

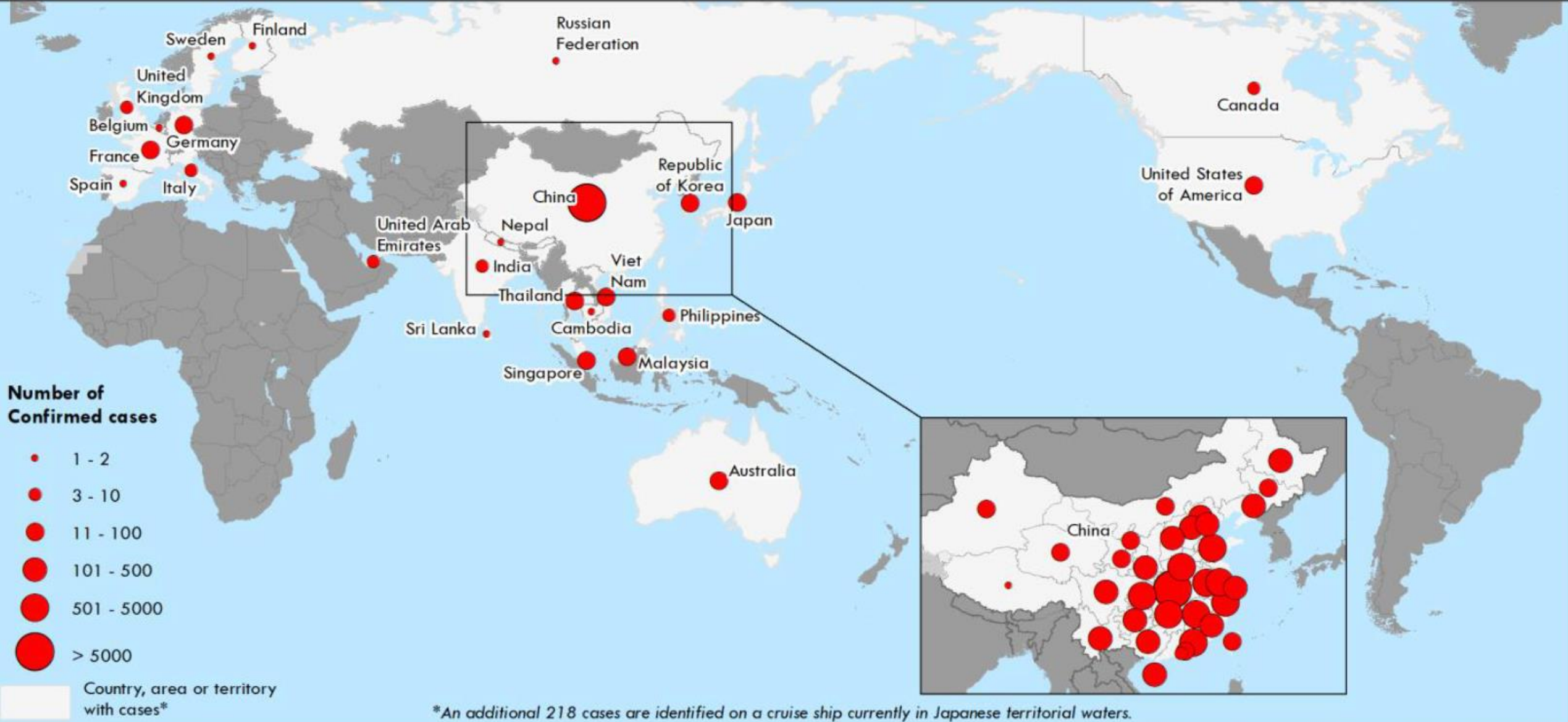
綜論嚴重特殊傳染性肺炎
臨床表徵及病程
2019-nCoV, SARS-CoV-2,
COVID-19

陽光耀

台北榮總 胸腔部

國立陽明大學 醫學院

Distribution of COVID-19 cases as of 14 February 2020



2019 Novel Coronavirus

[CDC](#) > [2019 Novel Coronavirus Home](#) > [Healthcare Professionals](#)

 [2019 Novel Coronavirus Home](#)

[2019-nCoV Situation Summary](#)

[About 2019-nCoV](#)

[Information for Travelers](#)

[Information for Businesses](#)

[Healthcare Professionals](#)

[Evaluating and Reporting PUI](#)

[Interim Guidance for EMS](#)

[Infection Control](#)

Interim Clinical Guidance for Management of Patients with Confirmed 2019 Novel Coronavirus (2019-nCoV) Infection

Updated February 11, 2020

This interim guidance is for clinicians caring for patients with confirmed 2019 novel coronavirus (2019-nCoV) infection. This update includes additional information regarding time from illness onset to hospital admission, detection of 2019-nCoV in extrapulmonary specimens, clarifies the type of advanced support observed among hospitalized patients and provides interim guidance for discontinuation of transmission-based precautions and in-home isolation. CDC will update this interim guidance as more information becomes available.

Clinical Presentation

There are a limited number of reports that describe the clinical presentation of

On This Page

[Clinical Presentation](#)

[Clinical Course](#)

[Diagnostic Testing](#)

[Laboratory and Radiographic Findings](#)

[Clinical Management and Treatment](#)

[Investigational Therapeutics](#)

臨床表徵

Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China (41 cases, 01/02/2020)

Chaolin Huang*, Yeming Wang*, Xingwang Li*, Lili Ren*, Jianping Zhao*, Yi Hu*, Li Zhang, Guohui Fan, Jiuyang Xu, Xiaoying Gu, Zhenshun Cheng, Ting Yu, Jiaan Xia, Yuan Wei, Wenjuan Wu, Xuelei Xie, Wen Yin, Hui Li, Min Liu, Yan Xiao, Hong Gao, Li Guo, Jungang Xie, Guangfa Wang, Rongmeng Jiang, Zhancheng Gao, Qi Jin, Jianwei Wang†, Bin Cao†

***Lancet* 2020; 395: 497–506**

Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study (99 cases, 01/20/2020)

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

***Lancet* 2020; 395: 507–13**

Comment

A novel coronavirus outbreak of global health concern



臨床表徵

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China (138 cases, 01/28/2020)

Dawei Wang, MD; Bo Hu, MD; Chang Hu, MD; Fangfang Zhu, MD; Xing Liu, MD; Jing Zhang, MD; Binbin Wang, MD; Hui Xiang, MD; Zhenshun Cheng, MD; Yong Xiong, MD; Yan Zhao, MD; Yirong Li, MD; Xinghuan Wang, MD; Zhiyong Peng, MD

JAMA. doi:10.1001/jama.2020.1585

Published online February 7, 2020.

Clinical characteristics of 2019 novel coronavirus infection in China (1099 cases, 01/29/2020)

Wei-jie Guan, Zheng-yi Ni, Yu Hu, Wen-hua Liang, Chun-quan Ou, Jian-xing He, Lei Liu, Hong Shan, Chun-liang Lei, David SC Hui, Bin Du, Lan-juan Li, Guang Zeng, Kowk-Yung Yuen, Ru-chong Chen, Chun-li Tang, Tao Wang, Ping-yan Chen, Jie Xiang, Shi-yue Li, Jin-lin Wang, Zi-jing Liang, Yi-xiang Peng, Li Wei, Yong Liu, Ya-hua Hu, Peng Peng, Jian-ming Wang, Ji-yang Liu, Zhong Chen, Gang Li, Zhi-jian Zheng, Shao-qin Qiu, Jie Luo, Chang-jiang Ye, Shao-yong Zhu, Nan-shan Z

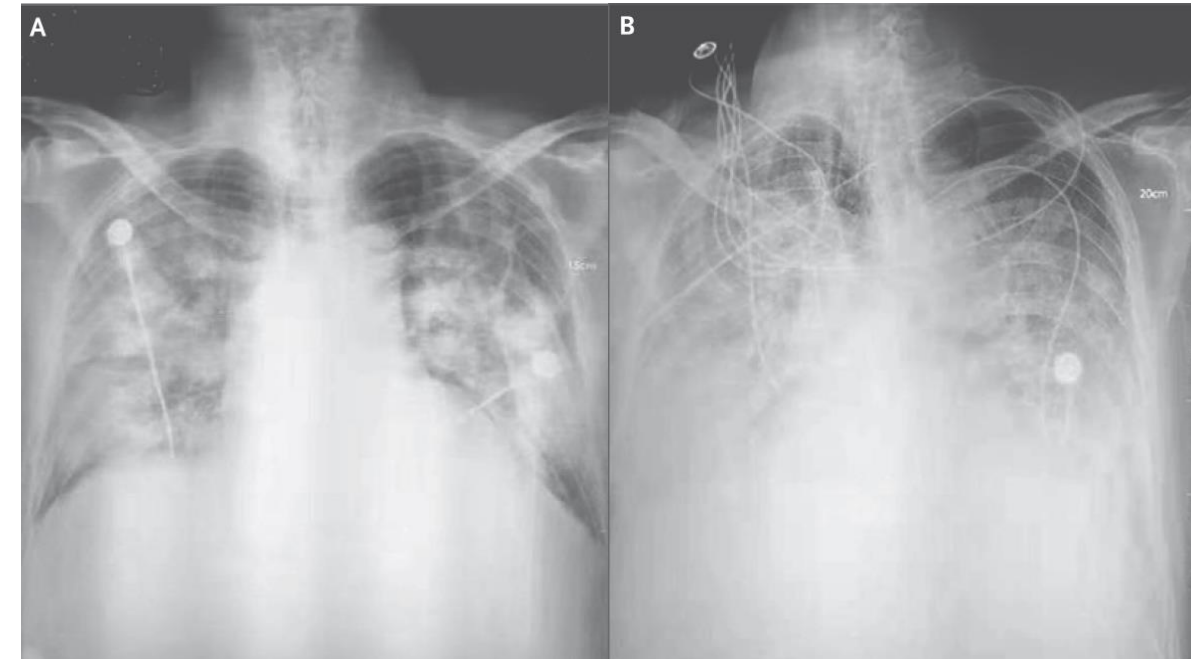
doi: <https://doi.org/10.1101/2020.02.06.20020974>



The NEW ENGLAND
JOURNAL of MEDICINE

A Novel Coronavirus from Patients with Pneumonia in China, 2019

- On December 31, 2019, China CDC dispatched a rapid response team conduct an epidemiologic and etiologic investigation in Wuhan.
- 49 y/o woman, 61 y/o man, 32 y/o man
- Fever, cough, chest discomfort and visited hospital in late Dec. 2019
- Contact history of seafood wholesale market
- 49 y/o woman and 32 y/o man recovered
- 61 y/o man progressed
 - Respiratory failure on day 7
 - Died on day 20

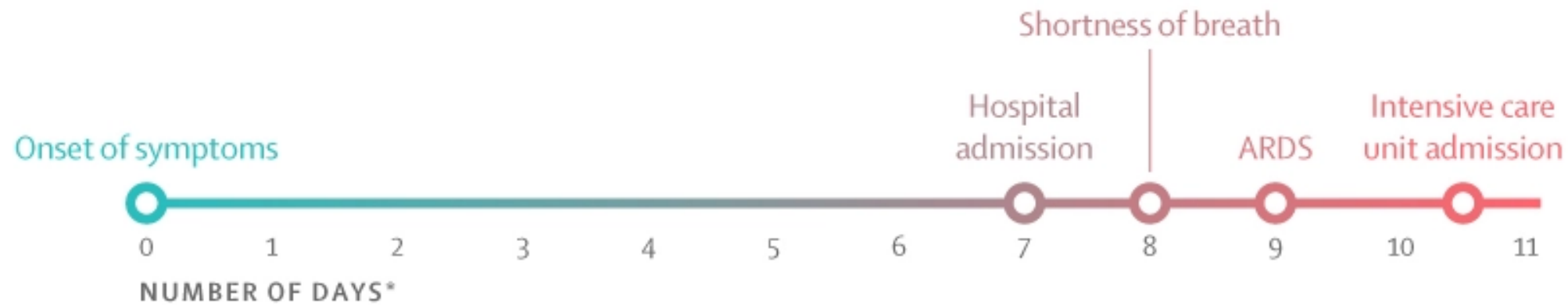


Day 8

Day 11

Admission 12/27/2019

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.

