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Disease burden from coronavirus disease 2019 symptoms among inpatients at the temporary military hospitals in Wuhan: A retrospective multi-center cross-sectional study

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|-------------------------------|---|
| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2021-048822 |
| Article Type: | Original research |
| Date Submitted by the Author: | 10-Jan-2021 |
| Complete List of Authors: | He, Mai-hong Li, Xiaoxiao; Fuzhou University, Tan, Qing Chen, Yong Kong, Yue You, Jian-ping Lin, Xian Lin, Ying Zheng, Qing |
| Keywords: | PUBLIC HEALTH, HEALTH ECONOMICS, HEALTH SERVICES ADMINISTRATION & MANAGEMENT |
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3 **1 Disease burden from coronavirus disease 2019 symptoms among inpatients**
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5 **2 at the temporary military hospitals in Wuhan: A retrospective multi-center**
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7 **3 cross-sectional study**
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23
24 30 The research ethics committee of the No. 900 Hospital of Joint Logistics Troop of People's Liberation
25

26 31 Army (PLA) gave ethical approval (The approval number: 2020-001).
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29 **32 Conflict of interest**
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31 33 None declared.
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34 **34 Funding source**
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36 35 This study was funded by Educational Research Project for Young and Middle-aged Teachers of Provincial
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38
39 36 Education Department of Fujian Province, China [Grant No. JAS19008]; Research Start-up Fund of
40

41
42 37 Fuzhou University, China [Grant No. CXRC201915]; Soft Science Fund of Fujian Province, China [Grant
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44
45 38 No. 2017R085].
46

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55 42 Conducted questionnaire and PTO processes: Xiao-xiao Li, Jian-ping You, and Yong Chen
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5 46 Drafted the article and revised it: Xiao-xiao Li and Mai-hong He
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7

8 47 All authors gave approval before submission.
9

10 48 **Acknowledgements**
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13 49 The authors thank the professional guidance and medical staff including managers, physicians,
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15
16 50 epidemiologists, sanitarian, and nurses in the target wards for their excellent assistance.
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For peer review only

ABSTRACT:

Aim: We aimed to establish a set of disability weights (DWs) for COVID-19 symptoms, evaluate the disease burden of inpatients, analyze the characteristics, and influencing factors of the disease.

Methods: DWs of COVID-19 symptoms were determined by the person-trade-off approach. The extracted medical records data of 2,702 randomly selected at three temporary military hospitals in Wuhan, China, were analyzed and used to calculate the disability adjusted life years (DALY). Means DALY between gender and age groups were tested. The relationship between DALY and age, gender, body mass index, length of stay, symptom duration before admission, and native place was determined by multiple line regression.

Results: For the DALY of each inpatient, severe expiratory dyspnea and mild cough and sore throat had the highest (0.399) and lowest (0.004) weights, respectively. The average synthetic DALY and daily DALY were 2.29 ± 1.33 and 0.18 ± 0.15 days, respectively. Fever and fatigue contributed the largest DALY at 31.36%; nausea and vomiting, and anxiety and depression contributed the least at 7.05%. There were significant differences between gender and age groups in both synthetic and daily DALY. Age, body mass index, length of stay, and symptom duration before admission were strongly related to both synthetic and daily DALY.

Conclusions: Although the disease burden was higher among females than in the males; however, their daily disease burdens were similar. The disease burden in the younger population was higher than that in the older population. Treatment at the hospitals relieved the disease burden efficiently, while delay in hospitalization could worsen it.

Keywords: COVID-19; Wuhan; Burden of disease; Bio-security; Symptom; Inpatient; Disability adjusted life years

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3 **73 Strengths and limitations**
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5 74 Our work firstly proposed the COVID-19 disability weights by each main symptom of COVID-19, and
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7
8 75 calculated the inpatient burden of disease caused by the symptoms.
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10 76 The validity of the symptoms of COVID-19 inpatient's data obtained from the military medical units are likely
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13 77 to be high.
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16 78 To determine the pure burden of disease caused by COVID-19 symptoms, this study excluded the inpatients with
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18 79 comorbidity, which makes the results more reliable.
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21 80 The PTO method has been questioned for having a lower test-retest reliability than the time-tradeoff technique,
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23 81 which is another common technique used in DALYs studies; and cultural differences may affect the
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26 82 determination of PTO values.
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29 83 Death cases are excluded, due to the reluctance of some family members to allow the use of their family
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31 84 members' death for a public study. By doing this, this study handled DALYs in the same way that we handled
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34 85 YLD.
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87 **Background**

88 The coronavirus disease (COVID-19) pandemic is both a global public health emergency and a major
89 bio-security event; it brings pain and loss to individuals and families, and a heavy burden to countries and
90 societies ^[1,2]. Scientific evaluation of the social and economic impact of the public health incident provides an
91 important way to determine the therapeutic effectiveness in medical institutions and an important basis for the
92 government to formulate relevant rescue policies and recovery measures. The economic burden of disease
93 (BOD) and injury include treatment costs as well as various forms of losses in life (e.g., death and loss of the
94 quality of life due to temporary or sustained decline in the quality of life) ^[3,4].

95 There are several new features of COVID-19 compared with those of severe acute respiratory syndrome
96 (SARS) and Middle East respiratory syndrome (MERS) ^[5]. The severe acute respiratory syndrome
97 coronavirus 2 (SARS-CoV-2) infection can cause symptoms such as fever, fatigue, cough, dyspnea, headache,
98 nausea, vomiting, abdominal pain, and diarrhea; in severe cases, it can lead to severe acute respiratory
99 syndrome, multiple organ failure, and even death ^[6-9]. As it is an emerging disease, the BOD caused by
100 COVID-19 is yet to be fully explored. Studying the BOD of COVID-19 and its symptoms will be helpful to
101 further deepen the understanding of the disease, its harm, and severity and to predict the developing trend
102 of the disease. Thus, public health authorities could improve the treatment and rehabilitation programs,
103 renew relief measures, and adjust public health policies appropriately.

104 Since the 1990s, the World Health Organization (WHO) and the World Bank have proposed indicators
105 to evaluate the BOD, that is, the disability-adjusted life years (DALY) measure. This single-utility measure
106 used to determine the burden attributable to a specific disease is calculated using the standard method
107 proposed by Murray and Lopez ^[10]. The DALY is a summary measure of population health that accounts for
108 both the years of life lost (YLLs) and years lost due to disability (YLDs). The DALY was first developed for
109 the primary purpose of quantifying the global burden of disease (GBD), expressed in terms of the relative

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3 110 magnitude of losses of healthy life associated with different causes of disease and injury ^[11]. Since then, the
4
5 111 DALY has been widely used globally to estimate the BOD at the national, international, and regional levels.
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8 112 In recent years, the DALY has been used to evaluate the BOD caused by some specific diseases. Qi et
9
10 113 al. comprehensively evaluated the direct and indirect BOD caused by Asian Lineage Avian Influenza A
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12 114 (H7N9) public health emergencies ^[12]. Zhang et al. evaluated and analyzed the BOD and related factors in
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14 115 hospitalized patients with coal workers' pneumoconiosis and provided the basis for improving relevant
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16 116 medical policy ^[13]. Bacellar et al. used similar method to assess the BOD in hospitalized elderly patients
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18 117 with neurological disorders in Brazil, and recommended measures to improve the treatment plan ^[14].
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20 118 Adopting the WHO approach, Pei and Li et al. formulated the disability weights (DWs) for chronic
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22 119 mountain disease, which was used to calculate the BOD among soldiers stationed at Tibet, and provided an
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24 120 important basis for evaluating the ability of troops to carry out tasks ^[15].
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31 121 The DALY method could provide important insights into public health studies and practice regarding
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33 122 COVID-19. This year, series of researches were conducted worldwide to estimate the BOD of COVID-19 in
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35 123 different regions, from multiple perspectives, and using different methods. Jo et al. adopted DW from
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37 124 previous similar causes to calculate the BOD due to COVID-19 in Korea including YLDs and YLLs ^[16]. Oh et
38
39 125 al. estimated the YLLs due to COVID-19 in 30 high-incidence countries using the WHO-provided data ^[17]. To
40
41 126 assess the socio-economic burden of COVID-19 pandemic in Italy, Nurchis et al. estimated YLLs and YLDs
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43 127 along with the productive YLL and the comparable DW of lower respiratory tract infection was adopted to
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45 128 estimate the YLDs ^[18]. Mohanty et al. examined COVID-19 impact in the USA, Italy, Germany, and
46
47 129 Sweden's longevity, years of potential life lost, and DALY, and also adopted similar diseases DW as proxy
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49 130 ^[19]. Furthermore, Ortiz-Prado et al. also assessed the BOD caused by COVID-19 in Ecuador by adopted other
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51 131 similar diseases DW ^[20].
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60 132 These researches not only contributed greatly to the understanding of COVID-19 BOD, but also

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3 133 provided the basis for the global COVID-19 public health services and related policy-making. However, in
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5 134 recent reports, the assessment of COVID-19 BOD remained at the macro level and relatively unclear. The
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8 135 challenge here relates to the fact that only the DWs from similar diseases were adopted, leaving COVID-19
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10 136 with a singular DW, which ignored the complexity of COVID-19 symptoms. Until now, limited reports exist
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13 137 on China's COVID-19 BOD, especially BOD based on each COVID-19 symptom, in detail. Thus, this study
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16 138 aimed to establish the DW for COVID-19 symptoms, to estimate the BOD among inpatients in Wuhan,
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18 139 China, and to analyze the characteristics and potential influencing factors. To design this technical approach,
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21 140 in this study we referred to the previous studies' methods to design this technical approach. The BOD
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24 141 caused by COVID-19 symptoms was evaluated according to the data from existing medical records.

25 26 142 **Method**

27 28 29 143 **Selection of the population groups**

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31 144 To counter the public health disaster and bio-security crisis caused by COVID-19 in Wuhan, PLA
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34 145 performed a series of non-combat military operations. These included the deployment of three temporary
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36 146 military hospitals: Huoshenshan Hospital (from March 2, to April 15, 2020), Taikang-Tongji Hospital
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39 147 (March 13, to April 16, 2020), and Guanggu Woman and Child Hospital (March 13, to April 16, 2020).
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41
42 148 The first hospital was a newly built one while the other two were civil medical facilities temporarily
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44 149 utilized by the PLA medical staff. While in operation, all the hospitals were designated as COVID-19
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47 150 special hospitals used to hospitalize COVID-19 patients only.

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49 151 All the analyzed inpatient data were selected randomly from the three temporary military hospitals'
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52 152 medical records using the same recording standard. The included inpatients' hospitalization period ranged
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55 153 from February 5 to April 5, 2020. The selection process conducted from May 25 to June 5, 2020 after the
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58 154 closure of the temporary hospitals is shown in Fig. 1. Data for 2,702 inpatients from the medical records
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60 155 were included in this study. All the inpatients treated by the military medical staff were from the military

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3 156 hospitals affiliated to the PLA.
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5 157 <Insert Fig. 1 here>
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8 158 The diagnosis and treatment method were according to the “Diagnosis and treatment standard of
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10 159 COVID-19 (7th edition)” published by the PRC central government [21]. All patients were hospitalized
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13 160 before the release of the 7th edition was reconfirmed according to the diagnostic criteria. The inclusion
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16 161 criteria were having been diagnosed of COVID-19 at the hospitals according to the standard guideline and
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18 162 been hospitalized and treated continuously at the hospitals. To determine the BOD caused by COVID-19,
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21 163 inpatients with records of any other morbidity (other infectious disease, other respiratory disease,
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24 164 psychiatric disease, tumor, pregnant and lactating women, chronic cardiac, liver, kidney, and neurological
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26 165 diseases) were excluded from the study. We also excluded cases of COVID-19 inpatient deaths, due to the
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29 166 reluctance of their family members to allow the use of their family members’ data for a public study.
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31 167 Similarly, cases with incomplete medical records were also excluded.
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33 34 168 **Establishment of the disability weights for COVID-19 symptoms** 35

36 169 DW is a key component of BOD analysis that represents the severity of an illness. DW ranges from 0 to 1,
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39 170 where 0 represents healthy life and 1 represents death [4]. The WHO has been conducting GBD studies for
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42 171 several years, with series of DWs derived for different health states that are the outcomes of different
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44 172 diseases [22-26].
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47 173 Because COVID-19 is a new infectious disease, no DWs existed for COVID-19 symptoms in the
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49 174 WHO’s DWs’ list; thus, we attempted to establish customized DWs for COVID-19 symptoms. First,
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52 175 COVID-19 symptoms were listed following the literature review of a series of newly published COVID-19
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55 176 clinical reports. Based on these, three rounds of questionnaires were completed by front-line medical staffs
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58 177 in the three military field hospitals in Wuhan to derive a raw list of COVID-19 symptoms for DWs
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60 178 establishment (questionnaire sample is shown in Additional file 1).

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3 179 Then, we convened a nine-expert panel composed of three senior respiratory physicians, two senior
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5 180 infectious disease physicians, one epidemiologist, one public health management expert, and two nursing
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8 181 experts. Based on the raw list of COVID-19 symptoms, the panel performed Delphi process to finally
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11 182 determine the symptom list for DWs creation [27].
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13 183 Then, the panel members performed the Person-Trade-Off (PTO) exercise to derive each symptom's
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16 184 DW by three levels of severities (health stages) [15, 28, 29]. The health stages were described on an A4-sized
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19 185 vignette that contained disease-specific information in simple terminologies. As a reference framework for
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21 186 this task, the panel members were provided with a WHO-GBD framework table, which displayed 7
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24 187 disability classes and 22 anchoring example conditions. The coefficient of variation (CV) was calculated to
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26 188 determine the need for additional rounds of discussion and reassignment of values.
27

28 189 **Data extraction**

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30 190 Basic information for the confirmed cases included the identification number (ID), age, gender, weight,
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33 191 height, native place, date of onset reported by patient, diagnostic conclusion, all the symptoms recorded by
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36 192 the medical staff, and inpatient and outpatient time. Nine age groups were created: <10, 10-19, 20-29,
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38 193 30-39, 40-49, 50-59, 60-69, 70-79, and >80 years. Body mass index (BMI) was calculated from each
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41 194 patient's weight and height, while duration of symptoms was determined as the length of stay + symptom
42
43 195 duration before hospitalization (by self-report in the medical record).
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46 196 To accurately extract the medical data from the records, we trained six staffs to standardize the criteria
47
48 197 of how to judge an inpatient with one or more symptoms in a day and how severe the symptoms were
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51 198 according to the medical records. During the data extraction, the six staffs were divided into three groups
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54 199 of two in each group and a cross-check was conducted when data were extracted from the records. The
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56 200 extraction process was conducted from May 29 to August 7, 2020.
57

58 201 **Calculation of DALY for COVID-19 symptoms**

59
60 202 The DALY was used to estimate the disease burden due to COVID-19 symptoms. The DALY for a disease

203 or health condition were calculated as the sum of the YLLs due to premature mortality in the population
 204 and the equivalent 'healthy' YLDs for incident cases of the health condition [4, 11, 30]. However, this study
 205 did not consider the death cases of COVID-19. Therefore, the DALY due to COVID-19 was equal to the
 206 YLDs. Thus, a patient's individual DALY was calculated case-by-case using the following formula [15]:

$$207 \quad \text{DALY} = \int_{x=\alpha}^{x=\alpha+L} DC x e^{-\beta x} e^{-r(x-\alpha)} dx \quad (1.0)$$

208 In this formula, D represents DW, K is an age weighting factor, C is a constant, r is the discount rate, a
 209 is age at the beginning, β is a parameter from the age weighting function, and L is life time with disability.
 210 We used the base case recommended by Murray and Lopez, with $C = 0.1658$, $r = 0.03$, $K = 1$, and $\beta = 0.04$
 211 [15, 31].

212 Considering that the COVID-19 inpatient's hospitalization time was relatively short, L in the formula
 213 (1.0) is shorter than 1 year, thus the age of each inpatient was treated as fixed. Accordingly, the formula
 214 was simplified into:

$$215 \quad \text{DALY} = DC x e^{-\beta x} \quad (2.0)$$

216 In formula 2.0, $C x e^{-\beta x}$ reflects the life value discounted by age. This function is based on the
 217 hypothesis that life value is different for different age groups: a person's life value increases after he/she is
 218 born and reaches the peak in one's youth; after that, the life value declines with age (Fig. 2). As a result, in
 219 calculating the DALY, although the symptoms are all the same, the DALY will differ for the different age
 220 groups.

221 <Insert Fig. 2 here>

222 In this study, a person's DALY was calculated as follows: 1) the cumulative duration (in days) of each
 223 health condition (a health condition is one type of symptom severity); 2) the health condition's duration
 224 was multiplied by the corresponding DW to get the DALY of each health condition; 3) all the health
 225 conditions' DALY was summed up into an inpatient's synthetic DALY for COVID-19; 4) the synthetic

226 DALY was divided by the patient's length of stay to get an inpatient's daily DALY. Considering that the
227 inpatient's length of stay was relatively short, the unit of DALY was set as days.

228 **Statistical analysis**

229 The demographic characteristics of the hospitalized patients by hospital, gender, and native place, were
230 calculated. The distribution of each symptom by each hospital, gender, and overall population, were
231 calculated. The means of signal symptom's DALY, synthetic DALY, DALY per day (daily DALY), age,
232 BMI, and symptoms course (including symptom duration before hospitalization, length of stay, and overall
233 duration) by hospital, gender, and age groups were calculated and compared by analysis of variance
234 (ANOVA) or t-test (for two groups only). The ratio difference of the cumulative duration (in days) of the
235 symptom severity levels (mild, moderate, and severe) was tested by chi-square test. The proportions of
236 BOD caused by each symptom by gender and age group, and in the entire sample population were
237 computed. DALY per 1,000 capita was also calculated by age group and gender. Besides, the proportion of
238 each symptom's duration in the whole study population was also calculated.

239 To test the relationship between the DALY and age, gender, BMI, and symptom duration, separate
240 linear regression analyses were performed using the DALY as the dependent variable and age, gender, BMI,
241 native place, symptom duration before hospitalization, and length of stay as the independent variables. In
242 the regression models, gender and native place were set as categorical variables while the others were
243 continuous variables. Synthetic DALY and daily DALY were analyzed, and each hospital's study
244 population and overall study population were also analyzed separately. IBM SPSS Statistics for Windows,
245 version 25.0 (IBM Corp., Armonk, N.Y., USA) was used to perform ANOVA and linear regression
246 analyses. In all the analyses, a *P*-value <0.05 was considered statistically significant.

247 **Patient and public involvement**

248 This was a multi-center retrospective cross-sectional descriptive study of COVID-19 inpatients in Wuhan,

the People's Republic of China (PRC). The study was performed after the closure of the three temporary military hospitals. None of the inpatients were involved in any health intervention. All individual data were anonymized prior to retrieval and analysis. Because the study only analyzed the data, the study design has no patient involved.

Results

Patient characteristics

The total number of included cases was 2,702 (that is 872, 921, and 909 selected cases from Taikang-Tongji, Huoshenshan, and Guanggu Woman and Child Hospitals, respectively). Table 1 shows the inpatients' demographic characteristics.

