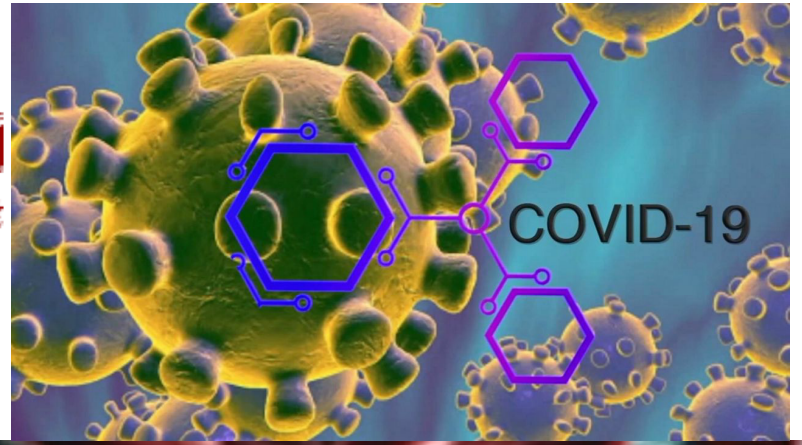
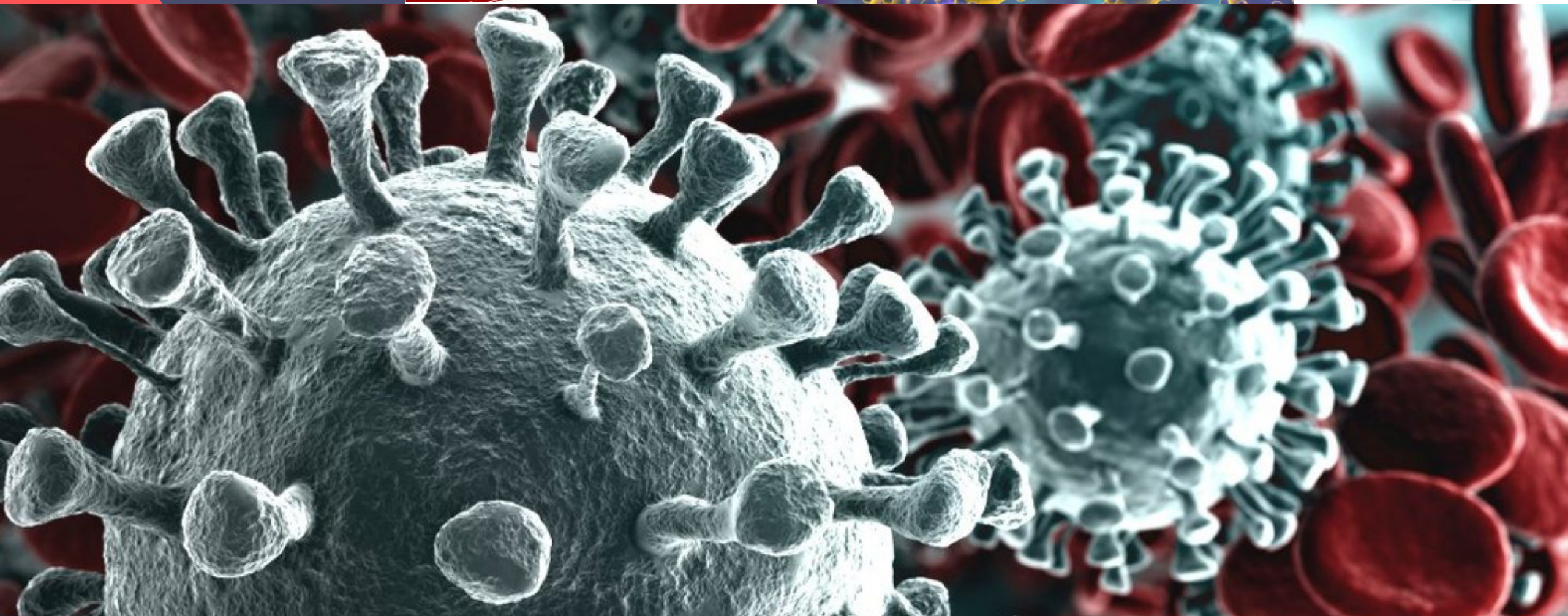
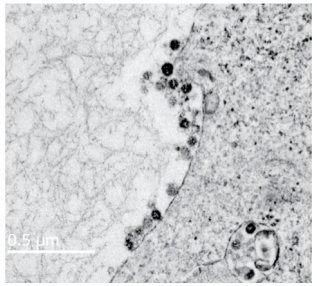
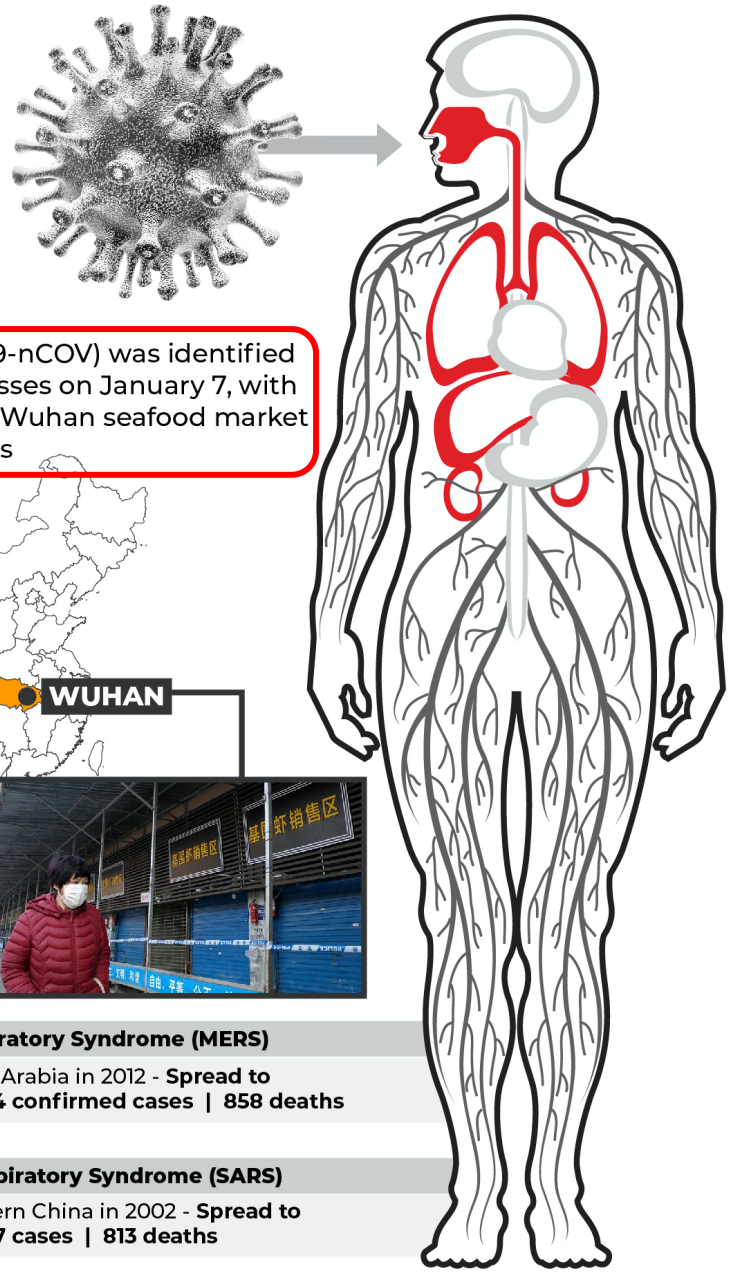

COVID-19


COVID-19

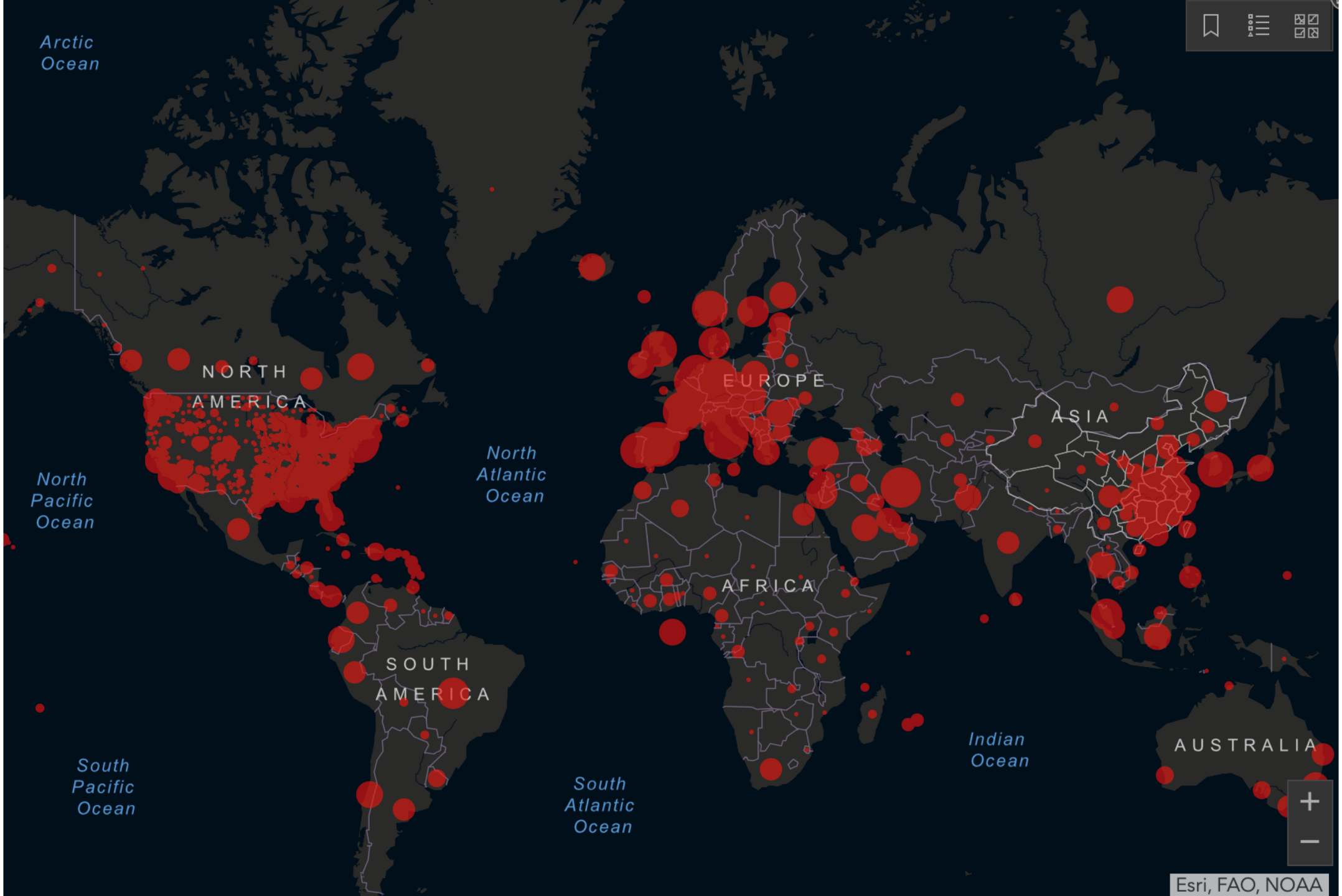


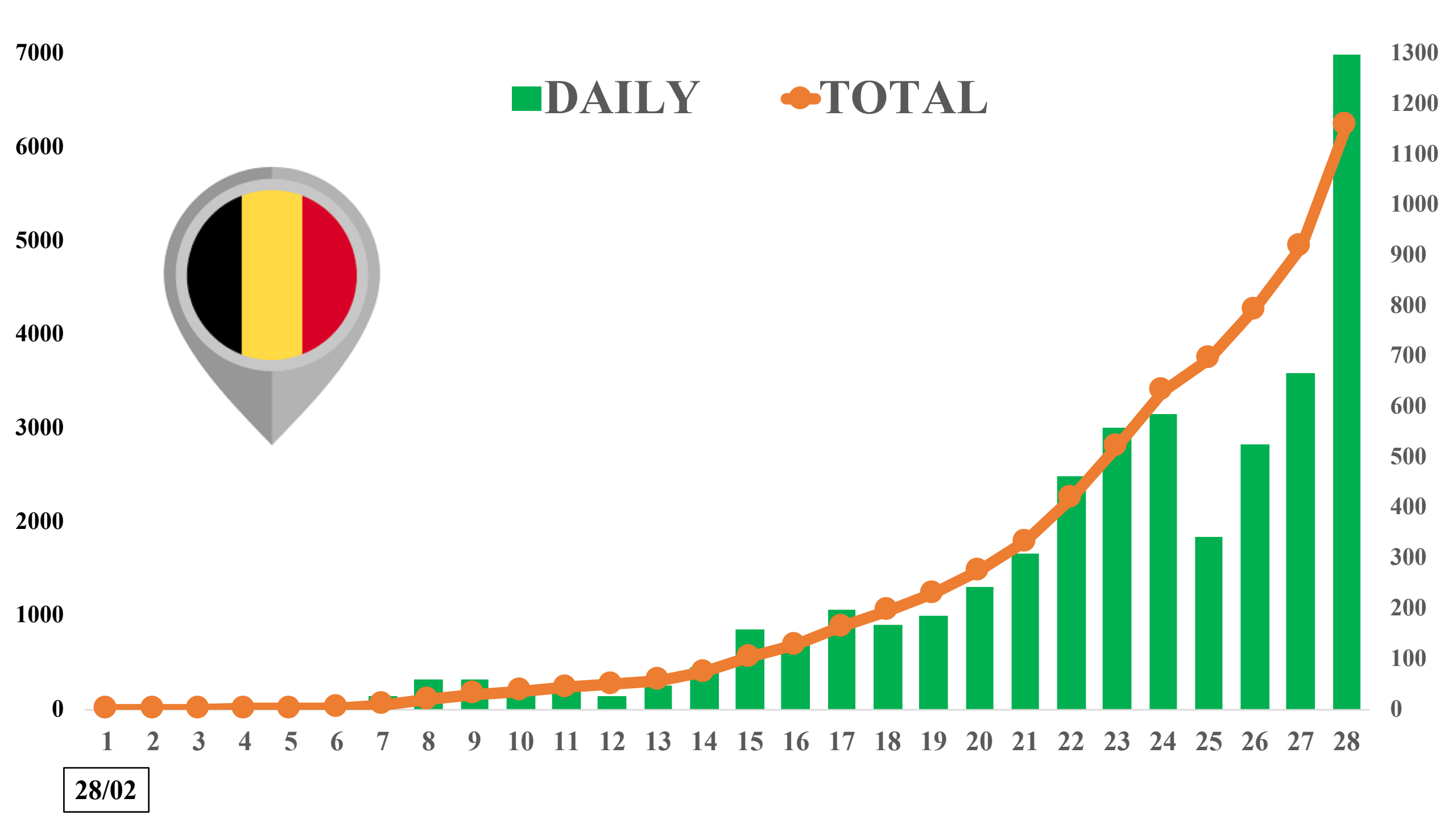
- ✓ On **December 31** 2019, China alerted WHO to several cases of unusual pneumonia in Wuhan (11M), in the central Hubei province. The virus was unknown (1st case = **December 8**).
- ✓ The Market was shut down on **January 1**.
- ✓ **40** similar cases are declared.
- ✓ On **January 5**, Chinese officials ruled out the possibility that this was a recurrence of the severe acute respiratory syndrome (SARS) virus
- ✓ On **January 7**, officials in Shangai announced they had identified a new virus, according to the WHO. The novel virus was named **2019-nCoV** or **SARS-CoV-2** (coronavirus family; pangolin/ turtle/snake)
- ✓ On **January 11**, a first case is reported in Thailand





