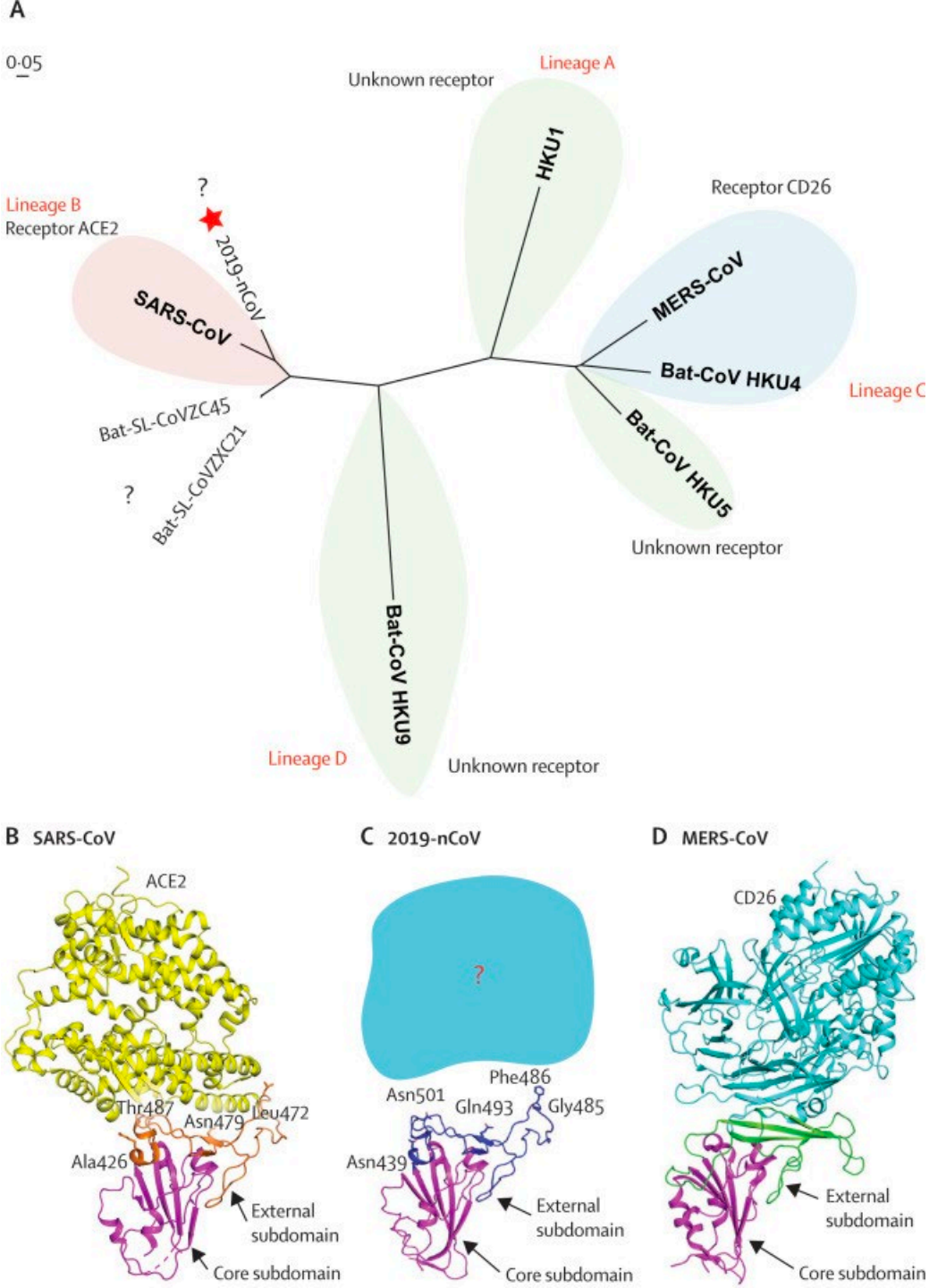
Singapore Clusters of SARS: “Super Shedding”



