RCSI Leading the world to better health

COVID-19 SARS-CoV-2 for health care workers

Samuel McConkey
Deputy Dean
RCSI

Contents

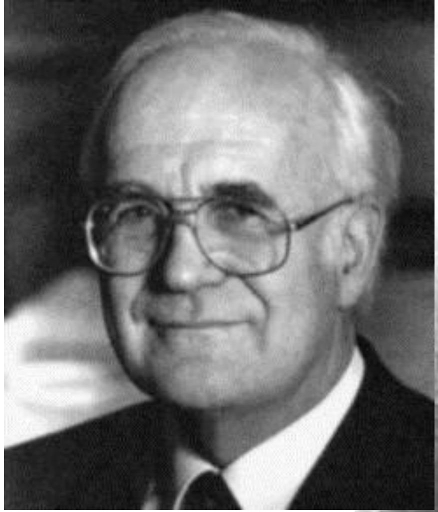
1. What happened
2. Clinical presentation
3. Complications
4. Management interventions
5. Outcomes
6. Health-care workers
7. What should we do

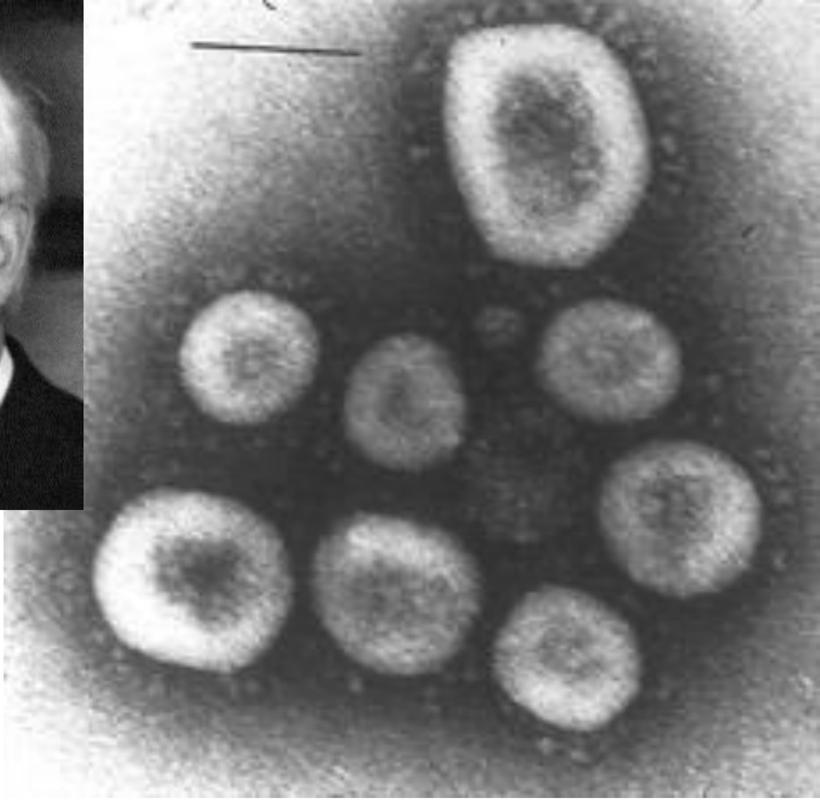
Coronaviruses

1965 HCoV OC43 (David A Tyrrell)
1967 HCoV 229E (from bats)
2003 SARS (from bats, via palm civet)
2004 HCoV NL63
2005 HCoV HKU3
2006 MERS (from bats)
2019 SARS-CoV-2
Cause 4 -15- 35% of URTI
and some LRTI and otitis media in children
even in people with pre-existing antibodies
More in winter and spring
Epidemics every 2 or 3 years

Big virus, largest RNA genome 20k base pairs
nsp12 RdRP has low error rate, nsp 10 proof reads
Ribavirin does not work

Killed easily by bleach, detergents, alcohol, soap, …





Coronavirus OC16. Proc Natl Acad Sci USA. 1967;57;933–940.

RCSI
Leading the world to better health

Context

- Wuhan city – central China 11m people
  - In Hubei province 55m people
- Pneumonia, fever and URTI linked to a seafood market, 41 cases by 27^{th} Dec
- Coronavirus
- Sequenced – like SARS
- Increasing cases
- Spread to rest of China despite controls
- Spread to other countries
- Isolation on a cruise ship does not work
- New cases and deaths in 70 countries

