The differential demographic pattern of Coronavirus Disease 2019 patient fatality outside Hubei and from six hospitals in Hubei, China: a descriptive analysis

Qing-Bin Lu
School of Public Health, Peking University

Hai-Yang Zhang
Beijing Institute of Microbiology and Epidemiology

Tian-Le Che
Beijing Institute of Microbiology and Epidemiology

Xi Chen
Wuhan No. 1 Hospital, Tongji Medical College, Huazhong University of Science and Technology

Rui Li
School of Health Sciences and Global Health Institute, Wuhan University

Wan-Li Jiang
Renmin Hospital of Wuhan University

Hao-Long Zeng
Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology

Xiao-Al Zhang
Beijing Institute of Microbiology and Epidemiology

Hui Long
Tianyou Hospital, Wuhan University of Science and Technology

Qiang Wang
Medical College, Wuhan University of Science and Technology

Ming-Qing Wu
Tianyou Hospital, Wuhan University of Science and Technology; Medical College, Wuhan University of Science and Technology

Zhi-Jie Zhang
School of Public Health, Fudan University

Yang Yang
College of Public Health and Health Professions, and Emerging Pathogens Institute, University of Florida

Li-Qun Fang
Beijing Institute of Microbiology and Epidemiology

Wei Liu (lwbime@163.com)
Beijing Institute of Microbiology and Epidemiology

Research Article

Keywords: Coronavirus Disease 2019, case fatality rate, epidemiological pattern, influencing factor, China

DOI: https://doi.org/10.21203/rs.3.rs-87627/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Background: The Coronavirus Disease 2019 (COVID-19) epidemic has been largely controlled in China, to the point where case fatality rate (CFR) data can be comprehensively evaluated.

Methods: Data on confirmed patients, with a final outcome reported as of 29 March 2020, were obtained from official websites and other internet sources. The hospitalized CFR (HCFR) was estimated, epidemiological features described, and risk factors for a fatal outcome identified.

Findings: The overall CFR in China was estimated to be 4.6% (95% CI 4.5%-4.8%). It increased with age and was higher in males than females. The highest CFR observed was in male patients ≥ 70 years old. Although the outcome of infection is generally worse for males, this adverse effect from male sex decreased as people get old. Differential age/sex CFR patterns across geographical regions were found: the age effect on CFR was greater in other provinces outside Hubei than in Wuhan. An effect of longer interval from symptom onset to admission was only observed outside Hubei, not in Wuhan. By performing multivariate analysis and survival analysis, the higher CFR was associated with older age, and male sex. Only in regions outside Hubei, longer interval from symptom onset to admission, were associated with higher CFR.

Interpretation: This up-to-date and comprehensive picture of COVID-19 CFR and its drivers will help healthcare givers target limited medical resources to patients with high risk of fatality.

Introduction

Coronavirus Disease 2019 (COVID-19) was first detected in Wuhan, central China in early December 2019 and rapidly swept through the whole country during the following month, with hundreds of cases reported in other continents by mid-February 2020.1,2 The etiological pathogen, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is suspected to have a zoonotic origin and causes common influenza-like illness including fever, cough, myalgia, sore throat and fatigue.2 Patients with severe pneumonia can experience acute respiratory distress syndrome and die of septic shock and multi-organ failure.3-7 As of 18 May 2020, more than 4.5 million cases had been reported worldwide, with more than 300,000 deaths from 216 countries. Case fatality rate (CFR) is a key epidemiologic parameter, which appears to vary substantially by geographic region and its estimation remains challenging. Especially in the case of countries in which the epidemic is still continuing, CFR estimation is based on dividing the observed number of fatalities by the number of confirmed cases. However, such an estimate might be severely biased due to both the long time from hospitalization to death or recovery, and the underreporting of mild or asymptomatic infections, especially during the early phase of the epidemic.4,8-10 In China, the epidemic has been largely brought to an end, with less than 10 new cases reported daily. This presents an opportunity to gain a complete understanding of the mortality data in China and to identify high risk populations for COVID-19 related deaths11, to support the development and implementation of effective public health surveillance and mitigation efforts for the current COVID-19 global pandemic.