Success with old-style public health tools: detect, isolate and quarantine



SARS: cumulative number of probable cases worldwide as of 25 June 2003 (N = 8 460 cases, 808 deaths)


A
0·05
Unknown receptor
Lineage A
HKU1
Receptor CD26
MERS-CoV
Bat-CoV HKU4
Lineage C
Bat-CoV HKU5
Unknown receptor
Lineage B
Receptor ACE2
?
2019-nCoV
SARS-CoV
Bat-SL-CoVZC45
?
Bat-SL-CoVZXC21
Bat-CoV HKU9
Lineage D
Unknown receptor
B SARS-CoV
ACE2
Thr487
Asn479
Leu472
Ala426
External subdomain
Core subdomain
C 2019-nCoV
?
Phe486
Asn501
Gln493
Gly485
Asn439
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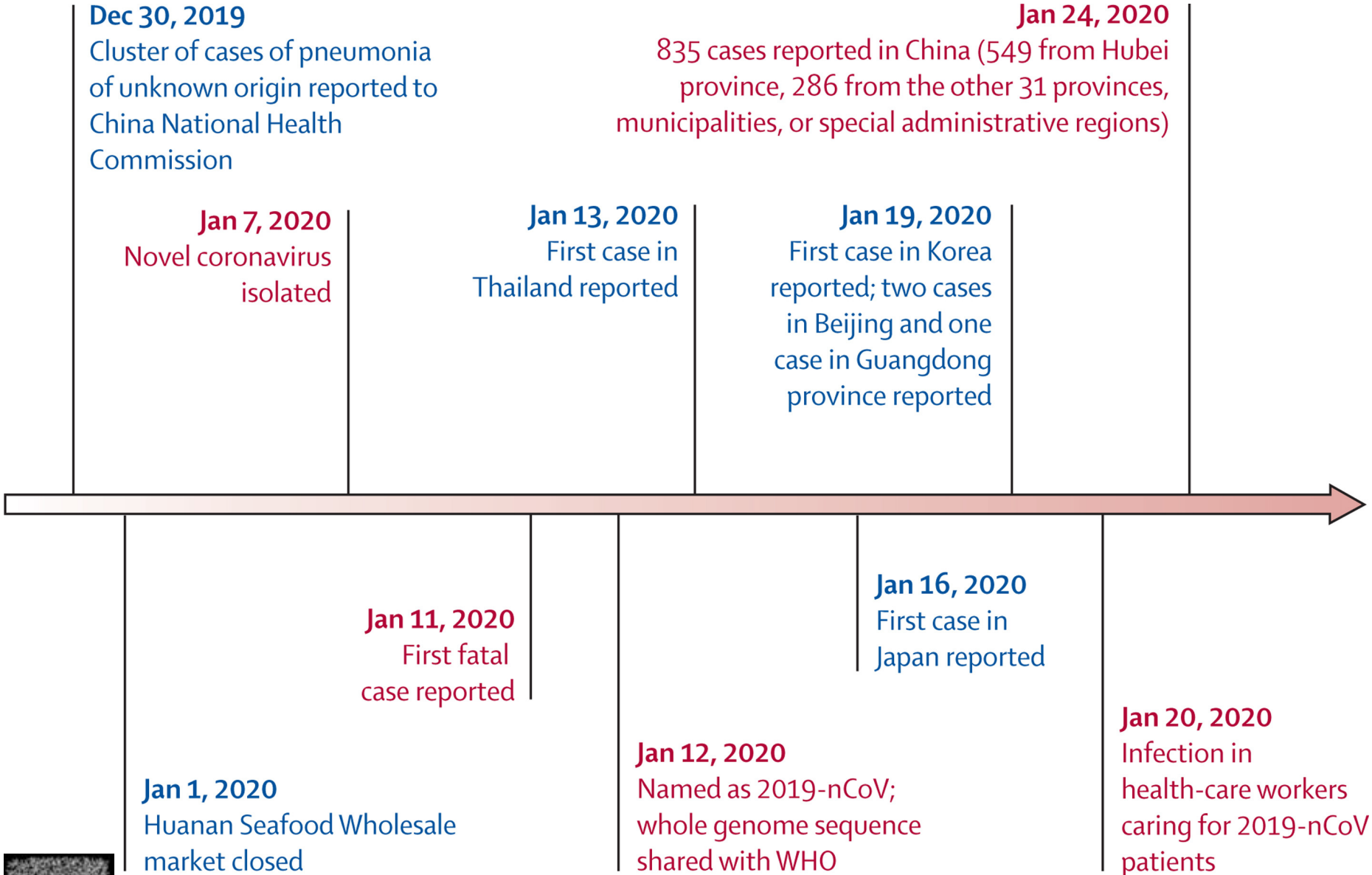
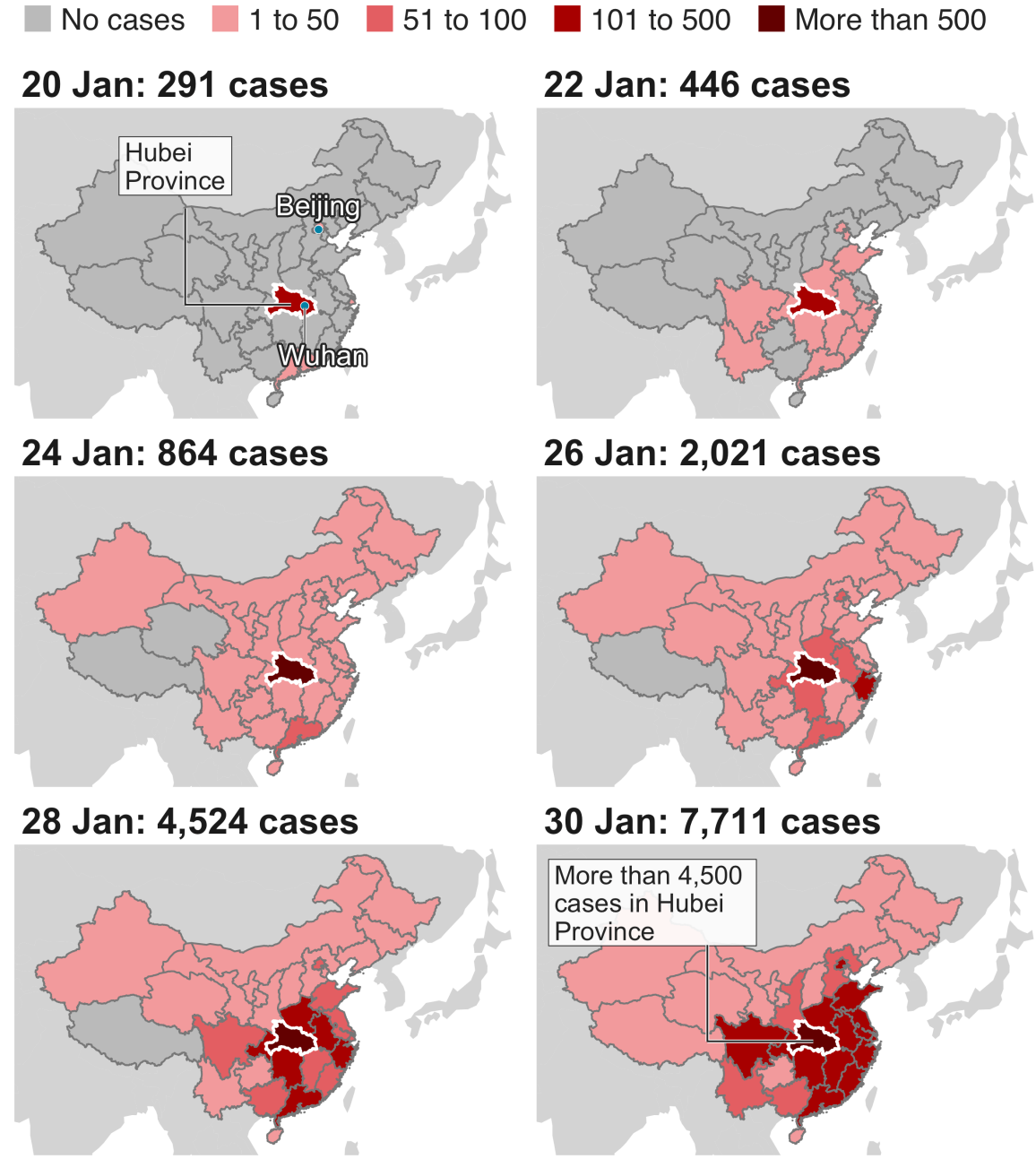
Core subdomain
D MERS-CoV
CD26
External subdomain
Core subdomain