Consensus, Nature Microbiol 2020


Arctic Ocean
NORTH AMERICA
EUROPE
ASIA
North Atlantic Ocean
North Pacific Ocean
AFRICA
SOUTH AMERICA
Indian Ocean
AUSTRALIA
South Pacific Ocean
South Atlantic Ocean
Esri, FAO, NOAA

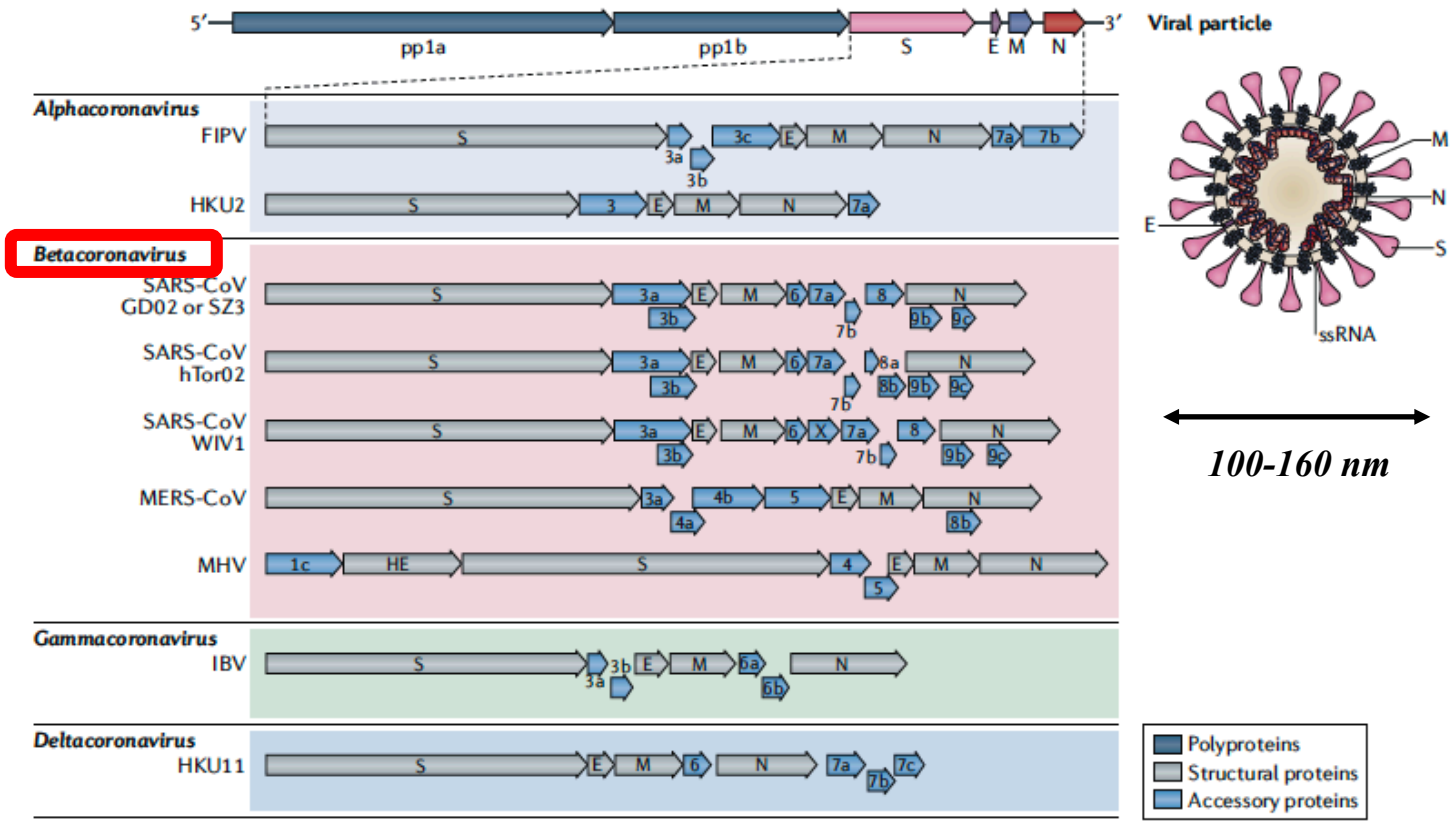

DAILY
TOTAL
7000
6000
5000
4000
3000
2000
1000
0
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
28/02

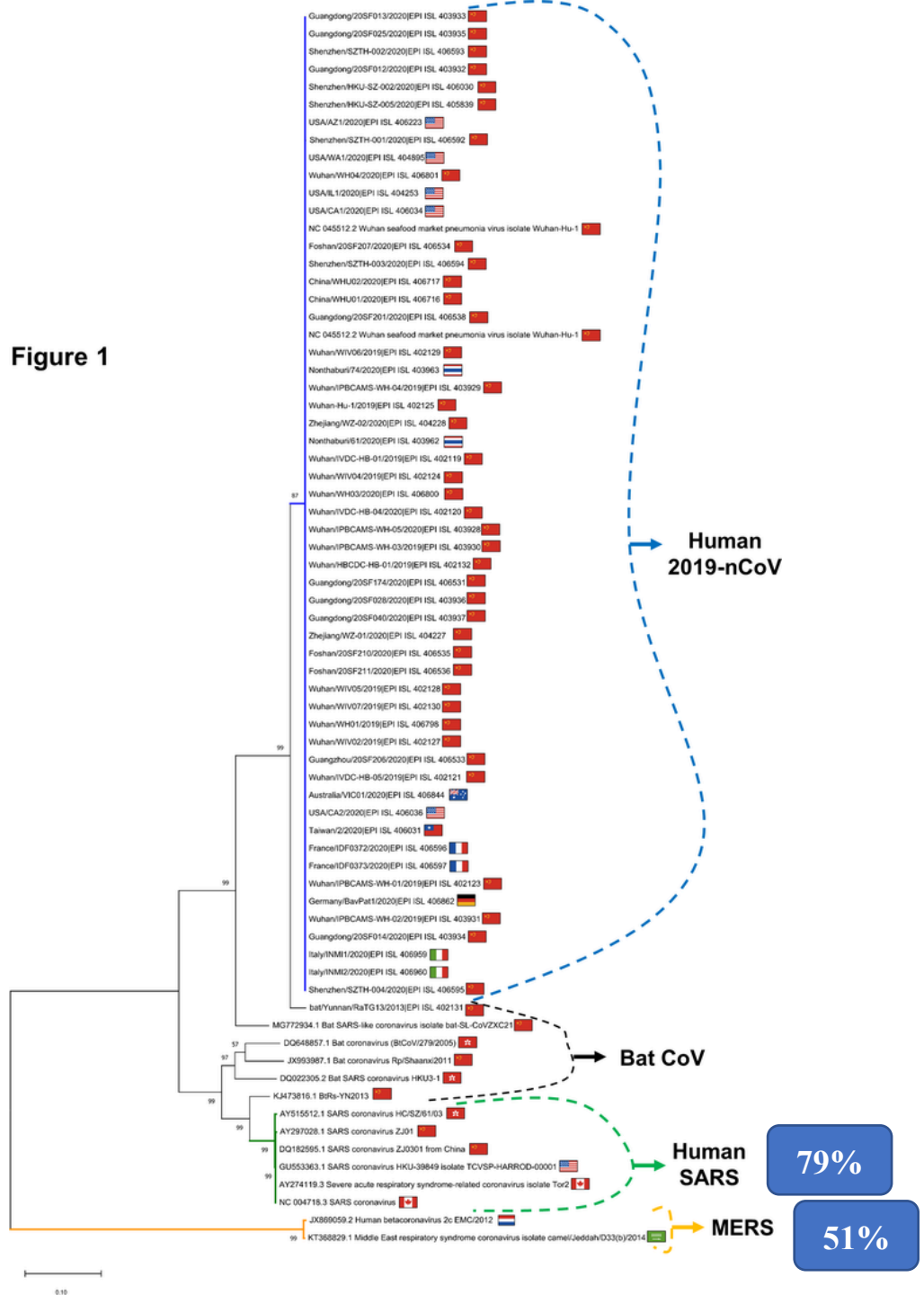
Origin and evolution of pathogenic coronaviruses

Jie Cui[1], *Fang Li*[2] *and Zheng-Li Shi*[1]*

NATURE REVIEWS | MICROBIOLOGY

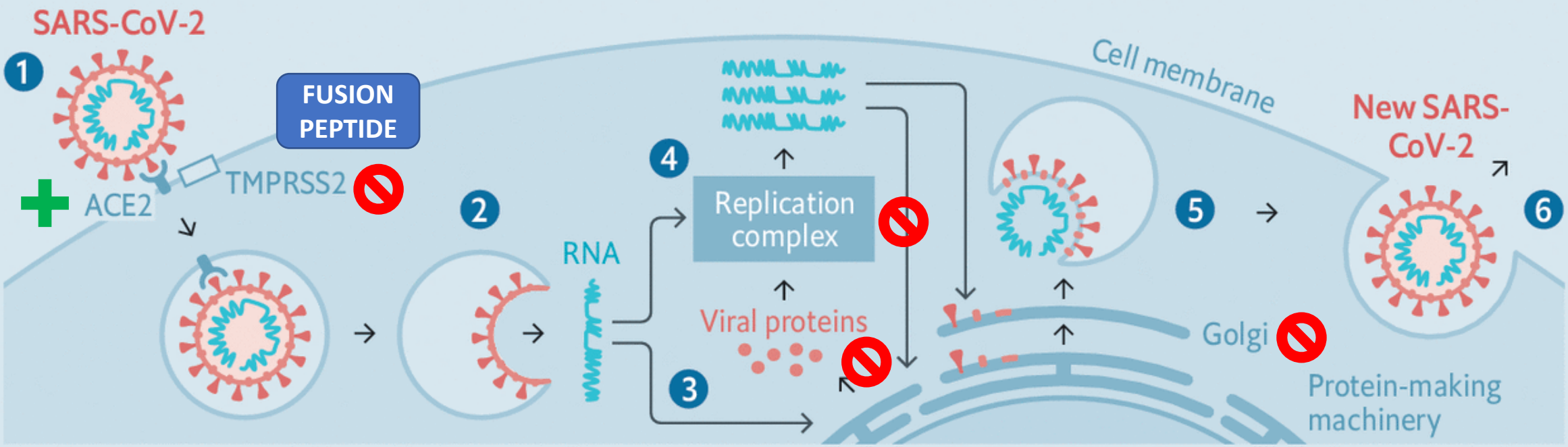
Figure 1



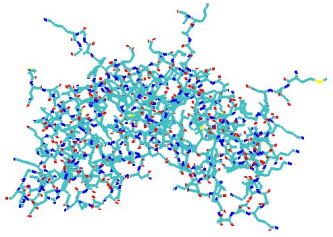


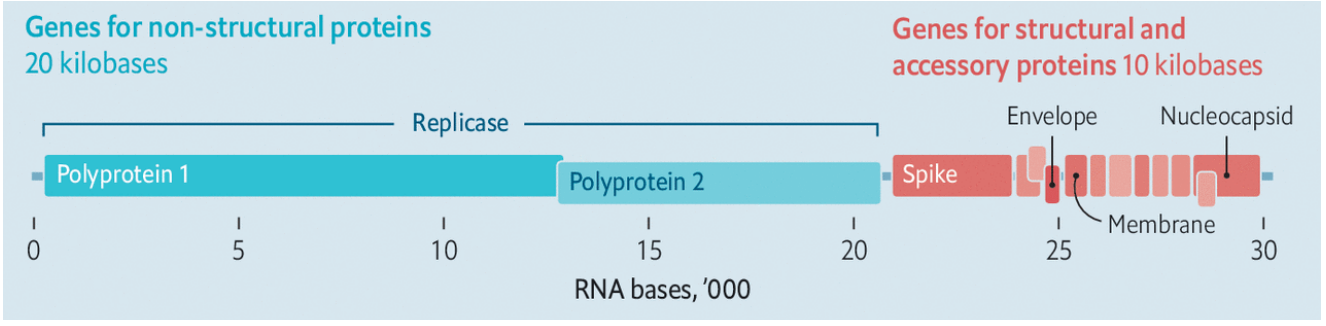
Lu, Lancet 2020
Hoffmann, Cell 2020

How SARS-CoV-2 replicates itself in the cells of those infected

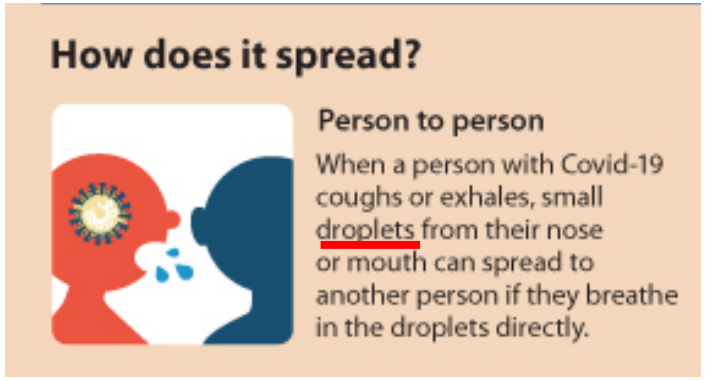


1 Spike protein on the virion binds to ACE2, a cell-surface protein. TMPRSS2, an enzyme, helps the virion enter 2 The virion releases its RNA 3 Some RNA is translated into proteins by the cell's machinery 4 Some of these proteins form a replication complex to make more RNA 5 Proteins and RNA are assembled into a new virion in the Golgi and 6 released