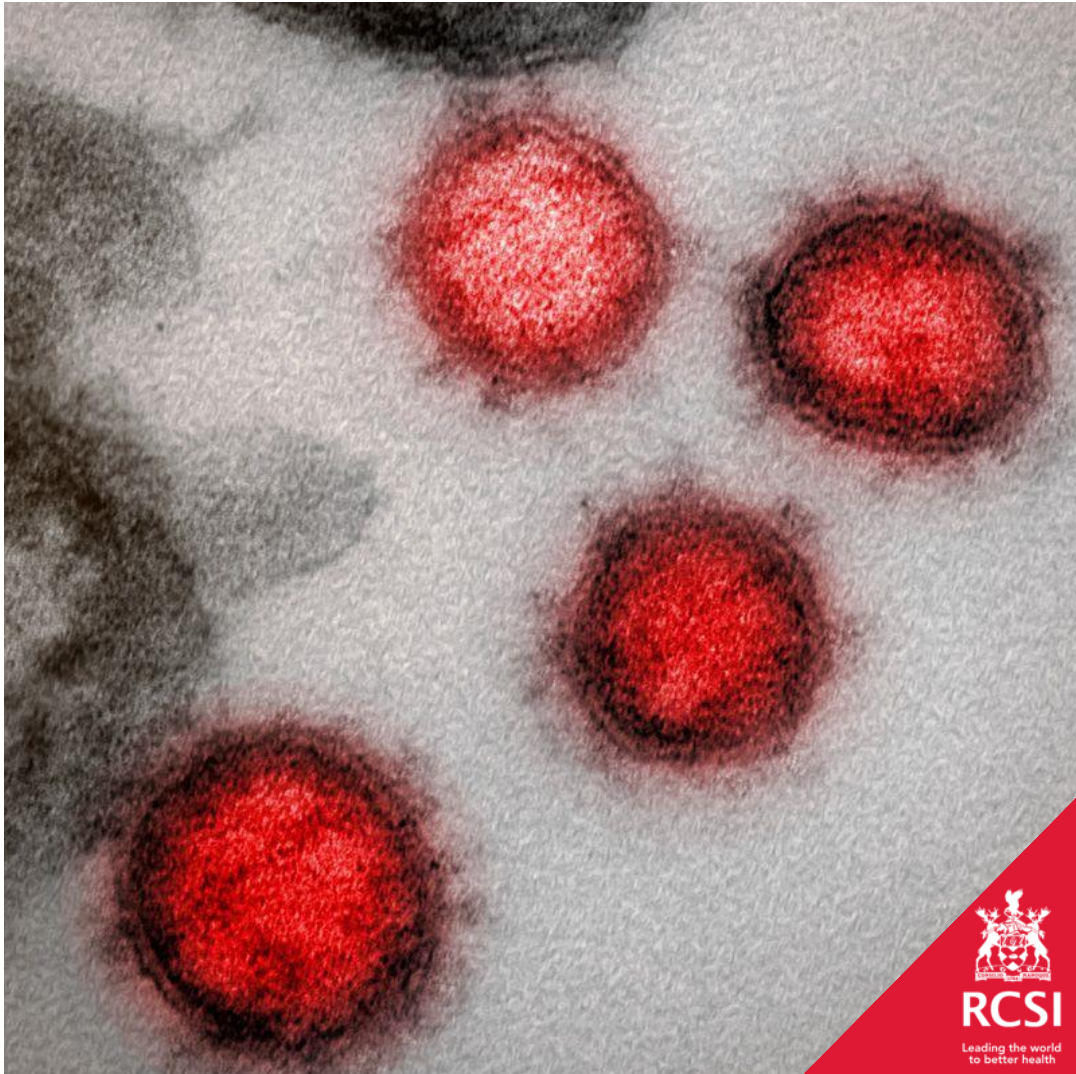
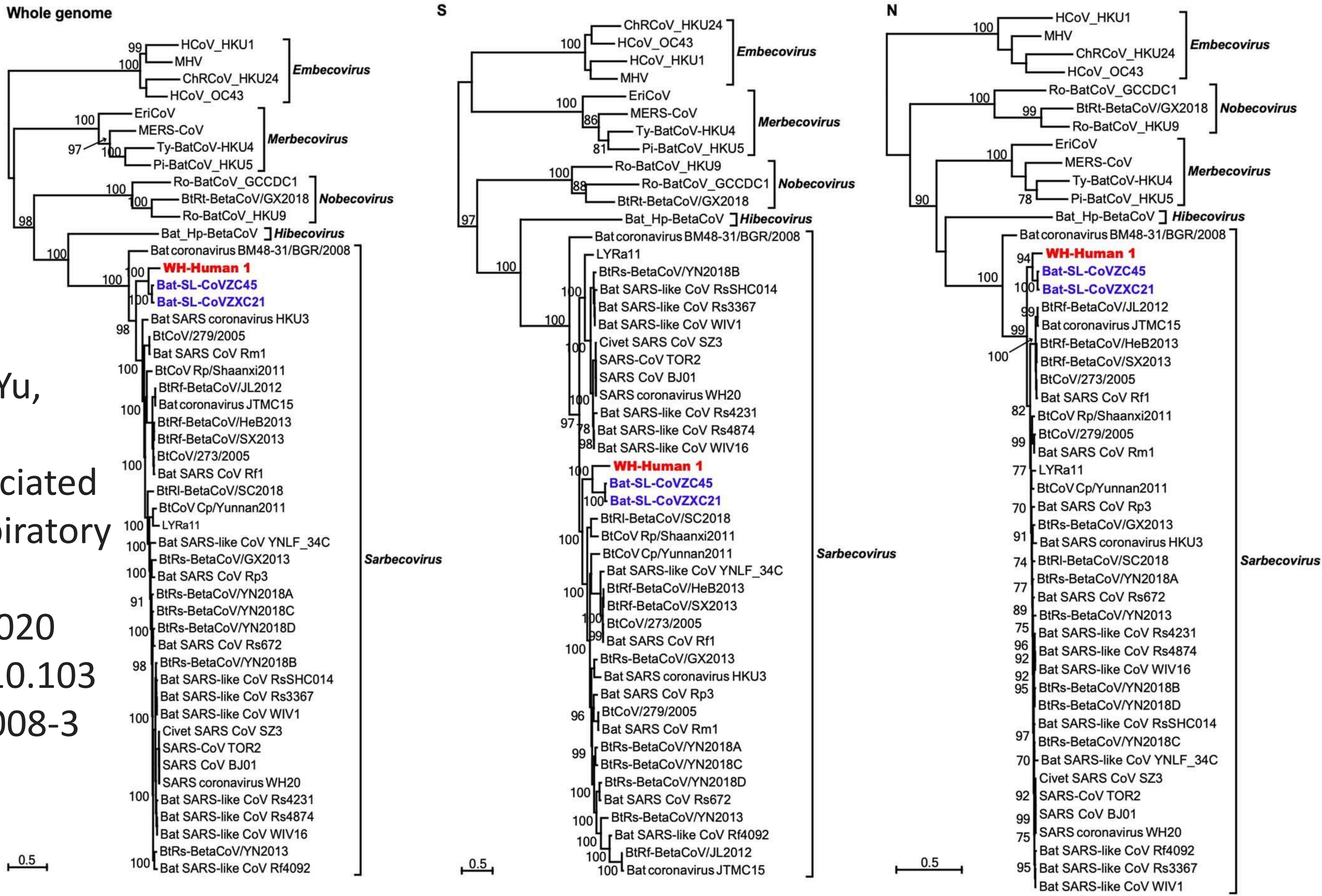


Fig. 5: Maximum likelihood phylogenetic trees of the nucleotide sequences of the whole genome, and *S* and *N* genes of WHCV and related coronaviruses



Wu, F., Zhao, S., Yu, B. *et al.* A new coronavirus associated with human respiratory disease in China. *Nature* (2020 https://doi.org/10.1038/s41586-020-2008-3

Pathological findings of COVID-19 associated with acute respiratory distress syndrome

Zhe Xu*, Lei Shi*, Yijin Wang*, Jiyuan Zhang, Lei Huang, Chao Zhang, Shuhong Liu, Peng Zhao, Hongxia Liu, Li Zhu, Yanhong Tai, Changqing Bai, Tingting Gao, Jinwen Song, Peng Xia, Jinghui Dong, Jingmin Zhao, Fu-Sheng Wang

Since late December, 2019, an outbreak of a novel coronavirus disease (COVID-19; previously known as 2019-nCoV)[1,2] was reported in Wuhan, China,[2] which has subsequently affected 26 countries worldwide. In general, COVID-19 is an acute resolved disease but it can also be deadly, with a 2% case fatality rate. Severe disease onset might result in death due to massive alveolar damage and progressive respiratory failure.[2,3] As of Feb 15, about 66 580 cases have been confirmed and over 1524 deaths. However, no pathology has been reported due to barely accessible autopsy or biopsy.[2,3] Here, we investigated the pathological characteristics of a patient who died from severe infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by obtaining biopsy samples at autopsy. This study is in

A 50-year-old man was admitted to a fever clinic on Jan 21, 2020, with symptoms of fever, chills, cough, fatigue and shortness of breath. He reported a travel history to Wuhan Jan 8–12, and that he had initial symptoms of mild chills and dry cough on Jan 14 (day 1 of illness) but did not see a doctor and kept working until Jan 21 (figure 1). Chest x-ray showed multiple patchy shadows in both lungs (appendix p 2), and a throat swab sample was taken. On Jan 22 (day 9 of illness), the Beijing Centers for Disease Control (CDC) confirmed by reverse real-time PCR assay that the patient had COVID-19.

He was immediately admitted to the isolation ward and received supplemental oxygen through a face mask. He was given interferon alfa-2b (5 million units twice daily,

Lancet Respir Med 2020
Published Online
February 17, 2020
https://doi.org/10.1016/S2213-2600(20)30076-X

*Contributed equally
Treatment and Research Center for Infectious Diseases (Z Xu MD, L Shi MD, J Zhang PhD, L Huang MD, C Zhang PhD, P Zhao MSc, H Liu BSc, J Song PhD, P Xia MSc, Prof F-S Wang MD), **Department of Pathology and Hepatology** (Y Wang PhD, S Liu MSc, L Zhu MSc, Prof Y Tai MD, T Gao BSc, Prof J Zhao MD), **Department of Respiration**

