

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. DOI: 10.1056/NEJMoa2002032

## Supplementary appendix

### Clinical characteristics of coronavirus disease 2019 in China

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#### **Methods**

##### ***Definitions of exposure and clinical complications***

\*\* In our study, exposure to wildlife denoted that a person in close contact with wildlife animals (bats, snakes, civet cats, etc.) or visiting either a wildlife retailer or a market selling wildlife within two weeks before the onset of respiratory symptoms. The cases with regular visit to the market without recalling the exposure date were, however, not considered as having definite exposure to the wildlife [E1].

\*\* Pneumonia was diagnosed as an acute respiratory disorder characterized by the presence of cough and at least one of the new-onset focal chest signs, fever for more than 4 days or dyspnoea/tachypnoea [E2].

\*\* Shock and acute respiratory distress syndrome (ARDS) were defined in accordance with the WHO interim guidance [E3].

\*\* Acute kidney injury was defined based on the highest serum creatinine level and urine output [E4]. Specifically, the diagnosis could be made based on any of the following criterion: an increase in serum creatinine levels by 0.3 mg/dl or greater (26.5  $\mu$ mol/l or greater) within 48 hours; or increase in serum creatinine levels to 1.5 times of the baseline level or greater, which was known or presumed to have occurred within 7 days; or urine volume of below 0.5 ml/kg/h for 6 consecutive hours.

\*\* The diagnosis of secondary bacterial or fungal infection was made in case of the occurrence of hospital-acquired pneumonia or bacteremia, plus a positive result of new pathogen culture from the blood and lower respiratory tract specimen (including sputum, bronchoalveolar lavage fluid or tracheal aspirate) obtained at least 8 hours after admission [E5].

\*\* Acute heart failure was defined as the clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality [E6].

\*\* Rhabdomyolysis was diagnosed if the muscle pain or muscle weakness took place on admission and the creatine kinase level was greater than 10 times the upper limit of normal [E7].

##### ***Assessment of exposure***

In this study, the history of contact with wildlife was documented through self-report by the patients. Among the patients who lived outside Wuhan, the absolute count and percentage of patients who were residents of Wuhan, patients who had a recent travel to Wuhan and patients who had a contact with people from Wuhan were reported, respectively. A recent travel to, nor contacted with people

from, Wuhan was inquired among the patients living outside of Wuhan.

### **Laboratory testing**

Laboratory confirmation of SARS-CoV-2 was achieved through the Chinese Center for Disease Prevention and Control (CDC) before January 23<sup>rd</sup>. Since January 24<sup>th</sup>, the National Health Commission has officially approved for confirmation of diagnosis in certified tertiary hospitals across all provinces/autonomous regions/provincial municipalities.

The uniform laboratory testing procedures were adopted across all provinces/autonomous regions/provincial municipalities in China.

The reverse-transcription polymerase chain reaction (RT-PCR) assay was conducted in accordance with the protocol established by the World Health Organization. Extraction of nucleic acids from the respiratory samples was performed with the commercialized nucleic acid extraction kits. The extracted nucleic acids were tested for SARS-CoV-2.

The following sequences of SARS-CoV-2 were adopted for the RT-PCR assays. For Open reading frame 1 ab fragment, the forward primer sequence was 5'-CCCTGTGGGTTTACACTTAA-3', the reverse primer sequence was 5'-ACGATTGTGCATCAGCTGA-3', and probe sequence was 5'-FAM-CCGTCTGCGGTATGTGGAAAGGTTATGG-BHQ1-3'.

For the N region of the viral sequence, the forward primer sequence was 5'-GGGGAAGTTCTCCTGCTAGAAT-3', the reverse primer sequence was 5'-CAGACATTTGCTCTCAAGCTG-3', and the probe sequence was 5'-FAM-TTGCTGCTGCTTGACAGATT-TAMRA-3'.

Amplifications were initially done at 50°C for 10 min and subsequently at 95°C for 5 min, followed by 40 cycles of 95°C for 10 s and 55°C for 40 s.

The cycle threshold (Ct) of 40 or greater denoted negative findings, whereas the Ct of less than 37 denoted the SARS-CoV-2 being detected. A Ct of greater than 37 but lower than 40 was considered susceptible value, and should be subject to re-testing. SARS-CoV-2 was reported as having been detected if the repeated Ct-value was less than 40 and an obvious peak was observed, or if the repeated Ct-value was less than 37.