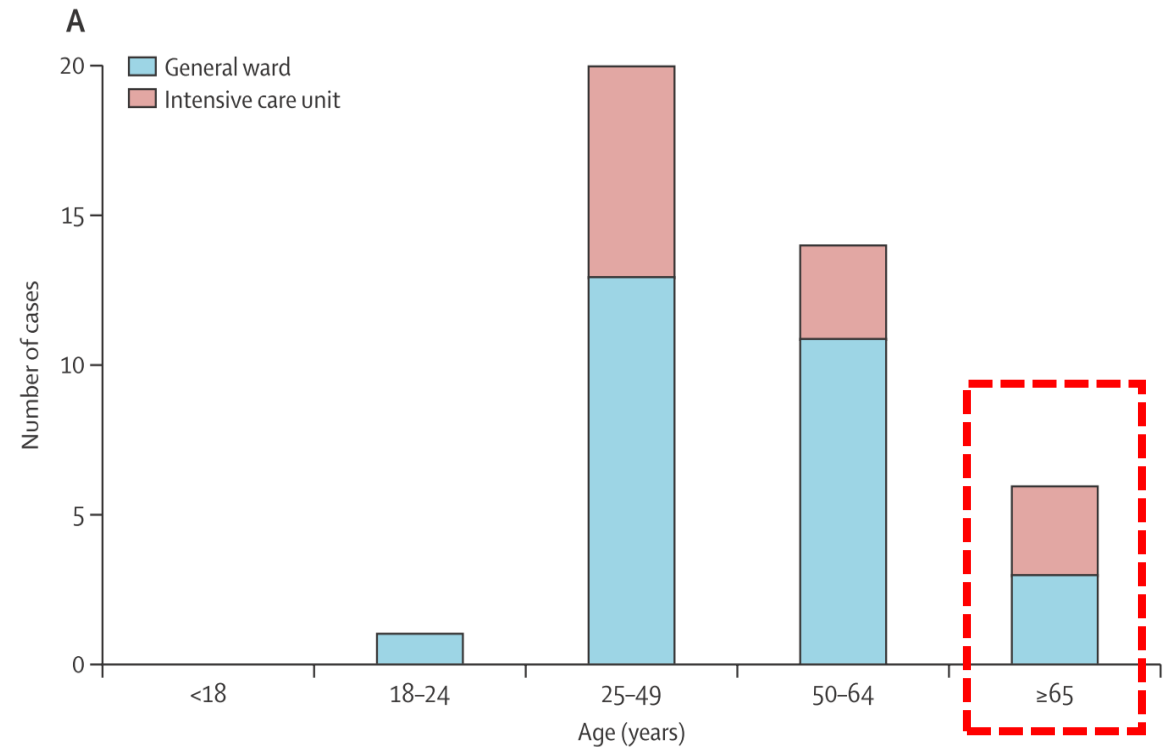
THE LANCET

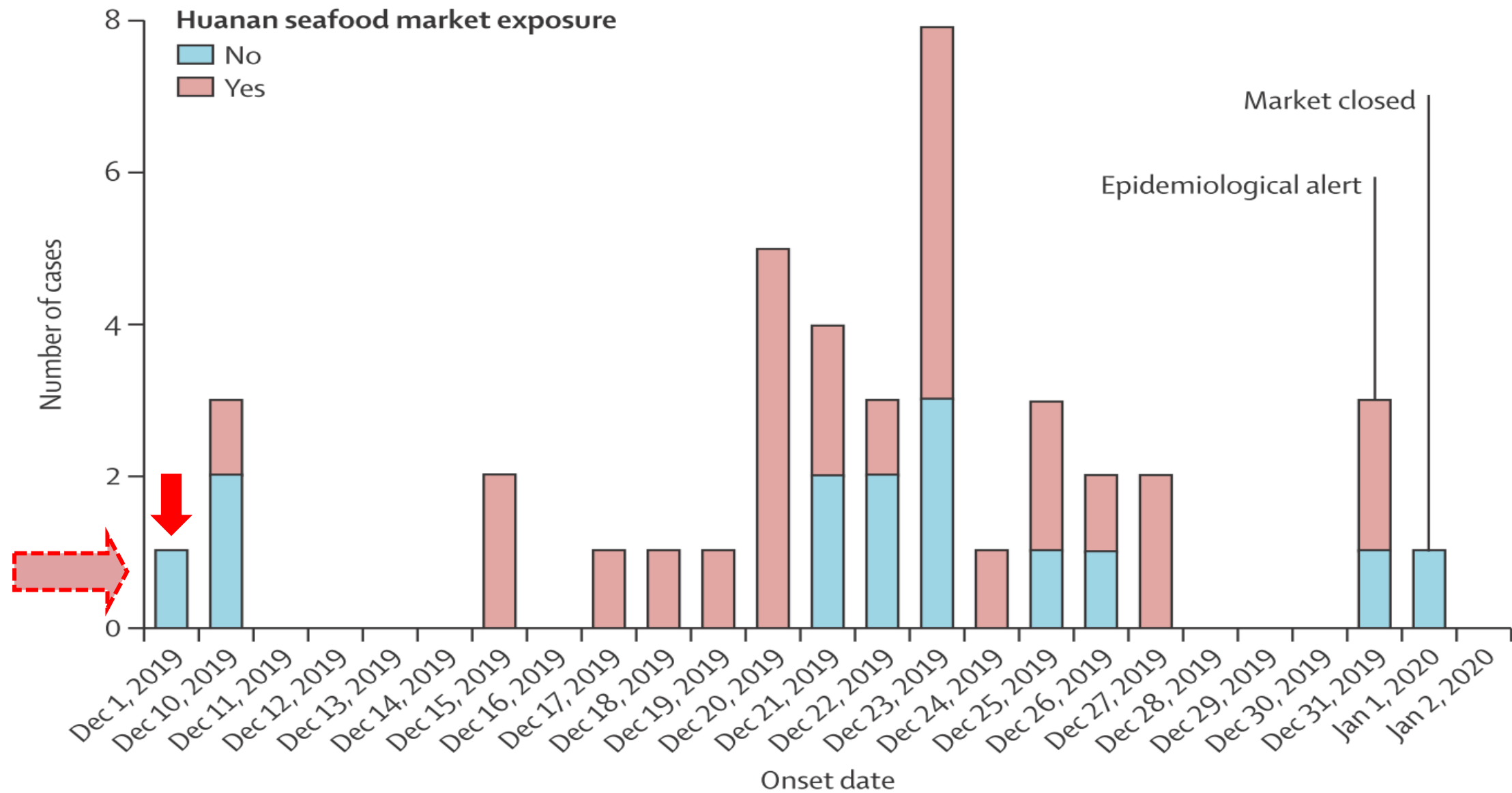
Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China

THE LANCET

- 41 2019-nCoV cases confirmed by RT-PCR and NGS
- 73% male, 32% with comorbidities
- Median age 49 years (IQR 41-58)
- 66% had seafood market exposure
- One family cluster
- illness onset to dyspnea 8 days, 10% 2nd infection
- 13 (**31.7%**) ICU care, **29% ARDS**, 24% NIV, 5% IMV, 5% ECMO
 - **6 (15%) died**

(41 cases, Jin Yintan Hospital, Wuhan, 01/02/2020)



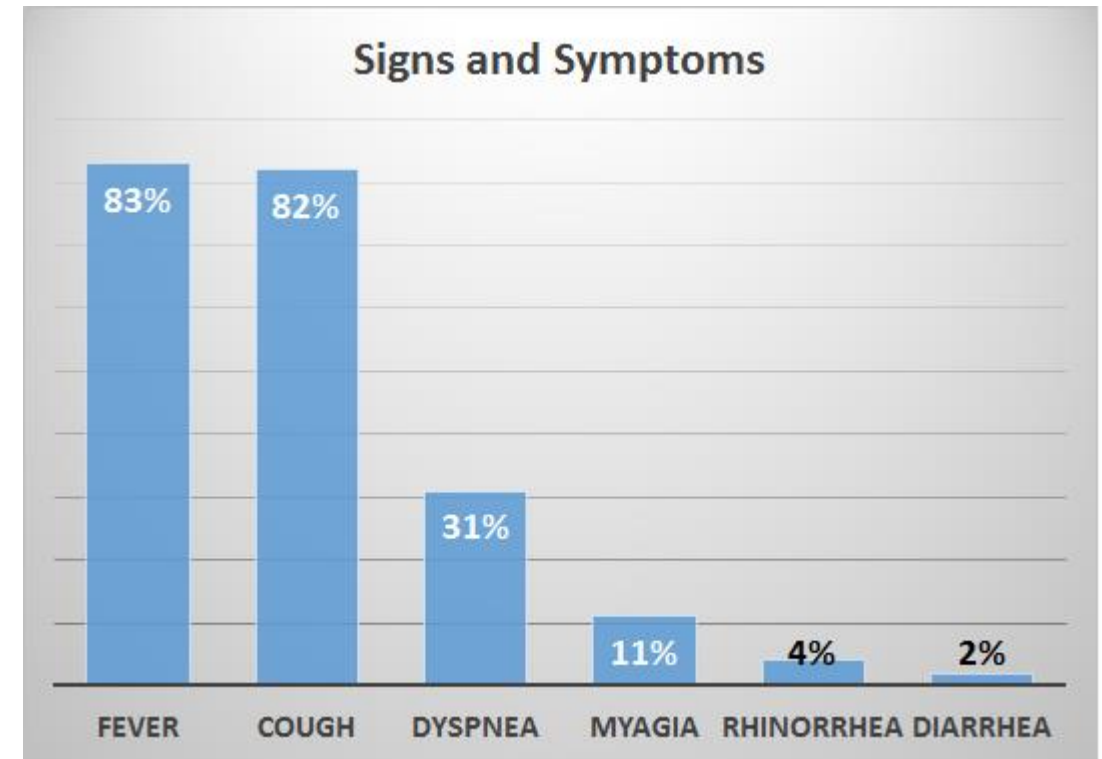
B

		All patients (n=41)	ICU care (n=13)	No ICU care (n=28)	p value
Signs and symptoms					
Fever		40 (98%)	13 (100%)	27 (96%)	0.68
Highest temperature, °C		..	22% <38°C	..	0.037
<37.3		1 (2%)	0	1 (4%)	..
37.3–38.0		8 (20%)	3 (23%)	5 (18%)	..
38.1–39.0	78%	18 (44%)	7 (54%)	11 (39%)	..
>39.0		14 (34%)	3 (23%)	11 (39%)	..
Cough	76%	31 (76%)	11 (85%)	20 (71%)	0.35
Myalgia or fatigue	44%	18 (44%)	7 (54%)	11 (39%)	0.38
Sputum production		11/39 (28%)	5 (38%)	6/26 (23%)	0.32
Headache		3/38 (8%)	0	3/25 (12%)	0.10
Haemoptysis		2/39 (5%)	1 (8%)	1/26 (4%)	0.46
Diarrhoea		1/38 (3%)	0	1/25 (4%)	0.66
Dyspnoea	55%	22/40 (55%)	12 (92%)	10/27 (37%)	0.0010

Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study (99 cases, 01/20/2020)

THE LANCET

- 99 2019-nCoV cases
- 68% male, 51% with comorbidities
- Median age 55 years (SD 13)
- 49% had seafood market exposure
- 23 (**23%**) ICU care, **17% ARDS**, 13% NIV, 4% IMV, 3% ECMO,
 - **11 (11%) died**

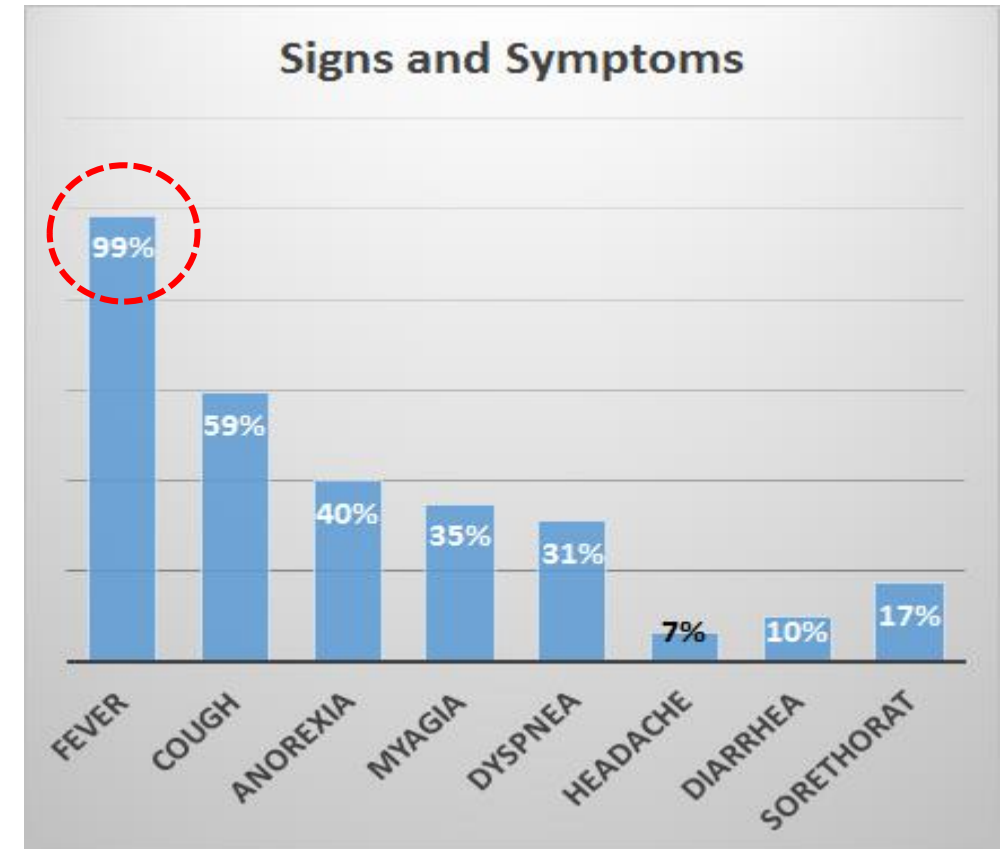


Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China

JAMA®

(138 cases, 01/28/2020, 武漢大學中南醫院)

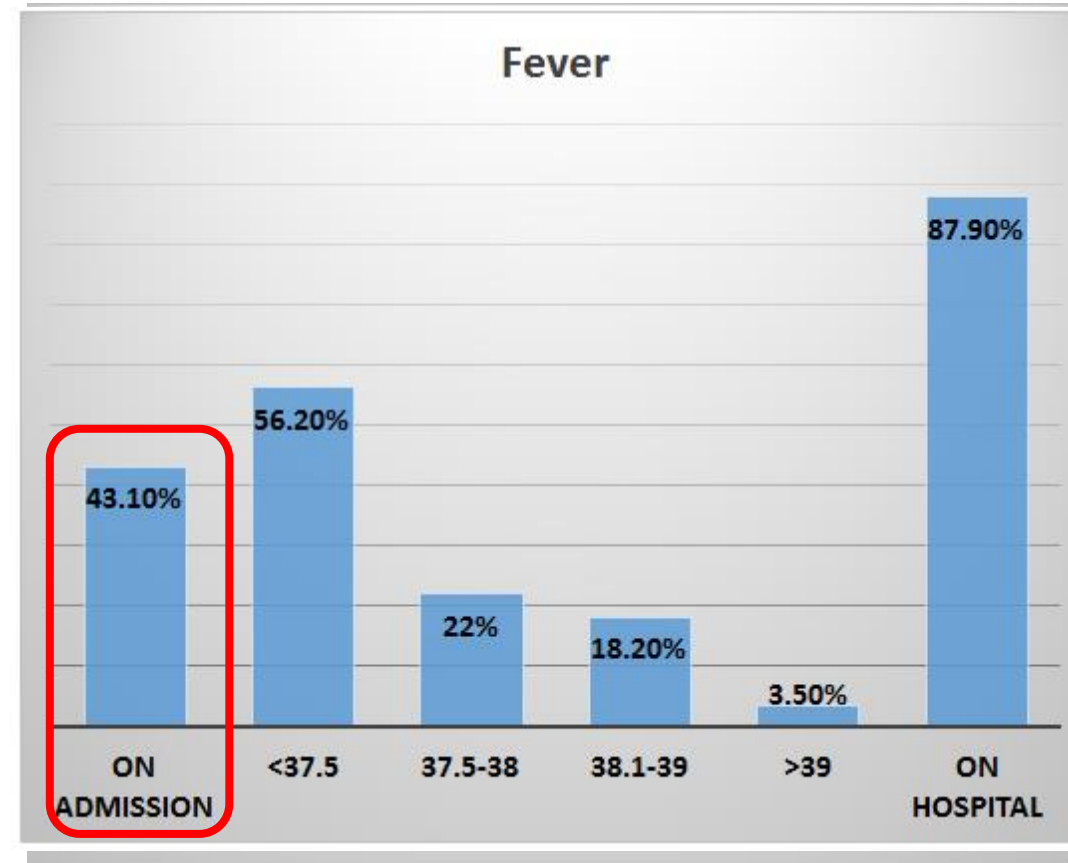
- 75% male, 46% with comorbidities (ICU vs. non-ICU 72% vs. 37%)
- Median age 56 years (IQR 42-68)
- Onset of symptom to dyspnea (5 days), ARDS (8 days)
- **Hospital-associated transmission:**
29% HCW, 12.3% hospitalized patients
- **8.7%** had seafood market exposure
- **26%** ICU care, **19.6% ARDS**, 12.3% IMV, 10.9% NIV, 2.9% ECMO,
 - **6 (4.3%) died**



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

Clinical characteristics of 2019 novel coronavirus infection in China (1099 cases, 01/29/2020)

- Multi-center case series study
- 1099 2019-nCoV cases from 552 hospitals
- 58.1% male, 23.2% with comorbidities
- Median age 47 years (IQR 42-68)
- **71.8%** had Wuhan contact history, **2% HCW**
- **Incubation time 3 days (0-24 days)**
- **5% ICU care**
 - **3.4% ARDS, 5.1% NIV, 2.2% IMV, 0.5% ECMO, 1.4% died**



Comparisons between 4 reports

	Huang et al.	Chen et al.	Wang et al.	Guan et al.
Case #	41	99	138	1099
Mean age	49	55	56	47
Male	73%	68%	75%	58.1%
Symptoms/signs				
Fever	98%	83%	99%	88%
Fever >38C	78%	?	?	59.2%
Cough	76%	82%	59%	68%
Dyspnea	55%	31%	31%	19%
Myalgia	44%	11%	35%	14.8%
Headache	8%	8%	7%	13.6%
Diarrhea	3%	2%	10%	3.7%
Sore throat	-	5%	17%	13.9%
ARDS	29%	17%	20%	3.4%
NIV	24%	13%	11%	5.1%
IMV	5%	4%	12%	2.2%
Mortality	15%	11%	4.3%	1.4%?