They were all Chinese: 1,326 female and 1,376 male inpatients; 2,618 were natives of Hubei province, while 84 were not. The mean age was 55.52 ± 16.09 years and 54.18 ± 15.85 years for female and male populations, respectively. The mean age for the male population was significantly lower ($P=0.03$). No significant difference was found in symptoms duration before hospitalization, length of stay, and overall duration of symptoms between female and male populations.

For age groups, there were significant difference in symptoms duration before hospitalization, length of stay, and overall duration of symptoms according to the ANOVA test ($P>0.05$). The least significant difference (LSD) test showed that in symptoms duration before hospitalization, age group 20-29 years had the lowest duration, whereas the group 60-69 years had highest age duration, with a significant difference between the groups ($P<0.05$).

Table 1: Demographic characteristics of inpatients

| Characteristics | Number of patients | Proportio |
|-----------------|--------------------|-----------|
|-----------------|--------------------|-----------|

| | | n |
|-------------------------|------|--------|
| Hospital | | |
| Taikang-Tongji | 872 | 32.27% |
| Huoshenshan | 921 | 34.09% |
| Guanggu Woman and Child | 909 | 33.64% |
| Gender | | |
| Female | 1326 | 49.07% |
| Male | 1376 | 50.93% |
| Native place | | |
| Hubei province | 2618 | 96.89% |
| Outside Hubei province | 84 | 3.11% |

271

272 Duration of symptoms

273 Table 2 shows the means for the inpatients age, BMI, symptoms duration before hospitalization, length of
 274 stay, and overall duration of symptoms by hospital, gender, and age group. There were no significant
 275 differences in age, symptoms duration before hospitalization, length of stay, and overall duration of
 276 symptoms among the three hospitals according to the ANOVA test ($P>0.05$). The inpatients' age ranged
 277 from 11 to 94 years, with a mean of 54.84 ± 15.98 years, while BMI ranged from 16.23 to 28.7, with a mean
 278 of 22.11 ± 1.94 . The length of stay ranged from 5 to 50 days, with a mean of 17.88 ± 7.38 days; the
 279 self-reported symptom duration before hospitalization ranged from 2 to 72 days, with a mean of
 280 24.11 ± 15.66 days. By combining the duration of inpatient and self-reported symptom duration before
 281 hospitalization, we obtained the duration of the symptoms, which ranged from 7 to 94 days, with a mean of

282 41.99±16.37 days.

283

284 **Table 2: Means of age, body mass index, symptoms duration before hospitalization, length of stay, and**

285 **overall duration of symptoms by hospital, gender, and age group of the inpatients**

| | Age | Body mass index | Symptoms duration before hospitalization | Length of stay | Overall duration of symptoms |
|---------------------------------|-------------|-----------------|--|----------------|------------------------------|
| Hospital | | | | | |
| Taikang-Tongji (n=872) | 54.76±15.75 | 22.25±1.92 | 24.36±15.92 | 17.92±7.42 | 42.28±16.57 |
| Huoshenshan (n=921) | 55.21±15.88 | 22.02±2.00 | 24.65±15.65 | 17.91±7.34 | 42.55±16.33 |
| Guanggu Woman and Child (n=909) | 54.53±16.29 | 22.07±1.90 | 23.34±15.40 | 17.80±7.39 | 41.15±16.21 |
| Gender | | | | | |
| Female (n=1326) | 55.52±16.09 | 22.14±1.92 | 24.11±15.40 | 18.11±7.34 | 42.22±16.04 |
| Male (n=1376) | 54.18±15.85 | 22.08±1.96 | 24.12±15.92 | 17.66±7.41 | 41.77±16.69 |
| Age group (years) | | | | | |
| <20 (n=49) | 15.59±2.53 | 21.79±2.19 | 24.61±14.01 | 13.22±5.67 | 37.84±13.16 |
| 20-29 (n=116) | 25.35±2.53 | 21.95±1.76 | 16.28±12.36 | 14.91±5.69 | 31.20±14.32 |
| 30-39 (n=305) | 34.87±2.84 | 22.21±1.98 | 23.77±16.68 | 15.79±6.71 | 39.56±17.44 |
| 40-49 (n=529) | 44.84±2.96 | 22.10±1.97 | 21.56±14.29 | 17.24±6.93 | 38.80±14.31 |
| 50-59 (n=592) | 54.68±2.80 | 22.13±1.97 | 23.83±15.81 | 17.98±7.20 | 41.81±16.15 |
| 60-69 (n=635) | 64.16±2.72 | 22.2±1.910 | 27.63±16.08 | 18.49±7.12 | 46.12±16.39 |
| 70-79 (n=306) | 73.96±2.88 | 21.99±1.84 | 25.12±15.95 | 20.34±8.09 | 45.46±16.04 |
| >79 (n=170) | 84.49±3.35 | 21.97±2.04 | 23.94±14.37 | 19.86±8.96 | 43.79±17.55 |
| Overall (n=2702) | 54.84±15.98 | 22.11±1.94 | 24.11±15.66 | 17.88±7.38 | 41.99±16.37 |

286

287 To further analyze the course of the disease (duration of symptom before hospitalization, length of
 288 stay, and overall duration of symptom), we drew line diagrams of the means by age group and gender (Figs.
 289 3 to 5). We also performed two-way ANOVA to test for the difference in the mean course of disease by age
 290 group and gender. The results showed that age was significantly associated with the three course of disease
 291 variables ($P<0.05$), whereas gender was not associated, and two factors had no significant interaction effect

292 ($P>0.05$).

293 <Insert Fig. 3, 4, and 5 here>

294 We also calculated each symptom's cumulative duration (in days) by three levels of severity in the
 295 overall sample population (Table 3). Fever and fatigue had the longest duration, with a cumulative duration
 296 of 26,863 days. The lowest cumulative duration occurred with anxiety and depression, which had 4,565
 297 days. By chi-square test, the proportion of severity differed significantly among different symptoms
 298 ($P<0.05$). Anxiety and depression had the highest proportion of severe conditions (30.54%), whereas cough
 299 and sore throat had the highest proportion of mild conditions (10.63%). Based on these findings,
 300 composition proportions of the cumulative duration (in days) by symptom in the whole study population
 301 are shown in Fig. 6a. Cough and sore throat contributed the largest part of the symptom duration, with a
 302 proportion of 32.06%, whereas anxiety and depression contributed the least, with a proportion of 3.72%.

303 <Insert Fig. 6 here>

304 **Table 3: Each COVID-19 symptom's cumulative duration (in days) in the study population**

| Symptoms | Mild | | Moderate | | Severe | | Overall duration (days) |
|----------------------------------|-------|-------|----------|-------|--------|-------|----------------------------|
| | Day | % | Day | % | Day | % | |
| Fever and fatigue | 2,231 | 8.31 | 20,846 | 77.60 | 3,785 | 14.09 | 26,863 |
| Muscular soreness | 334 | 3.08 | 8,220 | 75.71 | 2,303 | 21.21 | 10,858 |
| Dizziness and headache | 92 | 1.68 | 3,864 | 70.51 | 1,524 | 27.81 | 5,481 |
| Expiratory dyspnea | 104 | 1.83 | 4,096 | 72.23 | 1,471 | 25.94 | 5,672 |
| Cough and sore throat | 4,180 | 10.63 | 30,172 | 76.75 | 4,959 | 12.61 | 39,312 |
| Palpitations and chest tightness | 862 | 5.86 | 11,232 | 76.34 | 2,620 | 17.81 | 14,715 |
| Nausea and vomiting | 387 | 4.40 | 6,434 | 73.19 | 1,970 | 22.41 | 8,792 |

| | | | | | | | |
|-----------------------------|-------|------|--------|-------|--------|-------|---------|
| Abdominal pain and diarrhea | 150 | 2.36 | 4,534 | 71.30 | 1,675 | 26.34 | 6,360 |
| Anxiety and depression | 35 | 0.77 | 3,135 | 68.69 | 1,394 | 30.54 | 4,565 |
| Overall | 8,375 | 6.83 | 92,533 | 75.47 | 21,701 | 17.70 | 122,610 |

305 COVID-19, coronavirus disease 2019.

306

307 DWs of COVID-19 symptoms

308 After two rounds of the Delphi process by the panel, we developed a 9-item COVID-19 symptoms'
 309 list with six categories. Each symptom included three levels of severity (mild, moderate, and severe),
 310 thereby representing 27 health stages. Based on these, we derived the DWs for each health stage by the
 311 PTO exercise; along with the expert panel, a consensus was reached at the fifth round of the Delphi process
 312 (CV <0.5). Thus, the DWs of 27 COVID-19 health stages were derived; severe expiratory dyspnea had the
 313 highest weight of 0.399, while mild cough and sore throat had the lowest weight of 0.004, as shown in
 314 Table 4.

315

316 **Table 4: Disability weights for the symptoms of COVID-19**

| Category | Symptom categories | Health stages | DWs | 95% CI |
|-----------------------|------------------------|---------------|-------|---------------|
| Systemic symptoms | Fever and fatigue | Mild | 0.006 | (0.004-0.008) |
| | | Moderate | 0.051 | (0.036-0.066) |
| | | Severe | 0.133 | (0.089-0.177) |
| | Muscular soreness | Mild | 0.015 | (0.012-0.018) |
| | | Moderate | 0.054 | (0.041-0.067) |
| | | Severe | 0.110 | (0.059-0.113) |
| Neurological symptoms | Dizziness and headache | Mild | 0.028 | (0.019-0.037) |

| | | | | |
|---------------------------|----------------------------------|----------|-------|---------------|
| | | Moderate | 0.083 | (0.055-0.111) |
| | | Severe | 0.163 | (0.109-0.217) |
| Respiratory symptoms | Expiratory dyspnea | Mild | 0.045 | (0.040-0.050) |
| | | Moderate | 0.108 | (0.085-0.131) |
| | | Severe | 0.399 | (0.293-0.505) |
| | Cough and sore throat | Mild | 0.004 | (0.003-0.005) |
| | | Moderate | 0.011 | (0.008-0.014) |
| | | Severe | 0.034 | (0.023-0.045) |
| Cardiovascular symptoms | Palpitations and chest tightness | Mild | 0.041 | (0.029-0.053) |
| | | Moderate | 0.072 | (0.048-0.096) |
| | | Severe | 0.179 | (0.120-0.238) |
| Gastrointestinal symptoms | Nausea and vomiting | Mild | 0.009 | (0.006-0.012) |
| | | Moderate | 0.057 | (0.038-0.076) |
| | | Severe | 0.130 | (0.089-0.171) |
| | Abdominal pain and diarrhea | Mild | 0.011 | (0.008-0.014) |
| | | Moderate | 0.091 | (0.062-0.120) |
| | | Severe | 0.194 | (0.128-0.260) |
| Psychological symptoms | Anxiety and depression | Mild | 0.030 | (0.021-0.039) |
| | | Moderate | 0.120 | (0.084-0.156) |
| | | Severe | 0.366 | (0.243-0.489) |

317 COVID-19, coronavirus disease 2019; DWs, disability weights; CI, confidence interval

318 DALY of inpatients

319 According to the formula and DWs, the DALY of each inpatient for each symptom was calculated, as well

320 as their synthetic DALY and DALY per day. The composition proportion of DALY in the study population
 321 is shown in Fig. 6b. Among these, fever and fatigue contributed the largest part of the DALY, with a
 322 proportion of 31.36%, whereas nausea and vomiting and anxiety and depression contributed the smallest
 323 part, at 7.05%.

324 The mean and standard deviation of DALY by symptom by hospital, gender, and overall study
 325 population are shown in Table 5, and those by age group are shown in Table 6. The mean overall DALY in
 326 the overall study population was 2.29 ± 1.33 days, whereas the mean DALY per day was 0.18 ± 0.15 days.
 327 Among the three hospitals, no significant difference occurred with each symptom's DALY, the synthetic
 328 DALY, or the DALY per day in ANOVA test ($P > 0.05$). However, in the LSD test of the ANOVA,
 329 synthetic DALY in Huoshenshan Hospital was significantly lower than that in Taikang-Tongji ($P = 0.048$)
 330 and Guanggu Woman and Child ($P = 0.031$) Hospitals, respectively. The DALY per day in Huoshenshan
 331 Hospital was significantly lower than that in Guanggu Woman and Child Hospital ($P = 0.023$). The DALY
 332 for fever and fatigue, muscular soreness, palpitations and chest tightness, nausea and vomiting, and
 333 synthetic DALY was significantly lower for the male population than for the female population by t-test
 334 ($P > 0.05$). In the inpatient population the overall DALY per 1,000 capita was 6.28, in female and male
 335 population the overall DALY per 1,000 capita was 6.07 and 6.51 years respectively.

337 **Table 5: The mean DALY of COVID-19 inpatient by symptoms in each hospital, gender, and overall**
 338 **study population**

| Symptom | Taikang-Tongji (n=872) | Huoshenshan (n=921) | Guanggu Woman and Child (n=909) | Female (n=1326) | Male (n=1376) | Overall (n=2702) |
|-------------------|---------------------------|------------------------|------------------------------------|--------------------|------------------------|---------------------|
| Fever and fatigue | 0.72±0.60 | 0.70±0.59 | 0.73±0.63 | 0.75±0.61 | 0.69±0.60 [‡] | 0.72±0.61 |

| | | | | | | |
|----------------------------------|-----------|-------------|-----------|-----------|------------------------|-----------|
| Muscular soreness | 0.19±0.18 | 0.18±0.17 | 0.18±0.17 | 0.19±0.18 | 0.18±0.17 [‡] | 0.18±0.17 |
| Dizziness and headache | 0.14±0.18 | 0.13±0.17 | 0.14±0.20 | 0.13±0.17 | 0.14±0.19 | 0.14±0.18 |
| Expiratory dyspnea | 0.18±0.31 | 0.18±0.32 | 0.21±0.38 | 0.19±0.34 | 0.19±0.33 | 0.19±0.34 |
| Cough and sore throat | 0.18±0.12 | 0.18±0.12 | 0.18±0.13 | 0.18±0.12 | 0.18±0.13 | 0.18±0.12 |
| Palpitations and chest tightness | 0.41±0.45 | 0.37±0.40 | 0.39±0.43 | 0.42±0.44 | 0.36±0.41 [‡] | 0.39±0.43 |
| Nausea and vomiting | 0.16±0.24 | 0.16±0.23 | 0.17±0.24 | 0.17±0.25 | 0.15±0.23 [‡] | 0.16±0.24 |
| Abdominal pain and diarrhea | 0.18±0.30 | 0.16±0.26 | 0.17±0.24 | 0.17±0.26 | 0.16±0.28 | 0.17±0.27 |
| Anxiety and depression | 0.16±0.23 | 0.15±0.21 | 0.17±0.24 | 0.16±0.23 | 0.17±0.23 | 0.16±0.23 |
| Total DALY | 2.33±1.33 | 2.21±1.26* | 2.34±1.38 | 2.38±1.33 | 2.21±1.32 [‡] | 2.29±1.33 |
| DALY per day | 0.19±0.14 | 0.18±0.14** | 0.19±0.16 | 0.19±0.14 | 0.18±0.15 | 0.18±0.15 |

339 * $P < 0.05$ vs. Guanggu Woman and Child Hospital; [†] $P < 0.05$ vs. Taikang-Tongji Hospital; [‡] $P < 0.05$ vs. female.

340 DALY, Disability-adjusted life years.

341

342 **Table 6: COVID-19 inpatient DALY by symptoms and age group**

| Symptom | <20 years | 20-29 years | 30-39 years | 40-49 years | 50-59 years | 60-69 years | 70-79 years | >79 years |
|----------------------------------|-----------|-------------|-------------|-------------|-------------|-------------|-------------|-----------|
| | (n=49) | (n=116) | (n=305) | (n=529) | (n=592) | (n=635) | (n=306) | (n=170) |
| Fever and fatigue | 0.75±0.58 | 0.79±0.73 | 0.99±0.89 | 0.88±0.70 | 0.73±0.54 | 0.60±0.42 | 0.55±0.38 | 0.39±0.28 |
| Muscular soreness | 0.14±0.12 | 0.16±0.19 | 0.25±0.23 | 0.22±0.20 | 0.19±0.16 | 0.16±0.13 | 0.15±0.12 | 0.11±0.09 |
| Dizziness and headache | 0.15±0.18 | 0.13±0.16 | 0.17±0.22 | 0.16±0.22 | 0.16±0.21 | 0.11±0.13 | 0.10±0.11 | 0.08±0.09 |
| Expiratory dyspnea | 0.19±0.24 | 0.11±0.15 | 0.18±0.28 | 0.21±0.43 | 0.25±0.45 | 0.17±0.24 | 0.13±0.19 | 0.18±0.25 |
| Cough and sore throat | 0.20±0.09 | 0.25±0.13 | 0.26±0.15 | 0.21±0.14 | 0.18±0.12 | 0.15±0.09 | 0.14±0.08 | 0.09±0.06 |
| Palpitations and chest tightness | 0.33±0.43 | 0.54±0.54 | 0.51±0.61 | 0.47±0.5 | 0.37±0.35 | 0.37±0.34 | 0.31±0.33 | 0.17±0.17 |

| | | | | | | | | |
|-----------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Nausea and vomiting | 0.21±0.28 | 0.25±0.36 | 0.21±0.30 | 0.17±0.23 | 0.18±0.25 | 0.15±0.22 | 0.10±0.12 | 0.06±0.07 |
| Abdominal pain and diarrhea | 0.10±0.11 | 0.25±0.31 | 0.22±0.43 | 0.22±0.36 | 0.15±0.20 | 0.13±0.17 | 0.13±0.17 | 0.10±0.16 |
| Anxiety and depression | 0.21±0.25 | 0.18±0.24 | 0.21±0.28 | 0.20±0.28 | 0.19±0.25 | 0.14±0.16 | 0.09±0.12 | 0.06±0.08 |
| Synthetic DALY | 2.28±0.93 | 2.65±1.46 | 2.98±1.87 | 2.74±1.52 | 2.41±1.12 | 1.98±0.92 | 1.70±0.79 | 1.24±0.69 |
| DALY per day | 0.21±0.11 | 0.21±0.15 | 0.25±0.18 | 0.22±0.17 | 0.20±0.16 | 0.15±0.10 | 0.11±0.06 | 0.09±0.06 |

343 COVID-19, coronavirus disease 2019.

344 DALY, Disability-adjusted life years.

345

346 According to the ANOVA test, the mean DALY by age groups differed significantly for each
 347 symptom and also for the synthetic DALY and DALY per day ($P<0.05$). The DALY for both single
 348 symptoms and synthesized DALY had the tendency of an inverse U-shaped curve. The DALY increased
 349 with age, reached a peak in the prime of life, and then slowly decreased with age. In this study, the 40-49
 350 years age group had the highest DALY for expiratory dyspnea; while the 20-29 years group had the highest
 351 DALY for palpitations and chest tightness, nausea and vomiting, and abdominal pain and diarrhea. DALY
 352 for the other symptoms, synthetic DALY, and DALY per day peaked in those aged 20-29 years.

353 The composition of synthetic DALY for each symptom by hospital is shown in Fig. 7, and the
 354 composition of the synthetic DALY by gender and age group are shown in Fig. 8 and Fig. 9, respectively.