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## Results

### Tables

**Table S1. Clinical characteristics of the four patients whose stool specimens tested positive to SARS-CoV-2**

Patient No.	Sex	Age (yrs)	Severity	Diarrhea	Mechanical ventilation	ECMO
1	Male	66	Severe	Yes	No	Yes
2	Male	51	Severe	No	No	No
3	Female	18	Non-severe	No	No	No
4	Female	25	Non-severe	No	No	No

Abbreviation: ECMO, extracorporeal membrane oxygenation; SARS-CoV-2: severe acute respiratory syndrome coronavirus-2

**Table S2. Clinical characteristics of the four patients whose rectal swab specimens tested positive to SARS-CoV-2**

Patient No.	Sex	Age (yrs)	No. of days since onset	No. of days since hospitalization	2019-nCoV nucleic acids detected
1	Male	77	22	16	Pharyngeal swab (+), esophageal biopsy (+), gastric mucosa (+), rectal mucosa (+), duodenal mucosa (+)
2	Female	75	20	16	Pharyngeal swab switching from (+) to (-)
3	Male	60	13	8	Pharyngeal swab (+), esophageal biopsy (+), gastric mucosa (+), rectal mucosa (+), duodenal mucosa (+)
4	Male	44	9	8	Pharyngeal swab (+), urine (+)

Abbreviation: SARS-CoV-2 severe acute respiratory syndrome coronavirus-2

**Table S3. Summary characteristics of SARS-CoV-2, SARS-CoV, MERS-CoV and seasonal influenza**

Clinical characteristics	SARS-CoV-2	SARS-CoV	MERS-CoV	Seasonal influenza*
<b>Location</b>	Wuhan, China	Guangdong, China	Jeddah, Saudi Arabia	Worldwide
<b>Median and range of incubation period (days)</b>	4.0 (IQR: 2.0-7.0)	4.6 (2.0-14.0)	5.2 (2.0-13.0)	2.0 (1.0-7.0)
<b>Age (yrs)</b>	Mean: 47.0	Mean: 39.9	Median: 50	Mean: 23.4
<b>Adults (%)</b>	98.0	93.0	98.0	73.0
<b>Sex ratio (male: female)</b>	58.1%:41.9%	43.0%:57.0%	64.5%:35.5%	53.8%:46.2%
<b>Basic reproductive number</b>	2.2-2.68	2.0-3.0	<1.0	1.5
<b>Healthcare workers (%)</b>	3.6	23	9.8	NA
<b>Fever (%)</b>	83-98	99-100	98	36-100
<b>Cough (%)</b>	76-82	62-100	83	40-100
<b>Shortness of breath (%)</b>	31-55	40-42	72	7-100
<b>Diarrhea (%)</b>	2-3	20-25	26	4-25
<b>Any comorbidity (%)</b>	33	10-30	76	7.2-61
<b>Any chest radiograph abnormality (%)</b>	76.4	94-100	90-100	5.1-7.3
<b>Leukopenia (%)</b>	5-9	25-35	14	21
<b>Lymphopenia (%)</b>	35-63	68-85	32	68
<b>Thrombocytopenia (%)</b>	5-12	40-45	36	NA
<b>Abnormal liver function (%)</b>	5-37	20-30	11-14	8.8-10.1
<b>Needing mechanical ventilatory support (%)</b>	17-24	14-20	80.0	NA
<b>Time from onset of symptoms to ventilatory support (days)</b>	Mean: 9.3	Mean: 11.0	Median: 7.0	NA
<b>Time from onset of symptoms to death (days)</b>	Mean: 15.4	Mean: 23.7	Median: 11.5	NA
<b>Overall case-fatality rate (%)</b>	1.4-2.1	9.6	40.0	1.0-23.0 per 100,000
<b>Case-fatality rate with comorbidities (%)</b>	73.3	46.0	60.0	NA
<b>Factors associated with severe disease or death</b>	Greater disease severity, older age	Old age, males, high lactate dehydrogenase levels, high neutrophil count, comorbidities, lymphopenia	Immunocompromised, comorbidities, infection, low albumin, age >65 years	Increased age, pregnancy, Immunocompromised state, comorbidity, metabolic disorder