COVID-19 vs. MERS vs. SARS

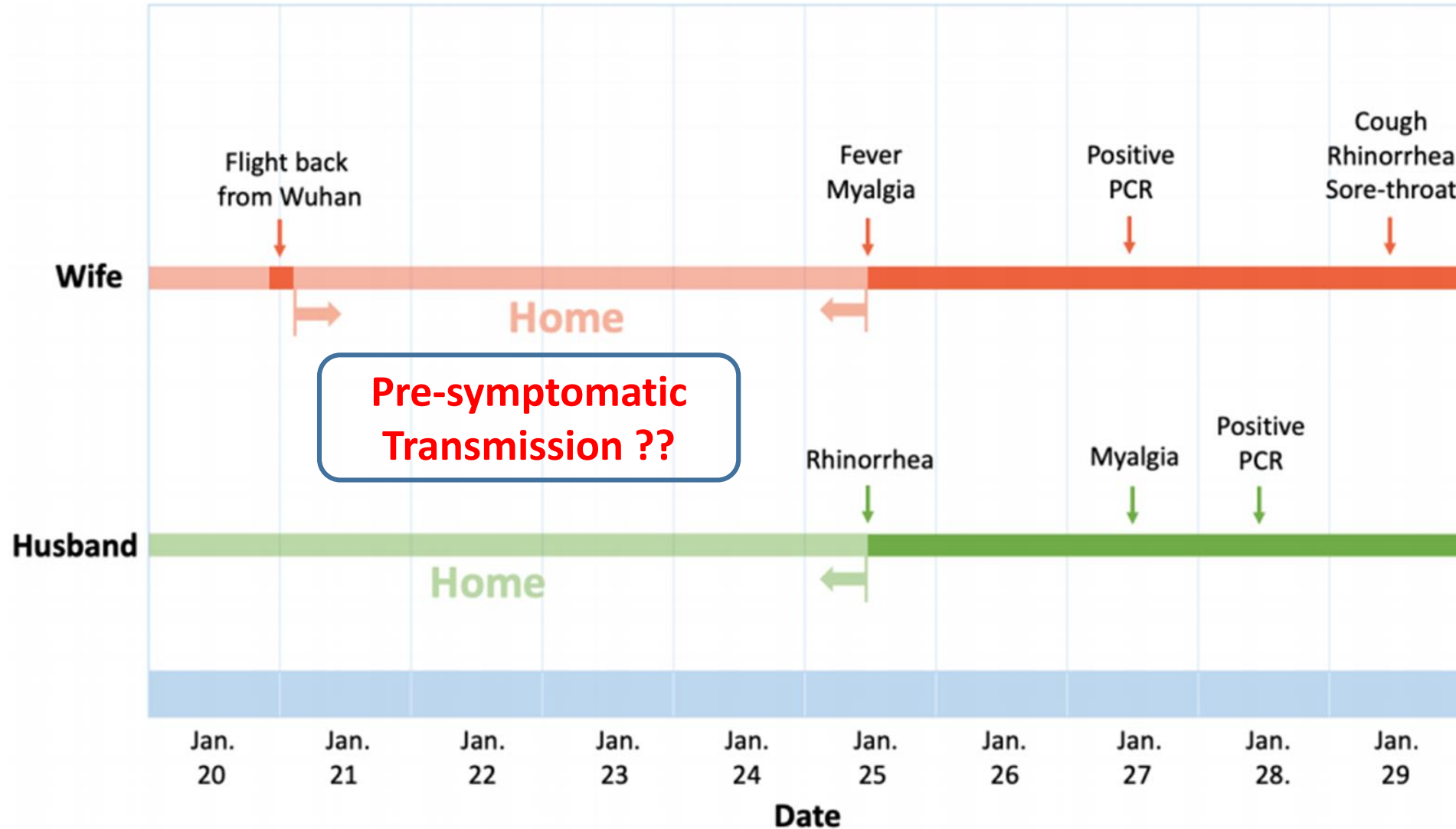
	SARS-CoV-2	MERS-CoV	SARS-CoV
Age (years)	47-56	56	39.9
Male	58-75%	76.70%	44%
Mortality[#]	2.3%	37%	10%
Ventilator support	6.1-12%	80%	14-20%
HCWs	2-29%	9.8%	23.1%
Symptoms			
Fever	83-98%	98%	99-100%
Dry cough	59-76%	47%	29-75%
Dyspnea	19-55%	72%	40-42%
Diarrhea	2-10%	26%	20-25%
Sore throat	5-17%	21%	13-25%

Data in China on 02/15/2020: mortality=1523/66492 (2.3%); severe cases=11053(16.6%).

A Locally Transmitted Case of SARS-CoV-2 Infection in Taiwan

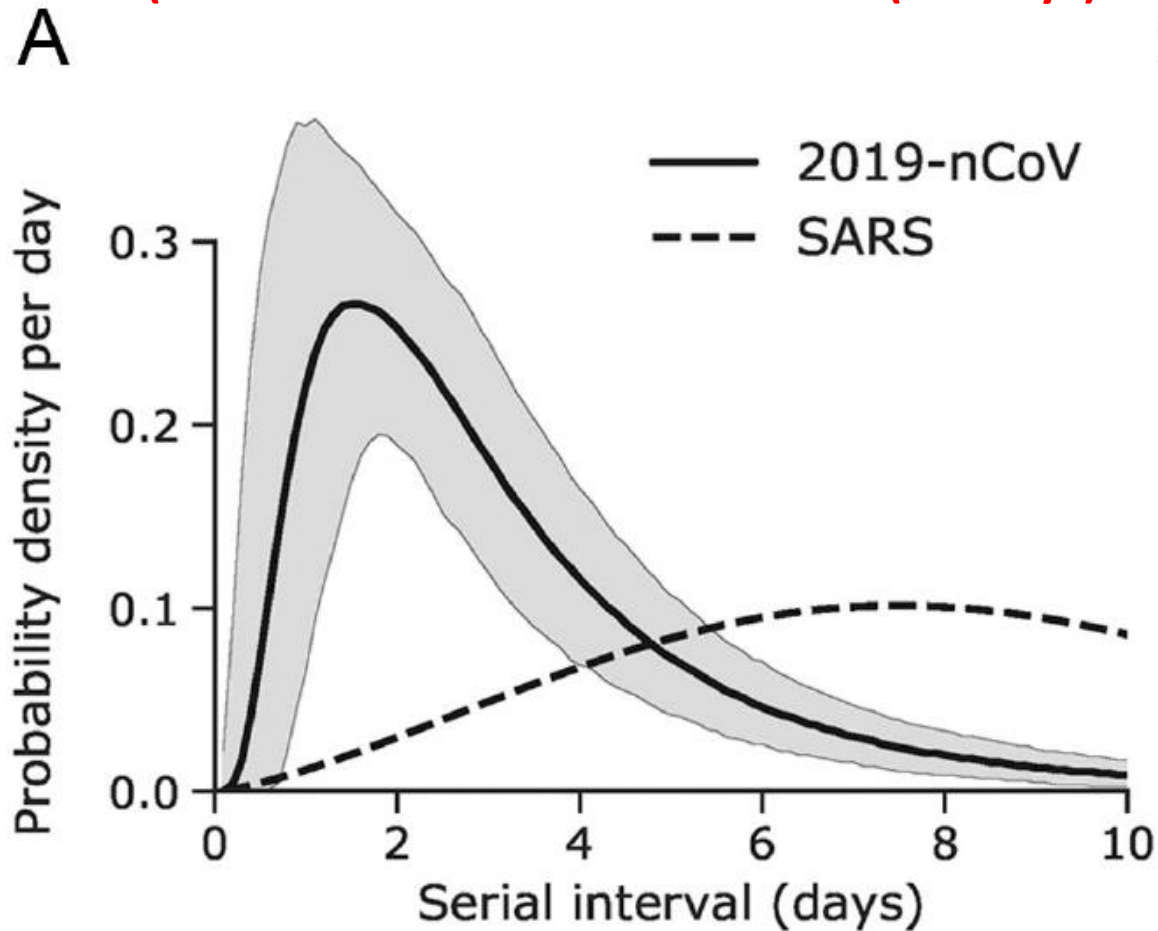


The NEW ENGLAND
JOURNAL of MEDICINE



Serial interval of 2019-nCoV infections

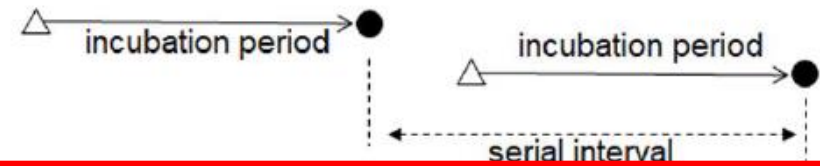
(Estimated median serial interval (2.6 days) shorter than the median incubation period (5.0 days))



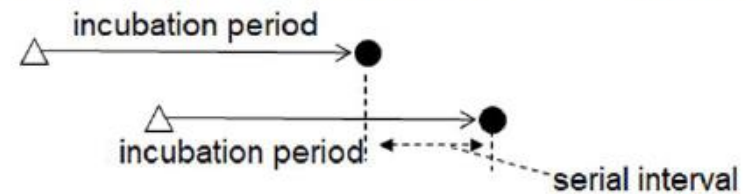
2.6 days

Incubation 5.0 days

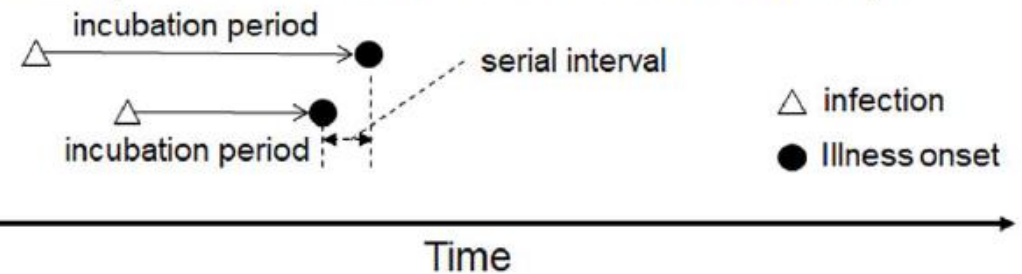
B Symptomatic transmission (incubation period \leq serial interval)



Pre-symptomatic transmission
(incubation period $>$ serial interval & serial interval $>$ 0)



Pre-symptomatic transmission
(incubation period $>$ serial interval & serial interval \leq 0)



medRxiv preprint doi:

<https://doi.org/10.1101/2020.02.03.20019497>

Laboratory and Radiographic Findings

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

THE LANCET

Patients (n=99)

Blood routine

Leucocytes ($\times 10^9$ per L; normal range 3.5–9.5)	7.5 (3.6)
Increased	Leukocytosis 24%
Decreased	9 (9%)
Neutrophils ($\times 10^9$ per L; normal range 1.8–6.3)	5.0 (3.3–8.1)
Increased	38 (38%)
Lymphocytes ($\times 10^9$ per L; normal range 1.1–3.2)	0.9 (0.5)
Decreased	Lymphopenia 35%
Platelets ($\times 10^9$ per L; normal range 125.0–350.0)	213.5 (79.1)
Increased	4 (4%)
Decreased	Thrombocytopenia 12%
Haemoglobin (g/L; normal range 130.0–175.0)	129.8 (14.8)
Decreased	Anemia 50%

Blood biochemistry

Alanine aminotransferase (U/L; normal range 9.0–50.0)	39.0 (22.0–53.0)
Increased	ALT↑ 28%
Aspartate aminotransferase (U/L; normal range 15.0–40.0)	34.0 (26.0–48.0)
Increased	AST↑ 35%
Total bilirubin ($\mu\text{mol/L}$; normal range 0.0–21.0)	15.1 (7.3)
Increased	T.bil↑ 18%
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	LDH↑ 76%

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%)