355 To visualize each symptom's DALY by age group and gender, we drew a thermal map for each
 356 subgroup's DALY per 1,000 capita (in days), as shown in Fig. 10. Fever and fatigue were in the most
 357 intense (red) area, while palpitations and chest tightness were the next intense area, for both female and
 358 male populations. Female population aged 30-39 years had the highest DALY score of 1,115 DALY (in
 359 days) per 1,000 capita. On the contrary, in the female population above 79 years, the lowest DALY

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3 360 temperature of 50 DALY (in days) per 1,000 capita was found.
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5 361 <Insert Fig. 7, 8, 9, and 10 here>
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8 362 We also identified the changing curves of the means synthetic DALY, DALY per day and by age
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10 363 groups and gender, as shown in Fig. 11 and Fig 12. The two-way ANOVA test showed that both age and
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12 364 gender significantly affected synthetic DALY ($P<0.05$); and there was a significant interaction effect
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14 365 between the two variables ($P=0.02$). However, when DALY per day was the dependent variable, the
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16 366 significant difference with gender was lost ($P=0.08$), whereas age remained significant ($P<0.05$), and the
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18 367 interaction effect between the two variables was also lost ($P=0.518$).
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23 368 <Insert Fig. 11 and 12 here>
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25 369 **Linear regression analyses**

26 370 The results of the multiple linear models are shown in Table 7. When synthetic DALY was set as the
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28 371 dependent variable, all of the four models were significant ($P<0.05$), with R^2 ranging from 0.214 to 0.240.
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30 372 In the four models, symptom duration before hospitalization and length of stay were significantly positively
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32 373 associated with synthetic DALY; while age was significantly negatively associated with the overall
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34 374 synthetic DALY. For gender and BMI, however, the four models showed different results. In the Guanggu
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36 375 Woman and Child Hospital model, gender and BMI were not significant ($P=0.098$ and $P=0.146$); in
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38 376 contrast, in the other three models, gender and BMI were significant, indicating that the female population
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40 377 had higher DALY than the male population ($P<0.05$), and high BMI population had higher DALY
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42 378 ($P<0.05$).
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51 379 When DALY per day was set as the dependent variable, all of the four models were significant
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53 380 ($P<0.05$), with R^2 ranging from 0.153 to 0.188. For age and symptom duration before hospitalization, the
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55 381 level of significance was the same as with model type I. Length of stay remained significant; however, the
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57 382 effectiveness was negatively reversed for DALY. For gender, the overall sample and Huoshenshan Hospital
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3 383 models were significant ($P=0.037$ and $P=0.022$, respectively), and for BMI, the overall sample and
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5 384 Taikang-Tongji Hospital models were significant ($P<0.001$ and $P=0.001$, respectively). In all the models,
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8 385 native place was not significant ($P>0.05$).
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Table 7 Linear regression analyses between COVID-19 inpatient’s DALY and individual variables

| Variable | Model Type I * | | | | | | | | Model Type II ** | | | | | | | |
|---|-----------------------|---------|-----------------------|---------|-----------------------|---------|-------------------------|---------|-----------------------|---------|-----------------------|---------|-----------------------|---------|-------------------------|---------|
| | Overall sample | | Taikang-Tongji | | Huoshenshan | | Guanggu Woman and Child | | Overall sample | | Taikang-Tongji | | Huoshenshan | | Guanggu Woman and Child | |
| | R ² =0.222 | | R ² =0.214 | | R ² =0.224 | | R ² =0.240 | | R ² =0.164 | | R ² =0.188 | | R ² =0.170 | | R ² =0.153 | |
| | β | P-value | β | P-value | β | P-value | β | P-value | β | P-value | β | P-value | β | P-value | β | P-value |
| Age | -0.415 | <0.001 | -0.431 | <0.001 | -0.388 | <0.001 | -0.429 | <0.001 | -0.290 | <0.001 | -0.288 | <0.001 | -0.269 | <0.001 | -0.312 | <0.001 |
| Gender | 0.069 | <0.001 | 0.070 | 0.020 | 0.088 | 0.003 | 0.048 | 0.098 | 0.037 | 0.037 | 0.047 | 0.123 | 0.070 | 0.022 | -0.002 | 0.956 |
| Symptom duration before hospitalization | 0.166 | <0.001 | 0.169 | <0.001 | 0.206 | <0.001 | 0.133 | <0.001 | 0.208 | <0.001 | 0.207 | <0.001 | 0.251 | <0.001 | 0.180 | <0.001 |
| Length of stay | 0.312 | <0.001 | 0.265 | <0.001 | 0.334 | <0.001 | 0.338 | <0.001 | -0.139 | <0.001 | -0.184 | <0.001 | -0.134 | <0.001 | -0.108 | 0.001 |
| Body mass index | 0.048 | 0.005 | 0.090 | 0.003 | 0.011 | 0.719 | 0.042 | 0.146 | 0.062 | <0.001 | 0.101 | 0.001 | 0.030 | 0.331 | 0.056 | 0.068 |
| Native place | 0.015 | 0.365 | 0.000 | 0.987 | -0.017 | 0.549 | 0.030 | 0.303 | 0.003 | 0.856 | -0.005 | 0.882 | -0.002 | 0.951 | 0.024 | 0.437 |

COVID-19, coronavirus disease 2019; DALY, disability-adjusted life years.

* Dependent variable is overall DALY; ** Dependent variable is DALY per day.

386 Discussion

387 BOD caused by COVID-19 and its symptoms in inpatient population is an indirect economic and social
388 burden; however, it is usually ignored by some public health authorities. According to this study, each
389 cured inpatient averagely lost about 2-3 days of healthy life due to COVID-19 symptoms and, on an
390 average, discounted almost 1/5th of the quality of life every day. If viewed from the population's
391 perspective, the indirect life loss per 1,000 inpatients was more than 6 years, even if death was not
392 considered. If we consider the increasing number of COVID-19 inpatients worldwide^[32], the indirect life
393 loss could be an enormous figure. Considering pre-hospitalization symptoms and temporary or permanent
394 loss of body function after patients are discharged from the hospital, the cumulative loss of life would be
395 several times more.

396 In general, inpatient's BOD caused by each symptom of COVID-19 in the three hospitals had a
397 relatively smaller gap; however, when the BOD was added together, inpatients at Huoshenshan Hospital
398 enjoyed a relatively lower overall BOD than the other two hospitals' inpatients. However, the gap was
399 small. This is accounted for by the greater investment of manpower and material resources at Huoshenshan
400 Hospital.

401 As far as the DWs are concerned, among the main symptoms of COVID-19, severe expiratory
402 dyspnea accounted for the most serious BOD, followed by the negative psychological symptoms such as
403 severe anxiety and depression. In actual cases, however, the prevalence of severe depression and dyspnea
404 among the inpatient population was not high. Although the prevalence and BOD of anxiety and depression
405 were not high, the ratios of their severity were notable and should be taken into consideration in medical
406 care. Among the inpatient population, the most common symptoms were cough and sore throat, but these
407 had low contribution to the BOD. In contrast, fever and fatigue caused most of the BOD. This suggests that
408 to reduce the BOD, the symptomatic treatment should focus on the symptoms that caused higher BOD.

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3 409 In general, the BOD of female inpatients was higher than that of male inpatients, which is similar to
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5 410 the findings in Korean report^[16]; however, when the BOD was shared per day in the hospitals, there were
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8 411 no significant differences. This indicated that the symptoms in female inpatients, in particular, during the
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10 412 period of hospitalization, were more serious (i.e., the symptoms fluctuated dramatically during
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13 413 hospitalization). In terms of the specific symptoms such as fever, fatigue, muscular soreness, palpitations,
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16 414 chest tightness, nausea, and vomiting; these could cause more BOD in female than in male populations. For
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18 415 the other symptoms, there was no significant difference between female and male populations in the BOD.
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21 416 Thus, cardiovascular and respiratory system symptoms in female inpatients were more serious, as were
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24 417 systemic symptoms, in particular, for the disease course. Consequently, more attention should be paid to
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26 418 female patients' cardiovascular and respiratory systems during the acute stage.

29 419 Contrary to the general thinking, the BOD of the younger population was found to be higher than that
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31 420 of the older population in our study. Both ANOVA and linear models support this conclusion. The main
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34 421 reason for this trend was that the "value" of life at different age stages was fully accounted for in the BOD
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37 422 evaluation. The illness among the youths and middle-aged could bring about greater personal, social, and
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39 423 economic losses. Although the symptoms in the elderly may be slightly more severe, it is more significant
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42 424 to reduce the disease burden in youths and middle-aged inpatients with COVID-19 from a macro-economic
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45 425 perspective when the medical resources are limited.

47 426 Whether for the synthetic DALY or DALY per day, most of the linear models indicated that the BOD
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50 427 for obese people was more serious. Studies have shown that obesity affects the immune function of the
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52 428 body, and burden borne by the organs in obese people is heavier than for in non-obese people. Obese
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55 429 people are not only more likely to suffer from various types of infection including COVID-19 but also
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58 430 experience more serious complications^[33, 34]. Therefore, in order to reduce the disease burden of obese
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60 431 people, it is necessary to strengthen the intervention on the symptoms of obese people.

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3 432 Although the synthetic DALY increased as the hospitalization time, DALY per day decreased
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5 433 significantly with hospitalization. Although the cumulative BOD increased, the BOD shared per day
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8 434 continuously reduced, and the trend of this reduction was very obvious. It indicated that the patients
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10 435 received better treatment during hospitalization, and the symptoms continued to reduce with the medical
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13 436 care process. In contrast, the longer the symptom duration before hospitalization, the heavier the BOD of
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16 437 inpatient time. It indicated that delaying the treatment may aggravate the BOD and lead to consumption of
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18 438 more medical resources. This finding suggests that earlier detection, diagnosis, and treatment of COVID-19
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21 439 are very important for the medical service system. In addition, teenagers and some older-aged groups,
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23
24 440 especially those aged above 60 years, exhibited longer duration of symptoms before hospitalization in our
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26 441 study. This suggests that teenagers and the older-aged groups may have difficulties in seeking medical
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29 442 treatment or lack vigilance of their own health, which could result in the consumption of more medical
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32 443 resources. This suggests that relevant social service departments should be strengthened to provide help and
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34 444 support for the teenagers and older ones.

445 **Conclusion**

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39 446 COVID-19 symptoms could cause heavy BOD to inpatients. The BOD for the female population was
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42 447 higher than that for the male population; however, the daily BOD between male and female inpatients were
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45 448 similar. When the changing life value with age was considered, the disease burden of the younger
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47 449 population was higher than that of the older population, except for teenagers. The treatment at the three
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50 450 military hospitals could have efficiently relieved the BOD of the inpatients, despite the similar treatment
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52 451 effect between them. Delay in hospitalization could worsen the BOD for patients with COVID-19. Thus,
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55 452 there is need for the deployment of adequate medical resources for the early hospitalization of patients with
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57 453 moderate or severe symptoms by the public health authority.

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3 455 **List of abbreviations**
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5 456 BOD: burden of disease
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8 457 COVID-19: coronavirus disease 2019
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10 458 DALY: disability-adjusted life years
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13 459 DW: disability weight
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16 460 PLA: people's liberation army
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18 461 GBD: global burden of disease
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21 462 WHO: World Health Organization
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23 463 YLDs: years lost due to disability
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26 464 YLLs: years of life lost
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31 466 **Declarations**
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33
34 467 **Ethics approval and consent to participate**
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36 468 The research ethics committee of the No.900 Hospital of Joint Logistics Troop of PLA gave ethical
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38
39 469 approval (approval number: 2020-001). None of the inpatients were involved in any health intervention. All
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41
42 470 the individual data were anonymized prior to retrieval and analysis, and they did not contain any
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44 471 individual's private information.
45
46

47 472 **Consent for publication**
48

49 473 Not applicable.
50
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52 474 **Availability of data and materials**
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54
55 475 The data that support the findings of this study are available from Wuhan Huoshenshan Hospital, Tongji
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57 476 Hospital, and Guanggu Womam & Child Hospital. However, restrictions will apply to the availability of
58

59
60 477 these data, which were used under license for the current study, and so are not publicly available. Data are

1
2
3 478 however available from the authors upon reasonable request and with permission of the health service
4
5 479 authority of Joint Logistics Troop of PLA.
6
7

8 480 **Competing interests**

9
10 481 The authors declare that they have no competing interests.
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12

13 482 **Funding**

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15 483 This study was funded by Educational Research Project for Young and Middle-aged Teachers (supporting
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17
18 484 XXL) [Funder: Provincial Education Department of Fujian Province, China; Grant No. JAS19008];
19
20 485 Research Start-up Fund (supporting XXL) [Funder: Fuzhou University, China; Grant No. CXRC201915];
21
22
23 486 Soft Science Fund (supporting MH) [Funder: Fujian Province, China; Grant No. 2017R085]. All the
24
25
26 487 funders had no role in design and conduct of the study; collection, management, analysis, and interpretation
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28
29 488 of the data; or preparation, review, and approval of the manuscript. The views expressed are those of the
30
31
32 489 authors and not necessarily those of the funders.
33

34 490 **Authors' contributions**

35
36 491 XXL and MH conceived and designed the studies; MH and XXL did literature search and review; XXL, JY,
37
38
39 492 and YC conducted questionnaire and PTO processes; XL1, QZ, and XL2 collected and extracted the data;
40
41
42 493 MHe, QT and YK contributed materials; XXL, JY, and YC analyzed and interpreted the data; XXL and
43
44
45 494 MH drafted the article and revised it. All the authors gave approval before submission.
46

47 495 **Acknowledgements**

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49
50 496 The authors thank the professional guidance and medical staff including managers, physicians,
51
52
53 497 epidemiologists, sanitarian, and nurses in the target wards for their excellent assistance.
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55 498 56 57 499 **Reference**

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29 580 **Figure legends**

30
31 581 **Fig. 1 Flow of inpatient selection**

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33 582 **Fig. 2: Curve of weighted life value changing with age**

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35 583 **Fig. 3: Duration of symptom before hospitalization changes with age group in female and male**
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37 584 **populations**

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39 585 **Fig. 4: Length of stay changes with age group in female and male populations**

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41 586 **Fig. 5: Overall duration of symptom changes with age group in female and male populations**

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43 587 **Fig. 6a: The composition proportion of accumulative duration (in day) by symptom in the study**
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45 588 **population**

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47 589 **Fig. 6b: The composition proportion of DALY by symptom in the study population**

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49 590 **Fig. 7: Composition of each military temporary hospital's synthetic DALY**

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51 591 **Fig. 8: Composition of each gender group's synthetic DALY**

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53 592 **Fig. 9: Composition of each age group's synthetic DALY**

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3 593 **Fig. 10: Thermal map of COVID-19 inpatient's DALY by gender and age group (DALY per 1000**
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5 594 **capita).**

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8 595 **Fig. 11: Synthetic DALY changes with age group in female and male populations**

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10 596 **Fig. 12: DALY per day changes with age group in female and male populations**

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16 598 **Additional file**

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18 599 File name: Additional file 1

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21 600 File format: DOC

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23 601 Title of data: questionnaire

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1,000 cases of COVID-19 inpatients' medical record data randomly selected from Taikang-Tongji Hospital

1,000 cases of COVID-19 inpatients' medical record data randomly selected from Huoshenshan Hospital

1,000 cases of COVID-19 inpatients' medical record data randomly selected from Guanggu Woman and Child Hospital

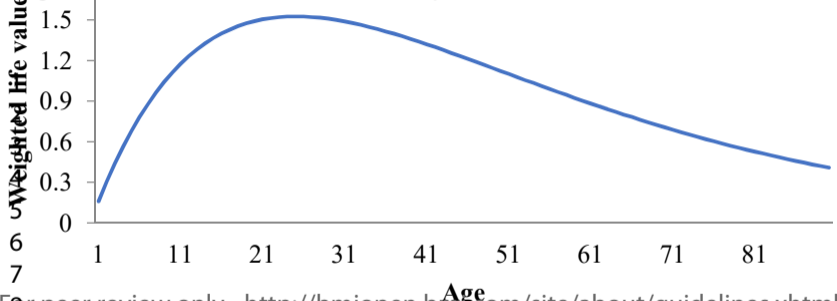
872 cases of COVID-19 inpatients' medical record data met the inclusion criteria

921 cases of COVID-19 inpatients' medical record data met the inclusion criteria

909 cases of COVID-19 inpatients' medical record data met the inclusion criteria

2,702 cases of COVID-19 inpatients' medical record

Fig. 1



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Fig. 2

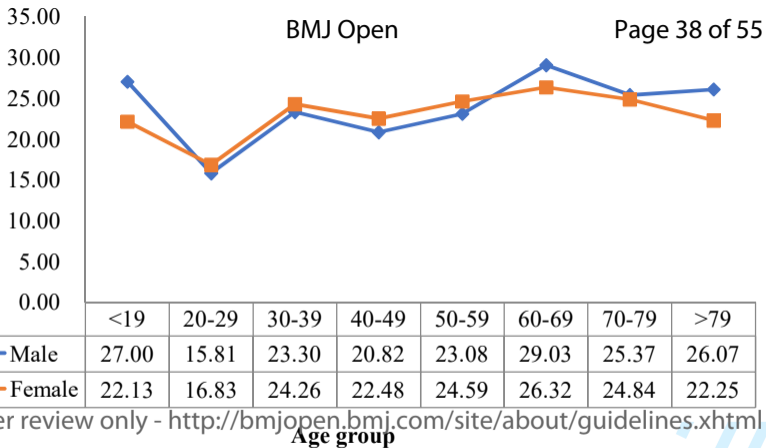


Fig. 3

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Duration day

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15.00
10.00
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| | <19 | 20-29 | 30-39 | 40-49 | 50-59 | 60-69 | 70-79 | >79 |
|--------|-------|-------|-------|-------|-------|-------|-------|-------|
| Male | 13.92 | 14.34 | 15.58 | 17.43 | 17.93 | 18.00 | 19.90 | 19.59 |
| Female | 12.50 | 15.57 | 16.02 | 17.00 | 18.03 | 18.95 | 20.82 | 20.07 |

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Age group

Fig. 4

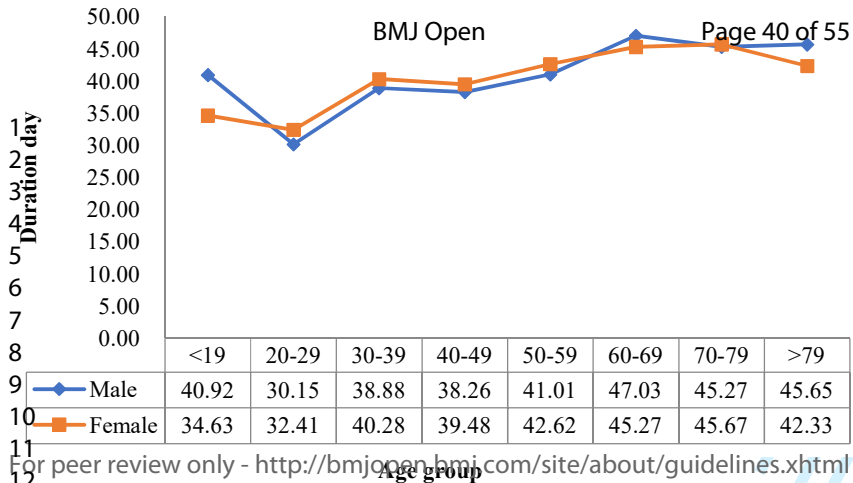


Fig. 5

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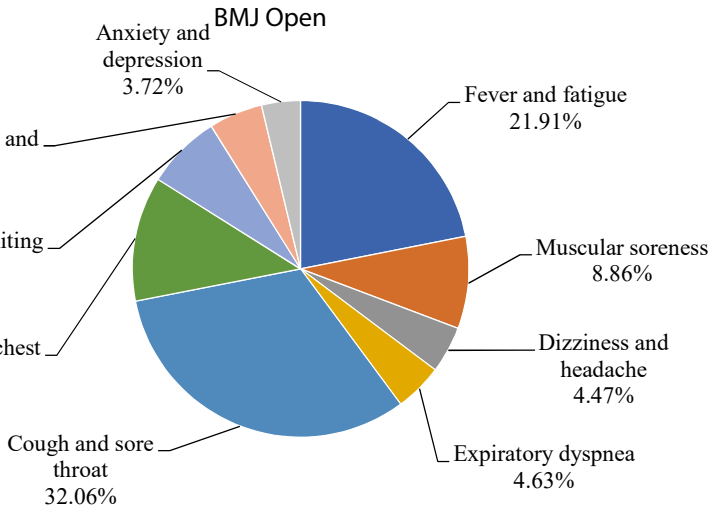