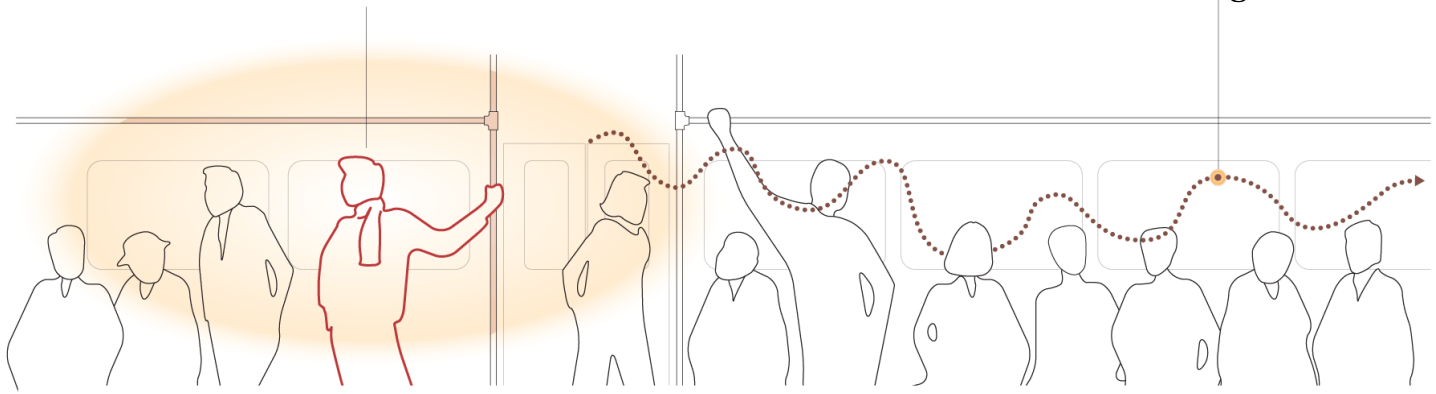
THE DISEASE = COVID-19



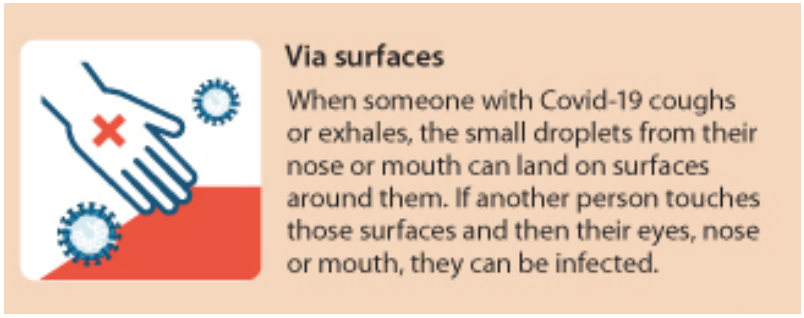
- ✓ **Coronaviruses** can travel only about six feet * from the infected person
- ✓ **Viral load** is higher in LRT than throat swab
- ✓ **SARS-CoV-2** has been found in tears (only if conjunctivitis)
- ✓ Viral RNA was also detected in **saliva**, **blood** (10%) and **stool** (40%) specimens
- ✓ **SARS-CoV-2** can live on surfaces: **85% of hospital surfaces** (how long ?)
- ✓ No (almost) vertical transmission (SARS-Cov2 + in placenta)

Poon, Nature Med 2020
Chan, Lancet 2020
Holshue, N Engl J Med 2020

Ong, JAMA 2020
Liu, J Infect 2020



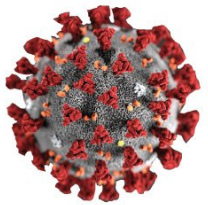
< 98 cm (MAX RISK)
< 183 cm (RISK)



Lauer, Ann Inter Med 2020

MEDIAN = 5 days
(ranges 1-17)

Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1



*Researchers used a nebulizer to simulate coughing or sneezing, and found that the virus became an aerosol

The NEW ENGLAND JOURNAL of MEDICINE

THE DISEASE

SUSPECTED CASE IS:

- ✓ Acute respiratory illness AND a **history of travel** to area reporting transmission of COVID-19 disease (14-18 days)
- ✓ Acute respiratory illness AND **contact** with a confirmed or probable COVID-19 case (14-18 days)
- ✓ A patient with severe acute respiratory infection AND requiring hospitalization AND with **no other aetiology** that fully explains the clinical presentation

THE DISEASE

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)
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%)

- ✓ Male (70%)
- ✓ Age: 55 years
- ✓ Comorbidities: 65%
- ✓ Evolution: 3-7 days

"Epidemic" phase:

- ✓ Syncope
- ✓ Tachycardia
- ✓ "Malaise"
- ✓ Gastro-intestinal

THE DISEASE

- **Biological parameters** :
  - NOT SPECIFIC
  - Lymphopenia (T-subtype?)
  - Thrombopenia
  - ⬆ AST/ALT (8-25%)
  - ⬆ D-dimers (>50%)
  - AKI (5-15% - CKD ?)
  - CK/TnT (5-10%)
  - Neuro ???

- **Almost no CO-INFECTION (on admission)**

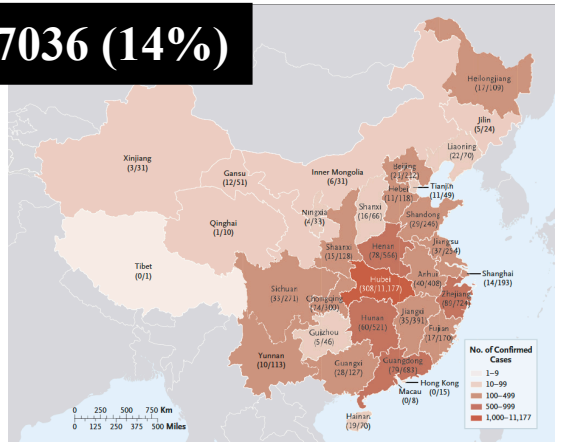
Lippi, Clin Chem Lab Med 2020
Li, J Med Virol 2020
Huang, Lancet 2020

	Patients (n=99)
(Continued from previous column)	
Infection-related biomarkers	
Procalcitonin (ng/mL; normal range 0·0–5·0)	0·5 (1·1)
Increased	6 (6%)
Interleukin-6 (pg/mL; normal range 0·0–7·0)	7·9 (6·1–10·6)
Increased	51 (52%)
Erythrocyte sedimentation rate (mm/h; normal range 0·0–15·0)	49·9 (23·4)
Increased	84 (85%)
Serum ferritin (ng/mL; normal range 21·0–274·7)	808·7 (490·7)
Increased	62 (63%)
C-reactive protein (mg/L; normal range 0·0–5·0)*	51·4 (41·8)
Increased	63/73 (86%)
Co-infection	
Other viruses	0
Bacteria	1 (1%)
Fungus	4 (4%)

Clinical Characteristics of Coronavirus Disease 2019 in China

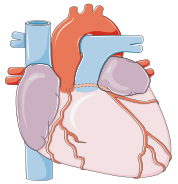
W. Guan, Z. Ni, Yu Hu, W. Liang, C. Ou, J. He, L. Liu, H. Shan, C. Lei, D.S.C. Hui, B. Du, L. Li, G. Zeng, K.-Y. Yuen, R. Chen, C. Tang, T. Wang, P. Chen, J. Xiang, S. Li, Jin-lin Wang, Z. Liang, Y. Peng, L. Wei, Y. Liu, Ya-hua Hu, P. Peng, Jian-ming Wang, J. Liu, Z. Chen, G. Li, Z. Zheng, S. Qiu, J. Luo, C. Ye, S. Zhu, and N. Zhong, for the China Medical Treatment Expert Group for Covid-19*

1099/7036 (14%)



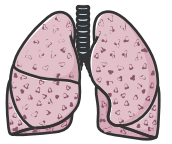
	ALL (n=1099)	Non-Severe (n=926)	Severe (n=173)
Age, years	47 (35-58)	45 (34-57)	52 (40-65)
Incubation, days	4 (2-7)	4 (2-7)	4 (2-7)
Comorbidities, %	24%	**21%**	**39%**
Abnormal CXR, %	59%	**54%**	**77%**
Abnormal CT-scan, %	86%	**84%**	**95%**
Thrombopenia, %	36%	**32%**	**58%**
Elevated CRP, %	61%	**57%**	**82%**
Elevated LDH, %	41%	**37%**	**58%**
Shock, %	1.1%	**0.1%**	**6.4%**
ARDS, %	3.4%	**1.1%**	**15.6%**
AKI, %	0.5%	**0.1%**	**2.9%**
Mortality, %	1.4%	**0.1%**	**8.1%**

THE DISEASE



Few patients in shock (4-17%)
“Acute cardiac injury” 10-50% in hospitalized patients
Myocarditis

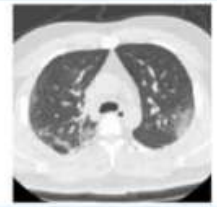
Severe lung involvement in 10-20%
25% of patients require ICU admission
MV in 8-45% in hospitalized patients
ARDS 17-30% in hospitalized patients

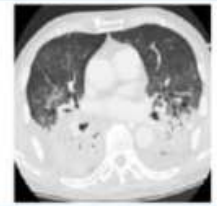


Wang, JAMA 2020 *Huang, Lancet 2020* *Han, Clin Chem Lab Med 2020* *Zhou, Lancet 2020*
Yang, J Infect 2020 *Chen, Lancet 2020* *Mao, medRxiv 2020* *Naicker, Kidney Int 2020*

Typical features according to current publications

Age Mean (SD) 55,5 (13-1), Male (68%)
Exposure to Huanan seafood market in Wuhan, China (49%)
Chronic medical underlying illness (51%)
Admission to Intensive Care Unit (23%)





INCUBATION PERIOD and ONSET OF SYMPTOMS 3 DAYS AGO

	FIRST WEEK				SECOND WEEK				
SETTING	WARD Illness day 4	WARD Illness day 5	WARD Illness day 6	WARD Illness day 7	WARD/ICU Illness day 8	ICU Illness day 9	ICU Illness day 10	ICU Illness day 11	LONG TERM INFO PENDING
REPEATED SAMPLING OF THE NASOPHARYNX AND TRACHEAL ASPIRATES (IF INTUBATED) BY rRT-PCR FOR THE COVID-19	Initial important viral shedding		Decrease of the viral shedding sometimes associated with transient respiratory deterioration		Respiratory failure, increase of the viral shedding and viremia or Decrease of the viral shedding, and superinfections			Duration of viral excretion unknown	
OXYGEN THERAPY AND MECHANICAL VENTILATION	NO		Consider oxygen support	FNC	FNC followed by MV	MV		MV	
ORGAN FAILURE	**Typical signs according to current publications** Fever, cough, and shortness of breath (15%) bilateral pneumonia (75%), lymphopenia (35%), thrombocytopenia (12%), prothrombin time decreased (30%), elevated liver enzyme levels (about 30%)		Deterioration of respiratory status with most often spontaneous recovery		ARDS If shock beware of superinfections ⚠ Possible renal failure Neurological failure unlikely Hemostasis disorders			YES	
CO-INFECTION/SUPERINFECTION	NOT LIKELY				Consider a possible HAP/VAP and other nosocomial infections (see text for diagnostic procedures)			Profound immune paralysis and late onset infections	
ANTIBIOTICS	NO				Consider antibiotic therapy			YES	
ANTIVIRAL AGENTS	NO				Consider antiviral agents if deterioration[a]				

FNC = flow nasal cannula; HFNC = high flow nasal cannula; HAP = healthcare-associated pneumonia; VAP = ventilator-associated pneumonia; MV = Mechanical ventilation;
[a] The use of immunomodulation including corticosteroids is unlikely but debated

Fig. 1 Global picture of severe cases

Bouadma L et al. Intensive Care Med

Viewpoint

ONLINE FIRST FREE

February 24, 2020

Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China

Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention

However, 14% were severe (ie, dyspnea, respiratory frequency ≥30/min, blood oxygen saturation ≤93%, partial pressure of arterial oxygen to fraction of inspired oxygen ratio <300, and/or lung infiltrates >50% within 24 to 48 hours), and 5% were critical (ie, respiratory failure, septic shock, and/or multiple organ dysfunction or failure) (Box).[1]

JAMA Internal Medicine | Original Investigation

Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China

n=201

FACTORS ASSOCIATED WITH ARDS

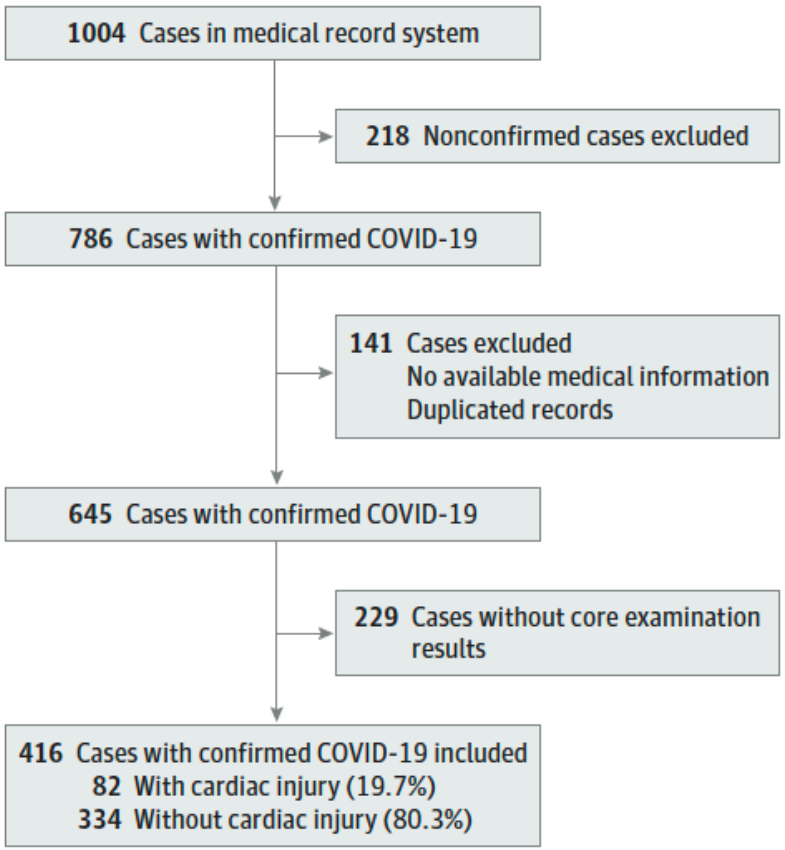
Table 1. Demographic Characteristics of Patients With Coronavirus Disease 2019 Pneumonia (continued)