Most of the previously published CFR data in China were derived from the first two month of documented COVID-19 cases, thus do not reflect the entire epidemic situation, and will be inevitably biased due to the uncertainty of the final patient outcome.10,12,13 Here, by using a most updated national dataset from Wuhan and provinces other than Hubei, we aimed to describe the key characteristics of deceased COVID-19 patients in China, to infer the different features from Wuhan and provinces other than Hubei, and to examine the epidemiological pattern of COVID-19 related death that might differ between age, sex, and epidemic regions and throughout the entire epidemic processes.

Material And Methods

Data sources

We used a range of different sources to curate the largest fatal cases database. First, we used official government sources and peer-reviewed scientific papers that reported primary data as the gold standard for data inclusion. Government sources included press releases on the official websites of Ministries of Health or Provincial Public Health Commissions, as well as updates provided by the official social media accounts of governmental or public health institutions. Second, to find additional details for each case or patient we augmented these data with online reports, mainly captured through news websites (e.g., https://www.163.com) or via news aggregators (e.g., https://bnonews.com/). We recorded all data sources in our database. Third, in some instances more detailed data are available, typically through peer-reviewed research articles, which were subsequently used to modify existing records in the database.

The data on confirmed patients with final clinical outcomes (death or recovered) in mainland China as of 29 March 2020 were compiled. All the cases were hospitalized. Data on cases included basic demographic information, clinical severity at diagnosis (severe vs. mild), and
The CFR were calculated based on the hospitalized patients in this study. Categorical variables were compared between groups with $\chi^2$ or Fisher’s exact tests, and continuous variables were compared between groups with either the Kruskal-Wallis test (for more than 2 groups) or Wilcoxon rank sum test (for 2 groups). A logistic regression model was used to identify risk factors for fatal outcome, using a case-control study. Ordinal Logistic regression model was used to analyze the related factors with clinical course of fatal cases. The competing risk model was presented to identify the potential risk factors for death considering discharge as the competing event. The nonparametric cumulative incidence curve was plotted. Sub-distribution hazard ratio (SHR) and 95% confidence interval (95% CI) were estimated. All statistical tests were 2-tailed at a nominal significance level of 0.05. All analyses were performed using Stata 14.0 (Stata Corp LP, College Station, TX).

Results

Epidemiological description of COVID-19 related mortality

Based on public released national data, a total of 3769 SARS-COV-2 related deaths were identified among 81470 confirmed cases up until 29 May 2020, an overall CFR of 4.6% (95% CI 4.5%-4.8%). Among the 3769 fatal cases, 2428 (64.4%) were male and 3089 (82.0%) were 60 years of age or older. The median age of all fatal cases was 70 (IQR 63-78) years.

Fatal cases were reported from 26 provinces, with most (CFR) from Hubei Province (97.1%, 3651/3769), especially from Wuhan (79.9%, 3011/3769), followed by Xiaogan city (3.4%, 129/3769), Huanggang city (3.3%,125/3769), and Ezhou city (1.6%, 59/3769) in Hubei Province (Figure S1; Table S1). Provinces other than Hubei collectively reported 2.9% (118/3769) of the fatal cases, with the highest CFR (4.0%, 95% CI 0.8%-11.1%) recorded in Xinjiang Uygur Autonomous Region, followed by Hainan Province (3.6%, 95% CI 1.3%-7.6%) and Heilongjiang Province (2.7%, 95% CI 1.4%-4.5%), with the lowest CFR (0.1%, 95% CI 0-0.4%) in Zhejiang Province. No deaths were reported in Jiangsu, Shanxi, Ningxia, Qinghai and Tibet Province. The CFR outside Hubei Province (0.9%, 95% CI 0.7%-1.0%, 118/13669) was significantly lower than that of Hubei Province (5.4%, 95% CI 5.2%-5.6%, 3651/67801, P<0.001, Figure S1; Table S1). The mortality rate in Wuhan city was 28 (95% CI 27-29) per 100,000, higher than other cities in Hubei Province (P<0.001). The CFR of Qingshan District in Wuhan city was the highest (8.3%, 95% CI 7.3%-9.4%, 225/2964), while the mortality rate was the highest [94 (95%CI 79-112) per 100,000] in Hannan District.