5% had Co-infection

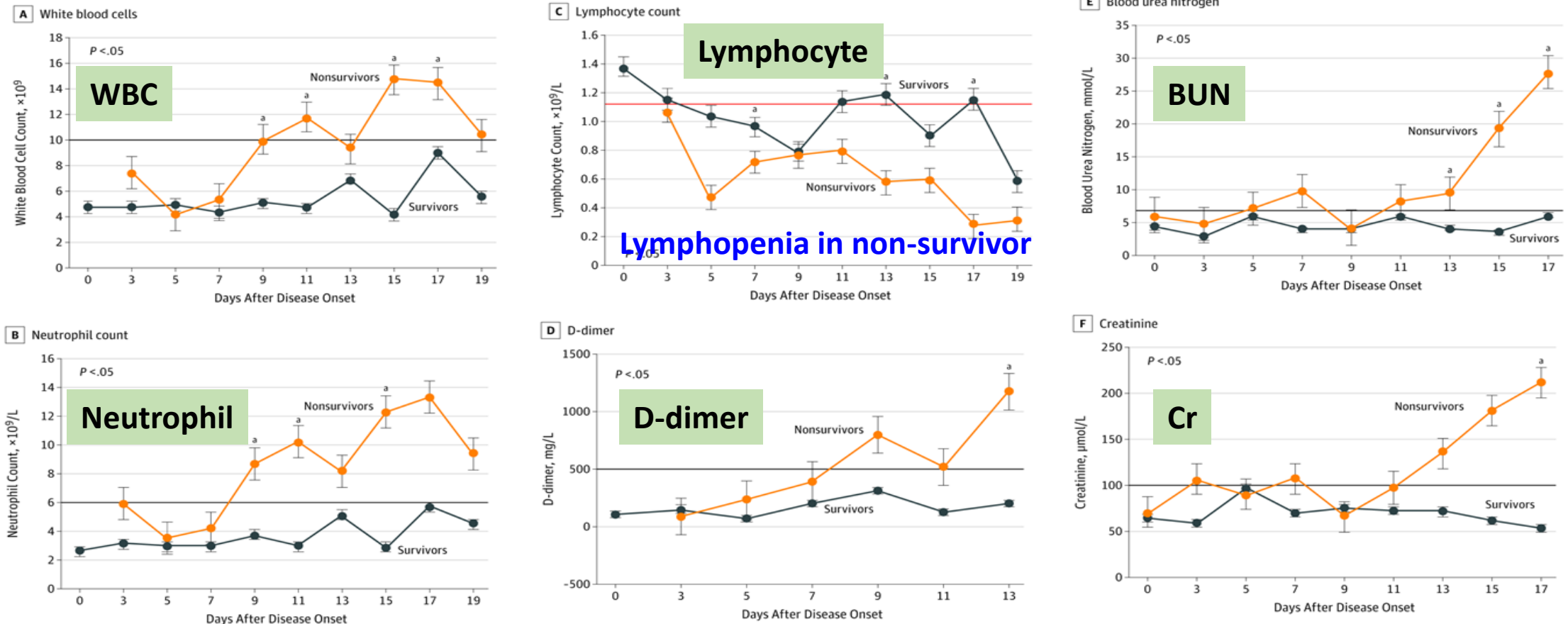
25% had unilateral lesion

14% had multiple GGO

Chen N, et al. The Lancet 2020

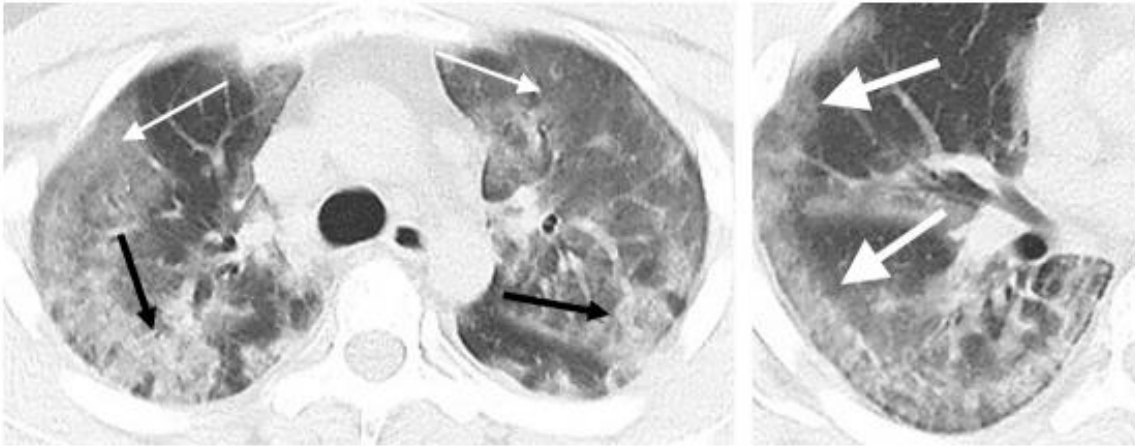
Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China

JAMA®



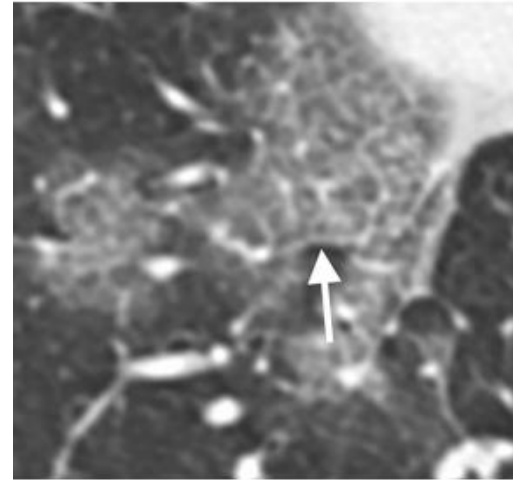
CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV)- Case Series

29 y/o male with fever and cough



GGO +consolidation
Peripheral distribution

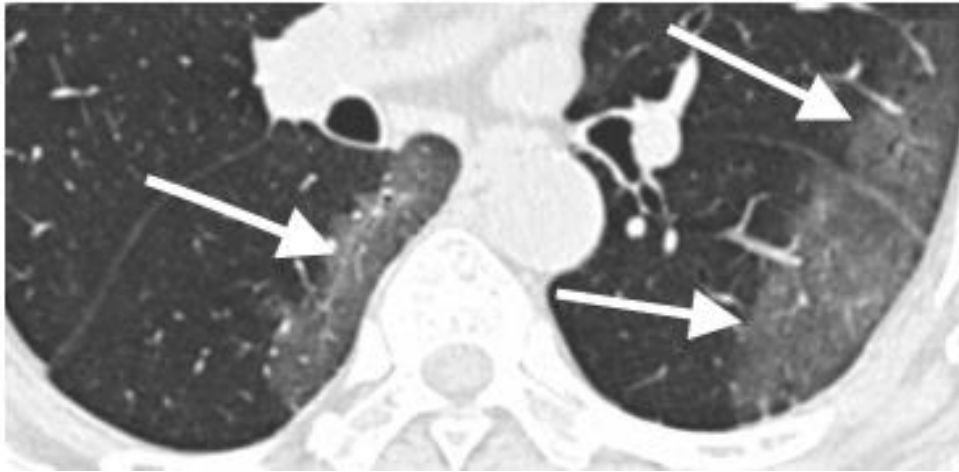
66 y/o male with fever and cough



Crazy-paving
Interlobular septal thickening

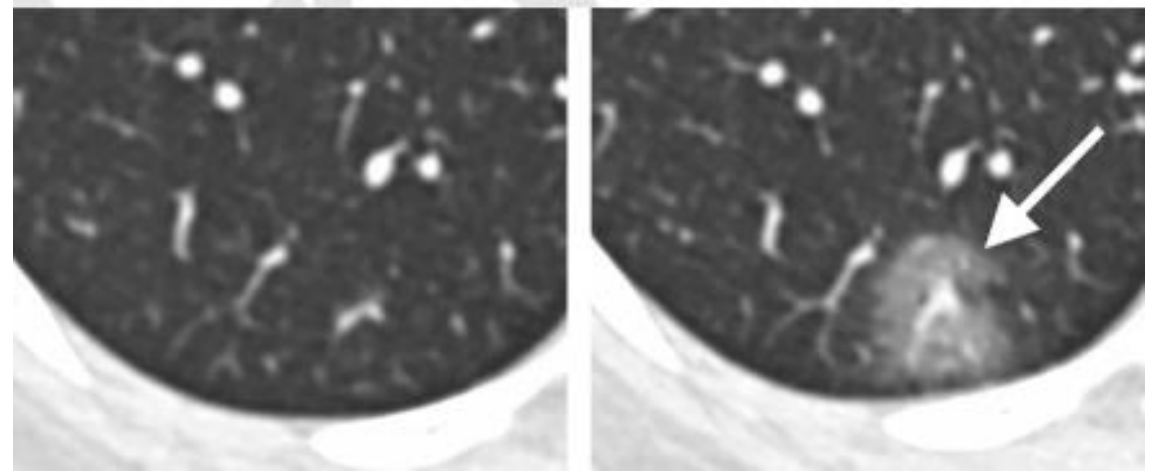
CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV)- Case Series

69 y/o male with fever and cough



Peripheral GGO

66 y/o male with fever and cough



Newly formed round GGO
3 days later

CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV)- Case Series

Ground-Glass Opacities and Consolidation	
Absence of Both Ground-Glass Opacities and Consolidation	3 (14)
Presence of Either Ground-Glass Opacities or Consolidation	18 (86)
Presence of Ground-Glass Opacities without Consolidation	12 (57)
Presence of Ground-Glass Opacities with Consolidation	6 (29)
Presence of Consolidation without Ground-Glass Opacities	0 (0)
Number of Lobes Affected	
0	3 (14)
1	1 (5)
2	2 (10)
3	3 (14)
4	4 (19)
5	8 (38)
More than 2 lobes affected	15 (71)
Bilateral Lung Disease	16 (76)