Fig. 6a

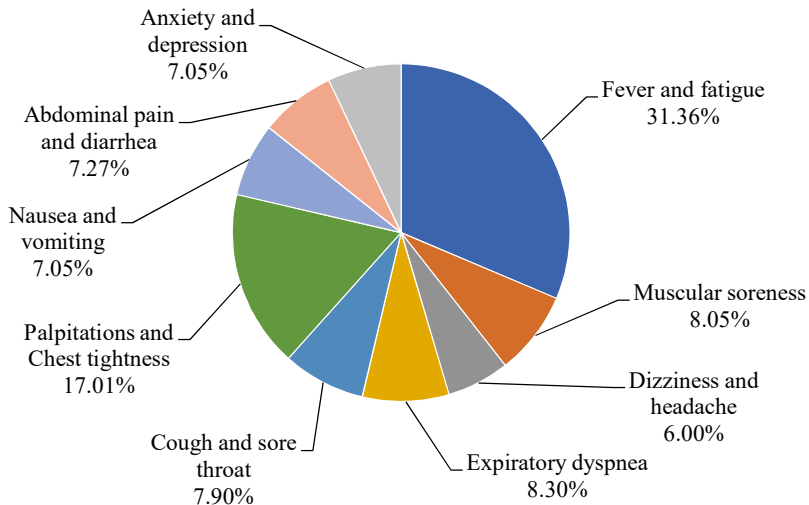
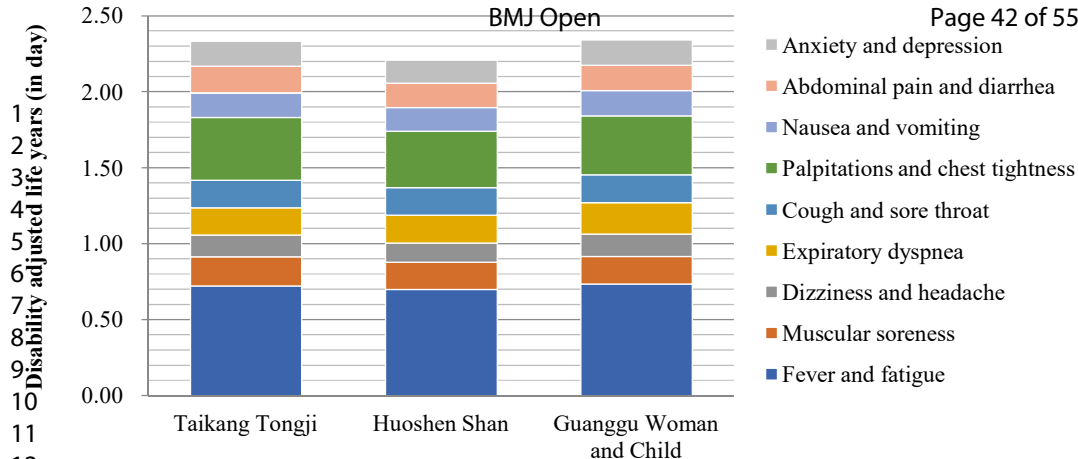
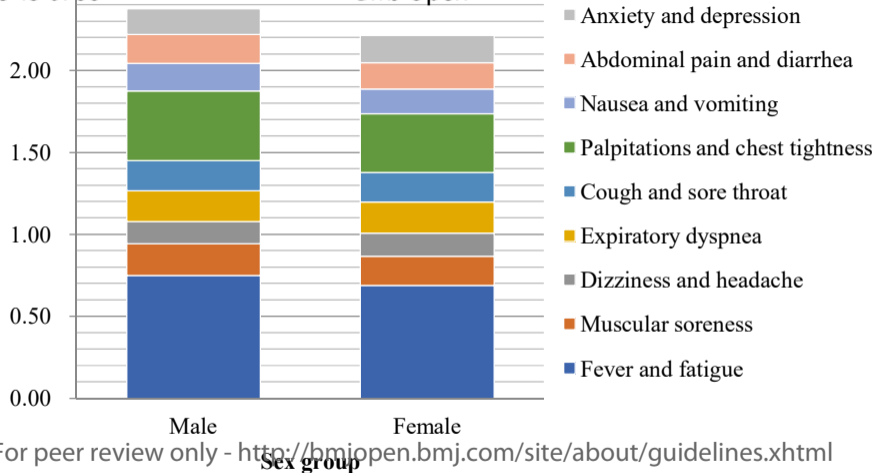


Fig. 6b



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Fig. 7



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Fig. 8

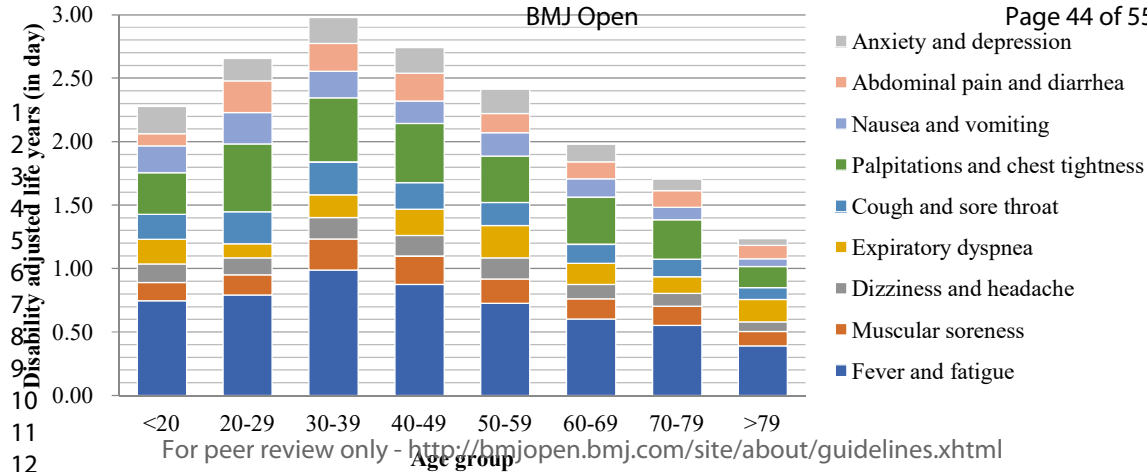


Fig. 9

| Male DALY/1000 captia (in days) | | | | | | | | | BMJ Open | Female DALY/1000 captia (in days) | | | | | | | | |
|---------------------------------|-----------------|------------------|------------------|------------------|------------------|------------------|---------------|---------------------|----------------------------------|-----------------------------------|---------------|------------------|------------------|------------------|------------------|------------------|-----------------|---------------|
| <19 (n=24) | 20-29 (n=54) | 30-39 (n=149) | 40-49 (n=234) | 50-59 (n=295) | 60-69 (n=328) | 70-79 (n=147) | >79 (n=95) | All age (n=1326) | Symptoms | All age (n=1376) | >79 (n=75) | 70-79 (n=159) | 60-69 (n=307) | 50-59 (n=297) | 40-49 (n=295) | 30-39 (n=156) | 20-29 (n=62) | <19 (n=25) |
| 639 | 789 | 1115 | 947 | 776 | 623 | 547 | 379 | 751 | Fever and fatigue | 689 | 412 | 559 | 584 | 677 | 821 | 868 | 796 | 855 |
| 162 | 174 | 276 | 233 | 201 | 163 | 157 | 117 | 193 | Muscular soreness | 177 | 107 | 145 | 154 | 187 | 215 | 217 | 146 | 121 |
| 134 | 150 | 176 | 151 | 159 | 109 | 94 | 83 | 134 | Dizziness and headache | 141 | 65 | 107 | 116 | 169 | 169 | 166 | 117 | 161 |
| 142 | 118 | 181 | 232 | 262 | 160 | 130 | 129 | 190 | Expiratory dyspnea | 191 | 236 | 133 | 177 | 247 | 189 | 175 | 108 | 243 |
| 202 | 275 | 271 | 210 | 183 | 151 | 146 | 87 | 183 | Cough and sore throat | 180 | 101 | 132 | 147 | 182 | 210 | 247 | 229 | 192 |
| 470 | 626 | 614 | 522 | 360 | 383 | 373 | 168 | 423 | Palpitations and Chest tightness | 358 | 162 | 252 | 357 | 373 | 423 | 401 | 457 | 193 |
| 149 | 263 | 238 | 192 | 187 | 151 | 124 | 59 | 171 | Nausea and Vomiting | 153 | 62 | 75 | 142 | 178 | 161 | 180 | 236 | 271 |
| 111 | 316 | 220 | 226 | 179 | 133 | 125 | 108 | 174 | Abdominal pain and Diarrhea | 160 | 100 | 138 | 137 | 126 | 213 | 220 | 187 | 80 |
| 266 | 203 | 202 | 194 | 184 | 135 | 85 | 50 | 157 | Anxiety and Depression | 166 | 63 | 92 | 137 | 197 | 210 | 209 | 153 | 164 |

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Fig. 10

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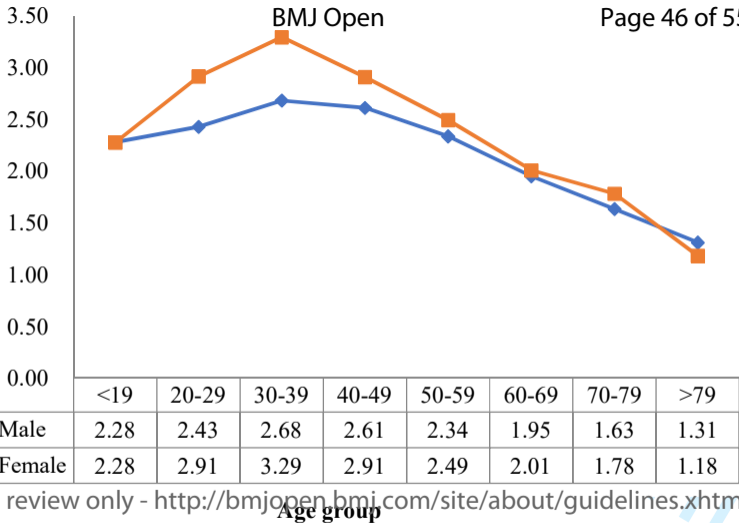
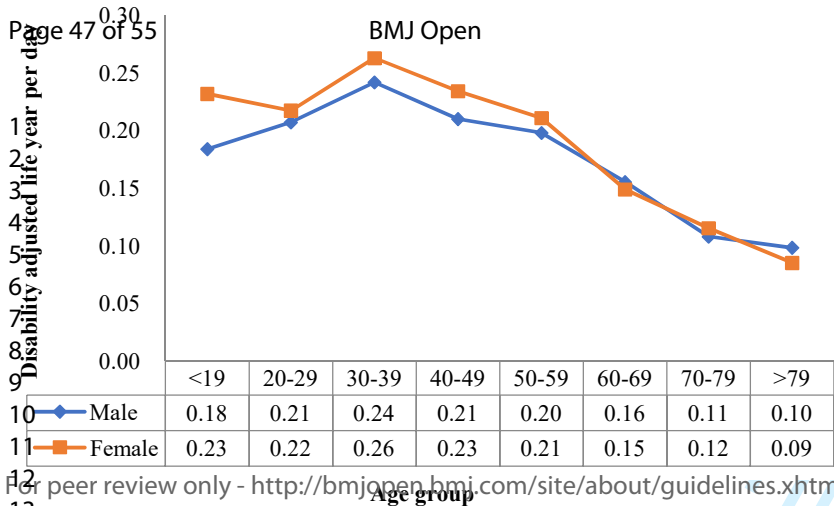


Fig. 11

**Fig. 12**

Additional file 1: Questionnaire

Front-line medical staff questionnaire on symptoms of COVID-19 (The first round)

Dear Sir/Madam:

This is a questionnaire on COVID-19 typical symptom. The aim is to generate a comprehensive list of typical symptoms of inpatient with COVID-19, which can be used to assess the disease burden caused by the symptoms. This study will adopt the method of disability adjusted life years (DALYs) of the World Health Organization (WHO) to evaluate inpatients' burden of disease caused by COVID-19 symptoms.

According to your clinical experience, please judge the raw list of category and symptoms summarized by the literature review (Table 1). The judgment items are included:

For category:

- (1) Whether the category should be included in the list;
- (2) Whether the name of the category is appropriate.

For symptoms:

- (1) Whether the symptom should be listed;
- (2) Whether the symptom should be classified into the current category;
- (3) Whether the name of the symptom is appropriate.

If you think it is necessary, please supplement the symptom list according to your clinical experience. You can add:

- (1) New categories if necessary;
- (2) New symptoms if necessary.

As a front-line clinical expert engaged in COVID-19 treatment, your knowledge about the symptoms of the disease is valuable. Therefore, your opinion is very important for this study. Please try your best to fill the list appropriately. All the information you fill in is for academic research only. We will not analyze your responses individually and will keep them anonymous. Please provide responses to the best of your knowledge.

According to the Delphi process, the opinions of each expert in this round will be anonymously submitted to other experts as reference, in the next round of questionnaire survey. You will also see the anonymous opinions of the other experts. This study is expected to be conducted in 2-3 rounds for a more consistent answer.

Thank you for your support and cooperation.

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The Research Group on COVID-19 Burden of Disease

Date: _____

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Table1: COVID-19 inpatient's symptom list for the burden of disease evaluation (Template)

| Category (Code) | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Symptom | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Should it be moved to another category? If yes, type the code |
|------------------------------|-------------------------------|-------------------------------|---|---------------------------------|-------------------------------|-------------------------------|---|---|
| Systemic symptoms (01) | | | | Fever | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Neurological symptoms (02) | | | | Headache | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Respiratory symptoms (03) | | | | Expiratory dyspnea | | | | |
| | | | | Cough | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Cardiovascular symptoms (04) | | | | Palpitations | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |

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| Category (Code) | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Symptom | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Should it be moved to another category? If yes, type the code |
|-------------------------------------|-------------------------------|-------------------------------|---|---------------------------------|-------------------------------|-------------------------------|---|---|
| | | | | Other symptom 2 (if necessary): | | | | |
| Gastrointestinal symptoms (05) | | | | Diarrhea | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Other category (06) (if necessary): | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Other category (07) (if necessary): | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |

If you have anything else to explain, please write here:

To confirm the above, please sign (or type here): _____

Date: _____

Front-line medical staff questionnaire on symptoms of COVID-19 (The second/third round)

Dear Sir/Madam:

Thank you for your cooperation and hard work in the last round of the questionnaire survey. The anonymous opinions of other experts in the last round have been sent to you as a reference. We retained all the consensus items in the last round of the expert consultation in the list. We also added the most favorite (approval rate > 50%) new items or the items that were proposed for adjustment (Table 1). Please supplement with the necessary items according to your own clinical experience and the opinions of other experts.

According to your clinical experience, please judge the newly added or adjusted category and symptom items:

For category:

- (1) Whether the category should be included in the list;
- (2) Whether the name of the category is appropriate.

For symptom:

- (1) Whether the symptom should be listed;
- (2) Whether the symptom should be classified into the current category;
- (3) Whether the name of the symptom is appropriate.

Besides, you also can add:

- (1) New categories if necessary;
- (2) New symptoms if necessary.

According to the Delphi process, the opinion of each expert in this round will be anonymous and submitted to other experts as reference, in the next round of the questionnaire survey. You will also see the anonymous opinions of the other experts. This study is expected to be conducted in 2-3 rounds for a more consistent answer.

Thank you for your support and cooperation.

The Research Group on COVID-19 Burden of Disease

Date: _____

Table1: COVID-19 inpatient's symptom list for the burden of disease evaluation (Template)

| Category (Code) | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Symptom | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Should it be moved to another category? If yes, type the code |
|------------------------------|-------------------------------|-------------------------------|---|---------------------------------|-------------------------------|-------------------------------|---|---|
| Systemic symptoms (01) | | | | Fever and fatigue * | | | | |
| | | | | Muscular soreness * | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Neurological symptoms (02) | | | | Headache | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Respiratory symptoms (03) | | | | Expiratory dyspnea | | | | |
| | | | | Cough | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Cardiovascular symptoms (04) | | | | Palpitations | | | | |
| | | | | Chest tightness * | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |

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| Category (Code) | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Symptom | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Should it be moved to another category? If yes, type the code |
|-------------------------------------|-------------------------------|-------------------------------|---|---------------------------------|-------------------------------|-------------------------------|---|---|
| | | | | | | | | |
| Gastrointestinal symptoms (05) | | | | Diarrhea | | | | |
| | | | | Vomiting * | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Psychological symptoms * (06) | | | | Anxiety and depression * | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Other category (07) (if necessary): | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |

* Newly proposed or adjusted item.

If you have anything else to explain, please write here:

To confirm the above, please sign (or type here): _____

Date: _____

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BMJ Open

Disease burden from COVID-19 symptoms among inpatients at the temporary military hospitals in Wuhan: A retrospective multi-center cross-sectional study

| | |
|---------------------------------|---|
| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2021-048822.R1 |
| Article Type: | Original research |
| Date Submitted by the Author: | 09-Mar-2021 |
| Complete List of Authors: | He, Mai-hong Li, Xiaoxiao; Fuzhou University, Tan, Qing Chen, Yong Kong, Yue You, Jian-ping Lin, Xian Lin, Ying Zheng, Qing |
| Primary Subject Heading: | Public health |
| Secondary Subject Heading: | Health economics |
| Keywords: | PUBLIC HEALTH, HEALTH ECONOMICS, HEALTH SERVICES ADMINISTRATION & MANAGEMENT |
| | |

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3 1 **Disease burden from COVID-19 symptoms among inpatients at the**
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5 2 **temporary military hospitals in Wuhan: A retrospective multi-center**
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7 **cross-sectional study**
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30 **Word count (excluding title page, abstract, references, figures and tables): 5252 words**

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2
3 31 **ABSTRACT:**

4
5 32 **Objectives:** We aimed to establish a set of disability weights (DWs) for COVID-19 symptoms, evaluate the
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8 33 disease burden of inpatients, and analyze the characteristics and influencing factors of the disease.

9
10 34 **Design:** This was a multi-center retrospective cross-sectional descriptive study.

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13 35 **Setting:** The medical records generated in three temporary military hospitals in Wuhan were analyzed in
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16 36 Fuzhou.