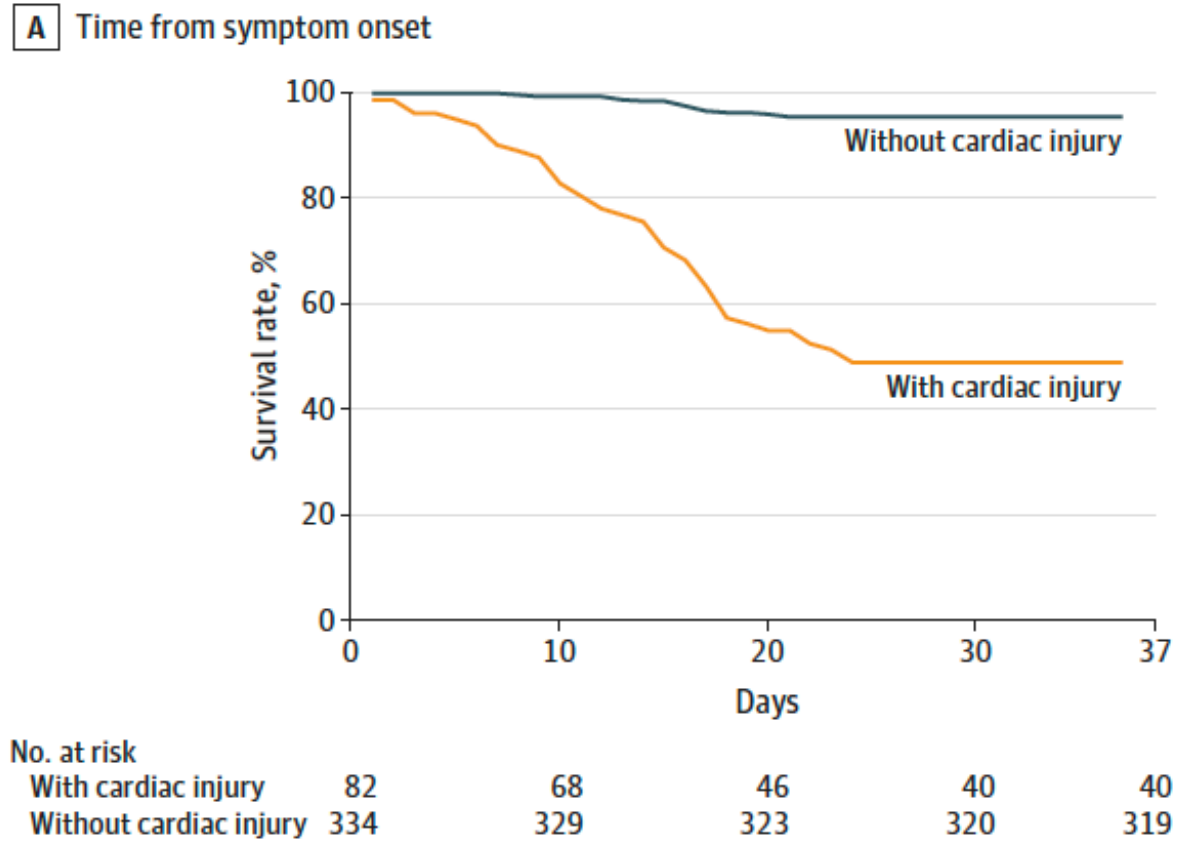
Study population	No. (%)
Clinical outcomes	
ARDS	84 (41.8)
ICU admission	53 (26.4)
Death	44 (21.9)

- ✓ *Age*
- ✓ *Highest Temperature*
- ✓ *Hypertension*
- ✓ *Diabetes*
- ✓ *D-Dimers*
- ✓ *Lymphopenia*
- ✓ *Biological variables*

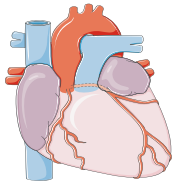
Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China

Shaobo Shi, MD; Mu Qin, MD; Bo Shen, MD; Yuli Cai, MD; Tao Liu, MD; Fan Yang, MD; Wei Gong, MMSC; Xu Liu, MD, PhD; Jinjun Liang, MD, PhD; Qinyan Zhao, MD, PhD; He Huang, MD, PhD; Bo Yang, MD, PhD; Congxin Huang, MD, PhD





THE DISEASE



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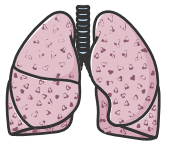
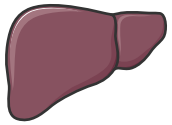
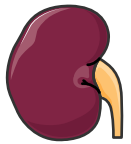




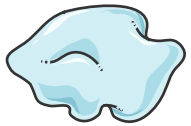
"Transaminitis" (2-9%)
Rare pancreatitis

Albuminuria (34-65%)
AKI (7-40%)
RRT (5-10%)



Dizziness, Headache, Anosmia – Stroke ? (5%)

Thrombopenia
Hypercoagulability



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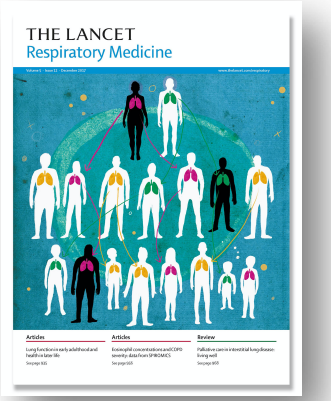


Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study

Xiaobo Yang, Yuan Yu*, Jiqian Xu*, Huaqing Shu*, Jia'an Xia*, Hong Liu*, Yongran Wu, Lu Zhang, Zhui Yu, Minghao Fang, Ting Yu, Yaxin Wang, Shangwen Pan, Xiaojing Zou, Shiying Yuan, You Shang*

	Survivors (n=20)	Non-survivors (n=32)	All patients (n=52)
Age, years	51·9 (12·9)	64·6 (11·2)	59·7 (13·3)
Age range, years			
30–39	6 (30%)	0	6 (11·5%)
40–49	3 (15%)	3 (9%)	6 (11·5%)
50–59	4 (20%)	9 (28%)	13 (25%)
60–69	6 (30%)	11 (34%)	17 (33%)
70–79	1 (5%)	7 (22%)	8 (15%)
≥80	0	2 (6%)	2 (4%)
Chronic medical illness	4 (20%)	17 (53%)	21 (40%)
Chronic cardiac disease	2 (10%)	3 (9%)	5 (10%)
Chronic pulmonary disease	2 (10%)	2 (6%)	4 (8%)
Cerebrovascular disease	0	7 (22%)	7 (13·5%)
Diabetes	2 (10%)	7 (22%)	9 (17%)
Malignancy	0	0	2 (4%)
Dementia	0	0	1 (2%)
Malnutrition	0	0	1 (2%)
Smoking	0	0	2 (4%)

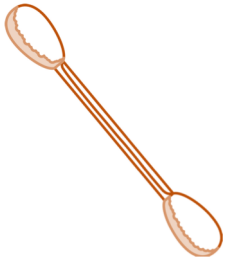
Comorbidities			
Acute respiratory distress syndrome	9 (45%)	26 (81%)	35 (67%)
Acute kidney injury	3 (15%)	12 (37·5%)	15 (29%)
Cardiac injury	3 (15%)	9 (28%)	12 (23%)
Liver dysfunction	6 (30%)	9 (28%)	15 (29%)
Hyperglycaemia	7 (35%)	11 (34%)	18 (35%)
Gastrointestinal haemorrhage	0	2 (6%)	2 (4%
Pneumothorax	1 (5%)	0	1 (2%)
Hospital-acquired pneumonia	40 (20%)	2 (6%)	7 (13·5%)
Bacteraemia	0	1 (3%)	1 (2%)
Urinary tract infection	0	1 (3%)	1 (2%)

Treatment			
High flow nasal cannula	17 (85%)	16 (50%)	33 (63·5%)
Mechanical ventilation	7 (35%)	30 (94%)	37 (71%)
Non-invasive	6 (30%)	23 (72%)	29 (56%)
Invasive	3 (15%)	19 (59%)	22 (42%)
Prone position ventilation	2 (10%)	4 (12·5%)	6 (11·5%)
Extracorporeal membrane oxygenation	1 (5%)	5 (16%)	6 (11·5%)
Renal replacement therapy	1 (5%)	8 (25%)	9 (17%)
Vasoconstrictive agents	2 (10%)	16 (50%)	18 (35%)
Antiviral agents	13 (65%)	10 (31%)	23 (44%)
Antibacterial agents	19 (95%)	30 (94%)	49 (94%)
Glucocorticoids	14 (70%)	16 (50%)	30 (58%)
Immunoglobulin	9 (45%)	19 (59%)	28 (54%)

DIAGNOSIS

EPIDEMIOLOGY NOT HELPFUL

ASPECIFIC
ASYMPTOMATIC (<10% ?)*



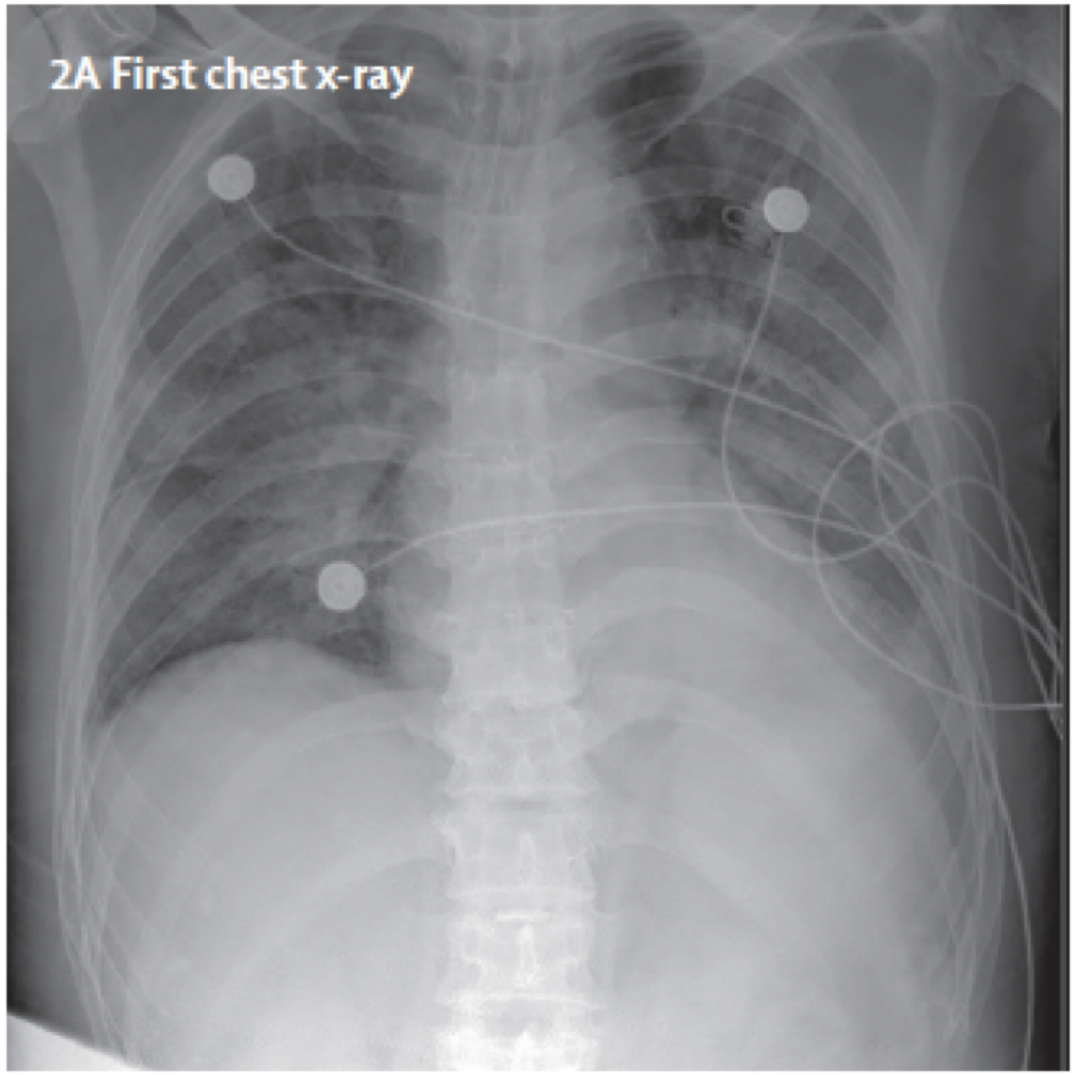
NP SWAB RT-PCR (FN 20%) – TEST FOR OTHER VIRUSES
BAL SWAB RT-PCR (FN NOT SEVERE)
BLOOD RT-PCR (PREDICTOR OF SEVERITY)

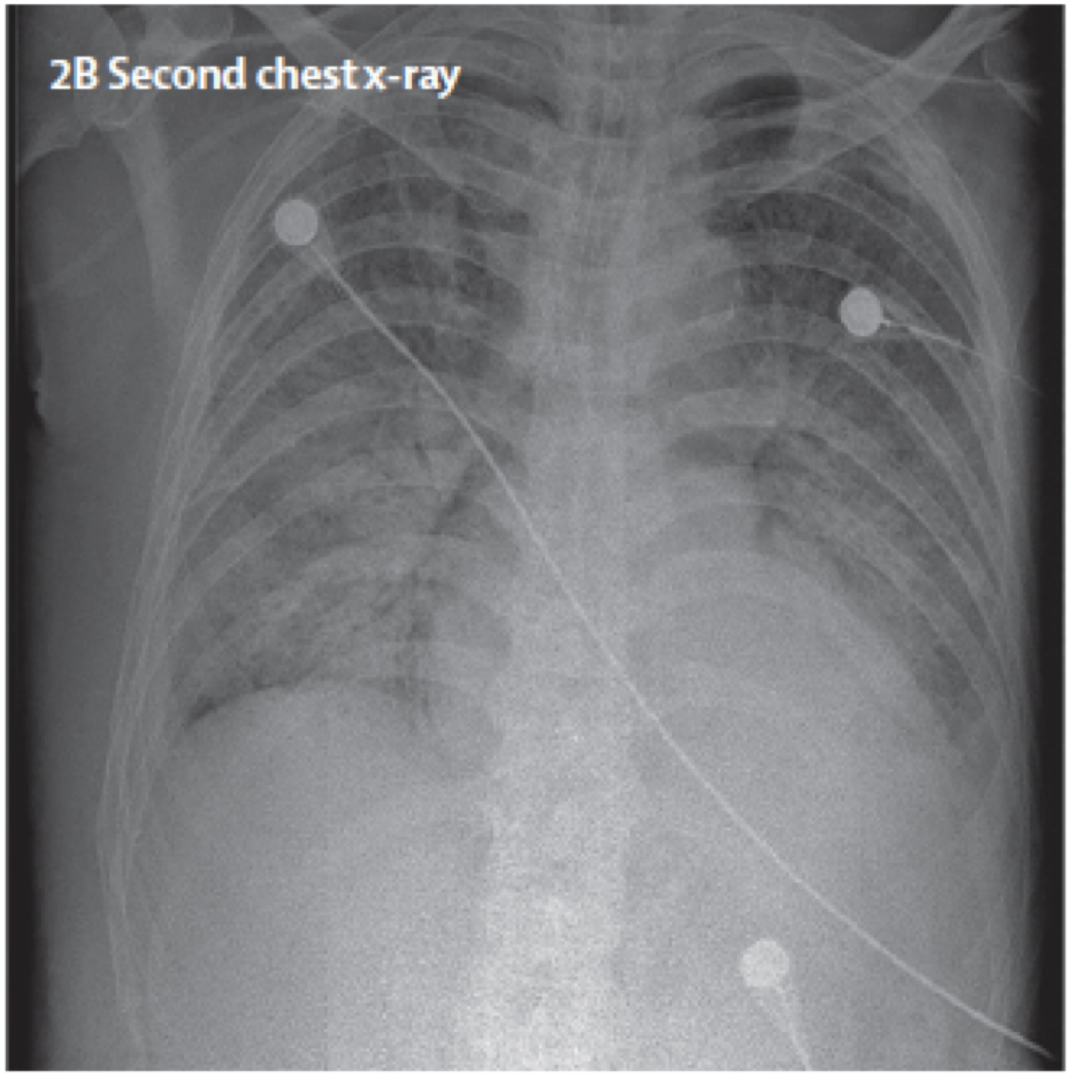
CHEST X-RAY (FN ON ADMISSION)
CHEST CT-SCAN (NP SWAB -)

NO SPECIFIC LAB TEST
IgM/IgG ?