Detailed information was obtained from all the 118 fatal patients outside Hubei Province, which represents all of the fatal cases reported by the government. Among these 63.0% were male and the median age was 73 (65-80) years, older than that of all fatal cases nationwide. For comparison, we used 443 fatal cases selected from six designated hospitals in Wuhan, with a comparable age (73 [IQR 64-81] years) and sex (61.6% male) distribution as those of fatal patients outside Hubei Province (Table 1).

For both groups, the CFR increased dramatically with age with a highly similar trend, i.e. starting from no deaths under 20 years of age, to a very low CFR <40 years of age, steadily increasing to >10% in 50-60 years old, and then higher in those ≥60 years of age (Table 1). Longer interval from disease onset to diagnosis and higher proportion of the interval >10 days from disease onset to hospital admission were observed for fatal patients from Wuhan than those from outside Hubei (10 vs. 6 days, P<0.001 and 33.4% vs. 17.8%, P=0.003, respectively). It is noteworthy that a significantly higher proportion of fatal cases entered hospital with mild disease in Wuhan than outside Hubei Province (48.8% vs. 5.1%, P<0.001), which was also related to a shorter clinical course (14 [IQR 9-22] vs. 17 [IQR 10-25] days, P=0.028).

Age- and sex-specific CFR that differed between Wuhan and outside Hubei

We further made a precise estimation of the age/sex CFR that was calculated in Wuhan, and outside Hubei Province in China. The CFR following SARS-COV-2 infection appeared to be higher in males, and increased with age; the highest CFR observed at the male patients ≥70 years old in both regions (Figure 1, Table S2). The outcome of COVID-19 patients was generally worse for males, but the magnitude of this difference was higher in Wuhan than in other provinces outside Hubei, with RR of death for males calculated as 1.94 (95% CI 1.59-2.36) vs. 1.49 (95% CI 1.03-2.17), respectively, compared to females (Table S3). CFR risk ratios also varied across age groups, which was seen in both regions. For example, in Wuhan city, the overall male to female CFR risk ratio in all age groups was 1.94 (95% CI 1.59-2.36), with the greatest
RR 2.94 (95% CI 1.60-5.38) observed for the 50-60 years of age group and the lowest RR 1.48 (95% 1.12-1.95) for the ≥70 years of age group. In a similar way, for outside Hubei Provinces, the overall male to female CFR risk ratio in all age groups was 1.49 (95% CI 1.03-2.17), with the greatest RR 3.06 (95% CI 0.83-11.34) observed in the 50-60 years of age group, and the lowest RR 1.35 (95% CI 0.83-2.21) for the ≥70 years of age group (Table S3).

The CFR following SARS-COV-2 infection appeared to increase with age, but with a magnitude greater in other provinces outside Hubei than in Wuhan. In Wuhan city, the age specific RR increased from 4.72 (95% CI 2.74-8.13) in the 50-60 years age group to 10.59 (95% CI 6.42-17.47) in the 60-70 years age group, to the highest RR of 40.00 (95% CI 24.68-64.84) in the ≥70 years age group. In contrast, for outside Hubei Province, a more significant effect of older age was observed: the RR increased from 7.88 (95% CI 2.77-22.40) in the 50-60 years age group, to 31.33 (95% CI 12.14-80.85) in the 60-70 years age group and to 147.37 (95% CI 59.34-366.00) in the ≥70 years age group (Table S3). The mortality rate in other provinces outside Hubei had a similar trend as that of CFR, which was low in both sex under 40 years old, and then increased along with the increase of age, and to higher extents in female (Figure 1C).

Risk factor analysis for fatal outcome

In univariate and multivariate logistic regression model, the odds of a fatal outcome of COVID-19 patients was significantly associated with age, sex and the interval from symptom onset to admission (Table S4 and Figure 2A). When data on fatal patients from Wuhan and other provinces outside Hubei Province were separately analyzed, the interval from symptom onset to admission were found in addition to be associated with a fatal outcome, but only in other provinces outside of Hubei and not in Wuhan. A long interval from symptom onset to admission was associated with higher CFR, with the OR estimated to be 4.68 (95% CI 2.49-8.82) for >10 days delay and 5.04 (95% CI 3.06-8.31) for 6-10 days compared to 1-5 days (Figure 2A and Table S4). In all three multivariate models, age remained the strongest risk factor. Patients ≥70 years old outside Hubei had the highest risk of death, with >167-fold increase compared to patients <50 years old (OR=167.05, 95% CI 65.78-424.18).