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18 37 **Participants:** Medical records of 2,702 inpatients generated from February 5 to April 5, 2020, were randomly
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21 38 selected for this study.

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23 39 **Primary and secondary outcome measures:** DWs of COVID-19 symptoms were determined by the
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26 40 person-trade-off approach. The inpatients' medical records were analyzed and used to calculate the
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29 41 disability-adjusted life years (DALY). The mean DALY was evaluated across sex and age groups. The
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32 42 relationship between DALY and age, sex, body mass index, length of hospital stay, symptom duration before
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35 43 admission, and native place was determined by multiple linear regression.

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37 44 **Results:** For the DALY of each inpatient, severe expiratory dyspnea, mild cough, and sore throat had the highest
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40 45 (0.399) and lowest (0.004) weights, respectively. The average synthetic DALY and daily DALY were 2.29 ± 1.33
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43 46 and 0.18 ± 0.15 days, respectively. Fever and fatigue contributed the most DALY at 31.36%, whereas nausea and
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46 47 vomiting and anxiety and depression contributed the least at 7.05%. There were significant differences between
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49 48 sex and age groups in both synthetic and daily DALY. Age, body mass index, length of hospital stay, and
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52 49 symptom duration before admission were strongly related to both synthetic and daily DALY.

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54 50 **Conclusions:** Although the disease burden was higher among women than men, their daily disease burdens were
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56
57 51 similar. The disease burden in the younger population was higher than that in the older population. Treatment at
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59
60 52 the hospitals relieved the disease burden efficiently, while a delay in hospitalization worsened it.

53 **Keywords:** COVID-19; Wuhan; Burden of disease; Bio-security; Symptom; Inpatient; Disability-adjusted life years

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2
3 **54 Strengths and limitations of this study**
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5 55 We calculated the inpatient disease burden according to disability weights of major symptoms of COVID-19.
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8 56 The validity of the large sampled medical records from the military medical units was high.
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10 57 To determine the pure burden of COVID-19 symptoms, comorbidity and mortality cases were excluded.
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13 58 Self-reported bias of symptom duration prior to hospital admission may be high.
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16 59 Cultural and ethnic differences and virus variation over time may have affected data comparison.
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60 BACKGROUND

61 The coronavirus disease (COVID-19) pandemic is both a global public health emergency and a major
62 bio-security event; it brings pain and loss to individuals and families and a heavy burden to countries and
63 societies.^[1,2] Scientific evaluation of the social and economic impact of the public health incident provides an
64 important way to determine the therapeutic effectiveness in medical institutions and an important basis for the
65 government to formulate relevant rescue policies and recovery measures. The economic burden of disease
66 (BOD) and injury include treatment costs and various forms of losses in life (e.g., death and poor quality of
67 life due to a temporary or sustained decline in the quality of life).^[3,4]

68 There are several new features of COVID-19 compared with severe acute respiratory syndrome (SARS)
69 and the Middle East respiratory syndrome (MERS).^[5] The severe acute respiratory syndrome coronavirus 2
70 (SARS-CoV-2) infection can cause symptoms such as fever, fatigue, cough, dyspnea, headache, nausea,
71 vomiting, abdominal pain, and diarrhea, and in severe cases, severe acute respiratory syndrome, multiple
72 organ failure, and even death.^[6-9] As it is an emerging disease, the BOD caused by COVID-19 remains
73 unclear. Studying the BOD and symptoms of COVID-19 will be helpful to deepen our understanding of the
74 disease, its harm, and severity and to predict the developing trend of the disease. Thus, public health
75 authorities could improve the treatment and rehabilitation programs, renew relief measures, and adjust
76 public health policies appropriately.

77 Since the 1990s, the World Health Organization (WHO) and the World Bank have proposed indicators
78 to evaluate the BOD, which is a measure of the disability-adjusted life years (DALY). This single-utility
79 measure used to determine the burden attributable to a specific disease is calculated using the standard
80 method proposed by Murray and Lopez.^[10] The DALY is a summary measure of population health
81 accounting for both the years of life lost (YLLs) and years lost due to disability (YLDs). The DALY was first
82 developed for quantifying the global burden of disease (GBD), expressed as the relative magnitude of losses

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3 83 of healthy life associated with different causes of disease and injury.^[11] Since then, the DALY has been
4
5 84 widely used globally to estimate BOD at the national, international, and regional levels.
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8 85 Recently, DALY has been used to evaluate the BOD of some specific diseases. Qi et al.
9
10 86 comprehensively evaluated the direct and indirect BOD of public emergencies caused by Asian Lineage
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13 87 Avian Influenza A (H7N9) infection.^[12] Zhang et al. evaluated the BOD and related factors in hospitalized
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16 88 patients with coal workers' pneumoconiosis and provided the basis for improving relevant medical
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19 89 policies.^[13] Bacellar et al. assessed BOD in hospitalized elderly patients with neurological disorders in
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22 90 Brazil and recommended measures to improve the treatment plan.^[14] Adopting the WHO approach, Pei and
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24
25 91 Li et al. formulated the disability weights (DWs) for chronic mountain disease, which was used to calculate
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27
28 92 the BOD among soldiers stationed in Tibet and helped evaluate the ability of troops to perform tasks.^[15]
29

30 93 The DALY method could provide important insights into public health studies and practice regarding
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32 94 COVID-19. This year, a series of research studies were conducted worldwide to estimate the BOD of
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35 95 COVID-19 in different regions, from multiple perspectives, and using different methods. Jo et al. adopted
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38 96 DWs from previous similar causes to calculate the BOD of COVID-19 in Korea, including YLDs and
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41 97 YLLs.^[16] Oh et al. estimated the YLLs due to COVID-19 in 30 high-incidence countries using the
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44 98 WHO-provided data.^[17] To assess the socio-economic burden of the COVID-19 pandemic in Italy, Nurchis et
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46
47 99 al. estimated YLLs and YLDs along with the productive YLLs, and the comparable DW of lower respiratory
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50 100 tract infection as adopted to estimate the YLDs.^[18] Mohanty et al. examined the impact of COVID-19 on the
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53 101 longevity, years of potential life lost, and DALY in the USA, Italy, Germany, and Sweden, and adopted DWs
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56 102 of similar diseases as proxy.^[19] Furthermore, Ortiz-Prado et al. assessed the BOD of COVID-19 in Ecuador
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59 103 by adopting the DWs of other similar diseases.^[20]
60

61 104 These studies not only contributed greatly to the understanding of BOD of COVID-19 but also provided
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64 105 the basis for global COVID-19 public health services and related policy-making. However, in recent reports,

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3 106 BOD assessment of COVID-19 remained at the macro level and relatively unclear, mainly because only the
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5 107 DWs from similar diseases were adopted, leaving COVID-19 with a singular DW, which ignored the
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8 108 complexity of COVID-19 symptoms. Until now, limited reports exist on China's COVID-19 BOD, especially
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11 109 based on each COVID-19. Thus, we aimed to establish the DW for COVID-19 symptoms, to estimate the
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13 110 BOD among inpatients in Wuhan, China, and to analyze the characteristics and potential influencing factors.
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16 111 To design this technical approach, we design a technical approach based on previous studies. The BOD of
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18 112 COVID-19 symptoms was evaluated from existing medical records.
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20 21 113 **METHOD**

22 23 114 **Selection of the population groups**

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26 115 To counter the public health disaster and bio-security crisis caused by COVID-19 in Wuhan, People's
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29 116 Liberation Army (PLA) performed a series of non-combat military operations, including the deployment of
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31 117 three temporary military hospitals [Huoshenshan Hospital (from March 2 to April 15, 2020),
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34 118 Taikang-Tongji Hospital (March 13 to April 16, 2020), and Guanggu Woman and Child Hospital (March
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36 119 13 to April 16, 2020)]. The first hospital was a newly built one, while the other two were civil medical
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39 120 facilities temporarily utilized by the PLA medical staff. While in operation, all the hospitals were
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42 121 designated as specialized COVID-19 hospitals.

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44 122 All the analyzed inpatient data were randomly selected from the three temporary military hospitals'
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47 123 medical records using the same recording standard. The included inpatients' hospitalization period ranged
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50 124 from February 5 to April 5, 2020. The selection process was conducted from May 25 to June 5, 2020, after
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52 125 the closure of the temporary hospitals (Fig. 1). Data for 2,702 inpatients were included in this study. All the
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55 126 inpatients treated by the military medical staff were from the military hospitals affiliated to the PLA.

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57 127 <Insert Fig. 1 here>
58

59
60 128 The diagnosis and treatment method were based on the "Diagnosis and treatment standard of

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3 129 COVID-19 (7th edition)” published by the People’s Republic of China’s (PRC) central government.^[21] The
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5 130 standard detailed laboratory tests for COVID-19, with pathogenic, serological, and chest image criteria,
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8 131 were included. All patients were hospitalized before the release of the 7th edition and were reconfirmed
9
10 132 according to the diagnostic criteria. The inclusion criteria were COVID-19 diagnosis at the hospitals
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12 133 according to the standard guideline and continuous treatment at these hospitals. To determine the BOD of
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14 134 COVID-19, inpatients with any other morbidity (other infectious diseases, other respiratory diseases,
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16 135 psychiatric disease, tumor, pregnancy and lactation, and chronic cardiac, liver, kidney, and neurological
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18 136 diseases) were excluded. We also excluded COVID-19 inpatient deaths due to the reluctance of their family
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20 137 members to allow the use of their data for a public study. Similarly, cases with incomplete medical records
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22 138 were excluded.
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29 139 **Establishment of the disability weights for COVID-19 symptoms**

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31 140 DW is a key component of BOD analysis that represents disease severity. It ranges from 0 to 1, where 0
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33 141 represents healthy life, and 1 represents death.^[4] WHO has been conducting GBD studies for several years,
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35 142 with series of DWs derived for different health states that are the outcomes of different diseases.^[22-26]
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39 143 Because COVID-19 is a new infectious disease, no DWs exist for COVID-19 symptoms in the
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41 144 WHO’s DWs list; thus, we attempted to establish customized DWs for COVID-19 symptoms. First,
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43 145 COVID-19 symptoms were listed following a literature review of newly published clinical reports on
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45 146 COVID-19. Three rounds of questionnaires were completed by front-line medical staff in the three military
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47 147 field hospitals in Wuhan to derive a raw list of COVID-19 symptoms for DWs establishment (questionnaire
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49 148 sample is shown in Additional file 1).
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54 149 Then, we convened a nine-expert panel composed of three senior respiratory physicians, two senior
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56 150 infectious disease physicians, one epidemiologist, one public health management expert, and two nursing
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58 151 experts. Based on the raw list of COVID-19 symptoms, the panel performed the Delphi process to
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3 152 determine the final symptom list for DWs creation.^[27]
4

5 153 Then, the panel members performed the Person-Trade-Off (PTO) exercise to derive each symptom's
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8 154 DWs by three levels of severities (health stages).^[15, 28, 29] The health stages were described on an A4-sized
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10 155 vignette that contained disease-specific information in simple terminologies. As a reference framework for
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13 156 this task, the panel members were provided with a WHO-GBD framework table, which displayed seven
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16 157 disability classes and 22 anchoring example conditions. The coefficient of variation (CV) was calculated to
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18 158 determine the need for additional rounds of discussion and reassignment of values.
19

20 159 **Data extraction**

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22 160 Basic information for the confirmed cases included the identification number (ID), age, sex, weight, height,
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25 161 native place, date of onset reported by the patient, diagnostic conclusion, symptoms recorded by the
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28 162 medical staff, and inpatient and outpatient time. Nine age groups were created: <10, 10-19, 20-29, 30-39,
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30 163 40-49, 50-59, 60-69, 70-79, and >80 years. Body mass index (BMI) was calculated, while the duration of
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33 164 symptoms was determined as the length of stay + symptom duration before hospitalization (self-reported in
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35 165 the medical record).
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38 166 To accurately extract the medical data from the records, we trained six staff members to standardize
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40 167 the criteria of judging an inpatient with one or more symptoms in a day and the symptom severity. During
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43 168 data extraction, the six staff members were divided into three groups of two in each group, and a
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46 169 cross-check was conducted when data were extracted from the records. The extraction process was
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48 170 conducted from May 29 to August 7, 2020.
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51 172 **Calculation of DALY for COVID-19 symptoms**

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53 173 The DALY was used to estimate the disease burden of COVID-19 symptoms. The DALY is calculated as
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56 174 the sum of the YLLs due to premature mortality in the population and the equivalent 'healthy' YLDs for
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58 175 incident cases of the health condition.^[4,11,30] However, we did not consider COVID-19-related deaths.
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3 176 Therefore, the DALY due to COVID-19 was equal to the YLDs. Thus, a patient's individual DALY was
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5 177 calculated using the following formula^[15]:

$$6 \quad 178 \quad \text{DALY} = \int_{x=\alpha}^{x=\alpha+L} DC x e^{-\beta x} e^{-r(x-\alpha)} dx \quad (1.0)$$

9
10 179 where D represents DW, K is an age weighting factor, C is a constant, r is the discount rate, a is the
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13 180 age at onset, β is a parameter from the age weighting function, and L is life time with disability. We used
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15
16 181 the base case recommended by Murray and Lopez, with $C = 0.1658$, $r = 0.03$, $K = 1$, and $\beta = 0.04$.^[15,31]

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18 182 Considering that the COVID-19 inpatient hospitalization time was relatively short, L in the formula
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21 183 (1.0) is shorter than 1 year; thus, the age of each inpatient was treated as fixed. Accordingly, the formula
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24 184 was simplified as follows:

$$25 \quad 26 \quad 185 \quad \text{DALY} = DCx e^{-\beta x} \quad (2.0)$$

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29 186 In formula 2.0, $Cx e^{-\beta x}$ reflects the life value discounted by age. This function is based on the
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32 187 hypothesis that life value is different for different age groups: a person's life value increases after they are
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34 188 born and reaches the peak in their youth; next, the life value declines with age (Fig.2). Hence, in
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37 189 calculating the DALY, DALY will differ for different age groups despite identical symptoms.

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39 190 <Insert Fig. 2 here>

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42 191 We calculated the DALY as follows: 1) the cumulative duration (in days) of each health condition (a
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44 192 health condition is one type of symptom severity); 2) the duration was multiplied by the corresponding DW
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47 193 to get the DALY of each health condition; 3) all the DALY values were summed up into an inpatient's
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50 194 synthetic DALY for COVID-19; 4) the synthetic DALY was divided by the patient's length of stay to get
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53 195 the daily DALY. Considering that the inpatient's length of stay was relatively short, the unit of DALY was
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55 196 set as days.

56 197 **Statistical analysis**

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58 198 The demographic characteristics of patients such as hospitalization, sex, and native place, were evaluated.

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3 199 The distribution of each symptom according to the hospital, sex, and overall population, was calculated.
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5 200 The mean DALY, synthetic DALY, daily DALY, age, BMI, and symptom course (including symptom
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8 201 duration before hospitalization, length of stay, and overall duration) based on the hospital, sex, and age
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10 202 groups were calculated and compared by analysis of variance (ANOVA) or t-test (for two groups only).
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13 203 The ratio difference of the cumulative duration (in days) of symptom severity levels (mild, moderate, and
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16 204 severe) was tested by a chi-square test. The proportions of BOD for each symptom by sex and age group,
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19 205 and in the entire sample population were computed. DALY per 1,000 capita was also calculated by age
20
21 206 group and sex. Each symptom's duration in the whole study population was also calculated.

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23
24 207 To test the relationship between DALY and age, sex, BMI, and symptom duration, separate linear
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26 208 regression analyses were performed using DALY as the dependent variable and age, sex, BMI, native place,
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29 209 symptom duration before hospitalization, and length of stay as independent variables. In the regression
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31 210 models, sex and native place were set as categorical variables while the others were continuous variables.
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33
34 211 Synthetic and daily DALY were analyzed, and each hospital's study population and overall study
35
36 212 population were analyzed separately. IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk,
37
38
39 213 N.Y., USA) was used for statistical analyses. A *P*-value <0.05 was considered statistically significant.

214 **Patient and public involvement**

215 This was a multi-center retrospective cross-sectional descriptive study of COVID-19 inpatients in Wuhan,
216
217 PRC. The study was performed after the closure of the three temporary military hospitals. None of the
218
219 inpatients were involved in any health intervention. All individual data were anonymized prior to retrieval
220
221 and analysis. Because only patient data were used, no patients were directly involved in the study.

219 **RESULTS**

220 **Patient characteristics**

221 Data of 2,702 inpatients (872, 921, and 909 from Taikang-Tongji, Huoshenshan, and Guanggu Woman and

222 Child Hospitals, respectively) were used. Table 1 shows the inpatients' demographic characteristics.

223 All were Chinese, and 1,326 were woman, whereas 1,376 were man; 2,618 were natives of Hubei
 224 province, while 84 were not. The mean age was 55.52 ± 16.09 years and 54.18 ± 15.85 years for female and
 225 male populations, respectively. The mean age of men was significantly lower ($P=0.03$). No significant
 226 difference was found in symptom duration before hospitalization, length of stay, and overall duration of
 227 symptoms between female and male populations.

228 For age groups, there were significant differences in the symptom duration before hospitalization,
 229 length of stay, and overall duration of symptoms according to the ANOVA test ($P>0.05$). The least
 230 significant difference (LSD) test showed that for 20-29 years age group had the least symptom duration,
 231 whereas the 60-69 years age group had the highest duration, with a significant difference between the
 232 groups ($P<0.05$).

233

234

Table 1: Demographic characteristics of inpatients

| Characteristics | Number of patients | Proportio n |
|-------------------------|--------------------|----------------|
| Hospital | | |
| Taikang-Tongji | 872 | 32.27% |
| Huoshenshan | 921 | 34.09% |
| Guanggu Woman and Child | 909 | 33.64% |
| Sex | | |
| Woman | 1326 | 49.07% |
| Man | 1376 | 50.93% |

Native place

| | | |
|------------------------|------|--------|
| Hubei province | 2618 | 96.89% |
| Outside Hubei province | 84 | 3.11% |

235

236 **Duration of symptoms**

237 Table 2 shows the mean age, BMI, symptom duration before hospitalization, length of stay, and overall
 238 duration of symptoms according to hospital, sex, and age group. There were no significant differences in
 239 age, symptom duration before hospitalization, length of stay, and overall duration of symptoms among the
 240 three hospitals according to the ANOVA test ($P>0.05$). The inpatients' age ranged from 11 to 94 years
 241 (mean, 54.84 ± 15.98 years), while BMI ranged from 16.23 to 28.7 (mean, 22.11 ± 1.94). The length of stay
 242 ranged from 5 to 50 days (mean, 17.88 ± 7.38 days), whereas the self-reported symptom duration before
 243 hospitalization ranged from 2 to 72 days (mean, 24.11 ± 15.66 days). By combining the inpatient and
 244 self-reported symptom duration before hospitalization, we obtained the total duration of symptoms, which
 245 ranged from 7 to 94 days (mean, 41.99 ± 16.37 days).