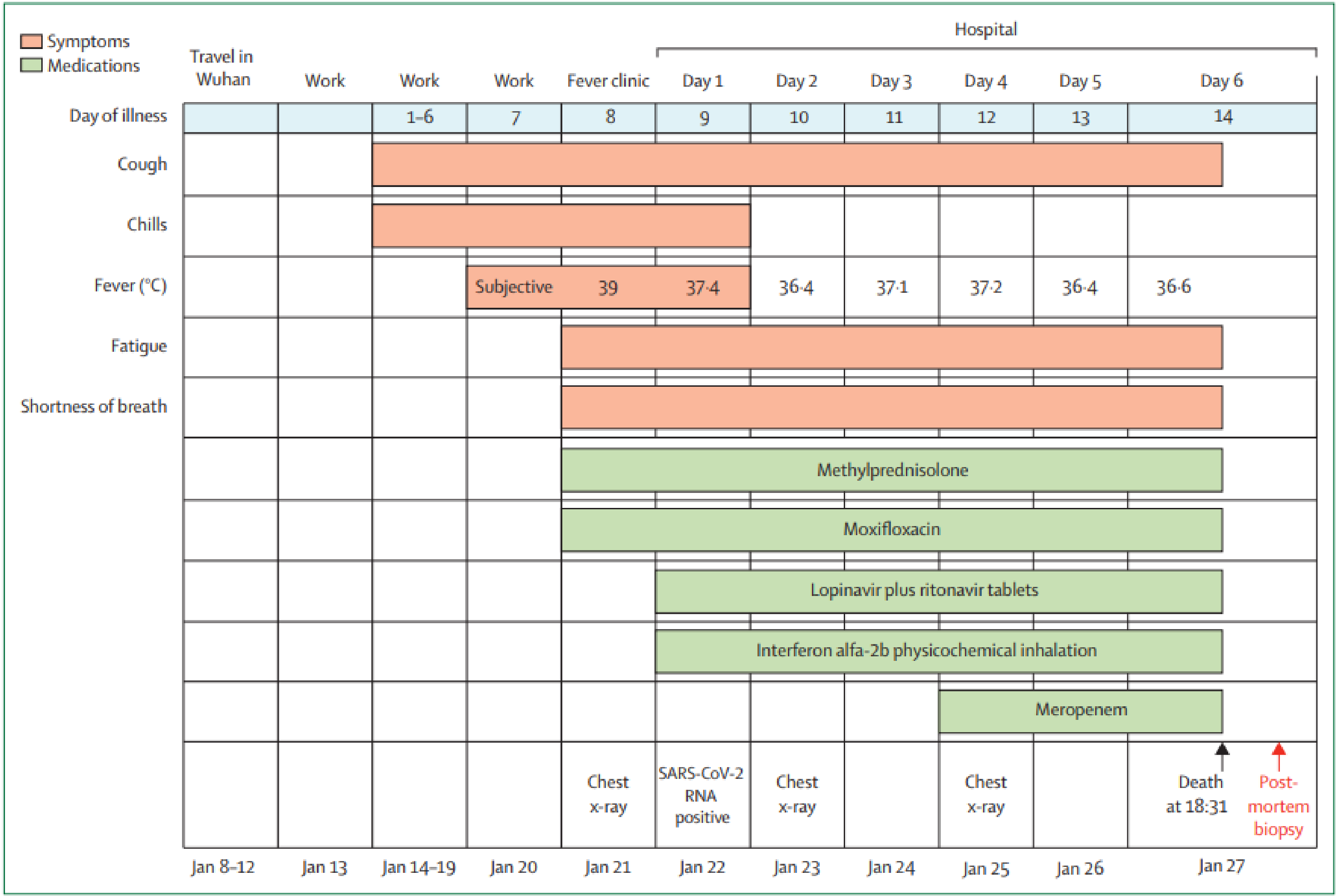


Figure 1: **Timeline of disease course according to days from initial presentation of illness and days from hospital admission, from Jan 8–27, 2020**
SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

Correspondence to:
Dr Fu-Sheng Wang, Treatment and Research Center for Infectious Diseases, The Fifth Medical Center of PLA General Hospital, National Clinical Research Center for Infectious Diseases, Beijing 100039, China
fswang302@163.com

or

Dr Jingmin Zhao, Department of Pathology and Hepatology, The Fifth Medical Center of PLA General Hospital, National Clinical Research Center for Infectious Diseases, Beijing 100039, China
jmzhao302@163.com