Chen, Emerging Microbes & Infections 2020

DIAGNOSIS





DIAGNOSIS

Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2

Xi Xu[1] · Chengcheng Yu[2] · Jing Qu[2] · Lieguang Zhang[2] · Songfeng Jiang[2] · Deyang Huang[2] · Bihua Chen[2] · Zhiping Zhang[2] · Wanhua Guan[2] · Zhoukun Ling[2] · Rui Jiang[2] · Tianli Hu[2] · Yan Ding[2] · Lin Lin[2] · Qingxin Gan[2] · Liangping Luo[1] · Xiaoping Tang[2] · Jinxin Liu[2]

SARS-CoV-2 RT-PCR+

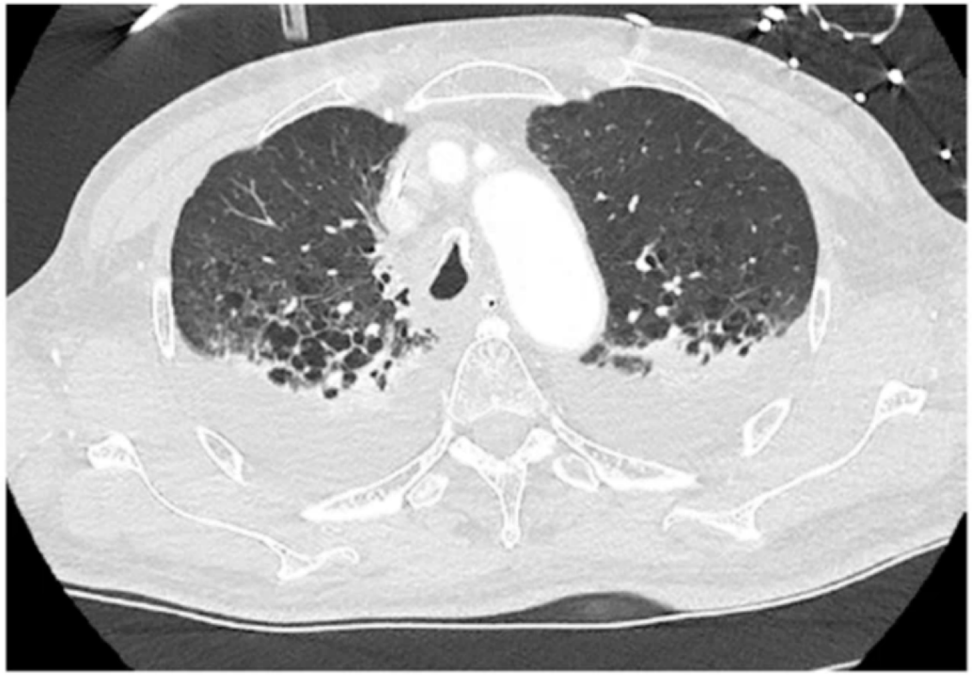
✓ Periphery distribution	51%
✓ **Bilateral involvement**	**59%**
✓ **Multifocal involvement**	**69%**
✓ Unifocal involvement	8%
✓ More than two lobes involved	59%
✓ **Ground glass opacification**	**72%**
✓ Consolidation	13%
✓ Crazy paving pattern	12%
✓ Cavitation	0%
✓ Pleural effusion	4%
✓ Pericardial effusion	1%
✓ Lymphadenopathy	1%

- ✓ **CT+ in >90% of patients with respiratory symptoms**
- ✓ **Mixed patterns more prevalent in symptomatic patients ***
- ✓ **COVID-19 pneumonia may occur in up to 20% of RT-CPR- patients**

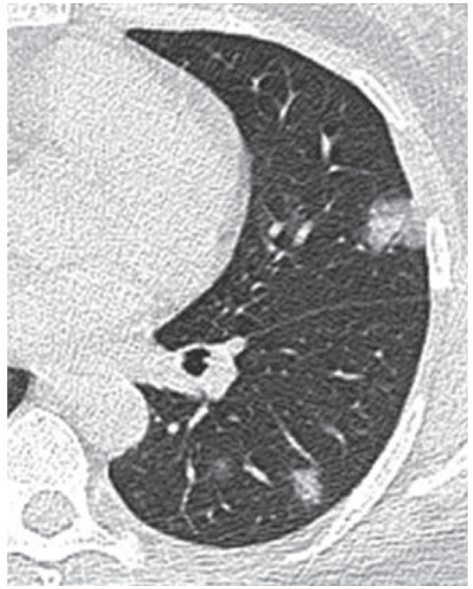
Shi, Lancet Infect Dis 2020
Ai, Radiology 2020
Inui, Radiology 2020

10-20% CT- on admission in patients with CLINICS + and RT-PCR + but without respiratory symptoms

Guan, medRxiv 2020
Yang, J Infect 2020
Chung, Radiology 2020

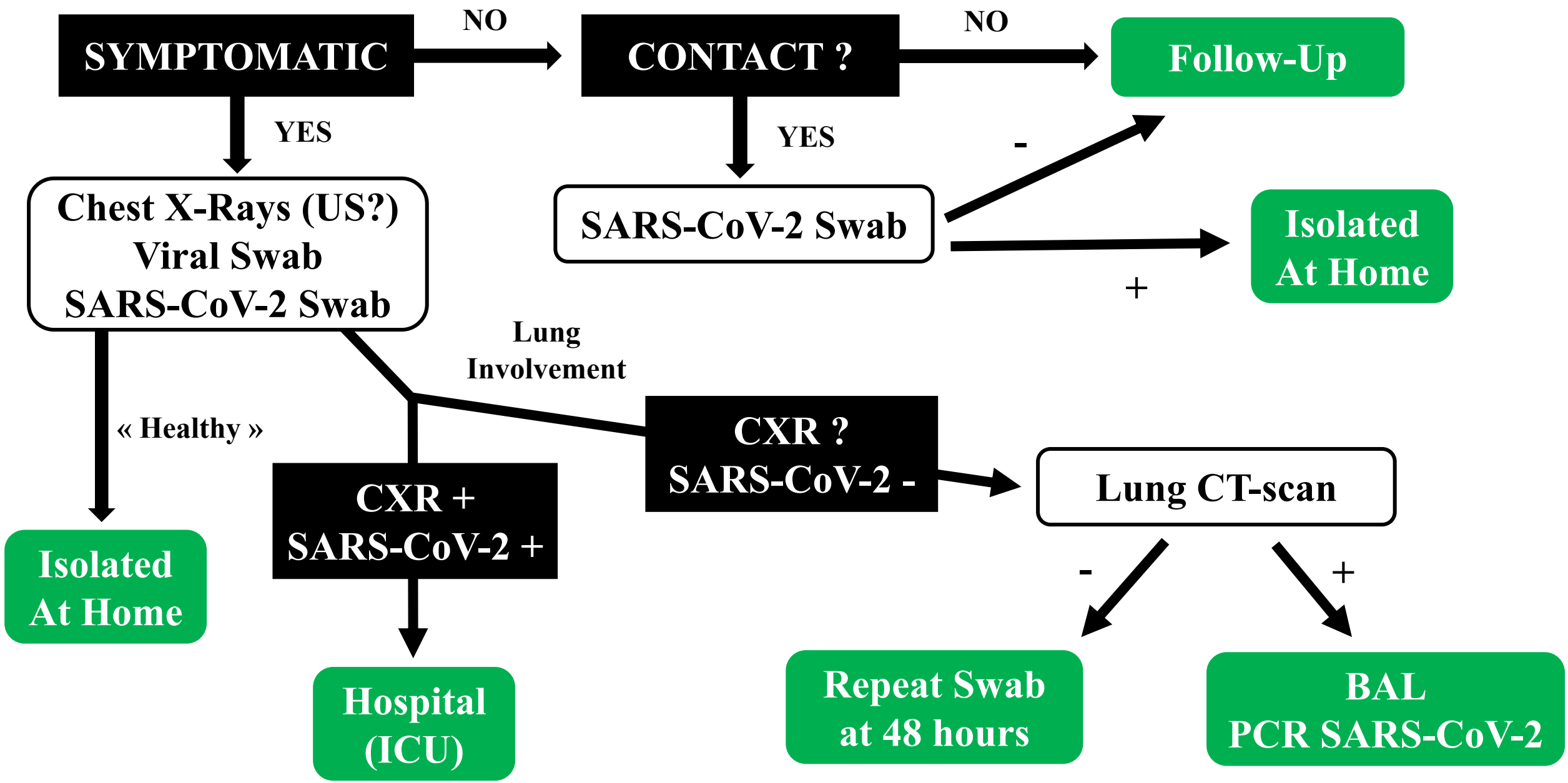


- ✓ Low rate of missed diagnosis of COVID-19 (4%)
- ✓ CT findings “peak” during illness days 6-11
- ✓ Evolution from ground-glass opacity to mixed patterns peak during illness days 12-17
- ✓ Halo sign > 60%
- ✓ Septal thickening, bronchiectasis, pleural thickening and subpleural involvement
- ✓ Not specific findings between viral pneumonias



Salehi, AJR 2020
Wang, Radiology 2020

DIAGNOSIS


SYMPTOMATIC
NO
CONTACT ?
NO
Follow-Up
YES
YES
-
Chest X-Rays (US?)
Viral Swab
SARS-CoV-2 Swab
SARS-CoV-2 Swab
Isolated
At Home
+
Lung
Involvement
« Healthy »
CXR ?
SARS-CoV-2 -
Lung CT-scan
CXR +
SARS-CoV-2 +
Isolated
At Home
-
+
Repeat Swab
at 48 hours
BAL
PCR SARS-CoV-2
Hospital
(ICU)


R.I.P


死神


?