Dec 30, 2019
Cluster of cases of pneumonia of unknown origin reported to China National Health Commission
Jan 7, 2020
Novel coronavirus isolated
Jan 13, 2020
First case in Thailand reported
Jan 19, 2020
First case in Korea reported; two cases in Beijing and one case in Guangdong province reported
Jan 24, 2020
835 cases reported in China (549 from Hubei province, 286 from the other 31 provinces, municipalities, or special administrative regions)
Jan 1, 2020
Huanan Seafood Wholesale market closed
Jan 11, 2020
First fatal case reported
Jan 12, 2020
Named as 2019-nCoV; whole genome sequence shared with WHO
Jan 16, 2020
First case in Japan reported
Jan 20, 2020
Infection in health-care workers caring for 2019-nCoV patients

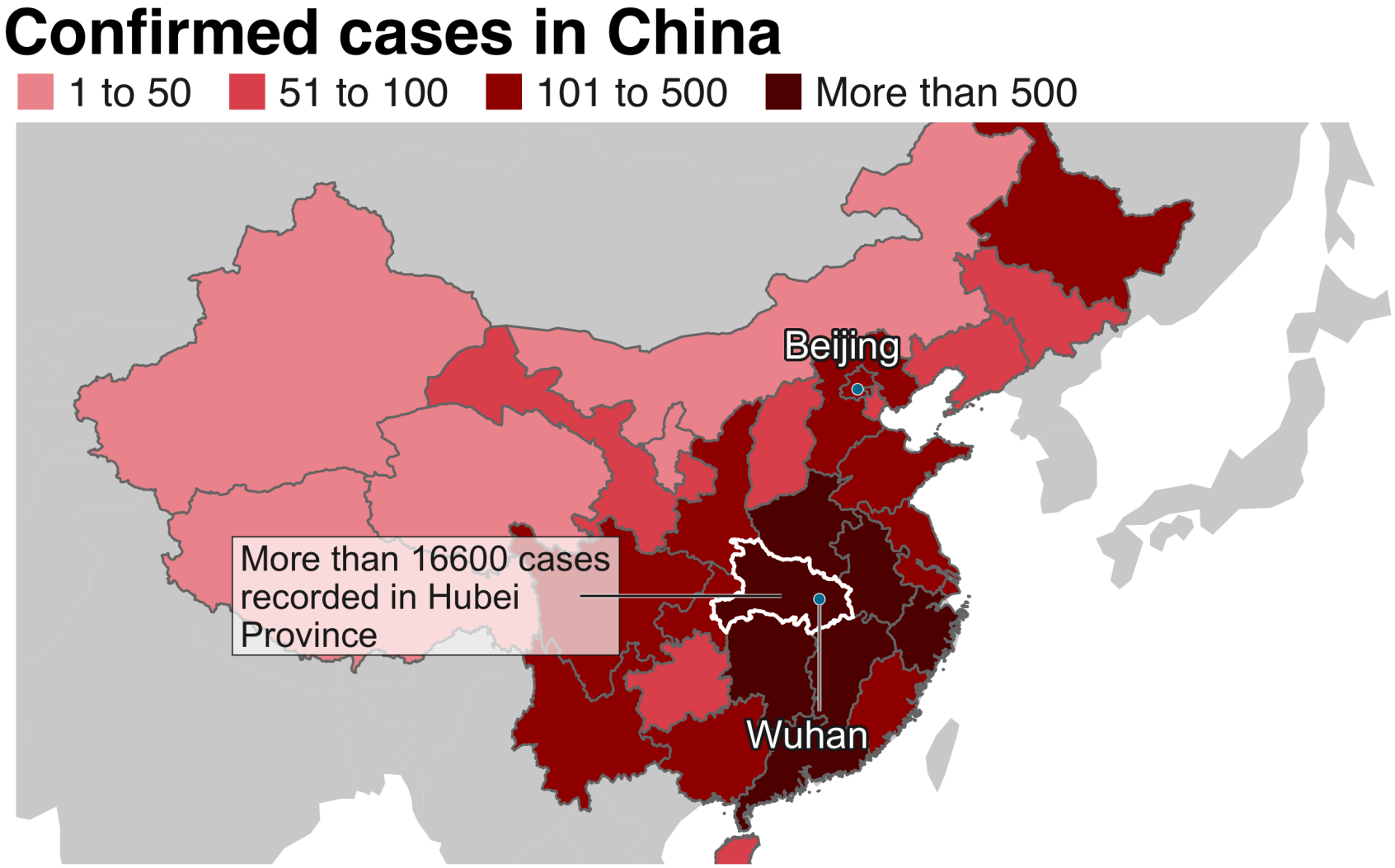
How the virus has spread in China



Source: China National Health Commission, BBC Research, 30 Jan