See Online for appendix

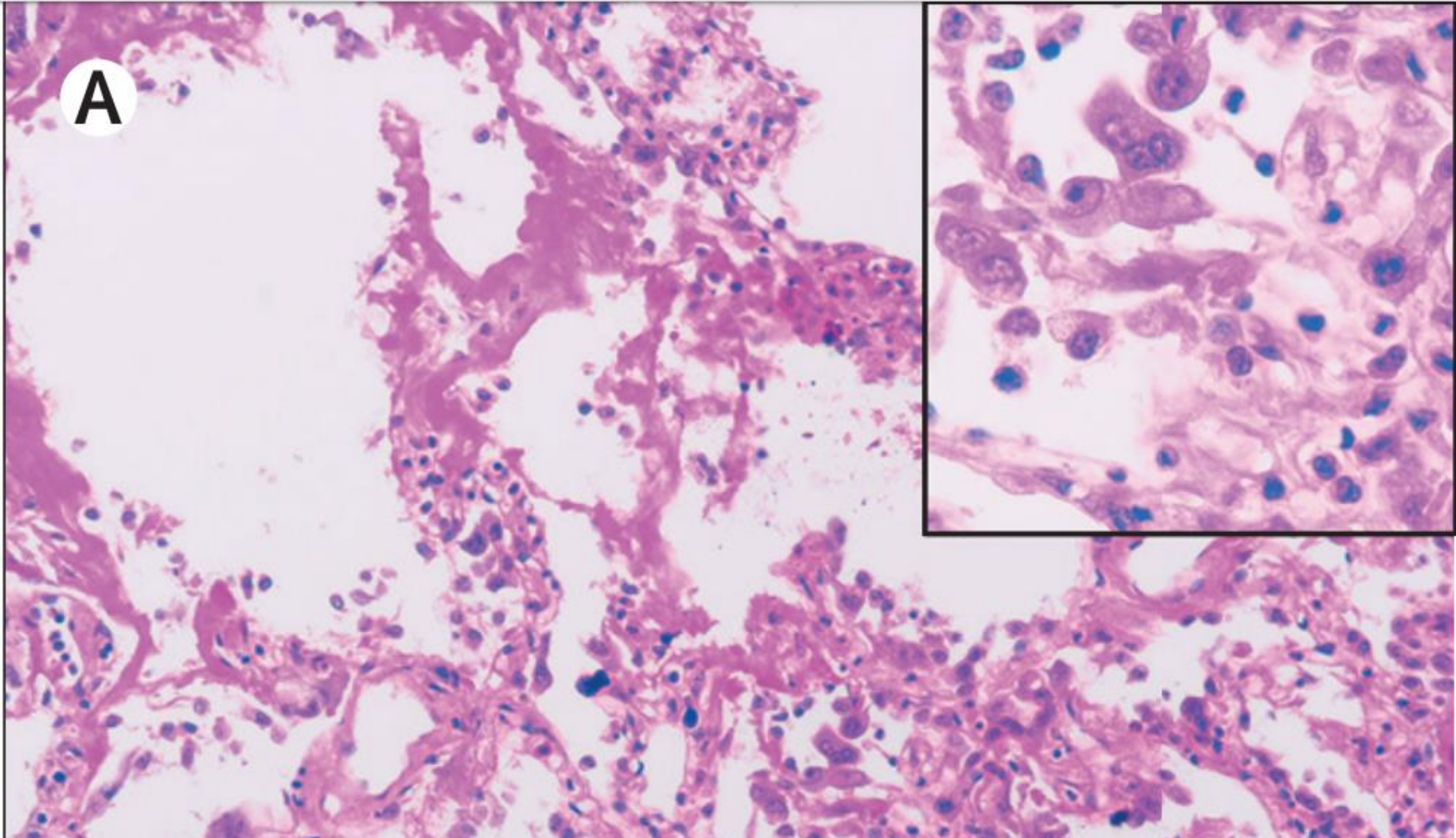

A

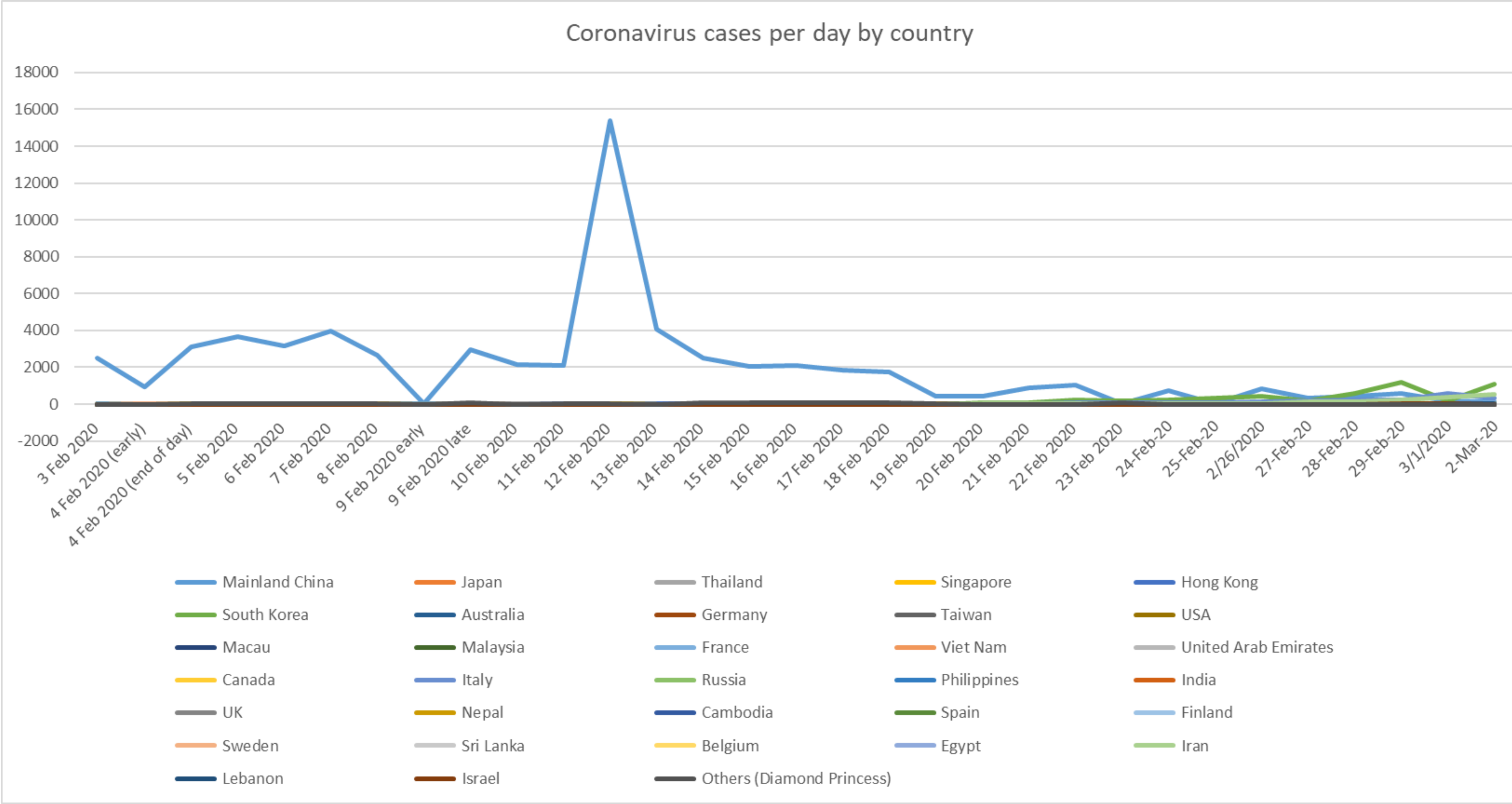
Table 1. Clinical Laboratory tests.

Measure	Reference range	Illness Day 8 Fever Clinic	Illness Day 10 Hospital Day 2	Illness Day 11 Hospital Day 3	Illness Day 12 Hospital Day 4	Illness Day 14 Hospital Day 6
Complete blood count						
White-cell count (×10^9/L)	3.97-9.15	3.19‡	2.23‡	7.07		6.28
Absolute neutrophil count (×10^9/L)	2-7	2.33‡	1.840‡	6.550		5.700
Absolute Lymphocyte count (×10^9/L)	0.8-4.0	0.66‡	0.280‡	0.340‡		0.310‡
Absolute monocyte count (×10^9/L)	0.12-1.0	0.20	0.110‡	0.160		0.250
Red-cell count (×10^12/L)	4.09-5.74	4.48	4.30	4.16		4.29
Hemoglobin (g/L)	131-172	143	135.00	134.00		134.00
Platelet count (×10^9/L)	85-303	124	154.00	188.00		205.00
Biochemical test						
Total protein (g/L)	60-83		60		55‡	56‡
Albumin (g/L)	35-55		34‡		30‡	30‡
Prealbumin (mg/L)	160-400		90‡			120‡
Alanine aminotransferase (ALT) (U/L)	5-40		69§	64§	70§	59§
Aspartate aminotransferase (AST) (U/L)	8-40		111§		83§	40
Lactate dehydrogenase (LDH) (U/L)	109-245		581§		617§	825§
Urea (mmol/L)	2.9-8.2		3.8		3.94	5.9
Creatinine(umol/L)	62-115		79		77	67
Sodium (mmol/liter)	136-145		135		135	145
Potassium (mmol/liter)	3.5-5.2		3.8		3.0‡	3.5
Chloride (mmol/liter)	93-108		97.6		98.7	109.3§
Arterial blood gas (ABG) **analysis**						
PH	7.35-7.45		7.5§	7.47§		7.27‡
Pressure of oxygen in arterial blood (mmHg)	80-100		63‡	74‡		28‡
Pressure of carbon dioxide in arterial blood (mmHg)	35-45		34	33‡		39
Base excess (mmol/L)	-2 - +2		3.2§	0.0		-9.1‡
Alveolar-arterial oxygen partial pressure difference (mmHg)			135.7§	331.2§		510.3§
Coagulation profile						
Prothrombin time (sec)	10.2-14.3		12.1	12.5		14.9§
International normalized ratio	0.8-1.2		1.05	1.09		1.31§
Fibrinogen (g/L)	2.0-4.0		5.28§	3.70		2.90
CRP (mg/L)	0.068-8.2	33.0§	44.3§	19.46§	19.73§	26.1§
Procalcitonin (ng/ml)	0-0.5		0.181	0.099	0.089	
Interleukin-6 (pg/ml)	0-7		18.89§	37.4§		18.25§