Survival probability over time for fatal cases and related factors for clinical course

The cumulative incidence probability of survival over time for fatal cases with SARS-COV-2 infection is presented by age, sex, and the interval from symptom onset to admission (Figure 2B; Table S5). The median clinical course of the fatal cases (duration from onset of symptoms to death) was 15 (IQR 9-22) days. About 32.1% (130/561) and 38.3% (215/561) patients died within 1-10 days and 11-20 days after symptom onset, respectively. The median clinical course of those cases which survived (duration from symptom onset to discharge) was 23 (IQR 18-30) days. Significant differences were observed in fatal outcome for cases with different age groups and sex (both P<0.001, Figure 3).

By fitting a multivariate ordinal logistic regression model to fatal case data, severe patients or the patients in Wuhan city when diagnosed were associated with a shorter clinical course, indicating a very rapid progress to a fatal outcome. A longer interval from symptom onset to hospital admission were all associated with a longer clinical course (Table S6).

Characteristics of fatal patients with mild pneumonia

There was 39.6% (222/561) of fatal cases who were admitted to hospital with mild pneumonia; the remainder 60.4% were admitted with severe pneumonia (Table S7). The median age of fatal cases admitted as mild was 75 (IQR 65-82) years, comparable with 72 (IQR 64-80) years for severe cases. The sex distribution was also comparable. Both the interval from onset of symptoms to diagnosis and the interval from onset of symptoms to admission were comparable between fatal cases with mild pneumonia and those with severe pneumonia.

The temporal pattern of CFR

The daily cumulative CFR was estimated by using the reported number of total fatal cases divided by the daily number of total confirmed cases reported (Figure 4). For Wuhan fatal cases, the CFR in January was significantly higher than during the later phase of the epidemic (Figure 4A). There was a clear peak in CFR during the week of 23-29 January 2020, followed by an obvious reduction thereafter to a stable level until recently. The national temporal trend was dominated by that of Wuhan city where both the total number of cases and fatal cases outweighs the other provinces (Figure 4A). In contrast, for provinces other than Hubei, there was an obvious low CFR observed during the first week of February, a period which corresponded to one week after Chinese spring festival travel rush; a tender increase was followed, bringing the CFR to the peaking level at the end of February (Week 6 of the epidemic); a decreasing trend was then observed after February, where the CFR was maintained at a stable level till the latest observation (Figure 4A).

The longitudinal CFR profiles were compared among different age groups and between Wuhan and outside Hubei Province. Generally, the CFR curve of three groups showed similar dynamic trends, but with much greater magnitude in the ≥70 years group than the other two
groups. For example, both the decrease of CFR at the end of February in Wuhan and the increase of CFR at the early February in other provinces outside Hubei were obvious and notable in the ≥70 years group than the other two age groups, remarkably contributing to the overall trend of CFR in both regions (Figure 4B, C).

**Discussion**

Assessing the mortality rate of emerging infections is challenging because of potential biases in case ascertainment and delays in counting the occurrence of deaths. This dilemma is rather obvious for COVID-19, where the estimated CFR differs between countries/regions, age, sex, and numerous other patient factors.\(^\text{16-21}\) In China, published CFR data is often presented as Wuhan data versus non-Wuhan data. As the initial epicenter of COVID-19, Wuhan experienced the chaos of changing diagnostic criteria and standard treatment regimens. Therefore it is not surprising that large CFR discrepancies have been reported in Wuhan, especially during the early epidemic phase. Among 41 hospitalized patients identified as having laboratory-confirmed SARS-COV-2 in Wuhan, six (15%) died.\(^\text{9}\) This represented the most severe state of the infection and inevitably an overestimation of the CFR. In a later series of 138 patients in one hospital in Wuhan, a much lower CFR was noted (4.3%)\(^\text{8}\) however this might have been underestimated due to a failure to account for delays between disease onset and final outcome. The national official statistics reported a CFR of 2.3% in China out of 44673 cases as of 11 February 2020;\(^\text{22}\) however, as with some other reports, each patient's eventual outcome was not determined.