246

247 **Table 2: Means of age, body mass index, symptom duration before hospitalization, length of stay, and**248 **overall duration of symptoms by hospital, sex, and age group of inpatients**

| | Age | Body mass index | Symptoms duration before hospitalization (days) | Length of stay (days) | Overall duration of symptoms (days) |
|---------------------------------|------------------|-----------------|---|-----------------------|-------------------------------------|
| Hospital | | | | | |
| Taikang-Tongji (n=872) | 54.76 ± 15.75 | 22.25 ± 1.92 | 24.36 ± 15.92 | 17.92 ± 7.42 | 42.28 ± 16.57 |
| Huoshenshan (n=921) | 55.21 ± 15.88 | 22.02 ± 2.00 | 24.65 ± 15.65 | 17.91 ± 7.34 | 42.55 ± 16.33 |
| Guanggu Woman and Child (n=909) | 54.53 ± 16.29 | 22.07 ± 1.90 | 23.34 ± 15.40 | 17.80 ± 7.39 | 41.15 ± 16.21 |
| Sex | | | | | |
| Woman (n=1326) | 55.52 ± 16.09 | 22.14 ± 1.92 | 24.11 ± 15.40 | 18.11 ± 7.34 | 42.22 ± 16.04 |
| Man (n=1376) | 54.18 ± 15.85 | 22.08 ± 1.96 | 24.12 ± 15.92 | 17.66 ± 7.41 | 41.77 ± 16.69 |

| Age group (years) | | | | | |
|-------------------|-------------|------------|-------------|------------|-------------|
| <20 (n=49) | 15.59±2.53 | 21.79±2.19 | 24.61±14.01 | 13.22±5.67 | 37.84±13.16 |
| 20-29 (n=116) | 25.35±2.53 | 21.95±1.76 | 16.28±12.36 | 14.91±5.69 | 31.20±14.32 |
| 30-39 (n=305) | 34.87±2.84 | 22.21±1.98 | 23.77±16.68 | 15.79±6.71 | 39.56±17.44 |
| 40-49 (n=529) | 44.84±2.96 | 22.10±1.97 | 21.56±14.29 | 17.24±6.93 | 38.80±14.31 |
| 50-59 (n=592) | 54.68±2.80 | 22.13±1.97 | 23.83±15.81 | 17.98±7.20 | 41.81±16.15 |
| 60-69 (n=635) | 64.16±2.72 | 22.2±1.910 | 27.63±16.08 | 18.49±7.12 | 46.12±16.39 |
| 70-79 (n=306) | 73.96±2.88 | 21.99±1.84 | 25.12±15.95 | 20.34±8.09 | 45.46±16.04 |
| >79 (n=170) | 84.49±3.35 | 21.97±2.04 | 23.94±14.37 | 19.86±8.96 | 43.79±17.55 |
| Overall (n=2702) | 54.84±15.98 | 22.11±1.94 | 24.11±15.66 | 17.88±7.38 | 41.99±16.37 |

249

250 To further analyze the disease course (duration of symptom before hospitalization, length of stay, and
 251 overall duration of symptom), we drew line diagrams of the means by age group and sex (Figs. 3 to 5). We
 252 also performed a two-way ANOVA to test for the difference in the mean course of the disease by age group
 253 and sex. The results showed that age was significantly associated with the disease variables ($P<0.05$), while
 254 sex was not, and that the two factors had no significant interaction ($P>0.05$).

255 <Insert Fig. 3, 4, and 5 here>

256 We also calculated each symptom's cumulative duration (in days) by three levels of severity in the
 257 overall sample population (Table 3). Fever and fatigue had the longest duration, with a cumulative duration
 258 of 26,863 days. The lowest cumulative duration was for anxiety and depression (4,565 days). By chi-square
 259 test, the proportion of severity differed significantly among different symptoms ($P<0.05$). Anxiety and
 260 depression had the highest proportion of severe conditions (30.54%), whereas cough and sore throat had the
 261 highest proportion of mild conditions (10.63%). The cumulative durations (in days) by symptoms are
 262 shown in Fig. 6a. Cough and sore throat contributed the maximum to symptom duration (32.06%), whereas
 263 anxiety and depression contributed the least (3.72%).

264 <Insert Fig. 6 here>

265 **Table 3: Each COVID-19 symptom's cumulative duration (in days) in the study population**

| Symptoms | Mild | | Moderate | | Severe | | Overall duration (days) |
|----------------------------------|-------|-------|----------|-------|--------|-------|----------------------------|
| | Day | % | Day | % | Day | % | |
| Fever and fatigue | 2,231 | 8.31 | 20,846 | 77.60 | 3,785 | 14.09 | 26,863 |
| Muscular soreness | 334 | 3.08 | 8,220 | 75.71 | 2,303 | 21.21 | 10,858 |
| Dizziness and headache | 92 | 1.68 | 3,864 | 70.51 | 1,524 | 27.81 | 5,481 |
| Expiratory dyspnea | 104 | 1.83 | 4,096 | 72.23 | 1,471 | 25.94 | 5,672 |
| Cough and sore throat | 4,180 | 10.63 | 30,172 | 76.75 | 4,959 | 12.61 | 39,312 |
| Palpitations and chest tightness | 862 | 5.86 | 11,232 | 76.34 | 2,620 | 17.81 | 14,715 |
| Nausea and vomiting | 387 | 4.40 | 6,434 | 73.19 | 1,970 | 22.41 | 8,792 |
| Abdominal pain and diarrhea | 150 | 2.36 | 4,534 | 71.30 | 1,675 | 26.34 | 6,360 |
| Anxiety and depression | 35 | 0.77 | 3,135 | 68.69 | 1,394 | 30.54 | 4,565 |
| Overall | 8,375 | 6.83 | 92,533 | 75.47 | 21,701 | 17.70 | 122,610 |

266 COVID-19, coronavirus disease 2019.

268 DWs of COVID-19 symptoms

269 After two rounds of the Delphi process by the panel, we developed a 9-item COVID-19 symptom list
 270 with six categories. Each symptom included three levels of severity (mild, moderate, and severe), thereby
 271 representing 27 health stages. Based on these, we derived the DWs for each health stage by the PTO
 272 exercise; along with the expert panel, a consensus was reached at the fifth round of the Delphi process (CV
 273 <0.5). Thus, the DWs of 27 COVID-19 health stages were derived; severe expiratory dyspnea had the
 274 highest weight of 0.399, while mild cough and sore throat had the lowest weight of 0.004 (Table 4).

276

Table 4: Disability weights for the symptoms of COVID-19

| Category | Symptom categories | Health stages | DWs | 95% CI |
|---------------------------|----------------------------------|---------------|-------|---------------|
| Systemic symptoms | Fever and fatigue | Mild | 0.006 | (0.004-0.008) |
| | | Moderate | 0.051 | (0.036-0.066) |
| | | Severe | 0.133 | (0.089-0.177) |
| | Muscular soreness | Mild | 0.015 | (0.012-0.018) |
| | | Moderate | 0.054 | (0.041-0.067) |
| | | Severe | 0.110 | (0.059-0.113) |
| Neurological symptoms | Dizziness and headache | Mild | 0.028 | (0.019-0.037) |
| | | Moderate | 0.083 | (0.055-0.111) |
| | | Severe | 0.163 | (0.109-0.217) |
| Respiratory symptoms | Expiratory dyspnea | Mild | 0.045 | (0.040-0.050) |
| | | Moderate | 0.108 | (0.085-0.131) |
| | | Severe | 0.399 | (0.293-0.505) |
| | Cough and sore throat | Mild | 0.004 | (0.003-0.005) |
| | | Moderate | 0.011 | (0.008-0.014) |
| | | Severe | 0.034 | (0.023-0.045) |
| Cardiovascular symptoms | Palpitations and chest tightness | Mild | 0.041 | (0.029-0.053) |
| | | Moderate | 0.072 | (0.048-0.096) |
| | | Severe | 0.179 | (0.120-0.238) |
| Gastrointestinal symptoms | Nausea and vomiting | Mild | 0.009 | (0.006-0.012) |
| | | Moderate | 0.057 | (0.038-0.076) |

| | | | | |
|------------------------|-----------------------------|----------|-------|---------------|
| | | Severe | 0.130 | (0.089-0.171) |
| | Abdominal pain and diarrhea | Mild | 0.011 | (0.008-0.014) |
| | | Moderate | 0.091 | (0.062-0.120) |
| | | Severe | 0.194 | (0.128-0.260) |
| Psychological symptoms | Anxiety and depression | Mild | 0.030 | (0.021-0.039) |
| | | Moderate | 0.120 | (0.084-0.156) |
| | | Severe | 0.366 | (0.243-0.489) |

277 COVID-19, coronavirus disease 2019; DWs, disability weights; CI, confidence interval

278 DALY of inpatients

279 According to the formula and DWs, the DALY of each inpatient for each symptom was calculated, as well
 280 as their synthetic DALY and daily DALY. The proportion of DALY in the study population is shown in
 281 Fig. 6b. Among these, fever and fatigue contributed the most in DALY (31.36%), whereas nausea and
 282 vomiting and anxiety and depression contributed the least (7.05%).

283 The mean and standard deviation of DALY for each symptom by hospital, sex, and overall study
 284 population are shown in Table 5, and those by age group are shown in Table 6. The mean overall DALY
 285 was 2.29 ± 1.33 days, whereas the mean daily DALY was 0.18 ± 0.15 days. No significant difference was
 286 noted in each symptom's DALY, synthetic DALY, or daily DALY among the hospitals ($P > 0.05$). However,
 287 in the LSD test, synthetic DALY in Huoshenshan Hospital was significantly lower than that in
 288 Taikang-Tongji ($P = 0.048$) and Guanggu Woman and Child ($P = 0.031$) Hospitals. The daily DALY in
 289 Huoshenshan Hospital was significantly lower than that in Guanggu Woman and Child Hospital ($P = 0.023$).
 290 The DALY for fever and fatigue, muscular soreness, palpitations and chest tightness, and nausea and
 291 vomiting, and synthetic DALY were significantly lower for men than for women ($P > 0.05$). In the inpatient
 292 population, the overall DALY per 1,000 capita was 6.28, whereas in the female and male populations, the

293 overall DALY per 1,000 capita was 6.07 and 6.51 years, respectively.

294

295 **Table 5: The mean DALY of COVID-19 inpatients or all symptoms, according to hospital, sex, and**

296 **overall study population**

| Symptom | Taikang-Tongji | Huoshenshan | Guanggu Woman and | Woman | Man | Overall |
|----------------------------------|------------------|-------------------------|------------------------|-----------|------------------------|-----------|
| | Hospital (n=872) | Hospital (n=921) | Child Hospital (n=909) | (n=1326) | (n=1376) | (n=2702) |
| Fever and fatigue | 0.72±0.60 | 0.70±0.59 | 0.73±0.63 | 0.75±0.61 | 0.69±0.60 [‡] | 0.72±0.61 |
| Muscular soreness | 0.19±0.18 | 0.18±0.17 | 0.18±0.17 | 0.19±0.18 | 0.18±0.17 [‡] | 0.18±0.17 |
| Dizziness and headache | 0.14±0.18 | 0.13±0.17 | 0.14±0.20 | 0.13±0.17 | 0.14±0.19 | 0.14±0.18 |
| Expiratory dyspnea | 0.18±0.31 | 0.18±0.32 | 0.21±0.38 | 0.19±0.34 | 0.19±0.33 | 0.19±0.34 |
| Cough and sore throat | 0.18±0.12 | 0.18±0.12 | 0.18±0.13 | 0.18±0.12 | 0.18±0.13 | 0.18±0.12 |
| Palpitations and chest tightness | 0.41±0.45 | 0.37±0.40 | 0.39±0.43 | 0.42±0.44 | 0.36±0.41 [‡] | 0.39±0.43 |
| Nausea and vomiting | 0.16±0.24 | 0.16±0.23 | 0.17±0.24 | 0.17±0.25 | 0.15±0.23 [‡] | 0.16±0.24 |
| Abdominal pain and diarrhea | 0.18±0.30 | 0.16±0.26 | 0.17±0.24 | 0.17±0.26 | 0.16±0.28 | 0.17±0.27 |
| Anxiety and depression | 0.16±0.23 | 0.15±0.21 | 0.17±0.24 | 0.16±0.23 | 0.17±0.23 | 0.16±0.23 |
| Total DALY | 2.33±1.33 | 2.21±1.26* | 2.34±1.38 | 2.38±1.33 | 2.21±1.32 [‡] | 2.29±1.33 |
| DALY per day | 0.19±0.14 | 0.18±0.14 ^{††} | 0.19±0.16 | 0.19±0.14 | 0.18±0.15 | 0.18±0.15 |

297 * $P < 0.05$ vs. Guanggu Woman and Child Hospital; † $P < 0.05$ vs. Taikang-Tongji Hospital; ‡ $P < 0.05$ vs. woman.

298 DALY, Disability-adjusted life years.

299

300 **Table 6: COVID-19 inpatient DALY by symptoms and age group**

| Symptom | <20 years | 20-29 years | 30-39 years | 40-49 years | 50-59 years | 60-69 years | 70-79 years | >79 years |
|---------|-----------|-------------|-------------|-------------|-------------|-------------|-------------|-----------|
|---------|-----------|-------------|-------------|-------------|-------------|-------------|-------------|-----------|

| | (n=49) | (n=116) | (n=305) | (n=529) | (n=592) | (n=635) | (n=306) | (n=170) |
|----------------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Fever and fatigue | 0.75±0.58 | 0.79±0.73 | 0.99±0.89 | 0.88±0.70 | 0.73±0.54 | 0.60±0.42 | 0.55±0.38 | 0.39±0.28 |
| Muscular soreness | 0.14±0.12 | 0.16±0.19 | 0.25±0.23 | 0.22±0.20 | 0.19±0.16 | 0.16±0.13 | 0.15±0.12 | 0.11±0.09 |
| Dizziness and headache | 0.15±0.18 | 0.13±0.16 | 0.17±0.22 | 0.16±0.22 | 0.16±0.21 | 0.11±0.13 | 0.10±0.11 | 0.08±0.09 |
| Expiratory dyspnea | 0.19±0.24 | 0.11±0.15 | 0.18±0.28 | 0.21±0.43 | 0.25±0.45 | 0.17±0.24 | 0.13±0.19 | 0.18±0.25 |
| Cough and sore throat | 0.20±0.09 | 0.25±0.13 | 0.26±0.15 | 0.21±0.14 | 0.18±0.12 | 0.15±0.09 | 0.14±0.08 | 0.09±0.06 |
| Palpitations and chest tightness | 0.33±0.43 | 0.54±0.54 | 0.51±0.61 | 0.47±0.5 | 0.37±0.35 | 0.37±0.34 | 0.31±0.33 | 0.17±0.17 |
| Nausea and vomiting | 0.21±0.28 | 0.25±0.36 | 0.21±0.30 | 0.17±0.23 | 0.18±0.25 | 0.15±0.22 | 0.10±0.12 | 0.06±0.07 |
| Abdominal pain and diarrhea | 0.10±0.11 | 0.25±0.31 | 0.22±0.43 | 0.22±0.36 | 0.15±0.20 | 0.13±0.17 | 0.13±0.17 | 0.10±0.16 |
| Anxiety and depression | 0.21±0.25 | 0.18±0.24 | 0.21±0.28 | 0.20±0.28 | 0.19±0.25 | 0.14±0.16 | 0.09±0.12 | 0.06±0.08 |
| Synthetic DALY | 2.28±0.93 | 2.65±1.46 | 2.98±1.87 | 2.74±1.52 | 2.41±1.12 | 1.98±0.92 | 1.70±0.79 | 1.24±0.69 |
| DALY per day | 0.21±0.11 | 0.21±0.15 | 0.25±0.18 | 0.22±0.17 | 0.20±0.16 | 0.15±0.10 | 0.11±0.06 | 0.09±0.06 |

301 COVID-19, coronavirus disease 2019.

302 DALY, Disability-adjusted life years.

303

304 According to the ANOVA test, the mean DALY by age groups differed significantly for each
 305 symptom and for the synthetic DALY and daily DALY ($P<0.05$). The DALY for both single symptoms
 306 and synthesized DALY had the tendency of an inverse U-shaped curve. The DALY increased with age,
 307 reached a peak in the prime of life, and then slowly decreased with age. In this study, the 40-49 years age
 308 group had the highest DALY for expiratory dyspnea, while the 20-29 years group had the highest DALY
 309 for palpitations and chest tightness, nausea and vomiting, and abdominal pain and diarrhea. DALY for the
 310 other symptoms, synthetic DALY, and daily DALY peaked in those aged 20-29 years.

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3 311 The composition of synthetic DALY for each symptom by hospital is shown in Fig. 7, and that by sex
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5 312 and age group is shown in Fig. 8 and Fig. 9, respectively.

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8 313 To visualize each symptom's DALY by age group and sex, we drew a thermal map for each subgroup's
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10 314 DALY per 1,000 capita (in days; Fig. 10). Fever and fatigue were in the most intense (red) area, while
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13 315 palpitations and chest tightness were in the next intense area, for both female and male populations. The
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16 316 female population aged 30-39 years had the highest DALY score of 1,115 days per 1,000 capita. Contrarily,
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18 317 in the female population above 79 years, the lowest DALY 50 days per 1,000 capita was found.

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20
21 318 <Insert Fig. 7, 8, 9, and 10 here>

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23
24 319 We also identified the changing curves of mean synthetic DALY and daily DALY age groups and sex
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26 320 (Fig. 11 and Fig 12). The two-way ANOVA showed that both age and sex significantly affected synthetic
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29 321 DALY ($P<0.05$), and there was a significant interaction effect between the two variables ($P=0.02$).
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31 322 However, when DALY per day was the dependent variable, the significant difference with sex was lost
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34 323 ($P=0.08$), whereas age remained significant ($P<0.05$), and the interaction effect between the two variables
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36 324 was also lost ($P=0.518$).