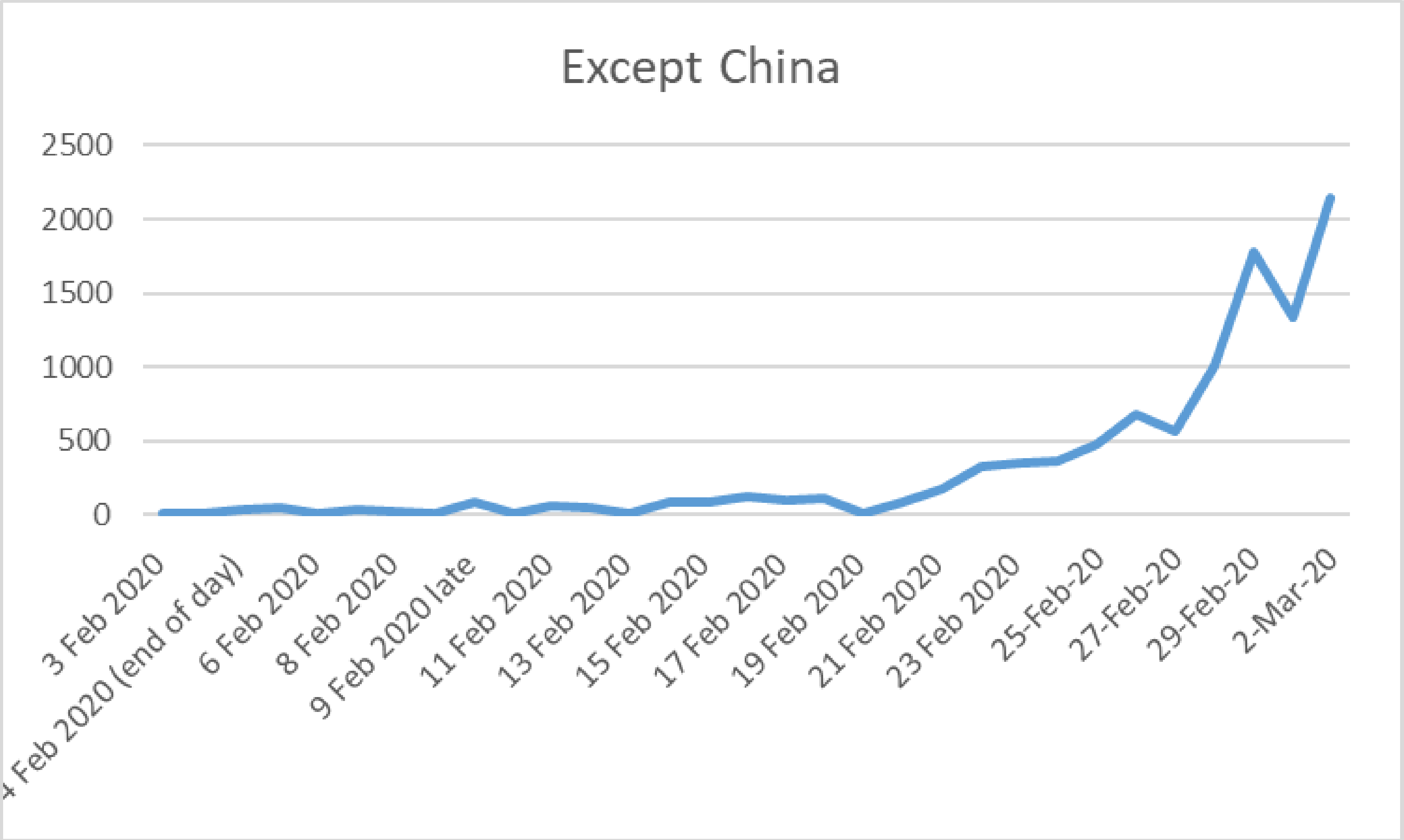
ABG analysis of Jan 27 was tested one hour before the patient died.

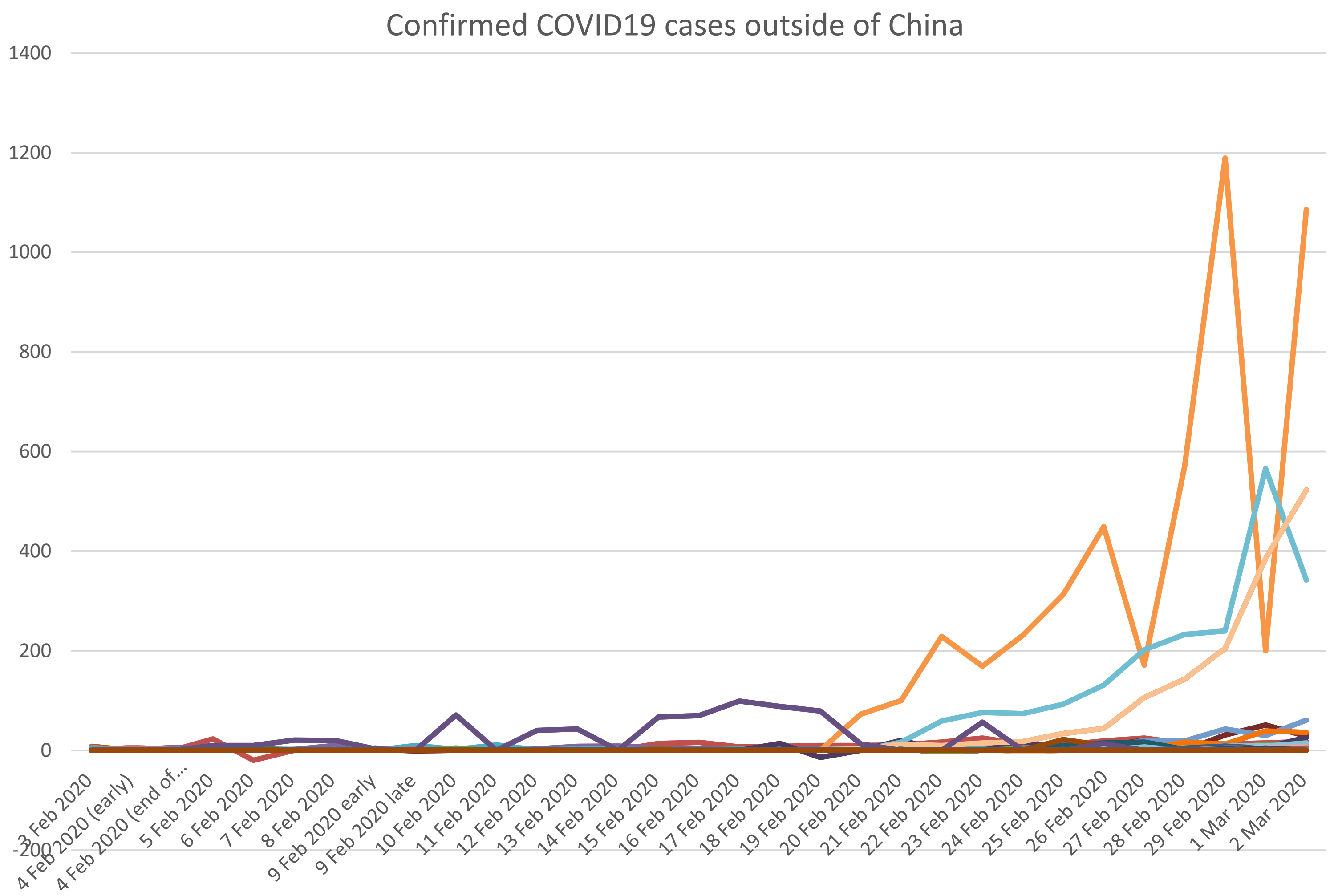
‡ The value in the patient was below normal.

§ The value in the patient was above normal.