21 cases

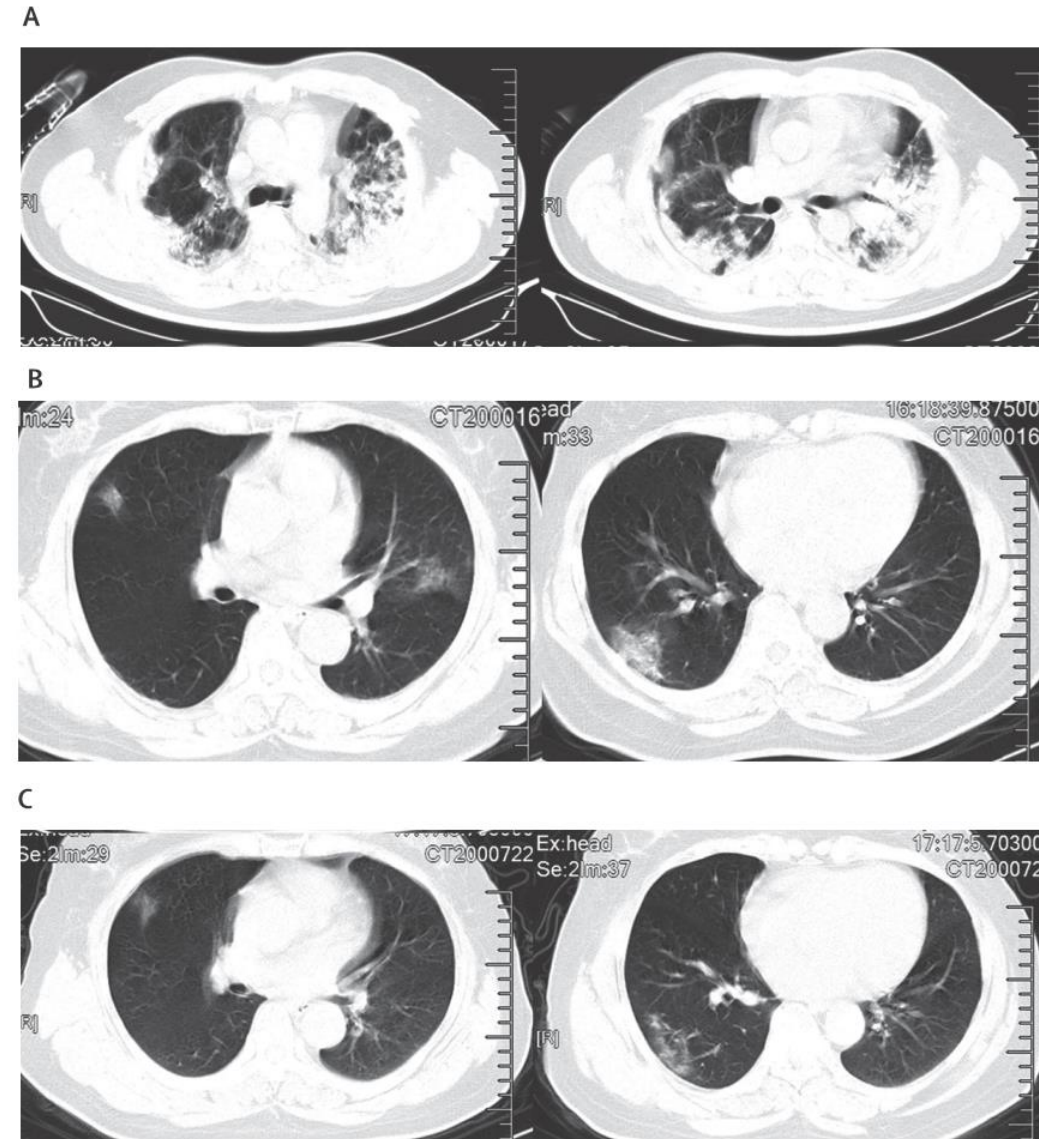
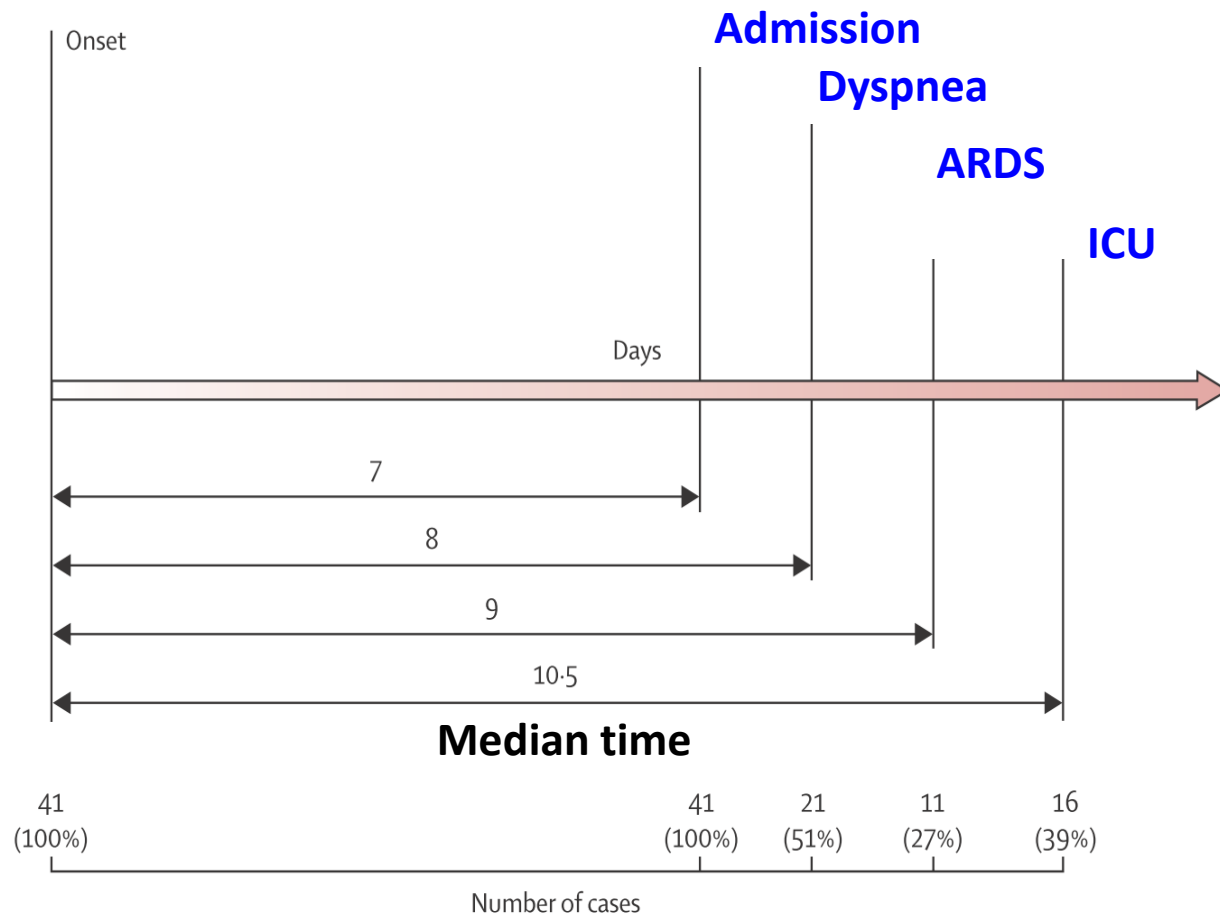
GGO: **86%**

GGO alone: **57%**

GGO +consolidation: **29%**

Consolidation alone: **0%**

Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China (41 cases, Mortality 15%)



98% had bilateral involvement

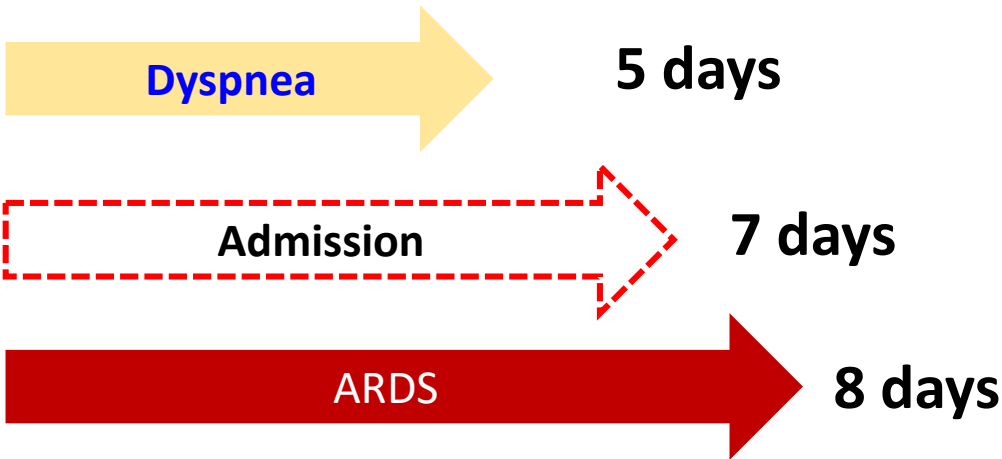
Lancet 2020; 395: 497–506

Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China



Mortality 4.3%

Time course



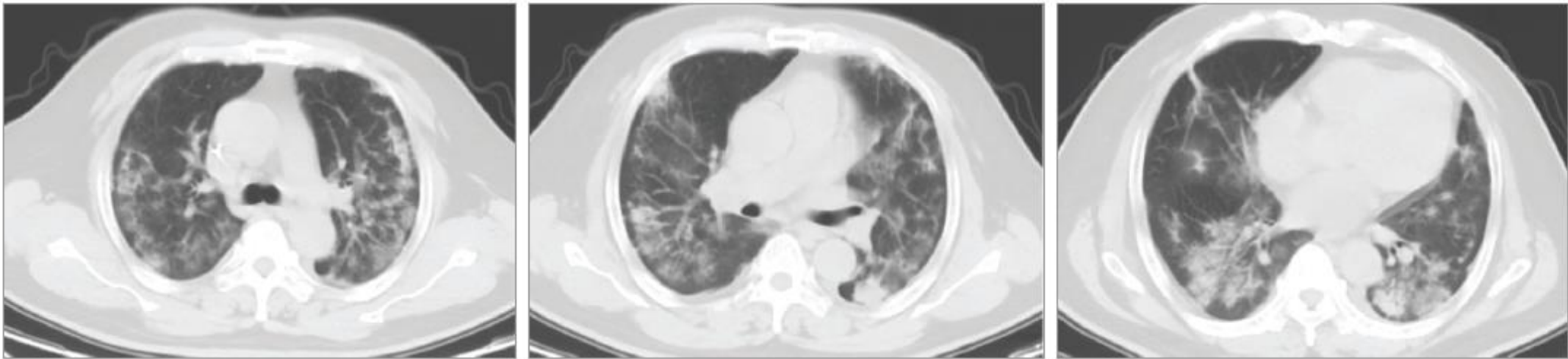
	Normal Range	Median (IQR) Total (N = 138)
White blood cell count, $\times 10^9/\text{L}$	3.5-9.5	4.5 (3.3-6.2)
Neutrophil count, $\times 10^9/\text{L}$	1.8-6.3	3.0 (2.0-4.9)
Lymphocyte count, $\times 10^9/\text{L}$	1.1-3.2	0.8 (0.6-1.1)
Prothrombin time, s	9.4-12.5	13.0 (12.3-13.7)
Activated partial thromboplastin time, s	25.1-36.5	31.4 (29.4-33.5)
Lactate dehydrogenase, U/L	125-243	261 (182-403)
Bilateral distribution of patchy shadows or ground glass opacity, No. (%)	NA	138 (100)

Figure 1. Chest Computed Tomographic Images of a 52-Year-Old Patient Infected With 2019 Novel Coronavirus (2019-nCoV)

A Computed tomography images on day 5 after symptom onset



B Computed tomography images after treatment on day 19 after symptom onset



A, Chest computed tomographic images obtained on January 7, 2020, show ground glass opacity in both lungs on day 5 after symptom onset. B, Images taken on January 21, 2020, show the absorption of bilateral ground glass

opacity after the treatment of extracorporeal membrane oxygenation from January 7 to 12 in the intensive care unit.