BBC

28,018 cases; 563 deaths; 195 exported cases to 27 countries; 45 local cases in 11 countries



Source: China National Health Commission, BBC Research, 05 Feb

BBC

Similarities between SARS-CoV and 2019-nCoV

- Homology of viral sequencing
- Origin: bats
- Cross-species jump through wildlife at a market
- Attacks lower respiratory tract (ACE2 inhibitor)
- Clinical picture very similar for the severe end

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

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

	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.

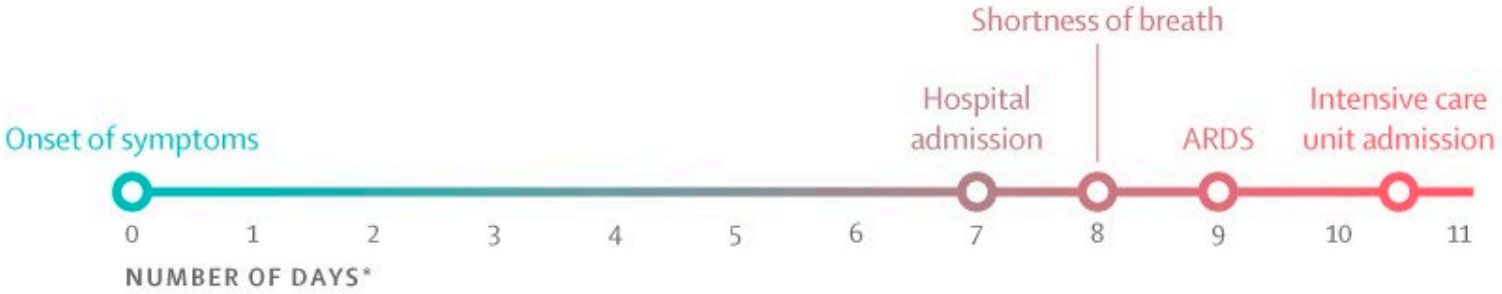
Table 1: **Demographics, baseline characteristics, and clinical outcomes of 99 patients admitted to Wuhan Jinyintan Hospital (Jan 1–20, 2020) with 2019-nCoV pneumonia**

	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.