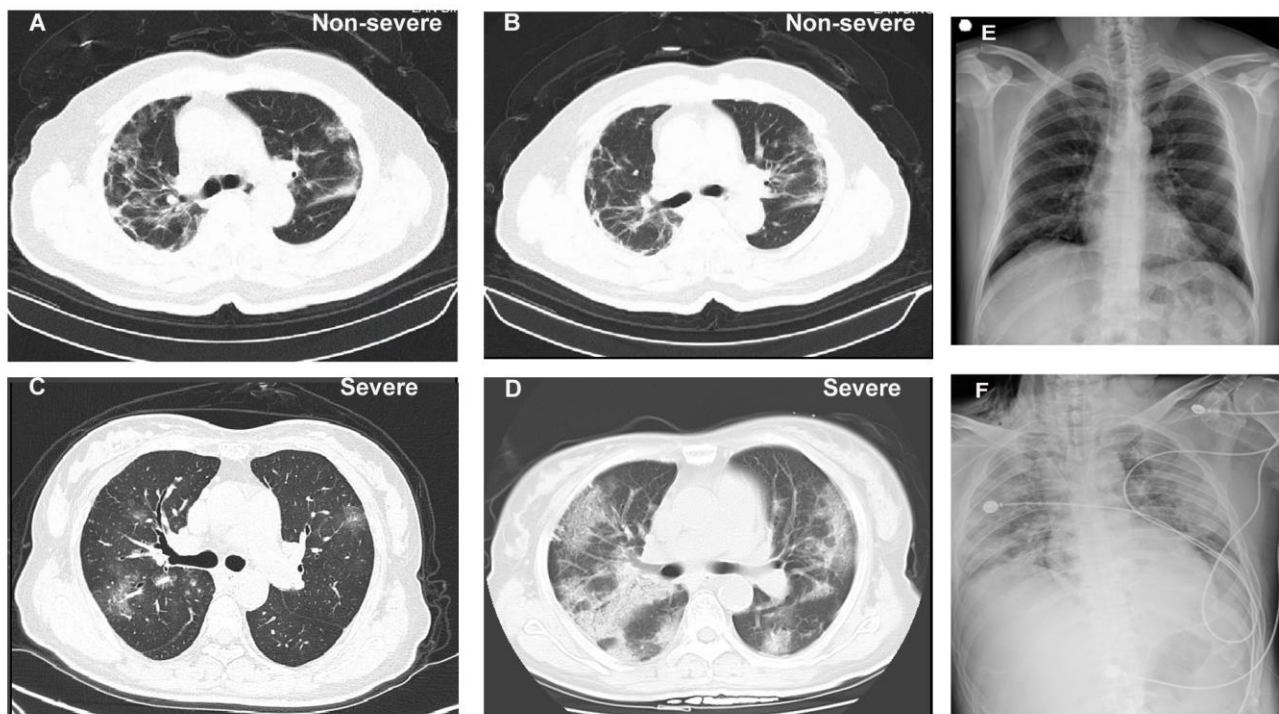
Data shown in the table above are derived from the reference **E1, E5, E8-E17**.

\* H1N1 infection after the year 2009 represented the seasonal influenza in this study.

Abbreviations: SARS-CoV, severe acute respiratory syndrome coronavirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; MERS-CoV, Middle East respiratory syndrome coronavirus, IQR: interquartile range; 95% CI: 95% confidence interval, NA: not applicable.

## Figure legends

**Figure S1. Representative chest radiographic manifestations in a non-severe and a severe case with COVID-19**



Transverse chest computed tomography imaging from a 50-year-old male with non-severe COVID-19, at 8 days after hospital admission (Panel A) and at 15 days after hospital admission (following the receipt of supportive treatment) (Panel B) showing multilobular and subpleural ground-glass opacity and consolidation. The transverse chest computed tomography imaging from a 60-year-old female with severe COVID-19 at 1 day after hospital admission (Panel C) showing multilobular ground-glass opacity and consolidation and at 4 days after hospital admission (following the receipt of supportive treatment) showing rapid radiologic progression, evidenced by multilobar subsegmental consolidation (Panel D).

Chest X-ray imaging from a 39-year-old male with non-severe COVID-19 after hospital admission demonstrating minor infiltrates in the right lower lobe (Panel E) and from 49-year-old male with severe COVID-19 after hospital admission demonstrating diffuse patchy shadowing and consolidation (Panel F).

COVID-19: coronavirus disease 2019