Here, based on the most recently released data as of March 17, the overall CFR in China is 4.4%, CFR increased with age and was higher in males than in females, the highest CFR being observed in male patients ≥70 years of age. We also identified major disparities in age- and sex-specific rates of CFR from SARS-CoV-2 in Wuhan versus other regions, the effect of age on CFR being greater outside Hubei provinces than Wuhan. The effect of longer interval from symptom onset and hospital admission was only observed outside Hubei Province. We suggest that the effect of these two variables were partially masked by the effect of differential medical care received between regions. Although no specific anti-viral therapy is available yet, supportive care is crucial for survival from severe respiratory disease.

Until recently, the male-female differences in COVID-19 morbidity and mortality have remained rarely investigated, especially regarding the differences within different age groups. Here we inferred detailed age- and sex-associated differences in CFR during the epidemic, which might reflect many different biological and behavioral factors. Although the outcome of infection is generally worse for males, this risk decreased in older age groups. Overall a poorer outcome of infection was seen as age increases, but this effect was more pronounced for females than males. Indeed, older age was consistently a risk for higher CFR, regardless of any other influencing factors, such as sex or comorbidities.\(^\text{23,24}\) Still the highest risk of death was observed for male patients ≥70 years of age, regardless of their geographic location.

Although the incidence data showed an approximately equal number of male and female cases, more men than women suffered from severe disease and died.\(^\text{17,25}\) The data from other countries demonstrated similar results.\(^\text{26}\) Adverse outcomes of COVID-19 have been associated with comorbidities, including hypertension, cardiovascular disease, and lung disease. These conditions are more prevalent in men and linked to behaviors such as smoking and drinking alcohol.\(^\text{26}\) Sex-based immunological differences have also been suggested as another potential explanation.\(^\text{4}\) During the pandemics, women were more likely to practice non-pharmaceutical behaviors - such as hand washing, face mask use and avoiding crowds - compared to men\(^\text{27}\), which may be in part responsible for the differences observed.

The current study also found a differential outbreak pattern between Wuhan and provinces outside Hubei. For Wuhan city, early in the outbreak, it is possible that more of the severe cases were detected and tested. High clinical volumes and underestimation of confirmed cases early in the epidemic might have contributed to this higher mortality rate in Wuhan. This surge might not reflect rapid death from severe disease, but rather might be due to the backlog in diagnostic confirmation caused by limited supplies and laboratory facilities early during the epidemic. Since 25 January, tests have become increasingly available for clinically suspected patients. The CFR calculated from Wuhan continued to decrease after a brief surge, however it remained higher than other provinces throughout the epidemic. Age, although reported to be an important factor in determining the risk of a fatal outcome, was not responsible for the higher CFR in Wuhan because the age effect was controlled in multivariate analysis. Rather, the higher CFR in Wuhan might be explained by case ascertainment. With thousands of serious cases, mild or asymptomatic cases that might account for most SARS-COV-2 infections would likely remain largely unrecognized. Accordingly, the official numbers of both cases and deaths reported from Wuhan represent the “tip of the iceberg”, potentially skewing CFR estimates towards patients presenting with more severe disease and a fatal outcome. We can infer that CFR truly differed between regions. The differences in medical care during a large epidemic versus care for single cases could be responsible for the differences in case fatality rates observed.

Whereas in other provinces early fatal cases were mainly attributed to imported sources with younger patient age and lower CFR, later on the fatal cases were mainly attributed to local transmission with higher CFR. We propose that there might be a higher CFR in local transmission
patients than those in imported case clusters, which has also been suggested in previous studies.\textsuperscript{28} Except for these two minor fluctuations, no reduction in CFR was observed for either of the regions until the end of the epidemic.

A small proportion of fatal patients exhibited only mild pneumonia, and this was more common in Wuhan. The mild disease in Wuhan was also associated with a rapid clinical progression to death, compared to those presenting with severe pneumonia. Consistent with the findings of Guan et al. 23.87\% of severe cases had no abnormal radiological findings, indicating that a severe outcome can occur even without associated severe lung pathology.\textsuperscript{10} In the study by Chen et al., SARS-COV-2 infection triggered a cytokine storm during the acute phase of disease that was related to an adverse patient outcome.\textsuperscript{4} This inflammatory reaction can cause very severe disease without extensive lung damage; also, such case progression might not be detected, during hospitalization.