Table 2: **Clinical characteristics and treatment of patients with 2019-nCoV pneumonia**

Timeline of coronavirus onset



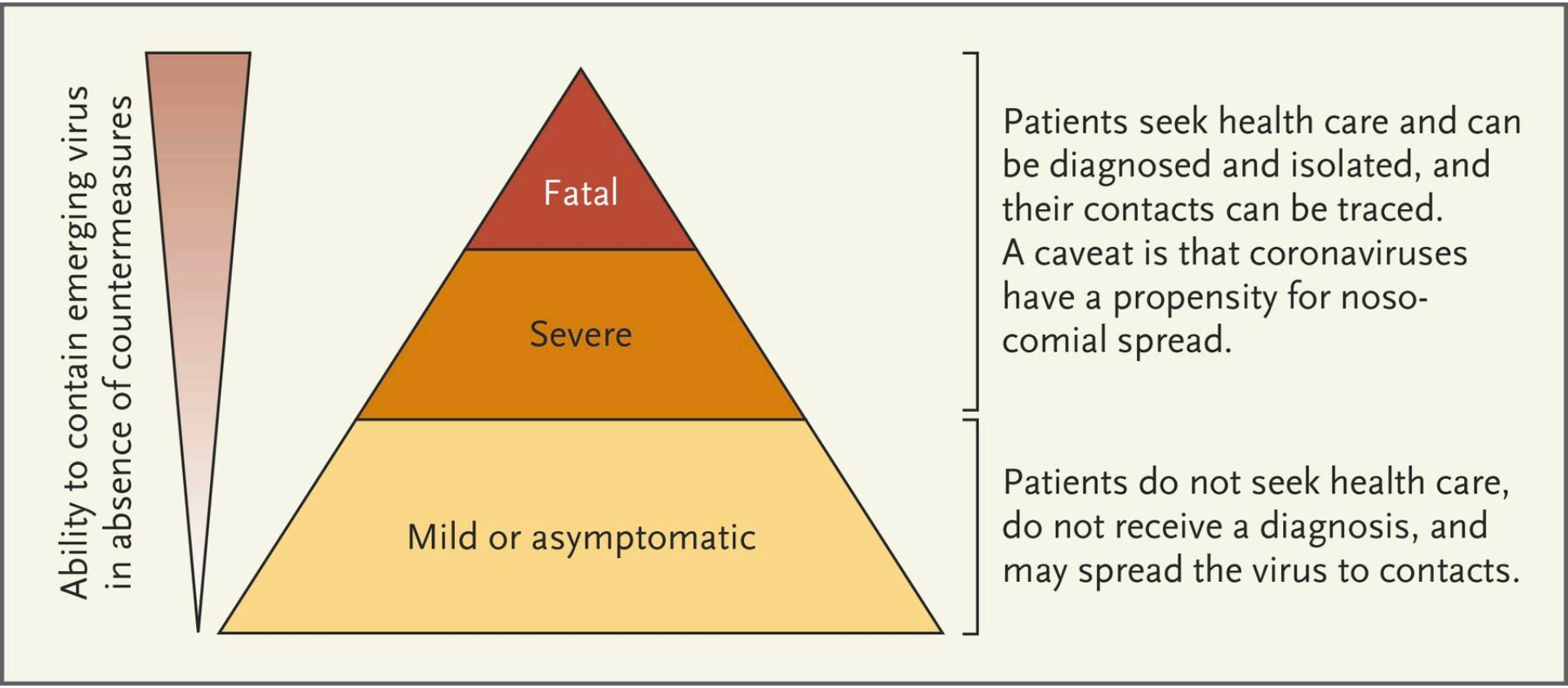
ARDS=Acute respiratory distress syndrome

*Median time from onset of symptoms, including fever (in 98% of patients), cough (75%), myalgia or fatigue (44%), and others.

THE LANCET

Public health tools

	Definition	Effective in following settings	Challenges
Isolation	Ill persons	Peak virus shedding and transmission occurs after symptoms occur	Early detection of cases
Quarantine	Contacts	Moderate incubation time (< 2 days too short.> 10 days impossible)	Depends on early detection of cases, and prompt contact tracing
Community containment	Social distancing, Community	Widespread community transmission where contacts cannot be identified anymore	Community acceptance Social unrest


Ability to contain emerging virus in absence of countermeasures
Fatal
Severe
Mild or asymptomatic
Patients seek health care and can be diagnosed and isolated, and their contacts can be traced. A caveat is that coronaviruses have a propensity for nosocomial spread.
Patients do not seek health care, do not receive a diagnosis, and may spread the virus to contacts.