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39 325 <Insert Fig. 11 and 12 here>

40 326 **Linear regression analyses**

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43 327 The results of the multiple linear models are shown in Table 7. When synthetic DALY was set as the
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46 328 dependent variable, all four models were significant ($P<0.05$), with R^2 ranging from 0.214 to 0.240. In the
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49 329 four models, symptom duration before hospitalization and length of stay were significantly positively
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51 330 associated with synthetic DALY, while age was significantly negatively associated with the overall
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54 331 synthetic DALY. For sex and BMI, however, the four models showed different results. In the Guanggu
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56 332 Woman and Child Hospital model, sex and BMI were not significant ($P=0.098$ and $P=0.146$); in the other
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59 333 three models, sex and BMI were significant, indicating that the female population had higher DALY than
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3 334 the male population ($P<0.05$), and that patients with a high BMI had higher DALY ($P<0.05$).
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5 335 When DALY per day was set as the dependent variable, all four models were significant ($P<0.05$), with
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8 336 R^2 ranging from 0.153 to 0.188. For age and symptom duration before hospitalization, the level of
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10 337 significance was the same as with model I. Length of stay remained significant; however, the effectiveness
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12 338 was negatively reversed for DALY. For sex, the overall sample and Huoshenshan Hospital models were
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14 339 significant ($P=0.037$ and $P=0.022$, respectively), and for BMI, the overall sample and Taikang-Tongji
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16 340 Hospital models were significant ($P<0.001$ and $P=0.001$, respectively). In all the models, native place was
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18 341 not significant ($P>0.05$).
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Table 7 Linear regression analyses between COVID-19 inpatient’s DALY and individual variables

| Variable | Model Type I * | | | | | | | | Model Type II ** | | | | | | | |
|---|-----------------------|---------|-----------------------|---------|-----------------------|---------|-------------------------|---------|-----------------------|---------|-----------------------|---------|-----------------------|---------|-------------------------|---------|
| | Overall sample | | Taikang-Tongji | | Huoshenshan | | Guanggu Woman and Child | | Overall sample | | Taikang-Tongji | | Huoshenshan | | Guanggu Woman and Child | |
| | R ² =0.222 | | R ² =0.214 | | R ² =0.224 | | R ² =0.240 | | R ² =0.164 | | R ² =0.188 | | R ² =0.170 | | R ² =0.153 | |
| | β | P-value | β | P-value | β | P-value | β | P-value | β | P-value | β | P-value | β | P-value | β | P-value |
| Age | -0.415 | <0.001 | -0.431 | <0.001 | -0.388 | <0.001 | -0.429 | <0.001 | -0.290 | <0.001 | -0.288 | <0.001 | -0.269 | <0.001 | -0.312 | <0.001 |
| Sex | 0.069 | <0.001 | 0.070 | 0.020 | 0.088 | 0.003 | 0.048 | 0.098 | 0.037 | 0.037 | 0.047 | 0.123 | 0.070 | 0.022 | -0.002 | 0.956 |
| Symptom duration before hospitalization | 0.166 | <0.001 | 0.169 | <0.001 | 0.206 | <0.001 | 0.133 | <0.001 | 0.208 | <0.001 | 0.207 | <0.001 | 0.251 | <0.001 | 0.180 | <0.001 |
| Length of stay | 0.312 | <0.001 | 0.265 | <0.001 | 0.334 | <0.001 | 0.338 | <0.001 | -0.139 | <0.001 | -0.184 | <0.001 | -0.134 | <0.001 | -0.108 | 0.001 |
| Body mass index | 0.048 | 0.005 | 0.090 | 0.003 | 0.011 | 0.719 | 0.042 | 0.146 | 0.062 | <0.001 | 0.101 | 0.001 | 0.030 | 0.331 | 0.056 | 0.068 |
| Native place | 0.015 | 0.365 | 0.000 | 0.987 | -0.017 | 0.549 | 0.030 | 0.303 | 0.003 | 0.856 | -0.005 | 0.882 | -0.002 | 0.951 | 0.024 | 0.437 |

COVID-19, coronavirus disease 2019; DALY, disability-adjusted life years.

* Dependent variable is overall DALY; ** Dependent variable is DALY per day.

342 DISCUSSION

343 The understanding of the symptoms and pathogenic mechanisms of COVID-19 has been updated
344 gradually.^[32] In addition to fever and dry cough, COVID-19 patients also have gastrointestinal symptoms
345 such as nausea and vomiting, diarrhea, abdominal discomfort, and abnormal liver function; the viral nucleic
346 acid can be detected in the patients' feces.^[33,34] A possible pathogenic mechanism of COVID-19 is the
347 following^[7,35]: a cytokine storm caused by viral infection leads to an increase in the neutrophil count, which
348 in turn results in the imbalance and excessive activation of the immune response and immune pathology,
349 focal proliferation of lung cells, and accumulation of multinucleated giant cells; this triggers apoptosis of
350 alveolar epithelial and endothelial cells, and diffuse alveolar injury and interstitial pulmonary fibrosis
351 resulting in progressive hypoxia and injury to the lungs, heart, liver, and other organs. Moreover, the
352 SARS-CoV-2 enters cells primarily through the angiotensin-converting enzyme 2 (ACE2) receptor.^[36]
353 ACE2 is not only highly expressed in type II alveolar epithelial cells but also in the small intestine,
354 duodenum, colon, and liver, suggesting that the virus may invade target organs in the digestive tract via the
355 ACE2 receptor, causing primary injury and digestive symptoms.^[37] In addition, anxiety, depression, and
356 other psychological stress responses can affect the response of the sympathetic nervous system and increase
357 systemic arterial pressure and heart rate.^[38] Anxiety and depression are also common in hospitalized
358 COVID-19 patients. This psychological stress may cause tachycardia and increase the left ventricular after
359 load, thus aggravating pulmonary edema and exacerbating the lung function. The emotional and
360 somatization symptoms caused by psychological stress may also affect the immune system through
361 neuroendocrine pathways, thereby affecting the patient's rehabilitation process and increasing the
362 BOD.^[39,40]

363 The burden of disease of COVID-19 and its symptoms in the inpatient population are an indirect
364 economic and social burden; however, these are ignored by some public health authorities. According to

1
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3 365 this study, each cured inpatient averagely loses about 2-3 days of healthy life due to COVID-19 symptoms
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5 366 and discounts almost 1/5th of the quality of life every day. If viewed from the population's perspective, the
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8 367 indirect life loss per 1,000 inpatients was more than 6 years, even if death was not considered. If we
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10 368 consider the increasing number of COVID-19 inpatients worldwide,^[41] the indirect life loss could be an
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13 369 enormous figure. Considering pre-hospitalization symptoms and temporary or permanent loss of body
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16 370 function after discharge, the cumulative loss of life would be many-fold higher. Inpatient BOD of each
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18 371 symptom of COVID-19 in the three hospitals had a relatively smaller difference; however, when the BOD
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21 372 was added, inpatients at Huoshenshan Hospital showed a relatively lower overall BOD than the other two
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24 373 hospitals' inpatients. However, the difference was negligible. This can be accounted for by the greater
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26 374 investment of manpower and material resources at Huoshenshan Hospital.

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29 375 Regarding DWs, among the main symptoms of COVID-19, severe expiratory dyspnea accounted for
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31 376 the most serious BOD, followed by negative psychological symptoms such as severe anxiety and
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34 377 depression. In actual cases, however, the prevalence of severe depression and dyspnea among the inpatient
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37 378 population was not high. Although the prevalence and BOD of anxiety and depression were not high, the
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39 379 ratios of their severity were not able and should be considered in medical care. Among the inpatient
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41
42 380 population, the most common symptoms were cough and sore throat, but these had a low contribution to
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45 381 the BOD. In contrast, fever and fatigue largely contributed to the BOD. This suggests that to reduce the
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47 382 BOD, symptomatic treatment should focus on symptoms that cause a higher BOD.

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49 383 The BOD of female inpatients was higher than that of male inpatients, which is similar to the findings
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51 384 in the Korean report^[16]; however, when the BOD was shared per day in the hospitals, there were no
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54 385 significant differences. This indicated that the symptoms in female inpatients during hospitalization were
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57 386 more severe (i.e., the symptoms fluctuated dramatically during hospitalization). Specific symptoms such as
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59 387 fever, fatigue, muscular soreness, palpitations, chest tightness, nausea, and vomiting could result in a higher

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3 388 BOD in female than in male inpatients. For other symptoms, there was no significant difference between
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5 389 female and male populations in the BOD. Thus, cardiovascular and respiratory symptoms in female
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8 390 inpatients were more severe, as were systemic symptoms. Consequently, more attention should be paid to
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11 391 female patients' cardiovascular and respiratory systems during the acute stage.

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13 392 Contrary to general thinking, the BOD of the younger population was higher than that of the older
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16 393 population. Both ANOVA and linear models supported this conclusion. The main reason for this trend was
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18 394 that the "value" of life at different age stages was fully accounted for in the BOD evaluation. The illness
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21 395 among youth and middle-aged individuals could bring about greater personal, social, and economic losses.
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24 396 Although the symptoms in the elderly may be slightly more severe, it is more significant to reduce the
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26 397 disease burden in youth and middle-aged inpatients with COVID-19 from a macro-economic perspective
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28
29 398 when the medical resources are limited.

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31 399 For the synthetic DALY or daily DALY, most linear models indicated that the BOD for obese people
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34 400 was more severe. Obesity affects the immune function of the body, and the burden borne by the organs in
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37 401 obese people is heavier than in non-obese people. Obese people are not only more likely to suffer from
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39 402 various types of infection, including COVID-19 but also experience more serious complications.^[42, 43]
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42 403 Therefore, to reduce the disease burden of obese people, it is necessary to strengthen the intervention in this
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45 404 population.

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47 405 Although synthetic DALY increased with the hospitalization duration, daily DALY decreased
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50 406 significantly. Although the cumulative BOD increased, the BOD shared per day continuously decreased,
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53 407 and the trend of this reduction was very obvious. It indicated that patients received better treatment during
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55 408 hospitalization, and that the symptoms continued to ameliorate with medical care. In contrast, the longer
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57 409 the symptom duration before hospitalization, the heavier the BOD of inpatient duration, indicating that
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60 410 delayed treatment may aggravate the BOD and lead to the consumption of more medical resources. This

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3 411 finding suggests that earlier detection, diagnosis, and treatment of COVID-19 are very important for the
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5 412 healthcare system. In addition, teenagers and some older age groups, especially those aged above 60 years,
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8 413 exhibited a longer duration of symptoms before hospitalization in our study. This suggests that these
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10 414 individuals may have difficulties in seeking medical treatment or lack vigilance of their own health, which
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13 415 could result in the consumption of more medical resources. Thus, relevant social service departments
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16 416 should be strengthened to provide help and support for teenagers and the elderly.

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18 417 There are some limitations to this study. First, because this was a retrospective study rather than a
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21 418 prospective study, the data acquired from the medical records may not be fully accurate. The duration of
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24 419 symptoms before admission can only rely on the self-report of the patients, which could cause potential
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26 420 self-reported bias. Notwithstanding, considering the relatively large sample, despite the compromise for
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29 421 potential bias, the macroscopic trend could be detected by statistical analysis.

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31 422 Second, the medical records were generated in the early stages of the COVID-19 outbreak when the
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34 423 knowledge about COVID-19 was limited. During that time, the diagnosis and treatment protocol of
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36 424 COVID-19 did not include symptoms such as ageusia and anosmia. Thus, there were only a few records of
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39 425 these symptoms in our data. Consequently, we did not include these as the main symptom in this study.
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42 426 However, because inpatients were in the acute stage of the disease, the discomfort from ageusia and
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44 427 anosmia could be clubbed with respiratory and gastrointestinal symptoms. When calculating the disease
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47 428 burden of respiratory and gastrointestinal symptoms, we could make up for the lack of disease burden
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50 429 caused by ageusia and anosmia. Meanwhile, in most cases ageusia and anosmia would more noticeable
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52 430 after discharge, when other acute symptoms gradually disappear. Thus, these symptoms could be treated as
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55 431 sequelae of COVID-19 rather than main symptoms of inpatients in the acute stage.

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57 432 Third, because this study is based on Chinese cultural and ethnic backgrounds in the early stage of the
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60 433 COVID-19 pandemic, these combined with virus variation over time may affect the comparability of the

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3 434 results worldwide. The DWs derived from this study may be limited and should consider regional DWs of
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5 435 COVID-19, which could be seen as a pilot study for international BOD study on COVID-19.

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8 436 Notwithstanding, our primary aim was to focus on the regional disease burden and public health
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10 437 management; the cultural difference may therefore not have a great impact on our findings.

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13 438 Moreover, to determine BOD only caused by COVID-19 symptoms, this study excluded inpatients
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15 439 with comorbidity. When the COVID-19 symptoms superimpose with other diseases, the effect could have
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17 440 been complex and could not have been easily evaluated using simple linear summarization function;
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19 441 moreover, quantitative differentiation of BOD purely caused by COVID-19 symptoms would have been
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21 442 challenging. Because the BOD of COVID-19 comorbidities will be helpful for understanding the
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23 443 COVID-19 burden, it should be considered in future studies. Thus, inpatients with pre-existing medical
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25 444 conditions were excluded, which could have affected the findings in the following two ways: a) the severity
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27 445 and disease duration may have been milder and shorter, respectively, and b) the exclusion of patients with a
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29 446 pre-existing psychiatric disease could have explained the short duration of reported anxiety and depression
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31 447 during hospitalization. Besides, deaths were excluded. Thus, this study evaluated DALY in the same way
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33 448 as YLD caused by symptoms during hospitalization.

34 449 **CONCLUSION**

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36 450 COVID-19 symptoms could cause heavy BOD in inpatients. The BOD for the female population was
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38 451 higher than that for the male population; however, the daily BOD between male and female inpatients was
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40 452 similar. When the changing life value with age was considered, the disease burden of the younger
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42 453 population was higher than that of the older population, except for teenagers. The treatment at the three
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44 454 military hospitals efficiently relieved the BOD of the inpatients, despite the similar treatment effects. Delay
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46 455 in hospitalization could worsen the BOD for patients with COVID-19. Thus, there is a need for the
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48 456 deployment of adequate medical resources for early hospitalization of patients with moderate or severe

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3 457 symptoms by the public health authority.
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8 459 **List of abbreviations**
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10 460 BOD: burden of disease
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13 461 COVID-19: coronavirus disease 2019
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16 462 DALY: disability-adjusted life years
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19 463 DW: disability weight
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22 464 PLA: people's liberation army
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25 465 GBD: global burden of disease
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28 466 WHO: World Health Organization
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31 467 YLDs: years lost due to disability
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34 468 YLLs: years of life lost
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37 469

38 470 **Acknowledgments:** The authors thank the professional guidance and medical staff, including managers,
39 471 physicians, epidemiologists, sanitarians, and nurses in the target wards for their excellent assistance.
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41

42 472 **Authors' contributions:** XXL and MH conceived and designed the studies; MH and XXL did literature
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45 473 search and review; XXL, JY, and YC conducted questionnaire and PTO processes; XL, QZ, and YL
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48 474 collected and extracted the data; MH, QT, and YK contributed materials; XXL, JY, and YC analyzed and
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51 475 interpreted the data; XXL and MH drafted the article and revised it. All the authors gave approval before
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54 476 submission.
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57 477 **Funding:** This work was funded by the Educational Research Project for Young and Middle-aged Teachers
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60 478 (supporting XXL) [Funder: Provincial Education Department of Fujian Province, China; Grant No.
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63 479 JAS19008]; Research Start-up Fund (supporting XXL) [Funder: Fuzhou University, China; Grant
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3 480 No.CXRC201915]; Soft Science Fund (supporting MH) [Funder: Fujian Province, China; Grant No.
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5 481 2017R085].

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8 482 **Disclaimer:** All the funders had no role in the design and conduct of the study; collection, management,
9
10 483 analysis, and interpretation of the data; or preparation, review, and approval of the manuscript. The views
11
12 484 expressed are those of the authors and not necessarily those of the funders.

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15 485 **Competing interests:** The authors declare that they have no competing interests.

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18 486 **Patient consent for publication:** Not applicable.

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21 487 **Availability of data and materials:** The data that support the findings of this study are available from
22
23 488 Wuhan Huoshenshan Hospital, Tongji Hospital, and Guanggu Woman & Child Hospital. However,
24
25 489 restrictions will apply to the availability of these data, which were used under license for the current study,
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27 490 and so are not publicly available. Data are available from the authors upon reasonable request and with
28
29 491 permission of the health service authority of Joint Logistics Troop of PLA.

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32 492 **Ethical Approval Statement:** The Research Ethics Committee of the No.900 Hospital of Joint Logistics
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34 493 Troop of PLA gave ethical approval (approval number: 2020-001). None of the inpatients were involved in
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36 494 any health intervention. All the individual data were anonymized prior to retrieval and analysis, and they
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38 495 did not contain any individual's private information.

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45 46 47 497 **REFERENCE**

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603 **Figure legends**

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24 604 **Fig. 1 Flow of inpatient selection**

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26 605 **Fig. 2: Curve of changes in the weighted life value with age**

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29 606 **Fig.3: Duration of symptoms before hospitalization by age group in female and male populations**

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31 607 **Fig.4: Length of hospital stay by age group in female and male populations**

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33 608 **Fig.5: Overall duration of symptom changes with age group in female and male populations**

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35 609 **Fig. 6a: The proportion of accumulative duration (in day) by symptoms in the study population**

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37 610 **Fig. 6b: The proportion of DALY by symptoms in the study population**

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39 611 **Fig. 7: Composition of each military temporary hospital's synthetic DALY**

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41 612 **Fig. 8: Composition of each sex group's synthetic DALY**

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43 613 **Fig. 9: Composition of each age group's synthetic DALY**

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45 614 **Fig. 10: Thermal map of COVID-19 inpatient's DALY by sex and age group (DALY per 1000**
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47 615 **capita).**

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49 616 **Fig. 11: Synthetic DALY changes with age group in female and male populations**

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51 617 **Fig. 12: DALY per day changes with age group in female and male populations**

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5 619 **Additional file**

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1,000 cases of COVID-19 inpatients' medical record data randomly selected from Taikang-Tongji Hospital

1,000 cases of COVID-19 inpatients' medical record data randomly selected from Huoshenshan Hospital

1,000 cases of COVID-19 inpatients' medical record data randomly selected from Guanggu Woman and Child Hospital

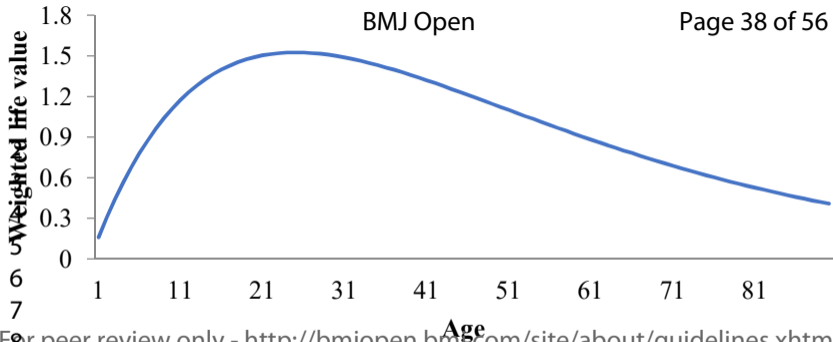
872 cases of COVID-19 inpatients' medical record data met the inclusion criteria

921 cases of COVID-19 inpatients' medical record data met the inclusion criteria

909 cases of COVID-19 inpatients' medical record data met the inclusion criteria

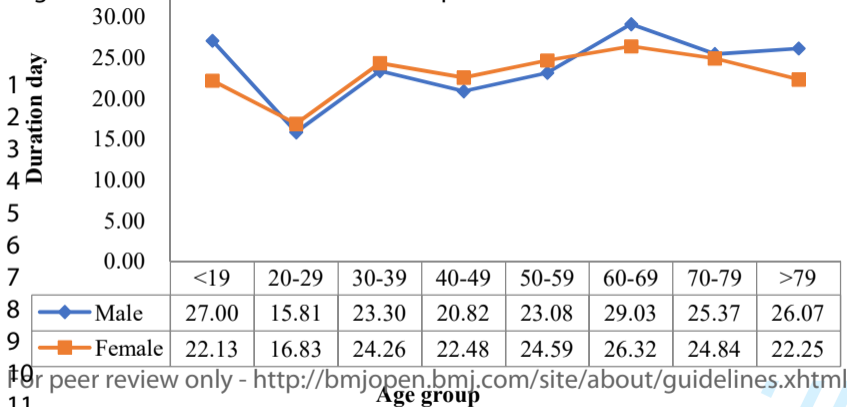
2,702 cases of COVID-19 inpatients' medical record