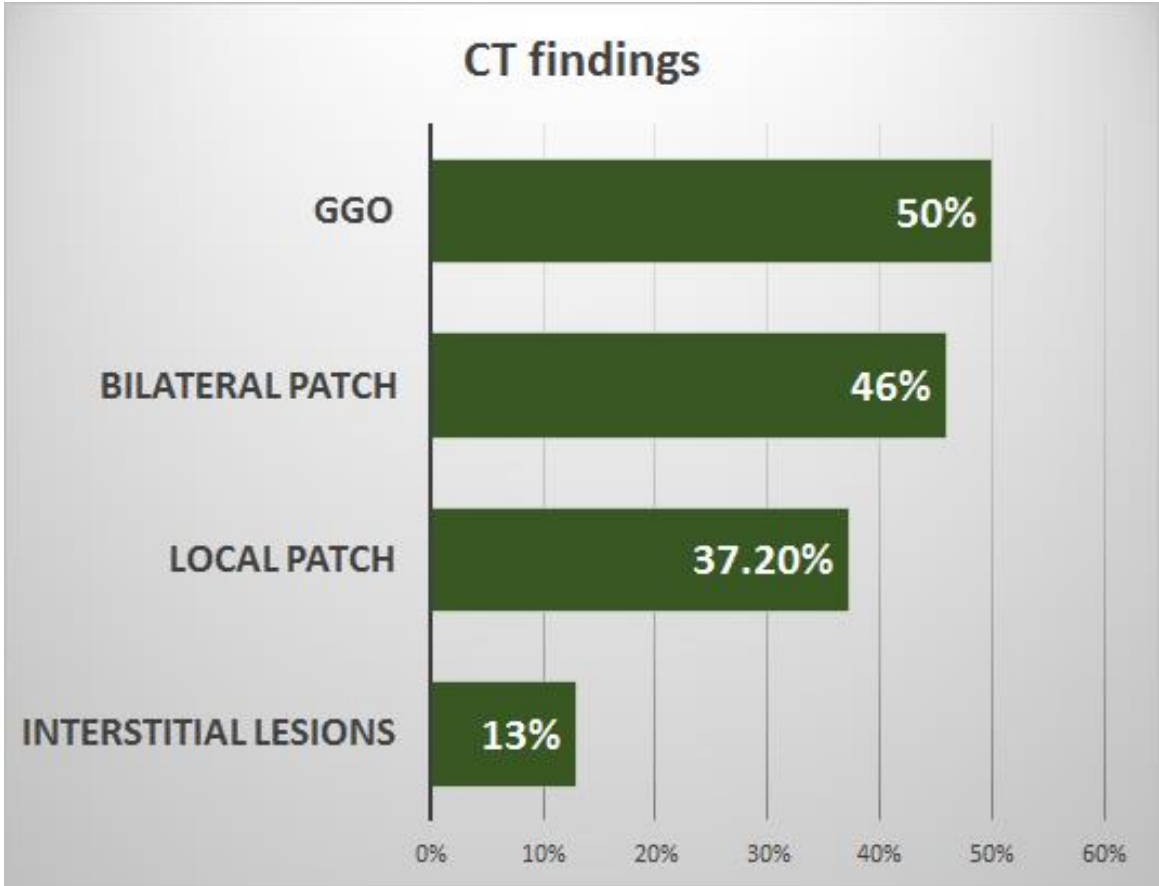
Wang D, et al. JAMA 2020

Clinical characteristics of 2019 novel coronavirus infection in China

1099 cases,
mortality 1.4%

81.2% Lymphopenia

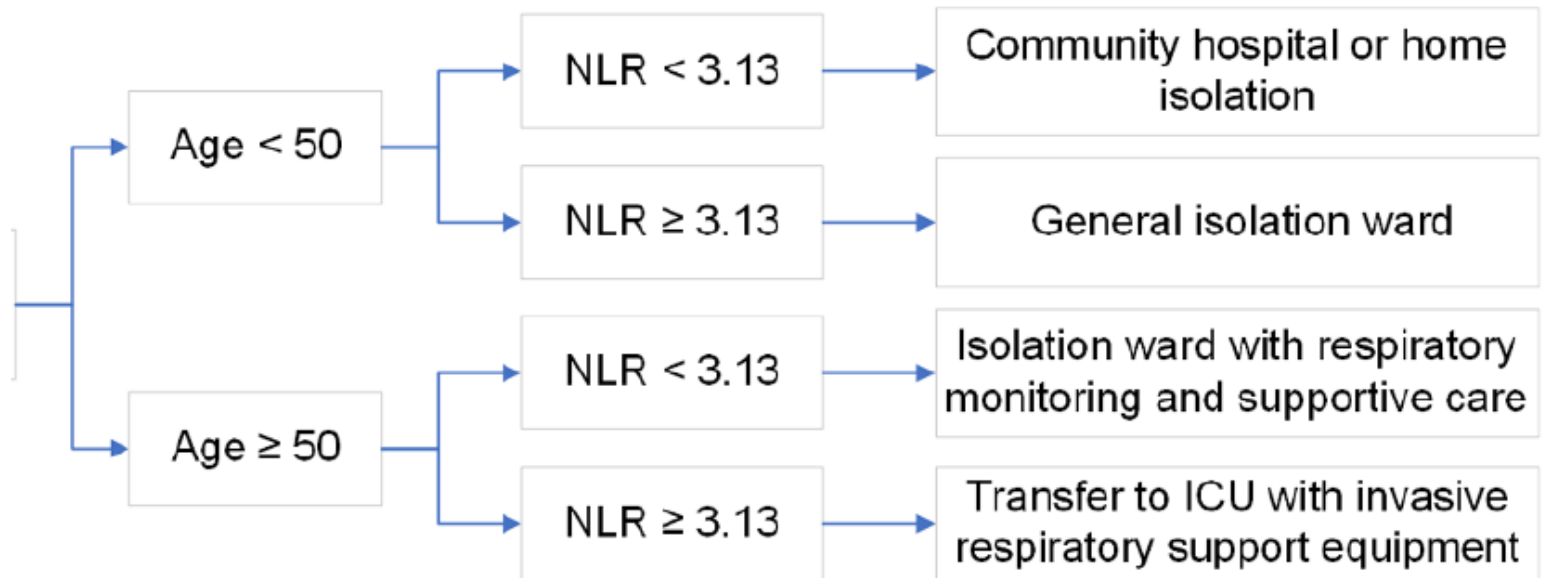
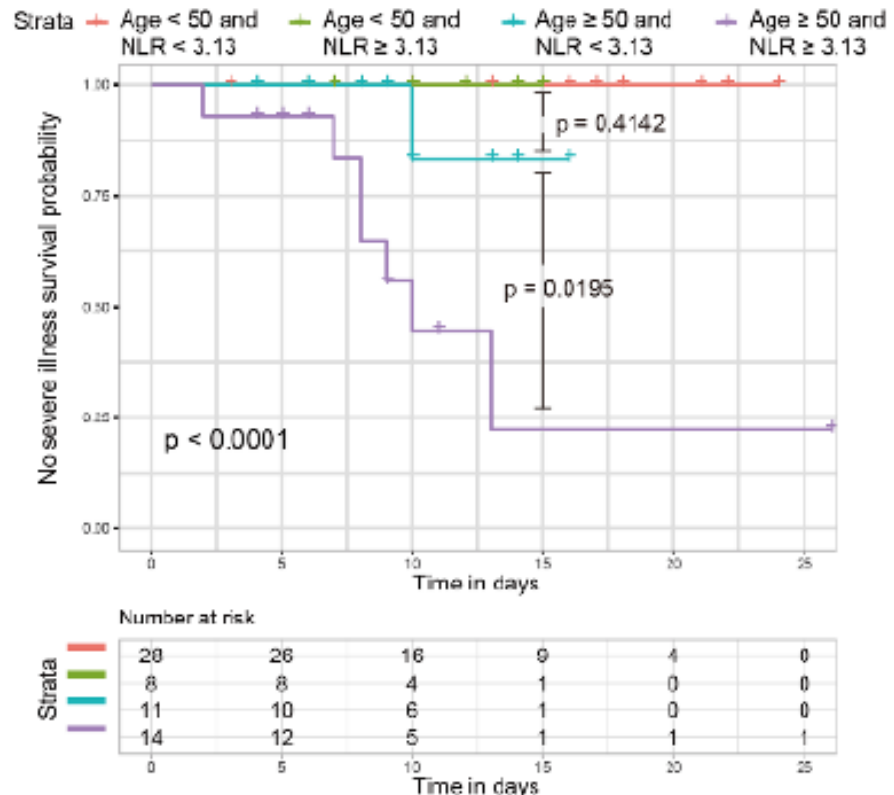
76.4% CT abnormal 14.7% CXR abnormal