This study was subject to the limitation that only hospitalized patients were included in the estimation. As described in previous studies, SARS-COV-2 infection can manifest as asymptomatic self-limited disease. In the absence of asymptomatically infected cases, or very mild cases of infection detected via immunology testing, we can only obtain an estimation of the hospitalized CFR.

In conclusion, the current study offers a detailed view on case fatality rate in relation to epidemiological data from both an epidemic center in which SARS-COV-2 transmission was intense and from regions in which the epidemic was well controlled. Epidemic curves from Wuhan and from provinces other than Hubei demonstrate the common feature of age as the main risk factor for CFR, especially among male patients, and that CFR remained relatively stable at the late epidemic. Differential demographic characteristics were found for the Wuhan fatal cases: 1) less effect on CFR at older ages or longer hospital admission delay, and 2) higher frequency of mild disease on admission to hospital. These findings might be explained by the profound differences in diagnostic capacity, health seeking behaviors and health care in Wuhan. This up-to-date and comprehensive description of COVID-2019 CFR and its drivers will help healthcare providers to target limited medical resources to patients with high risks of a fatal outcome.

\textbf{Declarations}

Competing interests: The authors do not have any commercial or other association that might pose a conflict of interest. All authors read and approved the final manuscript.

Funding: Natural Science Foundation of China.

\textbf{References}

1. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. \textit{N Engl J Med} 2020.

2. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. \textit{N Engl J Med} 2020.

3. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. \textit{N Engl J Med} 2020; 382(13): 1199-207.

4. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. \textit{Lancet} 2020; 395(10223): 507-13.

5. Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. \textit{Lancet} 2020; 395(10223): 514-23.

6. Fang Y, Zhang H, Xu Y, Xie J, Pang P, Ji W. CT Manifestations of Two Cases of 2019 Novel Coronavirus (2019-nCoV) Pneumonia. \textit{Radiology} 2020; 295(1): 208-9.

7. Liu Y, Yang Y, Zhang C, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. \textit{Sci China Life Sci} 2020; 63(3): 364-74.

8. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. \textit{JAMA} 2020.

9. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. \textit{Lancet} 2020; 395(10223): 497-506.

10. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. \textit{N Engl J Med} 2020; 382(18): 1708-20.

11. China CDC. Distribution of pneumonia outbreaks of novel coronavirus infection. 2020.

12. Chen R, Liang W, Jiang M, et al. Risk Factors of Fatal Outcome in Hospitalized Subjects With Coronavirus Disease 2019 From a Nationwide Analysis in China. \textit{Chest} 2020.
13. Liang WH, Guan WJ, Li CC, et al. Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Hubei (epicenter) and outside Hubei (non-epicenter): A Nationwide Analysis of China. *Eur Respir J* 2020.

14. National Health Commission of the People’s Republic of China. Diagnosis and Treatment Scheme of New Coronavirus Infected Pneumonia (5th). 2020. http://www.nhc.gov.cn/yzygj/s7653p/202002/d4b895337e19445f8d728fca1e3e13a/files/ab6bec7f936e64e7f998d802991203cd6.pdf (accessed 2020/2/8).

15. Fine JP, Gray RJ. A proportional hazards model for the Subdistribution of a competing risk. *ASA* 1999; 94(446): 496-509.

16. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. *JAMA* 2020.

17. Jin JM, Bai P, He W, et al. Gender Differences in Patients With COVID-19: Focus on Severity and Mortality. *Front Public Health* 2020; 8: 152.

18. Deng X, Yang J, Wang W, et al. Case fatality risk of the first pandemic wave of novel coronavirus disease 2019 (COVID-19) in China. *Clin Infect Dis* 2020.

19. Shi Q, Zhang X, Jiang F, et al. Clinical Characteristics and Risk Factors for Mortality of COVID-19 Patients With Diabetes in Wuhan, China: A Two-Center, Retrospective Study. *Diabetes Care* 2020.

20. Ma Y, Zhao Y, Liu J, et al. Effects of temperature variation and humidity on the death of COVID-19 in Wuhan, China. *Sci Total Environ* 2020; 724: 138226.

21. New York City Department of H, Mental Hygiene C-RT. Preliminary Estimate of Excess Mortality During the COVID-19 Outbreak - New York City, March 11-May 2, 2020. *MMWR Morb Mortal Wkly Rep* 2020; 69(19): 603-5.