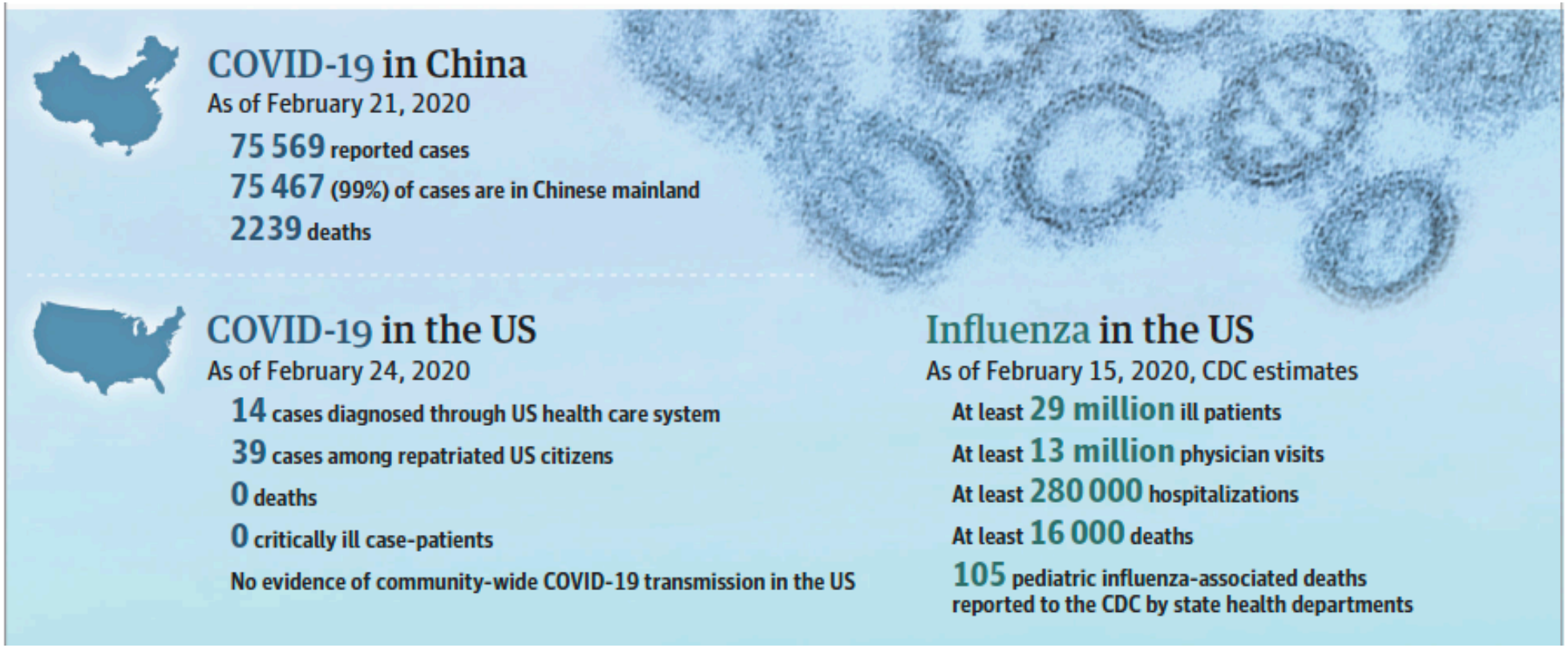
VIEWPOINT

Coronavirus Infections—More Than Just the Common Cold

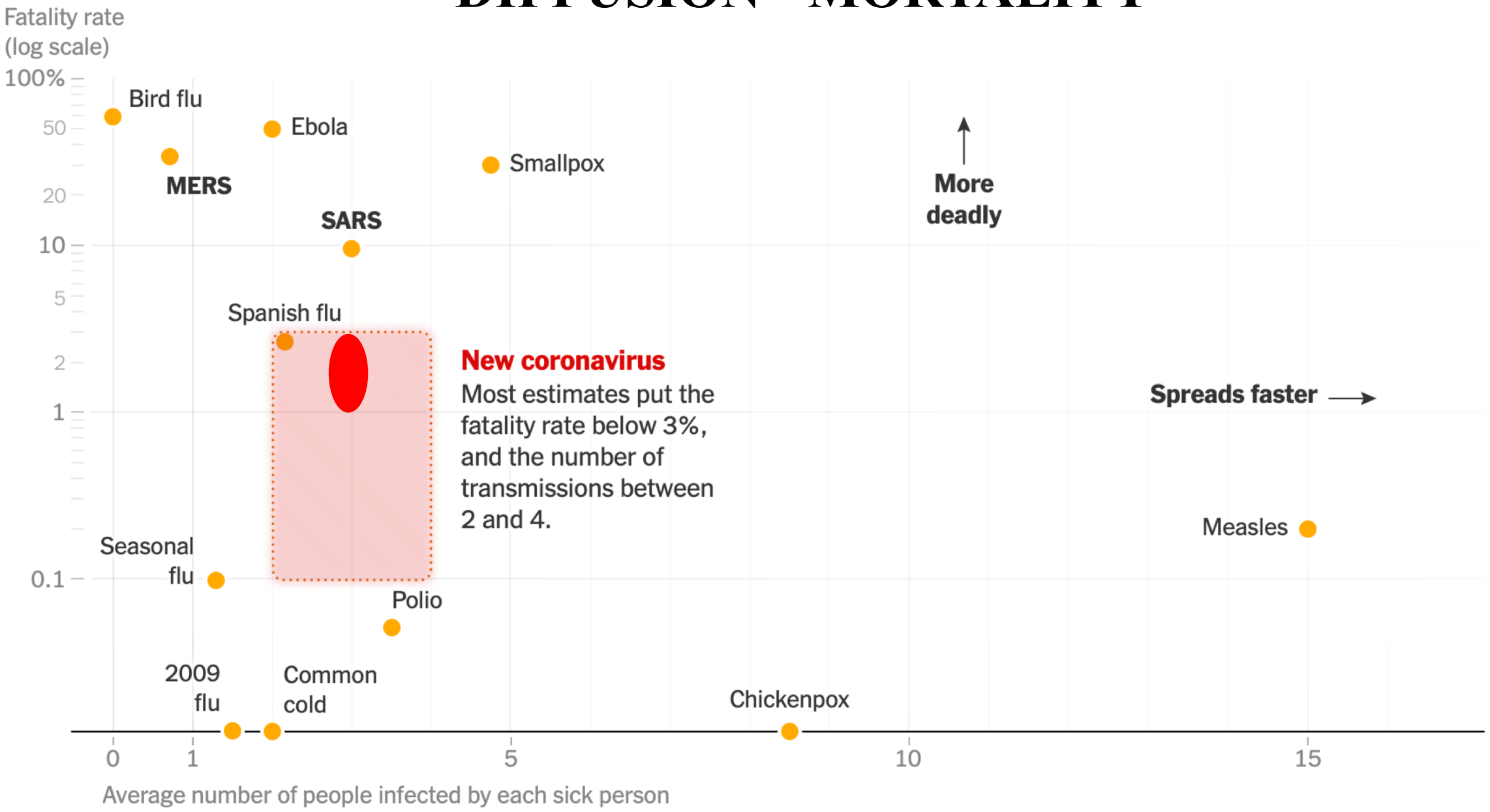
Catharine I. Paules, MD
Penn State University College of Medicine, Milton S. Hershey Medical Center, Hershey, Pennsylvania.

Hilary D. Marston, MD, MPH
National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.

Anthony S. Fauci, MD
National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.



DIFFUSION - MORTALITY



Viewpoint

ONLINE FIRST FREE

February 24, 2020

Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China

Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention

85%

15%

3-5%

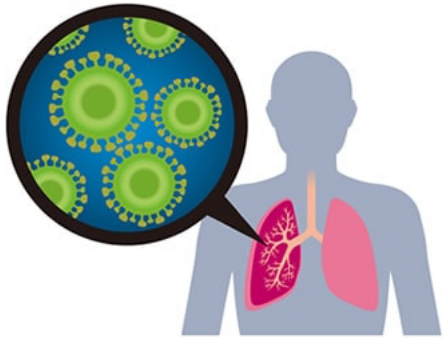
8%

0.1%

5-8%

42-62-%

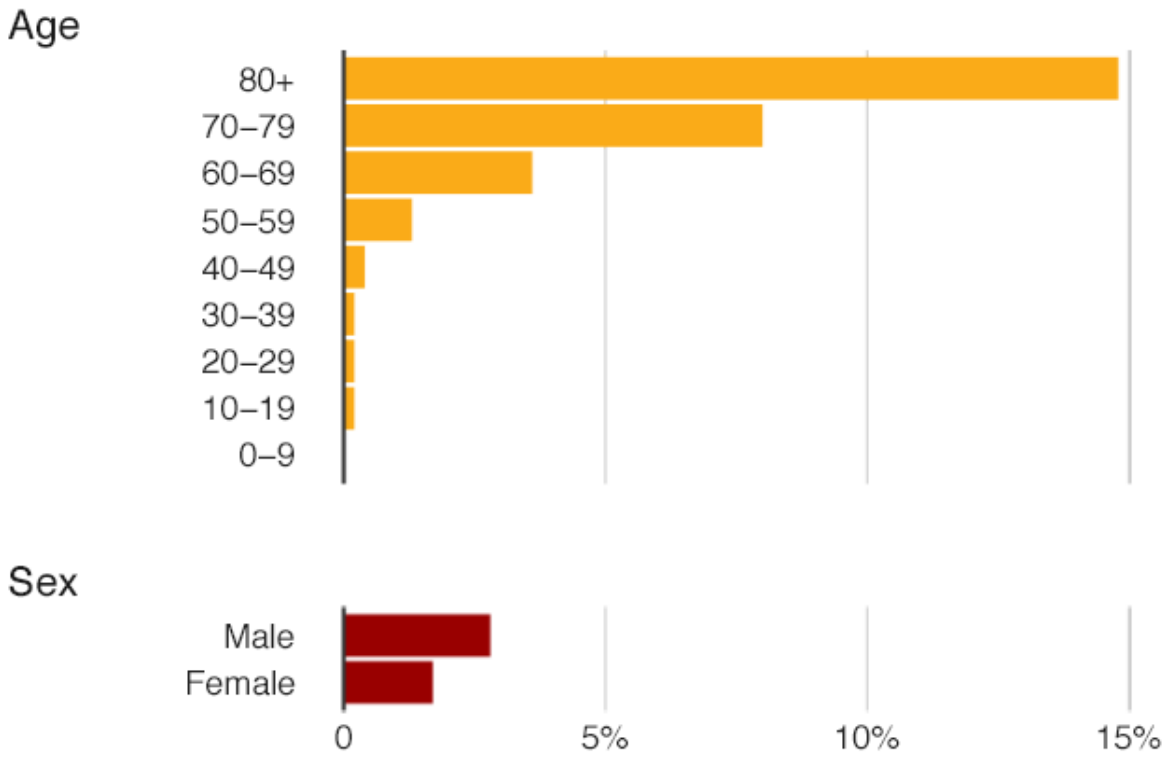
2-3%

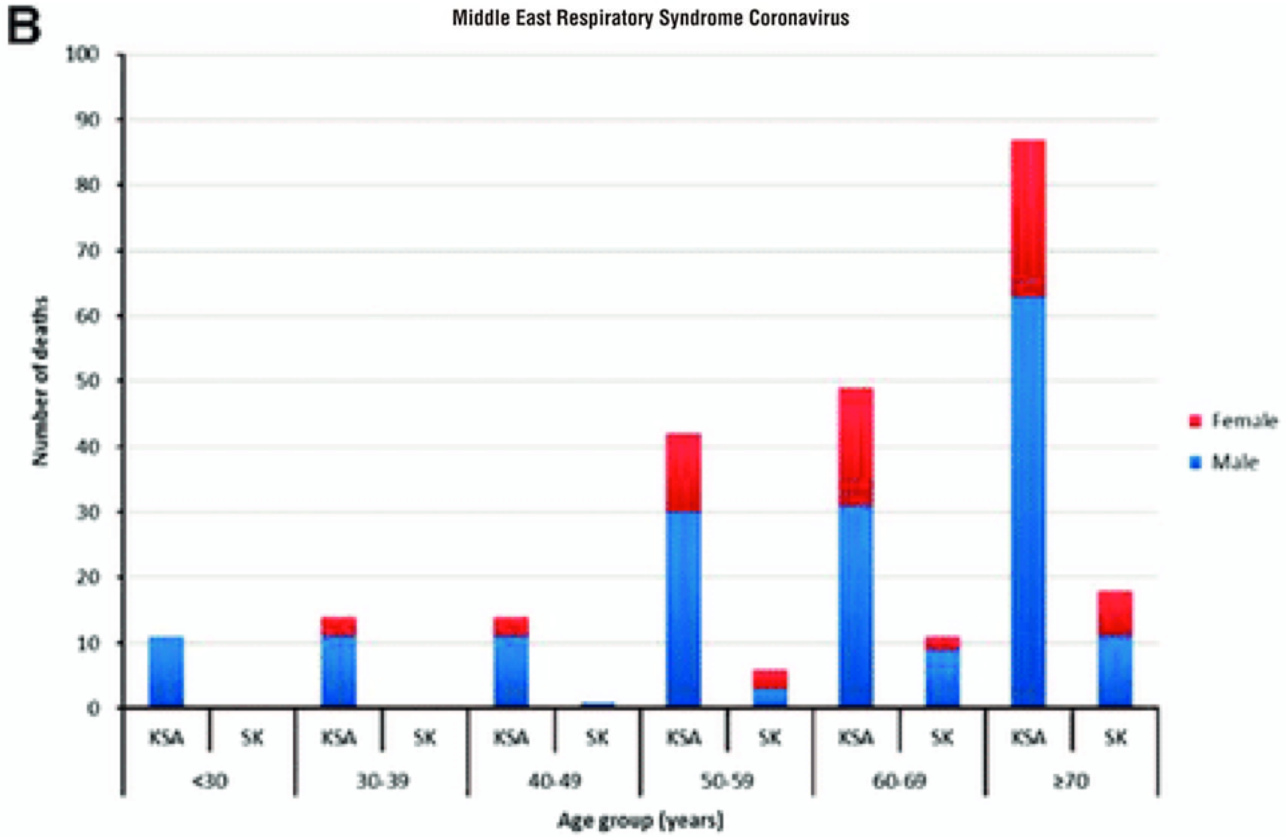


MERS-CoV

Middle East Respiratory Syndrome Coronavirus

Proportion of deaths among confirmed cases





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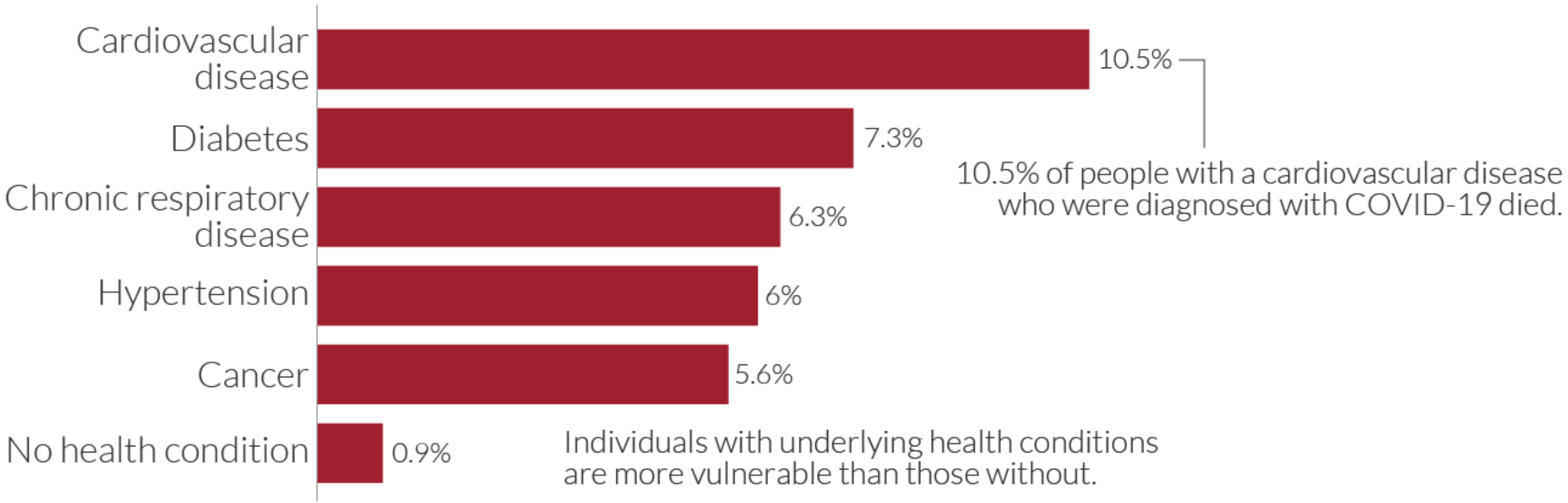


Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study

Fei Zhou, Ting Yu*, Ronghui Du*, Guohui Fan*, Ying Liu*, Zhibo Liu*, Jie Xiang*, Yeming Wang, Bin Song, Xiaoying Gu, Lulu Guan, Yuan Wei, Hui Li, Xudong Wu, Jiuyang Xu, Shengjin Tu, Yi Zhang, Hua Chen, Bin Cao*