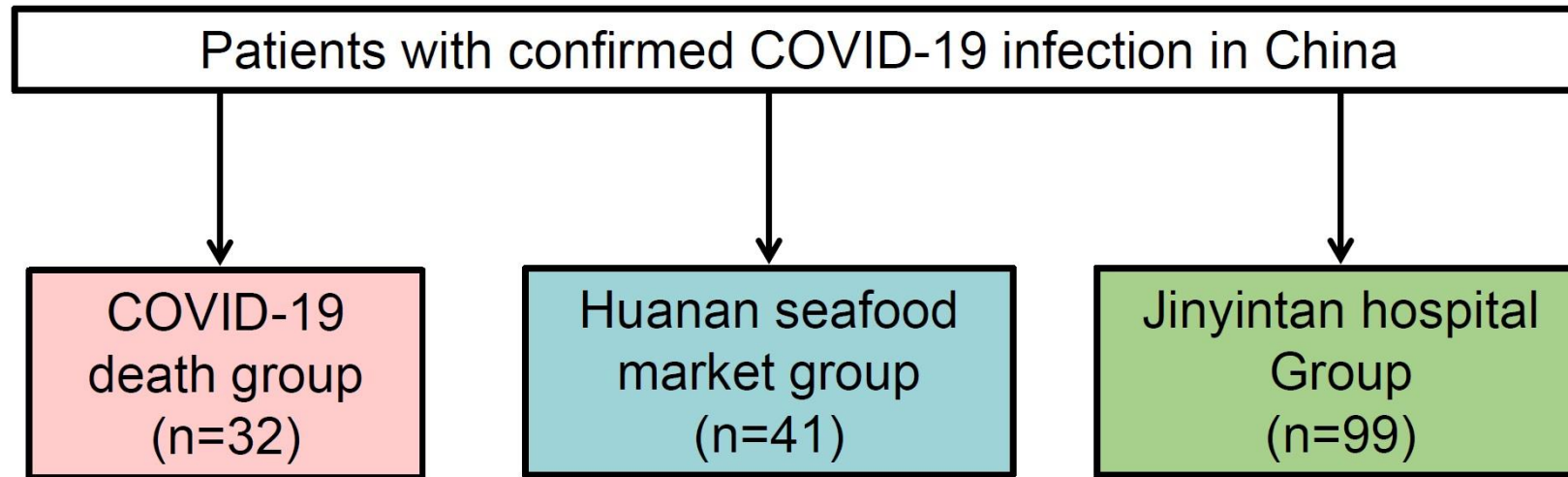


Risk factors for prognosis

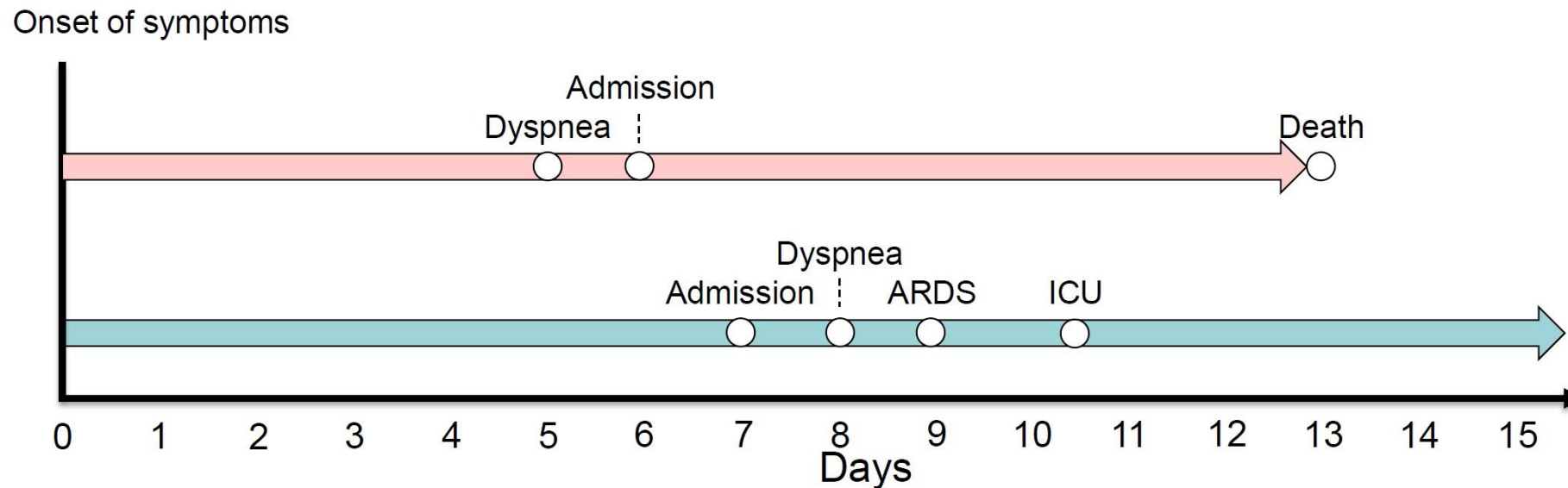
- **Neutrophil-to-Lymphocyte Ratio** Predicts Severe Illness Patients with 2019 Novel Coronavirus in the Early Stage (61 cases at Beijing Hospital)
- Patients with **age ≥ 50** and **NLR ≥ 3.13** facilitated severe illness, and they should rapidly access to **ICU**

C





Timeline of COVID-19 infection



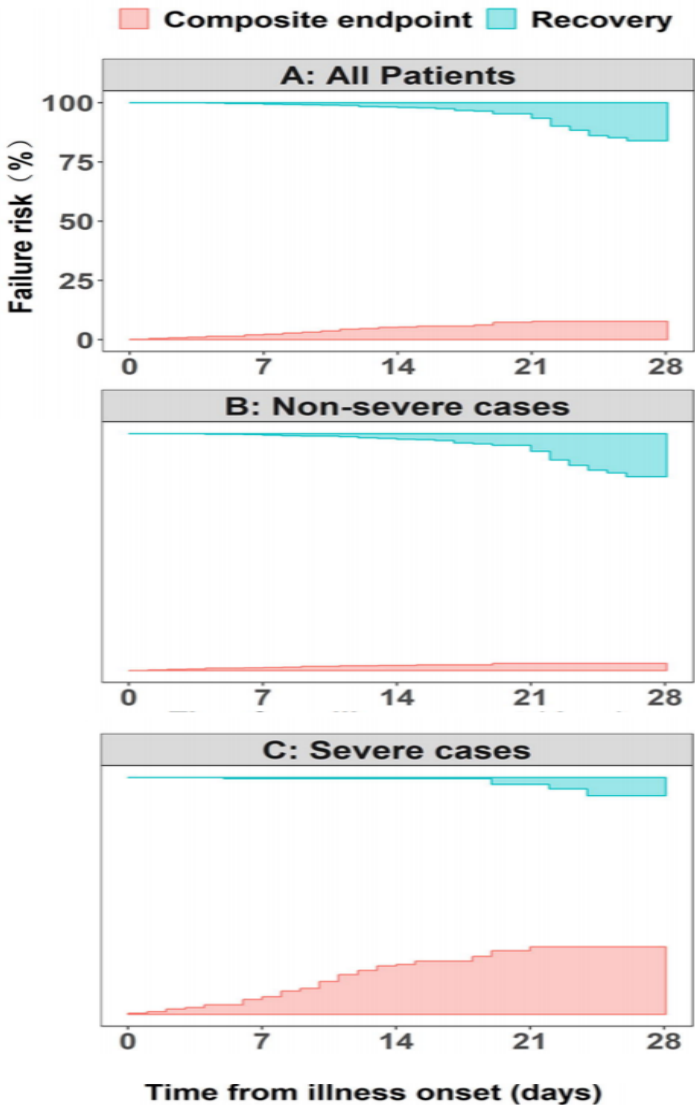
By courtesy of
Su VY, et al.
Unpublished
data

Clinical characteristics of 2019 novel coronavirus infection

Outcomes of 1,099 patients with COVID-19 (01/29/2020)

Characteristics	All patients	Disease severity			Composite endpoint		
		Non-severe (n=926)	Severe (n=173)	P value	Yes (n=67)	No (n=1032)	P value
Abnormalities on chest X-ray (%)	162/1099 (14.7)	12.5	26.6	<0.001	44.8	12.8	<0.001
Abnormalities on chest CT (%)	840/1099 (76.4)	73.7	91.3	<0.001	74.6	76.6	0.833
MV (NIV+IMV)— No., %	67/1099 (6.1)	0/926 (0.0)	67/173(38.7)	<0.001	40/67 (59.7)	27/1032 (2.6)	<0.001
ECMO	5/1099 (0.5)	0/926 (0.0)	5/173 (2.9)	<0.001	5/67 (7.5)	0/1032 (0.0)	<0.001
CRRT	9/1099 (0.8)	0/926 (0.0)	9/173 (5.2)	<0.001	8/67 (11.9)	1/1032 (0.1)	<0.001
Discharge from hospital	55/1099(5.0)	50/926(5.4)	5/173 (2.9)	0.230	1/67(1.5)	54/1032 (5.2)	0.249
Death	15/1099 (1.4)	1/926 (0.1)	14/173 (8.1)	<0.001	15/67 (22.4)	0/1032 (0.0)	<0.001
Recovered	9/1099 (0.8)	7/926 (0.8)	2/173 (1.2)	0.639	0/67 (0.0)	9/1032 (0.9)	1.000
Staying in hospital	1029/1099 (93.6)	875/926 (94.5)	154/173 (89.0)	0.011	51/67 (76.1)	978/1032 (94.8)	<0.001

Clinical characteristics of COVID-19 infection in China (1099 cases)



Composite endpoint: ICU admission/MV/death

Level	SDHR	P value
>65 v.s. ≤65	2.146	0.023
Female v.s. Male	1.061	0.860
Severe v.s. Non-severe	11.119	<0.001
Current-smokers v.s. non-smokers	0.648	0.290
Ever-Smokers v.s. non-smokers	1.323	0.590
Any underlying disease Yes v.s. No	1.312	0.470
ALT(U/L) or AST(U/L) >40 v.s. ≤40	1.569	0.180
Blood leukocytes (*10 ⁹ /L) >4 v.s. ≤4	3.985	0.008
Blood lymphocytes (*10 ⁹ /L) >1.5 v.s. ≤1.5	0.981	0.970
Ground-glass opacity on chest X-ray Yes v.s. No	0.415	0.140
Local patchy shadowing on chest X-ray Yes v.s. No	1.722	0.250
Diffuse patchy shadowing on chest X-ray Yes v.s. No	2.030	0.048
Interstitial on chest X-ray on admission Yes v.s. No	3.297	0.005
Interstitial abnormality on chest CT Yes v.s. No	0.552	0.170

0.5 4.5 8.5 12.5

**Epidemiological
and clinical
features of the
2019 novel
coronavirus
outbreak in
China
(4021 cases,
01/26/2020)**

Yang Yang, et al.
medRxiv 2020

Table 1. Estimates for adjusted case fatality rate (CFR) among 2019-nCoV patients, stratified by case type and baseline characteristics.				
Case type	Missing severity classified as mild	No. of cases	No. of deaths (Observed CFR, %)	CFR, % (95% CI)
Confirmed patients	4021 cases			
Gender				
Male	★	2213	44 (1.99)	4.45 (2.81, 6.93)
Female		1808	14 (0.77)	1.25 (0.43, 3.29)
Age Group				
<60 y		2969	15 (0.51)	1.43 (0.61, 3.15)
≥60 y	★	1052	43 (4.09)	5.30 (3.25, 8.46)
Severity				
Severe	★	927	47 (5.07)	6.23 (3.87, 9.79)
Mild	Yes	3094	11 (0.36)	1.16 (0.47, 2.69)
	No	2727	3 (0.11)	0.68 (0.13, 3.07)
Time from onset to diagnosis				
≤5 days ^{\$}		2054	18 (0.88)	1.34 (0.35, 5.12)
>5 days	★	1967	40 (2.03)	3.07 (2.02, 4.60)
Overall		4021	58 (1.44)	3.06 (2.02, 4.59)

Summary (clinical characteristic)

- The incubation period is estimated at ~5 days (95% CI, 4 to 7 days).
- **Fever (83–98%), cough (46%–82%),** myalgia or fatigue (11–44%), and SOB (31%) at illness onset.
- Fever may be prolonged and intermittent.
- **Asymptomatic infection** has been described.
- 1/3 to 1/2 of patients had **underlying medical comorbidities**.
- The most common laboratory abnormalities among patients with pneumonia on admission included leukopenia (9–25%), leukocytosis (24–30%), **lymphopenia (63%),** and elevated ALT and AST (37%).
- Most patients had normal serum levels of procalcitonin on admission.
- CT images shown **bilateral** multiple areas of consolidation and ground glass opacities are typical findings

Summary (disease process)

- Reports suggest the potential for clinical deterioration during the second week of illness.
- ICU patients were older (median age 66 years), and more underlying co-morbid conditions (72%).
- Between 23–32% of hospitalized pneumonia patients required ICU care.
- ARDS developed in 17–29% of hospitalized patients, and secondary infection in 10%.
- In ICU, 11% received HFNO, 42% NIV, and 47% IMV (4-10% in hospital). (ECMO, 3–7.5%)
- Among hospitalized patients with pneumonia, the Mortality has been reported as 4–15%. (risk factors: age>65, severe dx, delay diagnosis)
- ✓ However, because many infected persons have not yet recovered and may still die, the mortality rate and severity could be underestimated.