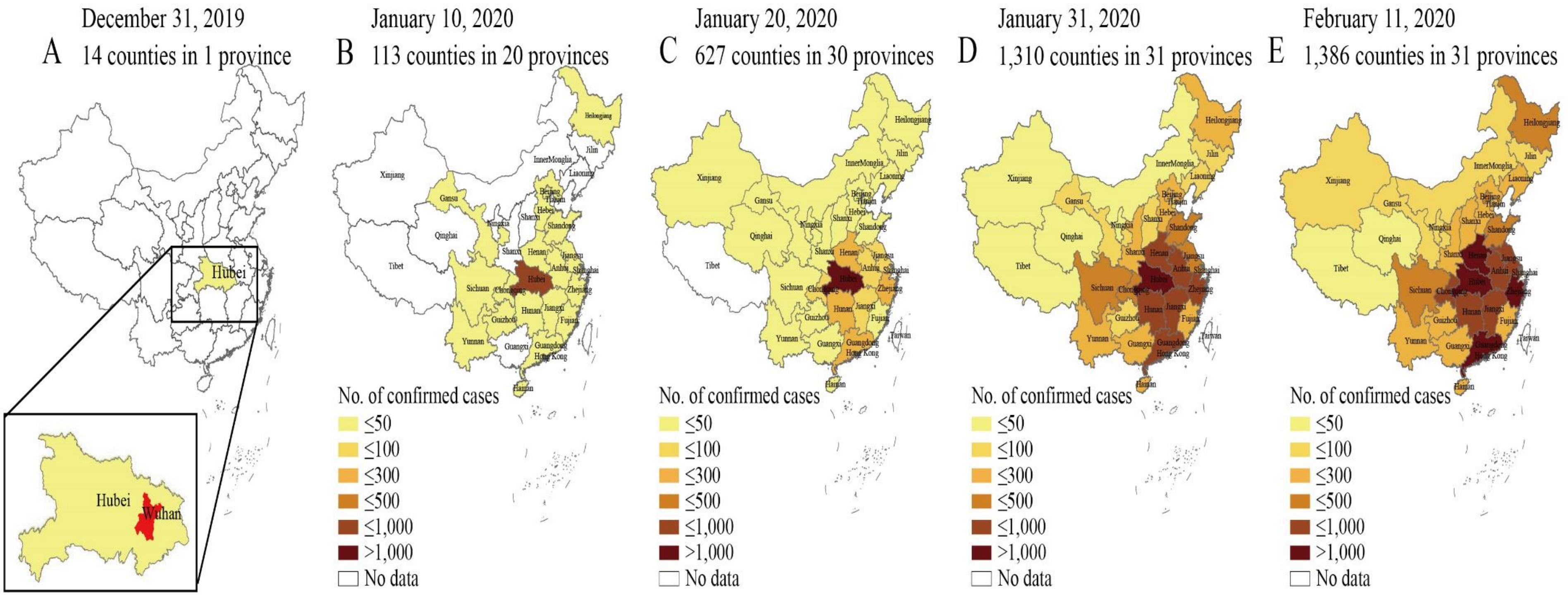


Coronavirus cases per day by country
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
3 Feb 2020
4 Feb 2020 (early)
4 Feb 2020 (end of day)
5 Feb 2020
6 Feb 2020
7 Feb 2020
8 Feb 2020
9 Feb 2020 early
9 Feb 2020 late
10 Feb 2020
11 Feb 2020
12 Feb 2020
13 Feb 2020
14 Feb 2020
15 Feb 2020
16 Feb 2020
17 Feb 2020
18 Feb 2020
19 Feb 2020
20 Feb 2020
21 Feb 2020
22 Feb 2020
23 Feb 2020
24-Feb-20
25-Feb-20
2/26/2020
27-Feb-20
28-Feb-20
29-Feb-20
3/1/2020
2-Mar-20
Mainland China
Japan
Thailand
Singapore
Hong Kong
South Korea
Australia
Germany
Taiwan
USA
Macau
Malaysia
France
Viet Nam
United Arab Emirates
Canada
Italy
Russia
Philippines
India
UK
Nepal
Cambodia
Spain
Finland
Sweden
Sri Lanka
Belgium
Egypt
Iran
Lebanon
Israel
Others (Diamond Princess)


Except China
2500
2000
1500
1000
500
0
3 Feb 2020
4 Feb 2020 (end of day)
6 Feb 2020
8 Feb 2020
9 Feb 2020 late
11 Feb 2020
13 Feb 2020
15 Feb 2020
17 Feb 2020
19 Feb 2020
21 Feb 2020
23 Feb 2020
25-Feb-20
27-Feb-20
29-Feb-20
2-Mar-20



Confirmed COVID19 cases outside of China
1400
1200
1000
800
600
400
200
0
-200
3 Feb 2020
4 Feb 2020 (early)
4 Feb 2020 (end of...
5 Feb 2020
6 Feb 2020
7 Feb 2020
8 Feb 2020
9 Feb 2020 early
9 Feb 2020 late
10 Feb 2020
11 Feb 2020
12 Feb 2020
13 Feb 2020
14 Feb 2020
15 Feb 2020
16 Feb 2020
17 Feb 2020
18 Feb 2020
19 Feb 2020
20 Feb 2020
21 Feb 2020
22 Feb 2020
23 Feb 2020
24 Feb 2020
25 Feb 2020
26 Feb 2020
27 Feb 2020
28 Feb 2020
29 Feb 2020
1 Mar 2020
2 Mar 2020

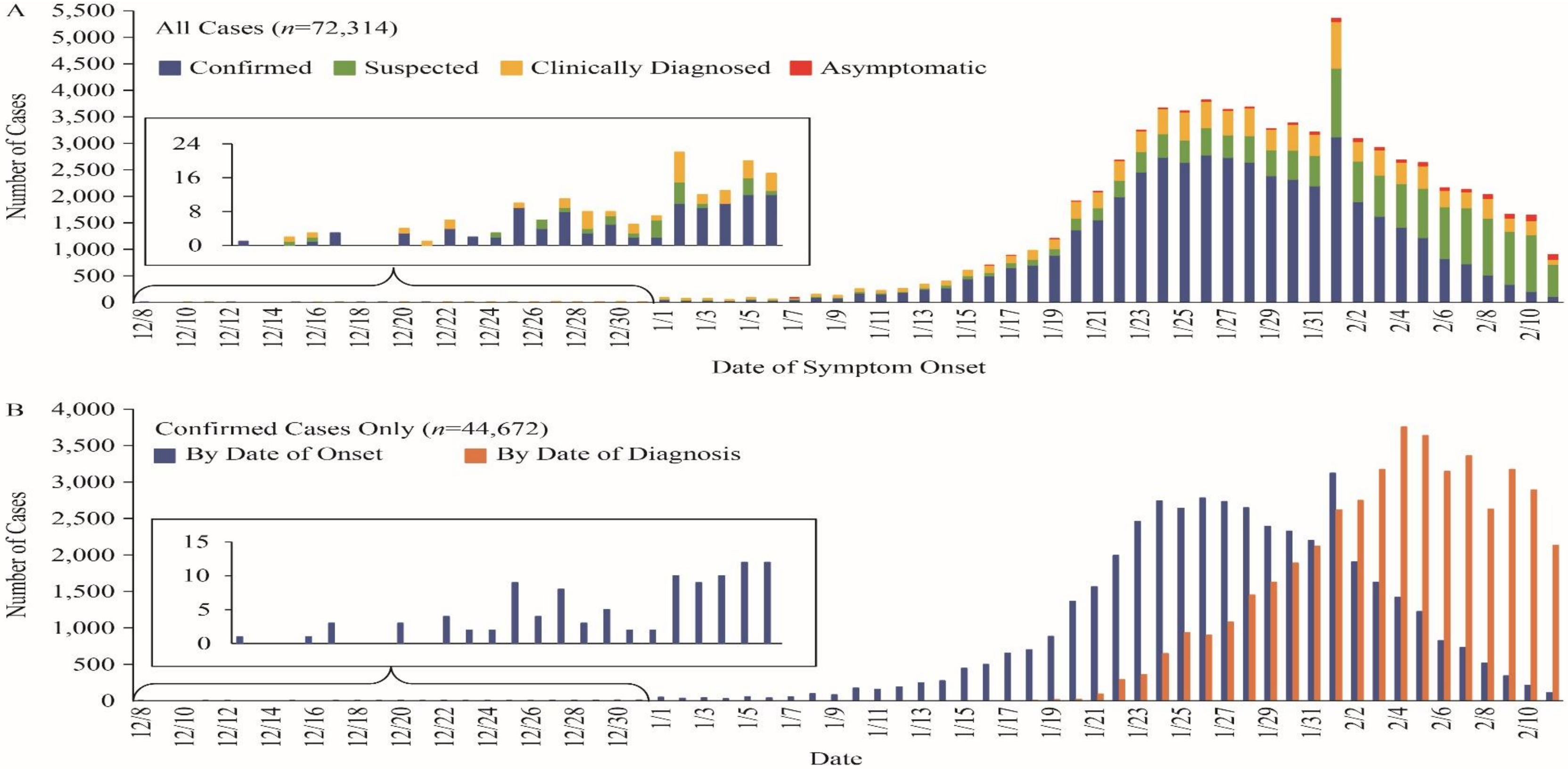


Geo-temporal spread of COVID-19 in China through February 11, 2020. (A) a total of 14 county-level administrative areas (hereafter counties) in Hubei Province only (inset) had reported cases as of December 31, 2019; (B) by January 10, 2020, 113 counties in 20 PLADs had reported cases with the highest prevalence still in Hubei Province; (C) nine days later, on January 20, 627 counties in 30 PLADs had reported cases and PLADs neighboring Hubei Province observed increasing prevalence; (D) by the end of January 31, 1310 counties across all 31 PLADs were affected and prevalence in the central, south, and south-central regions had risen dramatically; (E) by the end of February 11, 1,386 counties nationwide were affected and prevalence in the south-central PLADs had risen to the level of Hubei.