22. World Health Organization. Coronavirus disease (COVID-2019) situation reports. 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/.

23. Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J* 2020; 55(5).

24. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; 395(10229): 1054-62.

25. Wenham C, Smith J, Morgan R, Gender, Group C-W. COVID-19: the gendered impacts of the outbreak. *Lancet* 2020; 395(10227): 846-8.

26. Hall KS, Samari G, Garbers S, et al. Centring sexual and reproductive health and justice in the global COVID-19 response. *Lancet* 2020; 395(10231): 1175-7.

27. Moran KR, Del Valle SY. A Meta-Analysis of the Association between Gender and Protective Behaviors in Response to Respiratory Epidemics and Pandemics. *PLoS One* 2016; 11(10): e0164541.

28. Nie X, Fan L, Mu G, et al. Epidemiological characteristics and incubation period of 7,015 confirmed cases with Coronavirus Disease 2019 outside Hubei Province in China. *J Infect Dis* 2020.

### Tables

Table 1. Epidemiological and clinical characteristics of the 561 fatal cases with SARS-COV-2 infection as of 29 March 2020, the mainland of China
| Characteristic                               | All fatal cases | Outside Hubei (n=118) | Hospitals in Wuhan (n=443) | P value |
|---------------------------------------------|----------------|-----------------------|---------------------------|---------|
| Age, years, median (IQR)                    |                |                       |                           |         |
| <10                                         | 0 (0)          | 0 (0)                 | 0 (0)                     | 0.373   |
| 10−                                         | 0 (0)          | 0 (0)                 | 0 (0)                     | 0.373   |
| 20−                                         | 1 (0.18)       | 1 (0.85)              | 0 (0)                     |         |
| 30−                                         | 10 (1.78)      | 3 (2.54)              | 7 (1.58)                  |         |
| 40−                                         | 12 (2.14)      | 1 (0.85)              | 11 (2.48)                 |         |
| 50−                                         | 61 (10.87)     | 12 (10.17)            | 49 (11.06)                |         |
| 60−                                         | 144 (25.67)    | 30 (25.42)            | 114 (25.73)               |         |
| 70−                                         | 161 (28.70)    | 38 (32.20)            | 123 (27.77)               |         |
| ≥80                                         | 172 (30.66)    | 33 (27.97)            | 139 (31.38)               |         |
| Sex, n (%)                                  |                |                       |                           | 0.829   |
| Female                                      | 214 (38.15)    | 44 (37.29)            | 170 (38.37)               |         |
| Male                                        | 347 (61.85)    | 74 (62.71)            | 273 (61.63)               |         |
| Interval from disease onset to diagnosis, days, median (IQR) | 8 (3–14) | 6 (2–9) | 10 (4–15) | <0.001 |
| 1–5                                         | 168 (29.95)    | 46 (38.98)            | 122 (27.54)               | <0.001  |
| 6–10                                        | 157 (27.99)    | 47 (39.83)            | 110 (24.83)               |         |
| >10                                         | 236 (42.07)    | 25 (21.19)            | 211 (47.63)               |         |
| Interval from disease onset to admission, days, median (IQR) | 6 (2–11) | 6 (2–8) | 6 (2–11) | 0.054  |
| 1–5                                         | 255 (45.45)    | 59 (50.00)            | 196 (44.24)               | 0.003   |
| 6–10                                        | 137 (24.42)    | 38 (32.20)            | 99 (22.35)                |         |
| >10                                         | 169 (30.12)    | 21 (17.80)            | 148 (33.41)               |         |
| Severity of disease                         |                |                       |                           | <0.001  |
| Mild                                        | 222 (39.57)    | 6 (5.08)              | 216 (48.76)               |         |
| Severe                                      | 339 (60.43)    | 112 (94.92)           | 227 (51.24)               |         |
| Clinical course, median (IQR)               |                |                       |                           |         |
| Mild                                        | 15 (9–22)      | 17 (10–25)            | 14 (9–22)                 | 0.028   |
| Severe                                      | 15 (9–23)      | 17 (5–32)             | 15 (9–22)                 | 0.847   |
| IQR: interquartile range.                   |                |                       |                           |         |