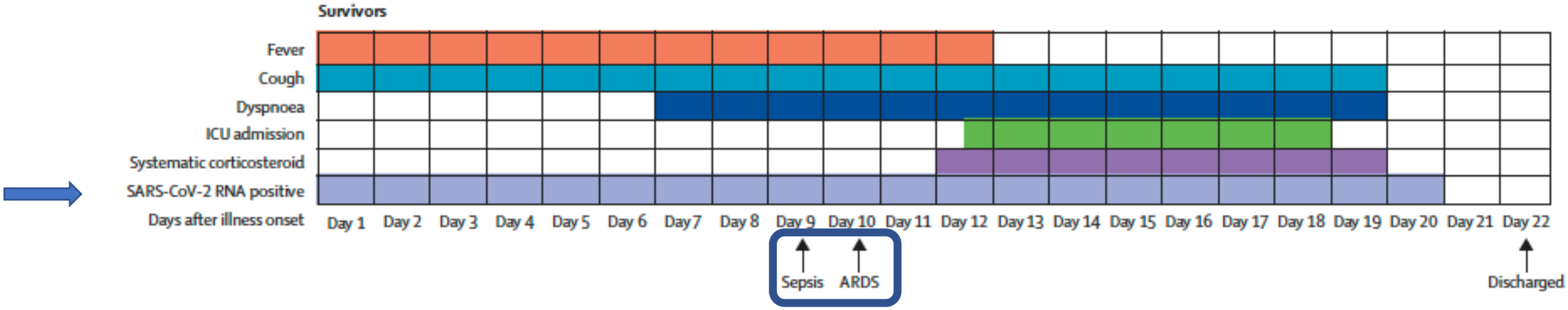
n=191

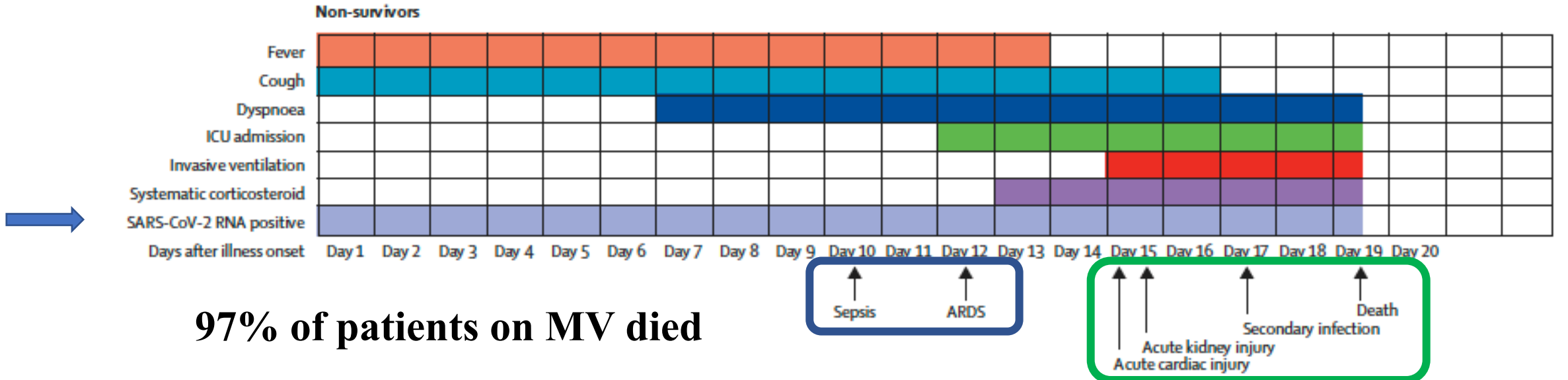
58/191
28%

	Univariable OR (95% CI)	p value	Multivariable OR (95% CI)	p value
Demographics and clinical characteristics				
Age, years*	1·14 (1·09–1·18)	<0·0001	1·10 (1·03–1·17)	0·0043
> 1 D-dimer, μg/mL	20·04 (6·52–61·56)	<0·0001	18·42 (2·64–128·55)	0·0033
SOFA score	6·14 (3·48–10·85)	<0·0001	5·65 (2·61–12·23)	<0·0001

Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study

Fei Zhou, Ting Yu*, Ronghui Du*, Guohui Fan*, Ying Liu*, Zhibo Liu*, Jie Xiang*, Yeming Wang, Bin Song, Xiaoying Gu, Lulu Guan, Yuan Wei, Hui Li, Xudong Wu, Jiuyang Xu, Shengjin Tu, Yi Zhang, Hua Chen, Bin Cao*





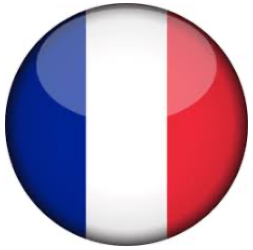
97% of patients on MV died

1386 Mil
81285
3287
58.6/M
4.0%

82 Mil
29406
2234
358.0/M
7.5%

17 Mil
7431
434
437.1/M
5.8%

60 Mil
74386
7503
1239.8/M
10.1%



67 Mil
25233
1331
376.0/M
5.2%

9 Mil
6398
49
710.9/M
0.7%

327 Mil
68905
1037
210.7/M
1.5%

9 Mil
11575
172
1286.1/M
1.4%

11 Mil
6235
220
566.8/M
3.5%

47 Mil
56188
4089
1195.4/M
7.2%

67 Mil
9529
465
142.2/M
4.8%

10 Mil
3522
60
352.0/M
1.7%

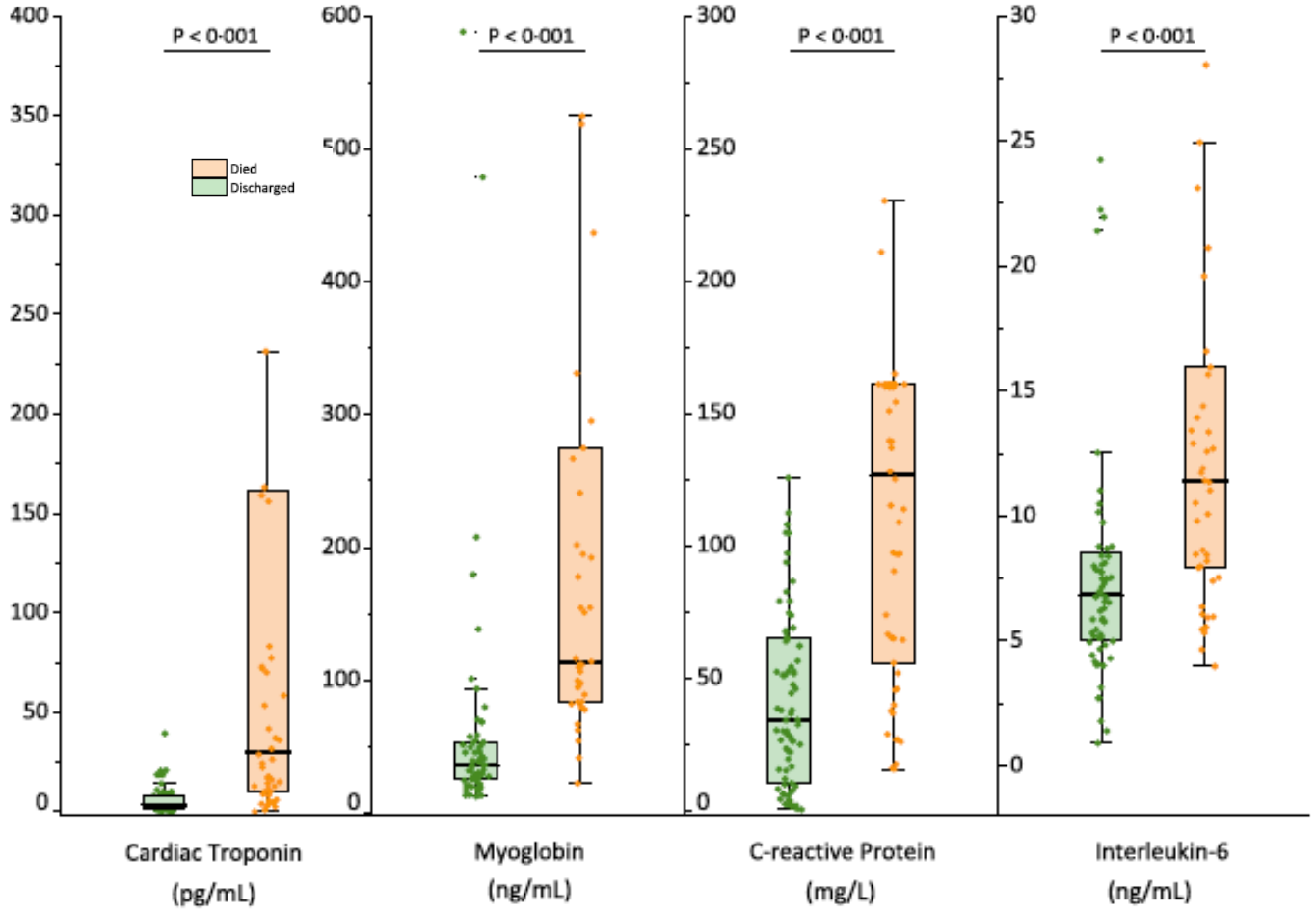
83 Mil
40421
229
487.0/M
0.5%

51 Mil
9241
131
181.2/M
1.4%

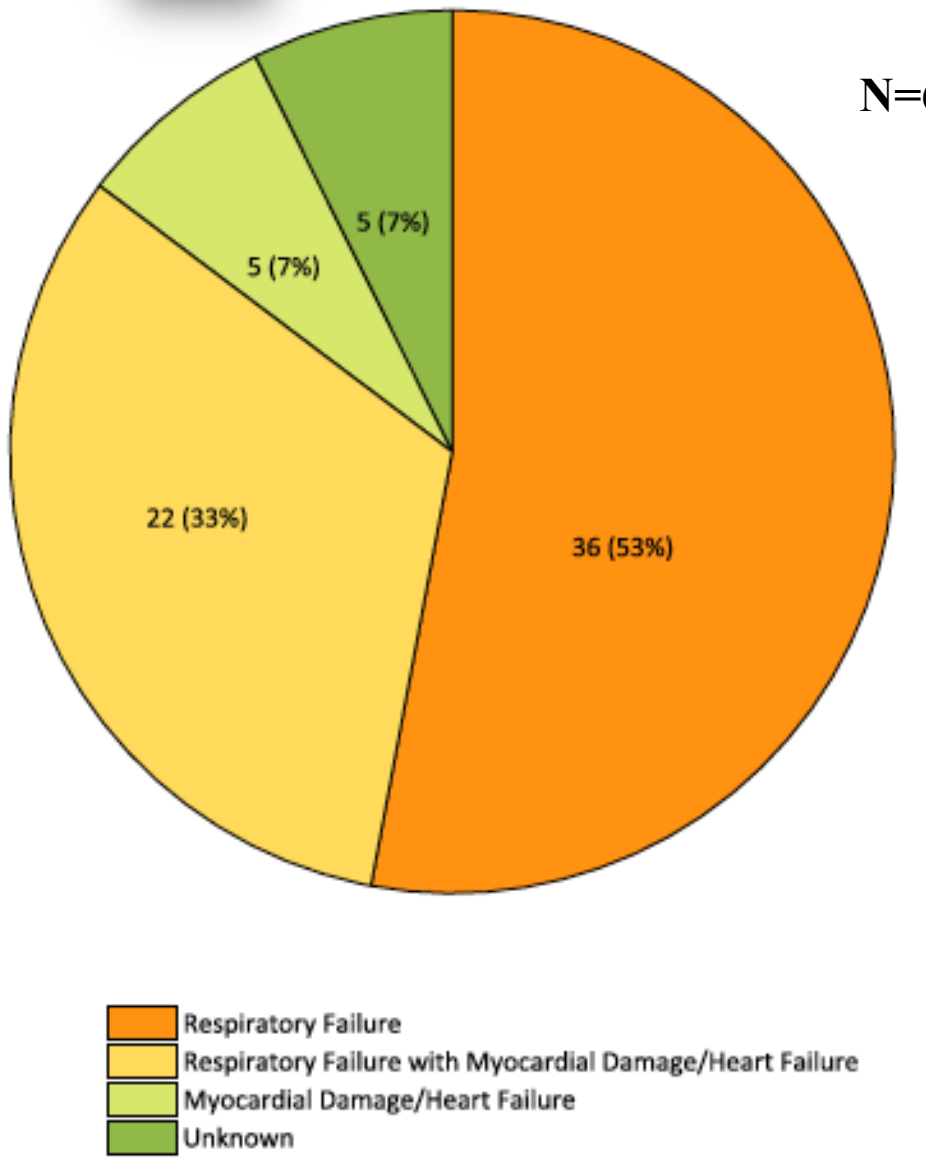
38 Mil
3405
36
89.7/M
1.0%

Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China

Qiurong Ruan[1,2], Kun Yang[3], Wenxia Wang[4], Lingyu Jiang[5] and Jianxin Song[4*]



N=68



TREATMENT – SUPPORTIVE CARE

- **RESPIRATORY SUPPORT**
  - ✓Oxygen therapy
  - ✓*HFOT? CPAP ? NIV ?*
    - ✓*Aerosol dispersion ? (up to 1m < air leakage and PEEP!)*
    - ✓*Failure (MERS > SARS) ?*
    - ✓*High-risk patients = Low PF and MOF*
  - ✓Mechanical ventilation
    - ✓Low TV (protective)
    - ✓High PEEP (> 15 cmH20)
  - ✓Prone Positioning
  - ✓ECMO (3-5%)

- ✓ **Disposable, single-use systems**
- ✓ **Breathing with closed mouths (HFOT)**
- ✓ **Condensation in the circuit cleaned**

- **PREVENT COMPLICATIONS (VAP, CLABSI – 10%)**
- **ANTIBACTERIAL ? (macrolides – interactions +++)**

TREATMENT – ANTIVIRALS

Testing, testing

Promising drugs to treat covid-19

Drug	Current use	Original mode of action	Being tested?
Chloroquine	Antimalarial	Heme polymerase inhibitor	Yes
Kaletra (ritonavir + lopinavir)	HIV	Protease inhibitor	Yes
Interferon alfa-2b	Hepatitis-C	Immune modulator	Yes
Remdesivir	Experimental	Nucleotide analogue	Yes
Favipiravir	Influenza	RNA polymerase inhibitor	Yes
Actemra (tocilizumab)	Rheumatoid arthritis; covid-19	Anti-inflammatory	Approved*
Kevzara (sarilumab)	Rheumatoid arthritis	Anti-inflammatory	Trials expected

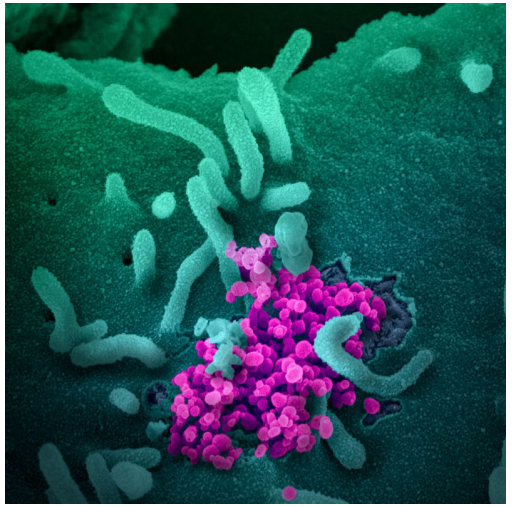
Source: WHO, adapted from landscape analysis, 17th February 2020

*For use on covid-19 in China, March 2020

The Economist

TREATMENT - ANTIVIRALS

- **Hydroxychloroquine**
  - *200 mg q12h (7 days)*



- **ANTIVIRALS = no proof at today !!!!**
  - *Lopinavir/Ritonavir (SARS = Reduction of ARDS occurrence)*
    - *400 mg q12h (5-7 days)*
  - *Remdesivir (experimental MERS = reduction of viral load)*
    - *200 mg loading dose then 100 mg/d (10-14 days)*
  - *Umifenovir (better outcome in 69 patients)*
  - *Oseltamivir*

- **Ribavirine + IFN discouraged (MERS)**
- **Plasma exchange (or IVIG?)**
- **VACCINES ??**

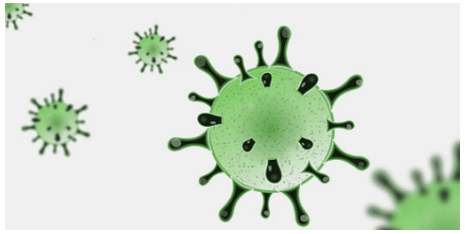
TREATMENT - OTHERS

- **IMMUNOMODULATION**
  - *Camrelizumab = anti-PD1*
  - *Tocilizumab = IL-6*
  - *Baricitinib = Janus kinase inhibitor*

- **OTHERS**
  - *Telmisartan or Losartan ?*

TREATMENT - OTHERS

Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19)



Surviving Sepsis Campaign

Recommendation:

45. In critically ill adults with COVID-19, we **suggest against** the routine use of standard intravenous immunoglobulins (IVIG) (Weak recommendation, very low-quality evidence).