The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team

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

China CDC Weekly,2020, 2(null)
http://dx.doi.org/null



Epidemiological curves of COVID-19 in China through February 11, 2020. (A) the epidemiological curve shows the progression of illness in the outbreak over time from December 8, 2019 to February 11, 2020. A total of 72,314 cases are shown and confirmed cases (blue) are compared to suspected cases (green), clinically diagnosed cases (yellow), and asymptomatic cases (red). The inset shows a zoomed-in view of all days in December, when total daily count remained below 24 cases; (B) the epidemiological curve shows the progression of illness in the outbreak over time from December 8, 2019 to February 11, 2020 for confirmed cases only (blue). The number of cases diagnosed each day is also shown for confirmed cases only (orange). The inset shows a zoomed-in view of all days in December, when total daily count remained below 15 cases.

The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team

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

China CDC Weekly,2020, 2(null)
http://dx.doi.org/null

TABLE 1. Patients, deaths, and case fatality rates, as well as observed time and mortality for n=44,672 confirmed COVID-19 cases in Mainland China as of February 11, 2020.

Baseline Characteristics	Confirmed Cases, N (%)	Deaths, N (%)	Case Fatality Rate, %	Observed Time, PD	Mortality, per 10 PD
Overall	44,672	1,023	2.3	661,609	0.015
Age, years					
0–9	416 (0.9)	–	–	4,383	–
10–19	549 (1.2)	1 (0.1)	0.2	6,625	0.002
20–29	3,619 (8.1)	7 (0.7)	0.2	53,953	0.001
30–39	7,600 (17.0)	18 (1.8)	0.2	114,550	0.002
40–49	8,571 (19.2)	38 (3.7)	0.4	128,448	0.003
50–59	10,008 (22.4)	130 (12.7)	1.3	151,059	0.009
60–69	8,583 (19.2)	309 (30.2)	3.6	128,088	0.024
70–79	3,918 (8.8)	312 (30.5)	8.0	55,832	0.056
≥80	1,408 (3.2)	208 (20.3)	14.8	18,671	0.111
Sex					
Male	22,981 (51.4)	653 (63.8)	2.8	342,063	0.019
Female	21,691 (48.6)	370 (36.2)	1.7	319,546	0.012
Occupation					
Service industry	3,449 (7.7)	23 (2.2)	0.7	54,484	0.004
Farmer/laborer	9,811 (22.0)	139 (13.6)	1.4	137,992	0.010
Health worker	1,716 (3.8)	5 (0.5)	0.3	28,069	0.002
Retiree	9,193 (20.6)	472 (46.1)	5.1	137,118	0.034
Other/none	20,503 (45.9)	384 (37.5)	1.9	303,946	0.013
Province					

Article Contents

Abstract
Introduction
Method
Results
Discussion
Acknowledgements

References

FIGURE1
FIGURE2
FIGURE3
FIGURE4
TABLE1
TABLE2

Province					
Hubei	33,367 (74.7)	979 (95.7)	2.9	496,523	0.020
Other	11,305 (25.3)	44 (4.3)	0.4	165,086	0.003
Wuhan-related exposure*					
Yes	31,974 (85.8)	853 (92.8)	2.7	486,612	0.018
No	5,295 (14.2)	66 (7.2)	1.2	71,201	0.009
Missing	7,403	104	2.8	103,796	0.010
Comorbid condition†					
Hypertension	2,683 (12.8)	161 (39.7)	6.0	42,603	0.038
Diabetes	1,102 (5.3)	80 (19.7)	7.3	17,940	0.045
Cardiovascular disease	873 (4.2)	92 (22.7)	10.5	13,533	0.068
Chronic respiratory disease	511 (2.4)	32 (7.9)	6.3	8,083	0.040
Cancer (any)	107 (0.5)	6 (1.5)	5.6	1,690	0.036
None	15,536 (74.0)	133 (32.8)	0.9	242,948	0.005
Missing	23,690 (53.0)	617 (60.3)	2.6	331,843	0.019
Case severity§					
Mild	36,160 (80.9)	–	–	–	–
Severe	6,168 (13.8)	–	–	–	–
Critical	2,087 (4.7)	1,023 (100)	49.0	31,456	0.325
Missing	257 (0.6)	–	–	–	–
Period (by date of onset)					
Before Dec 31, 2019	104 (0.2)	15 (1.5)	14.4	5,142	0.029
Jan 1–10, 2020	653 (1.5)	102 (10.0)	15.6	21,687	0.047
Jan 11–20, 2020	5,417 (12.1)	310 (30.3)	5.7	130,972	0.024
Jan 21–31, 2020	26,468 (59.2)	494 (48.3)	1.9	416,009	0.012
After Feb 1, 2020	12,030 (26.9)	102 (10.0)	0.8	87,799	0.012

Effects of SARS 2

Chinese CDC report n=55,000

Fever	88%
Dry cough	68%
Fatigue	38%
Sputum	33%
SOB	18%
Sore throat	13%
HA	13%
Myalgia/arthralgia	14%
Chills	11%
N,V	5%
Diarrhoea	4%

Rarely completely asymptomatic

80% of cases were mild, Sats >93%
14% severe PaO2/FiO2 <300mmHg
6% critical with respiratory failure,
occasionally other organ failure
Crude Fatality rate was 3.8% dropped to
0.7% later with better care
Outside Wuhan 0.7%

Time to recovery – 2 weeks if mild
3-6 weeks if severe
Onset - > severe takes 1 week
Onset -> death takes 2 – 8 weeks

Effects of SARS 2 SOFA scores

Lung dysfunction

20%

Acute Kidney Injury

<1%

Heart

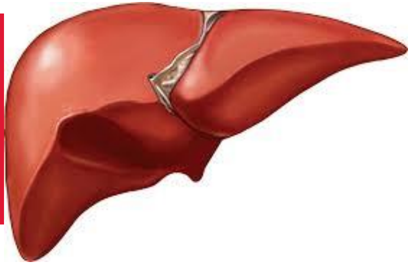
A few

Delerium

??

Liver failure

??



Coagulopathy

A few

What do I think will happen?

On 2 Feb 2020: a range of possible expectations

Best case –	lots of suspected cases and no or few confirmed no clusters, no transmission
Expected scenario –	like the Dec 2019 influenza
Worst case-	20% attack ratio and 2% mortality, 20,000 deaths

RCSI
Leading the world to better health

What do I think will happen?

Today 5 March 2020

Best case– very many clusters and some uncontrolled community transmission in Ireland leading to something like the Dec 2019 seasonal influenza, widespread economic and social disruption

Expected scenario – like the 1918/19 Spanish influenza, a once in a century event, overwhelming of the health care system, massive economic disruption

Worse case- 80% attack ratio and 3.8% mortality
challenge to our free liberal democratic government
long term change in our way of life

RCSI
Leading the world to better health

What can we do for patients?

Artificial homeostasis for SARS-CoV-2

Measure and monitor, and intervene to maintain metabolic parameters within normal range

Oxygen

H_2O, H^+, CO_2, blood pressure, renal function, glucose, Na, K, Cl, Ca, Mg, albumin, PO_4, red cells, platelets, polymorphs, skin care, venous embolism prophylaxis, stress ulcer prevention, enteral nutrition, chemical sedation, replace clotting factors.