Notable differences between SARS and nCoV

Epidemiological similarities

Mean incubation period 5.2 days (95% confidence interval [CI], 4.1 to 7.0), with the 95th percentile of the distribution at 12.5 days.

Mean serial interval of 7.5 days (95% CI, 5.3 to 19)

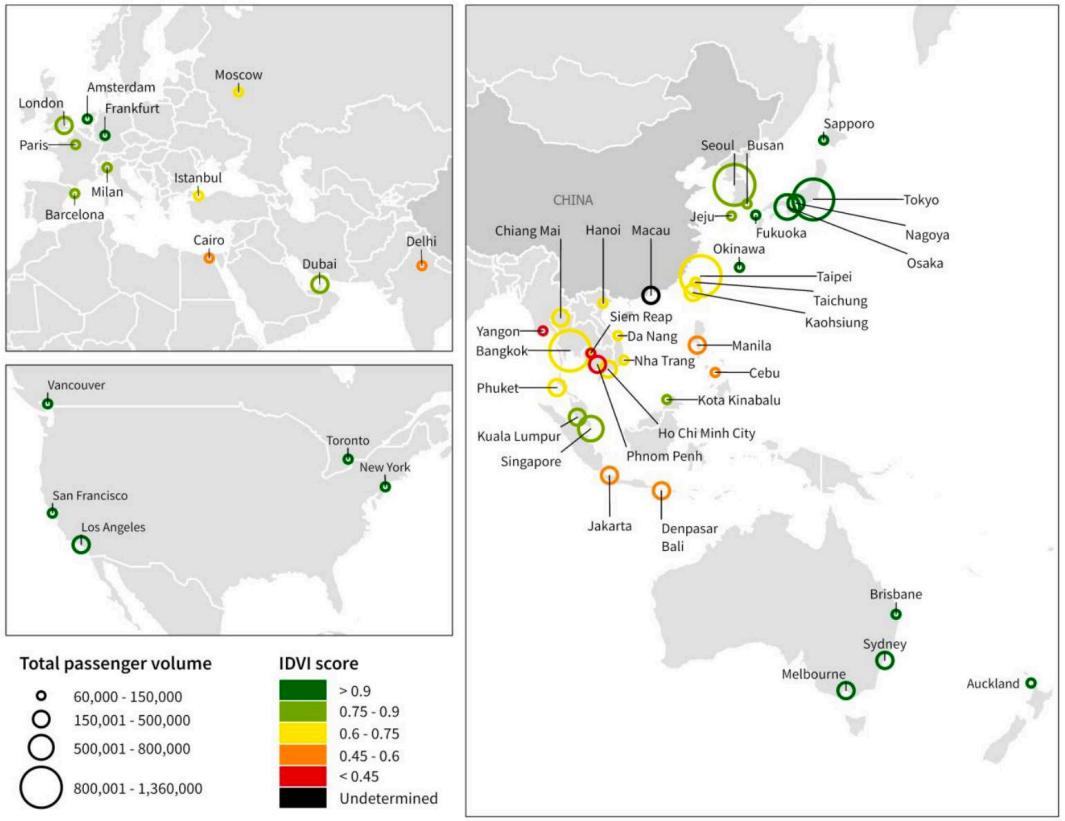
Basic reproductive number of 2.2 (95% CI, 1.4 to 3.9).

Epidemiological differences

- Transmission by pre-symptomatic persons
- Infectious period??
- CFR lower, but how high?

Potential for global spread of a novel coronavirus from China

Bogoch I et al. Journal of Travel Medicine 2020



Conclusions

Many unknowns remain. Until we know those answers, all efforts need to scale-up to implement old-school public health tools.

Where new cases are imported they do not need to trigger new outbreaks if systems are in place to detect, isolate and quarantine.

We need strong political will and –even in the European context- some top-down approach