Recommendation

47. In critically ill adults with COVID-19:

47.1. we **suggest against** the routine use of lopinavir/ritonavir (weak recommendation, low quality evidence).

47.2. **There is insufficient evidence to issue a recommendation** on the use of other antiviral agents in critically ill adults with COVID-19.

Recommendation

48. **There is insufficient evidence to issue a recommendation** on the use of recombinant rIFNs, alone or in combination with antivirals, in critically ill adults with COVID-19.

Recommendation

49. **There is insufficient evidence to issue a recommendation** on the use of chloroquine or hydroxychloroquine in critically ill adults with COVID-19.

Recommendation

50. **There is insufficient evidence to issue a recommendation** on the use of tocilizumab in critically ill adults with COVID-19.

TREATMENT

Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury

	Outcomes of corticosteroid therapy*	Comment
MERS-CoV	Delayed clearance of viral RNA from respiratory tract[2]	Adjusted hazard ratio 0·4 (95% CI 0·2–0·7)
SARS-CoV	Delayed clearance of viral RNA from blood[5]	Significant difference but effect size not quantified
SARS-CoV	Complication: psychosis[6]	Associated with higher cumulative dose, 10 975 mg *vs* 6780 mg hydrocortisone equivalent
SARS-CoV	Complication: diabetes[7]	33 (35%) of 95 patients treated with corticosteroid developed corticosteroid-induced diabetes
SARS-CoV	Complication: avascular necrosis in survivors[8]	Among 40 patients who survived after corticosteroid treatment, 12 (30%) had avascular necrosis and 30 (75%) had osteoporosis
Influenza	Increased mortality[9]	Risk ratio for mortality 1·75 (95% CI 1·3–2·4) in a meta-analysis of 6548 patients from ten studies
RSV	No clinical benefit in children[10,11]	No effect in largest randomised controlled trial of 600 children, of whom 305 (51%) had been treated with corticosteroids

CoV=coronavirus. MERS=Middle East respiratory syndrome. RSV=respiratory syncytial virus. SARS=severe acute respiratory syndrome. *Hydrocortisone, methylprednisolone, dexamethasone, and prednisolone.

Table: **Summary of clinical evidence to date**

IV steroids are discouraged (delayed ARN clearance) **– Inhaled ???**

JAMA Internal Medicine | Original Investigation

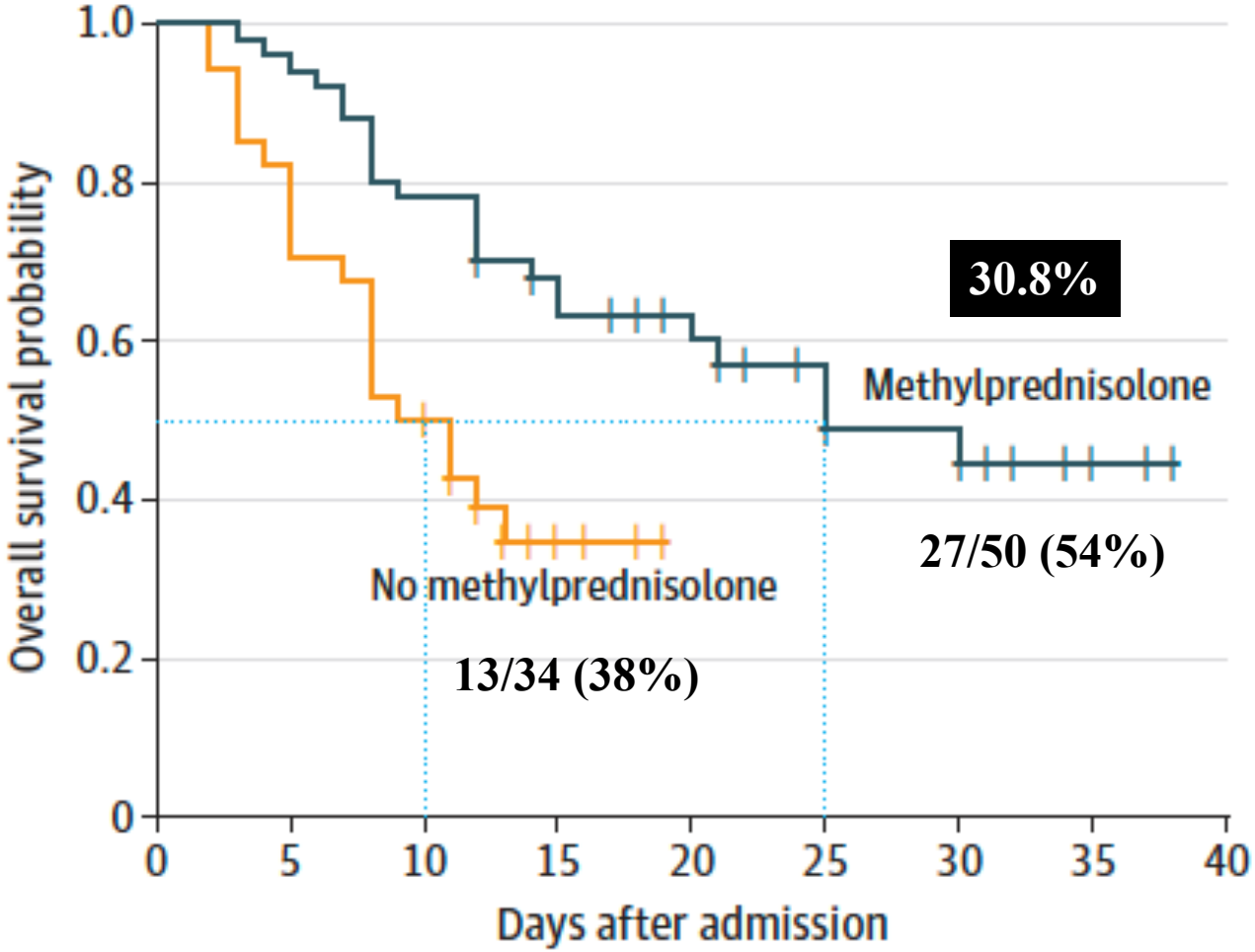
Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China

n=201

Table 1. Demographic Characteristics of Patients With Coronavirus Disease 2019 Pneumonia (continued)

Study population	No. (%)
Clinical outcomes	
ARDS	84 (41.8)
ICU admission	53 (26.4)
Death	44 (21.9)

Mortality = 66% if MV (n=67)

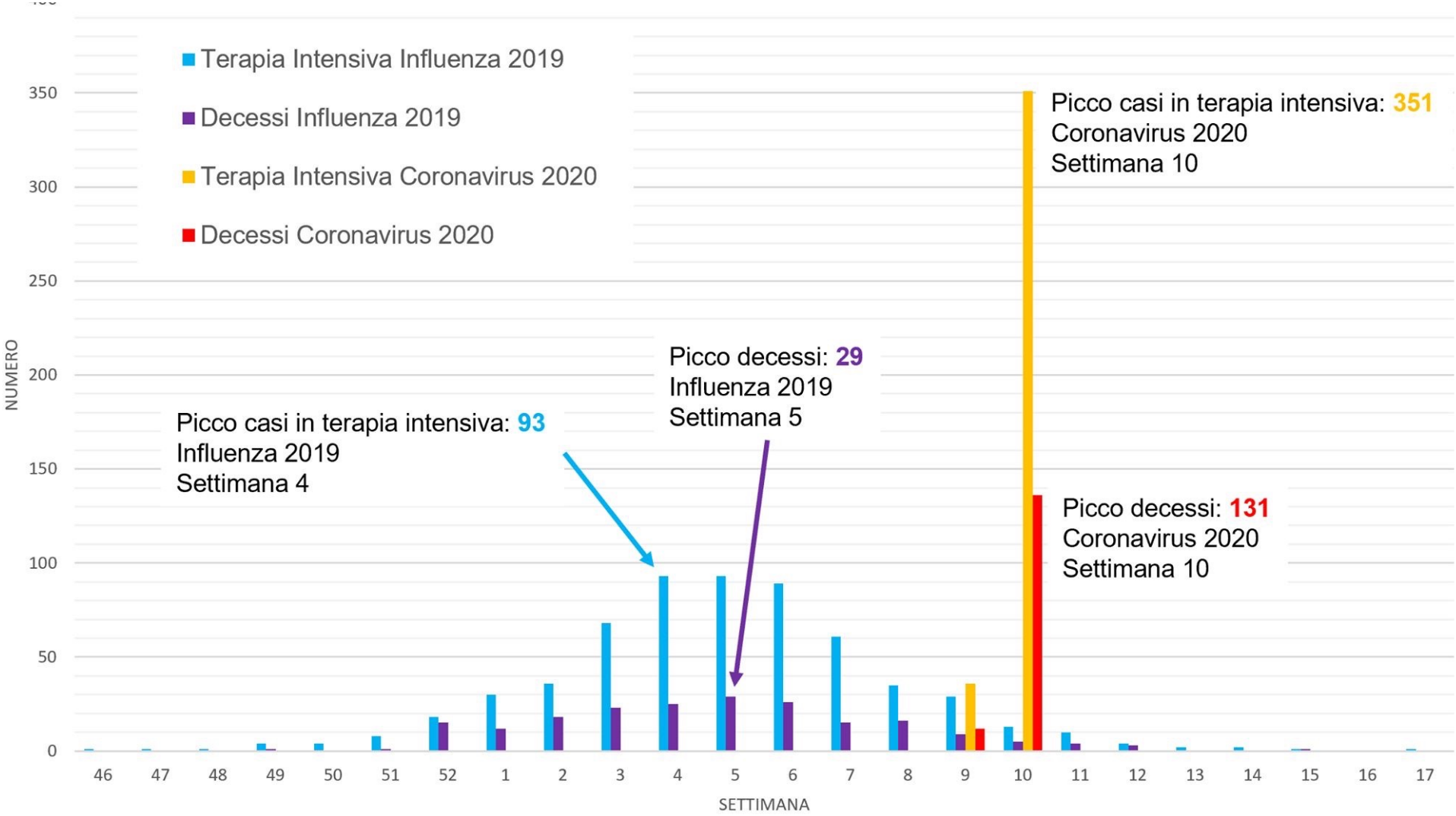


ORGANISATION

	Demands	Difficulties	Potential solutions
Space	Double or triple ICU beds to cope with the surge of critically ill patients requiring mechanical ventilation and other supportive care	Limited physical space with specific functionalities such as electricity, medical gas, and suction Not designed for infectious diseases spreading via respiratory droplets or contact	Post-anesthesia care unit and ED as primary backup space General wards with adequately ventilated rooms as secondary backup space after remodeling Infection prevention and control measures designed by infection control professionals
Supplies	Bedside monitors, ventilators, CRRT machine, ECMO, portable X-ray equipment PPE, such as N95 mask, googles, face shields, long-sleeved gowns, and gloves	Information about epidemic less predictable during the initial phase Information about patient characteristics unavailable during the initial phase	Provision of update and predicted estimates of the epidemic by public health authorities List of PPE and medical devices/equipment for stockpiling Prediction of supply based on patient volume, staffing, and real-time consumption of PPE
Staff	Staffing of the medical rescue team, including intensivists, intensive care nurses, and respiratory therapists	Lack of knowledge about infection control and prevention Heavy workload and associated risk of contamination Burnout	Training provided by infection control professionals Duration of every shift no longer than 6–8 h Preparation of reserve medical rescue team for substitution Psychological consultation for healthcare workers

CRRT **continuous renal replacement therapy,** ***ECMO*** **extracorporeal membrane oxygenation,** ***ICU*** **intensive care unit,** ***PPE*** **personal protection equipment,** ***SARI*** **severe acute respiratory infection**

ORGANISATION - ICU



Fonte dati: https://www.epicentro.iss.it/influenza/ - http://www.protezionecivile.gov.it/

ORGANISATION – NOSOCOMIAL PREVENTION

- ✓In one study, **41%** of patients were presumed to be related to transmission within the hospital
  - ✓12% **hospitalized for other reasons**
  - ✓29% **healthcare workers**

Wu, JAMA 2020

- ✓**Health-care personnel infected**
  - ✓**3.8%** (1716 out of 44672)
  - ✓**14.8%** cases classified as severe or critical
  - ✓**5** Deaths

Zunhyou, JAMA 2020

- ✓**2339 (8.4% of all cases) in Italy**

Grasselli, JAMA 2020

Reader survey

‘No one is allowed out’: your stories from the coronavirus outbreak

The outbreak of a new coronavirus is wreaking havoc worldwide. In China, the epicentre of the epidemic, the virus has infected tens of thousands of people and killed some 2,600. Unprecedented measures meant to contain the spread have brought millions of lives to a halt, and the effects have touched economies and global supply chains. The restrictions have also brought challenges to scientists. Some have suspended their usual research to study the coronavirus. Others have had their work or personal lives disrupted by laboratory closures and travel restrictions. In a *Nature* reader poll, more than 600 of you told us that the coronavirus had affected your lives. These are some of your stories.

The deserted streets of Wuhan, China, where the outbreak originated.

‘People are dying’

Charles C. Y. Xu, McGill University, Montreal, Canada