Minimise onwards transmission to staff and other patients (Pods)

Clinical trials of RNA polymerase and protease inhibitors

The unknowns

What is the death rate for COVID19?

What is the R0, under different levels of social distancing?

How can we rapidly scale up health care services?

Can we reach 99-100% compliance about how to don, to doff, to label, clean and bag samples?

The extent of asymptomatic transmission?

Is there strong evidence that closing school works?

Does closing factories work?

Does closing public transport work?

Closing airports?

Staying at home?

Balancing and predicting the economic impact of above

What can we do as a community?

Copy the Chinese Government

Very thorough compliant identification, contact tracing, self isolation at home for 14 days e.g. 900 teams of 5 people in each, digital records

Scale up Health-care to look after the sick and prevent in-hospital transmission – re-training

Social distancing, >2m or outside

Maintain essential services- water, food, electricity, internet, GPS, phones, media, health-care, security, governance, culture

What can we do as individuals ?

Listen to Tony Holohan, CMO
hse.ie

If unwell and travelled from an affected area self-isolate and call GP

If well read the HSE, HPSC and DFA advice

Respiratory etiquette, tissue, bin, wash hands

Re-assure, reaffirm and teach others

Travel with DFA advice

Enjoy life, sports, music, dancing, friends, family, culture, volunteering

In hospitals

Contingency planning

Plan for safe assessment of referred patients

- 20 per day (have done)
- 200 per day (can do)
- 2000 per day?

Plan for safe effective care for people with respiratory failure

- 10 in our hospital (can do)
- 100 in our hospital (can do)
- 1000 in our region?
- 10,000 in our region?

Plan for safe effective mechanical ventilation

- 10 in our hospital (can do)
- 50 in our hospital (can do)
- 200 in our region?
- 3000 in our region?

Build more, re-purpose, re-designate spaces

Recruit, train and organise staff

Plan for the worst

Attack ratio of 80% == 4 million in Ireland

20% respiratory failure == 800,000

Perhaps over 1 or 2 months

Hopefully over 6 – 12 - 24 months

6% mechanical ventilation = 240,000

RCSI

Leading the world to better health

Research

Meticulous data collection

Audit of artificial homeostasis for SARS-2

Clinical trials of existing protease inhibitors

Clinical trials of new RdRP, remdesivir

Vaccine development

Artificial Intelligence using mobile phone location data for contact tracing

Behavioural science understanding of how best to teach staff, relatives and patients

Social determinants of health

RCSI
Leading the world to better health

Nationally

All government multi-sectoral approach
Detailed, tested business continuity plans for all essential services
Re-allocation of staff to contact tracing
Balance the social and economic costs of distancing
Create surge capacity for identification and testing
Create surge capacity in hospitals for ID care
Create surge capacity in hospitals for ICU care
Use fast AI for contact tracing with GPS data
Legal controls of mass gatherings
Who and how to enforce a cordon sanitaire
Support factories to make gowns, masks gloves
Support the farmers to feed us and export
Support pharma to make vaccines, anti-virals and O2
Identify critical areas which are struggling and assist
Legal changes that are needed
Decisions about staying at home, enforcement, support
Decisions about closing transport, enforcement, support

Support and advice for businesses to do their own continuity plans – nominated designate

- working from home, VC, TC, email
- use of IT
- analysis and mitigation of supply chain
- analysis and mitigation of sales
- treasury and financing
- travel, trade and export disruptions
- managing internal communications

RCSI
Leading the world to better health

Social cohesion

To do this we need wide social cohesion and co-operation

To achieve social cohesion and co-operation we need widespread social trust

To achieve social trust we need a widespread perception of social equality

To achieve a perception of social equality we need social equality

To achieve social equality we need a basic living wage for all, access to pre-school, 1st, 2nd 3rd level education for all, access to health care and affordable housing

RCSI

Leading the world to better health

Leading the world to better health

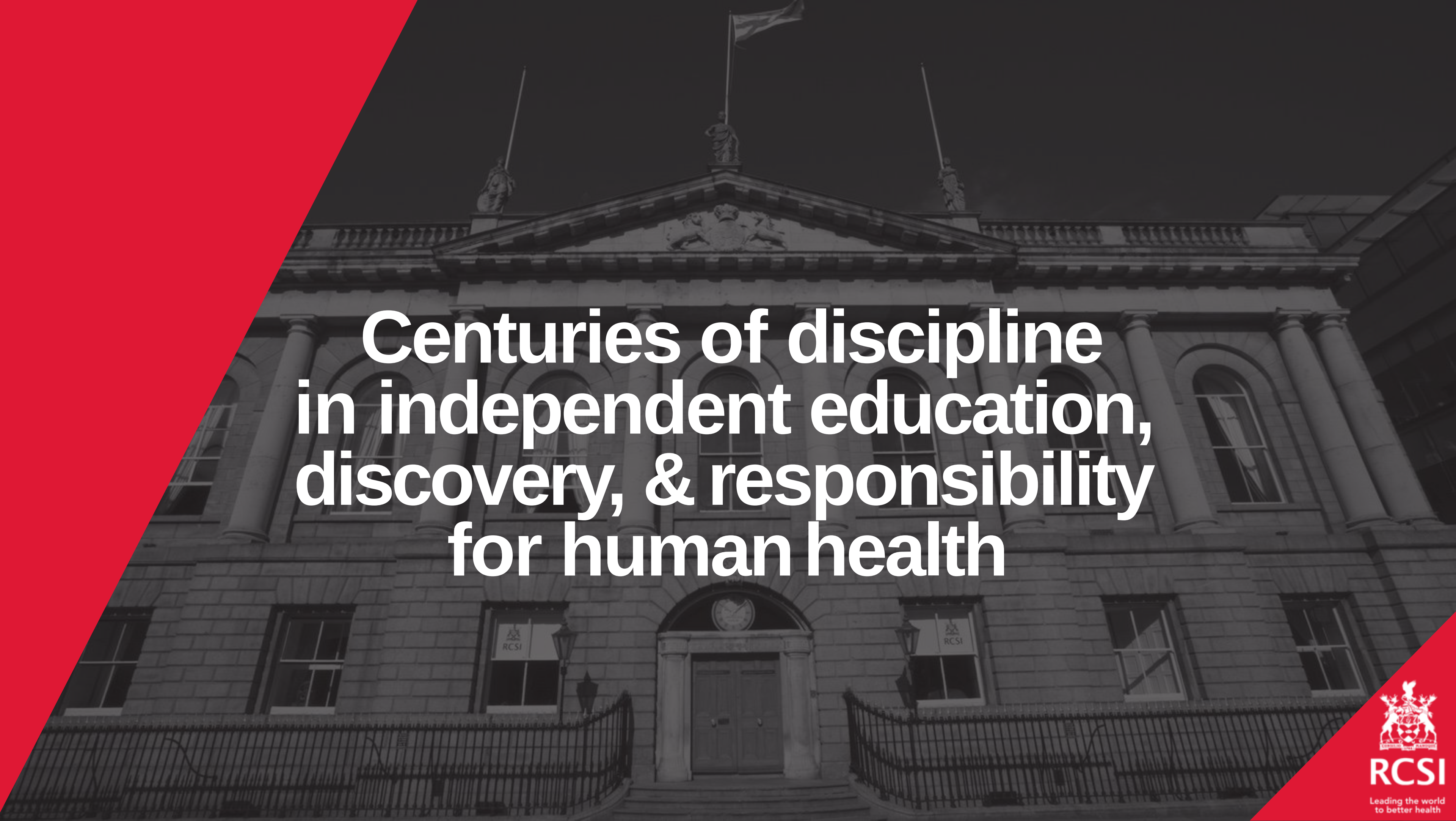
RCSI

Leading the world to better health

RCSI Leading the world to better health

Thank you

Samuel McConkey
smcconkey@rcsi.ie



Centuries of discipline in independent education, discovery, & responsibility for human health

RCSI
Leading the world to better health