Fig. 1



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Fig. 2

**Fig. 3**

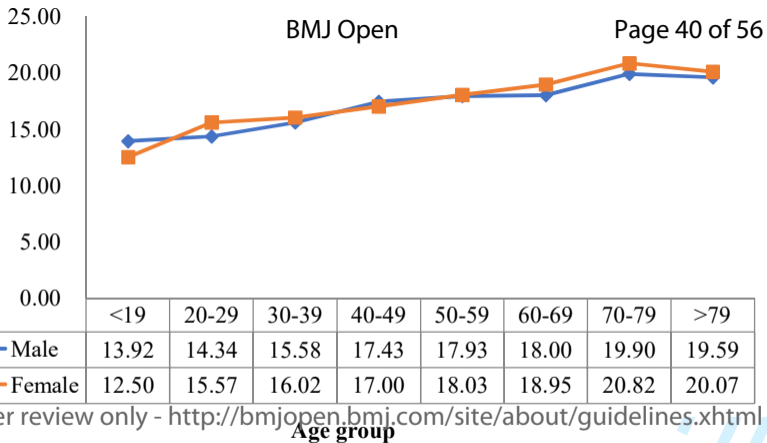
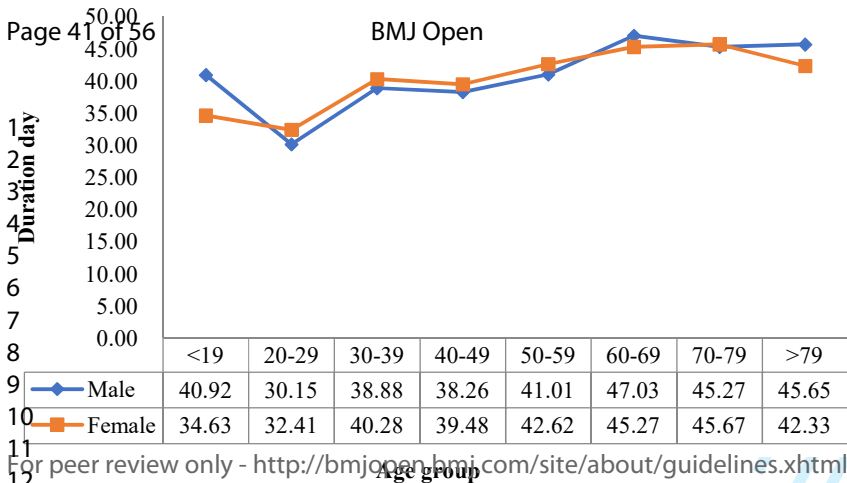


Fig. 4

**Fig. 5**

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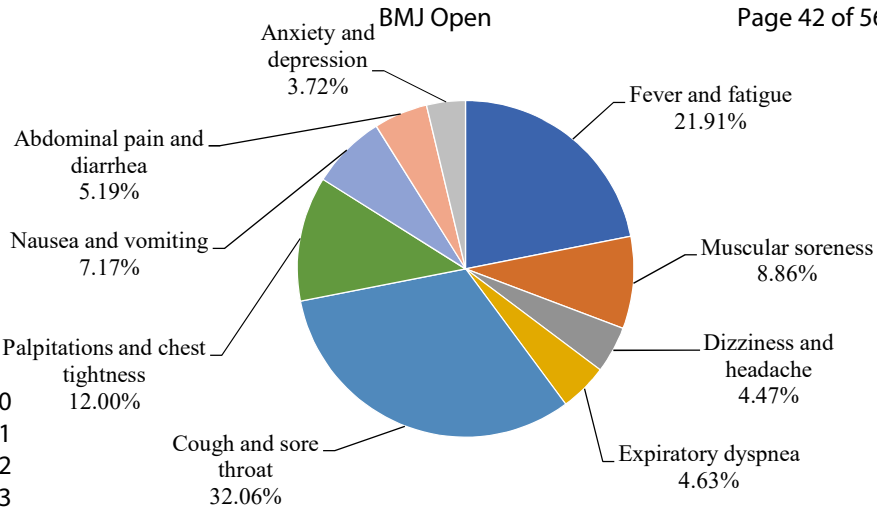


Fig. 6a

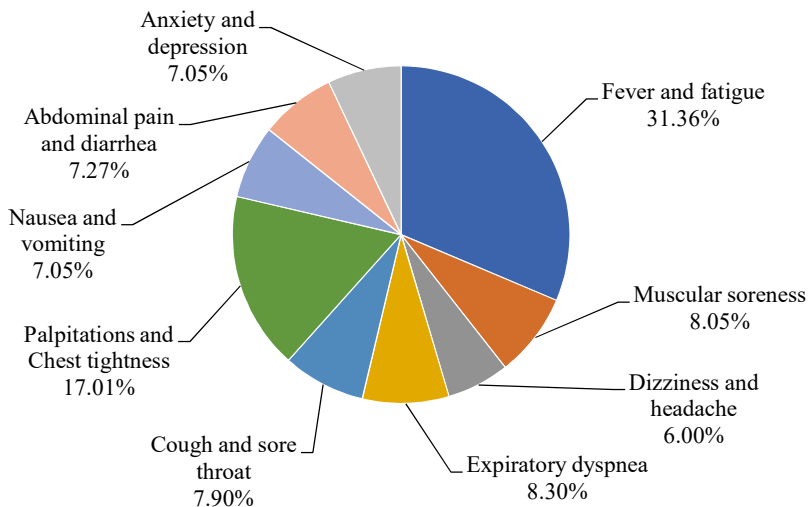


Fig. 6b

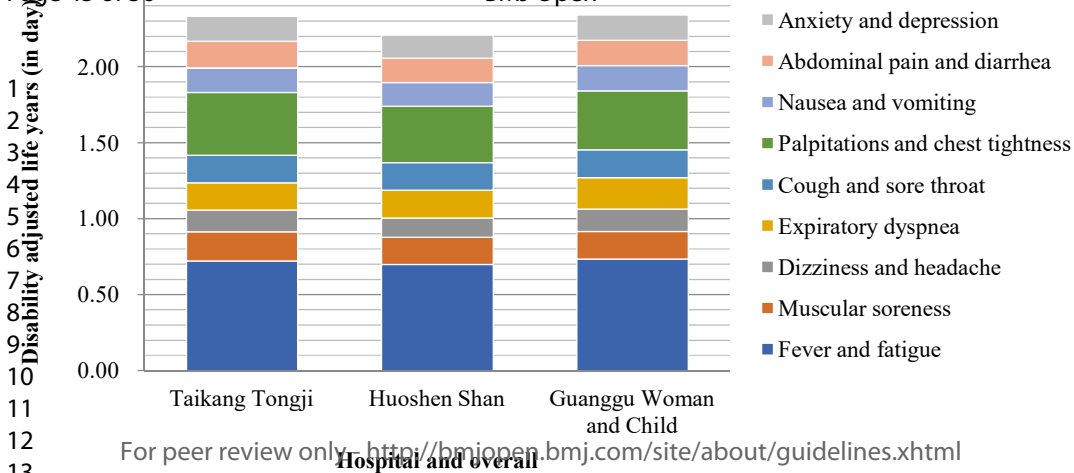


Fig. 7

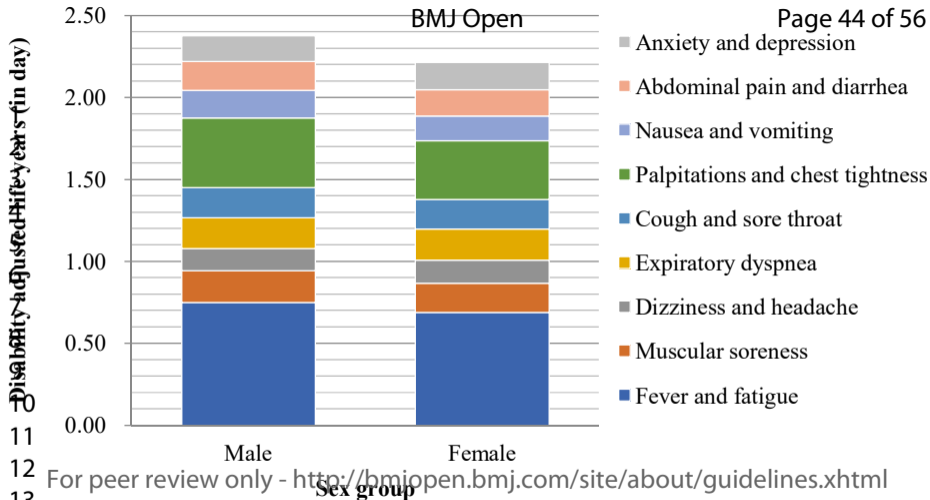


Fig. 8

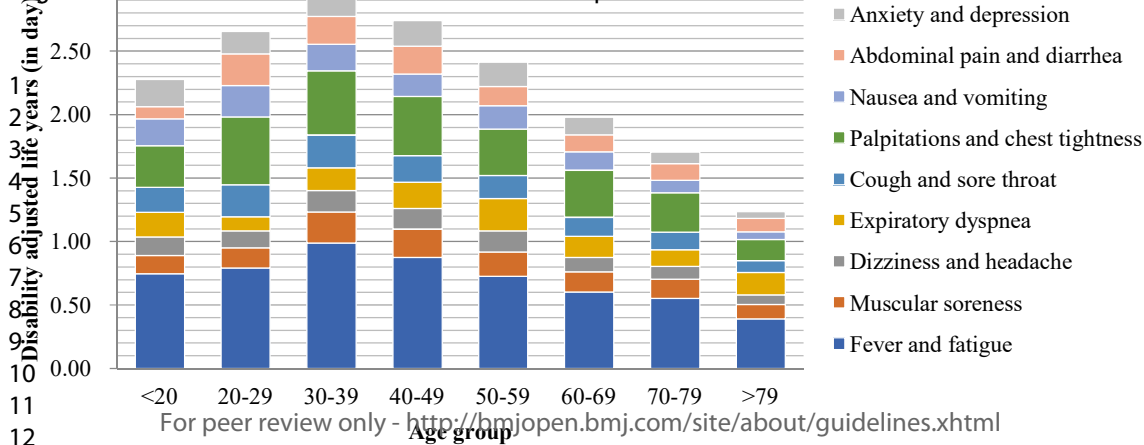
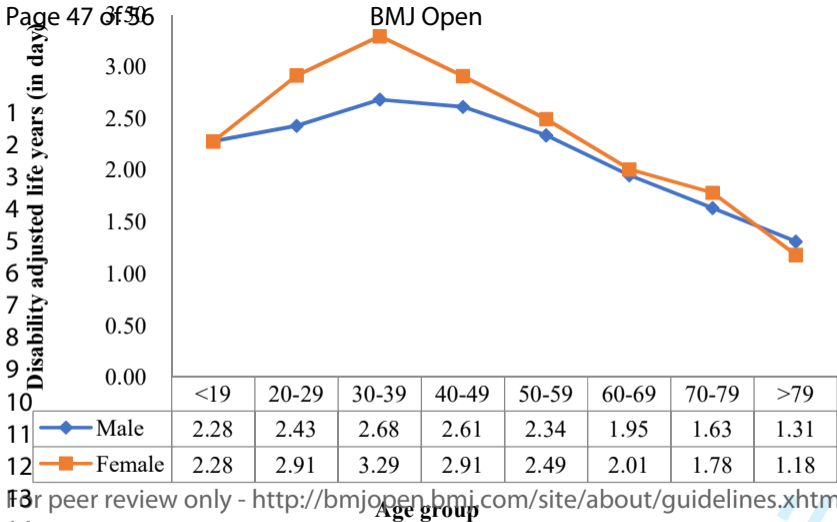


Fig. 9

| Male DALY/1000 captia (in days) | | | | | | | | | BMJ Open | Female DALY/1000 captia (in days) | | | | | | | | |
|---------------------------------|-----------------|------------------|------------------|------------------|------------------|------------------|---------------|---------------------|----------------------------------|-----------------------------------|---------------|------------------|------------------|------------------|------------------|------------------|-----------------|---------------|
| <19 (n=24) | 20-29 (n=54) | 30-39 (n=149) | 40-49 (n=234) | 50-59 (n=295) | 60-69 (n=328) | 70-79 (n=147) | >79 (n=95) | All age (n=1326) | Symptoms | All age (n=1376) | >79 (n=75) | 70-79 (n=159) | 60-69 (n=307) | 50-59 (n=297) | 40-49 (n=295) | 30-39 (n=156) | 20-29 (n=62) | <19 (n=25) |
| 639 | 789 | 1115 | 947 | 776 | 623 | 547 | 379 | 751 | Fever and fatigue | 689 | 412 | 559 | 584 | 677 | 821 | 868 | 796 | 855 |
| 162 | 174 | 276 | 233 | 201 | 163 | 157 | 117 | 193 | Muscular soreness | 177 | 107 | 145 | 154 | 187 | 215 | 217 | 146 | 121 |
| 134 | 150 | 176 | 151 | 159 | 109 | 94 | 83 | 134 | Dizziness and headache | 141 | 65 | 107 | 116 | 169 | 169 | 166 | 117 | 161 |
| 142 | 118 | 181 | 232 | 262 | 160 | 130 | 129 | 190 | Expiratory dyspnea | 191 | 236 | 133 | 177 | 247 | 189 | 175 | 108 | 243 |
| 202 | 275 | 271 | 210 | 183 | 151 | 146 | 87 | 183 | Cough and sore throat | 180 | 101 | 132 | 147 | 182 | 210 | 247 | 229 | 192 |
| 470 | 626 | 614 | 522 | 360 | 383 | 373 | 168 | 423 | Palpitations and Chest tightness | 358 | 162 | 252 | 357 | 373 | 423 | 401 | 457 | 193 |
| 149 | 263 | 238 | 192 | 187 | 151 | 124 | 59 | 171 | Nausea and Vomiting | 153 | 62 | 75 | 142 | 178 | 161 | 180 | 236 | 271 |
| 111 | 316 | 220 | 226 | 179 | 133 | 125 | 108 | 174 | Abdominal pain and Diarrhea | 160 | 100 | 138 | 137 | 126 | 213 | 220 | 187 | 80 |
| 266 | 203 | 202 | 194 | 184 | 135 | 85 | 50 | 157 | Anxiety and Depression | 166 | 63 | 92 | 137 | 197 | 210 | 209 | 153 | 164 |

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Fig. 10

**Fig. 11**

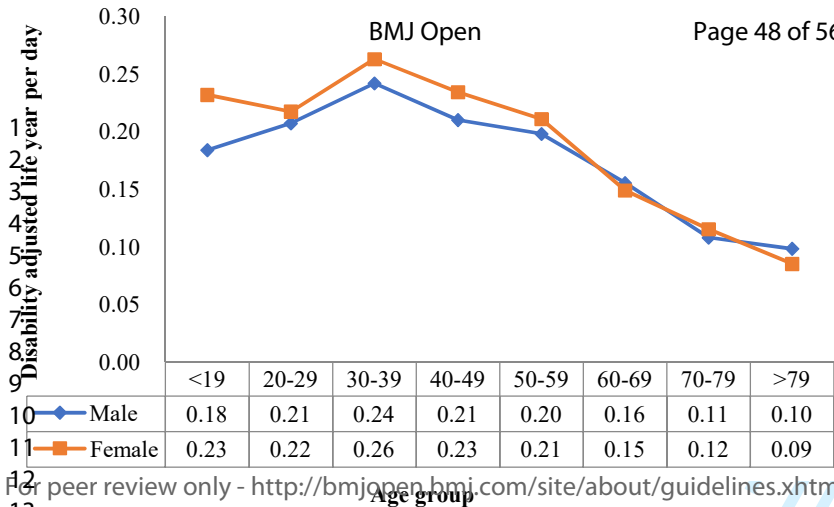


Fig. 12

Additional file 1: Questionnaire

Front-line medical staff questionnaire on symptoms of COVID-19 (The first round)

Dear Sir/Madam:

This is a questionnaire on COVID-19 typical symptom. The aim is to generate a comprehensive list of typical symptoms of inpatient with COVID-19, which can be used to assess the disease burden caused by the symptoms. This study will adopt the method of disability adjusted life years (DALYs) of the World Health Organization (WHO) to evaluate inpatients' burden of disease caused by COVID-19 symptoms.

According to your clinical experience, please judge the raw list of category and symptoms summarized by the literature review (Table 1). The judgment items are included:

For category:

- (1) Whether the category should be included in the list;
- (2) Whether the name of the category is appropriate.

For symptoms:

- (1) Whether the symptom should be listed;
- (2) Whether the symptom should be classified into the current category;
- (3) Whether the name of the symptom is appropriate.

If you think it is necessary, please supplement the symptom list according to your clinical experience. You can add:

- (1) New categories if necessary;
- (2) New symptoms if necessary.

As a front-line clinical expert engaged in COVID-19 treatment, your knowledge about the symptoms of the disease is valuable. Therefore, your opinion is very important for this study. Please try your best to fill the list appropriately. All the information you fill in is for academic research only. We will not analyze your responses individually and will keep them anonymous. Please provide responses to the best of your knowledge.

According to the Delphi process, the opinions of each expert in this round will be anonymously submitted to other experts as reference, in the next round of questionnaire survey. You will also see the anonymous opinions of the other experts. This study is expected to be conducted in 2-3 rounds for a more consistent answer.

Thank you for your support and cooperation.

The Research Group on COVID-19 Burden of Disease

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Table1: COVID-19 inpatient’s symptom list for the burden of disease evaluation (Template)

| Category (Code) | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Symptom | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Should it be moved to another category? If yes, type the code |
|------------------------------|-------------------------------|-------------------------------|---|---------------------------------|-------------------------------|-------------------------------|---|---|
| Systemic symptoms (01) | | | | Fever | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Neurological symptoms (02) | | | | Headache | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Respiratory symptoms (03) | | | | Expiratory dyspnea | | | | |
| | | | | Cough | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Cardiovascular symptoms (04) | | | | Palpitations | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |

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| Category (Code) | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Symptom | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Should it be moved to another category? If yes, type the code |
|-------------------------------------|-------------------------------|-------------------------------|---|---------------------------------|-------------------------------|-------------------------------|---|---|
| | | | | Other symptom 2 (if necessary): | | | | |
| Gastrointestinal symptoms (05) | | | | Diarrhea | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Other category (06) (if necessary): | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Other category (07) (if necessary): | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |

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If you have anything else to explain, please write here:

To confirm the above, please sign (or type here): _____

Date: _____

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Front-line medical staff questionnaire on symptoms of COVID-19 (The second/third round)

Dear Sir/Madam:

Thank you for your cooperation and hard work in the last round of the questionnaire survey. The anonymous opinions of other experts in the last round have been sent to you as a reference. We retained all the consensus items in the last round of the expert consultation in the list. We also added the most favorite (approval rate > 50%) new items or the items that were proposed for adjustment (Table 1). Please supplement with the necessary items according to your own clinical experience and the opinions of other experts.

According to your clinical experience, please judge the newly added or adjusted category and symptom items:

For category:

- (1) Whether the category should be included in the list;
- (2) Whether the name of the category is appropriate.

For symptom:

- (1) Whether the symptom should be listed;
- (2) Whether the symptom should be classified into the current category;
- (3) Whether the name of the symptom is appropriate.

Besides, you also can add:

- (1) New categories if necessary;
- (2) New symptoms if necessary.

According to the Delphi process, the opinion of each expert in this round will be anonymous and submitted to other experts as reference, in the next round of the questionnaire survey. You will also see the anonymous opinions of the other experts. This study is expected to be conducted in 2-3 rounds for a more consistent answer.

Thank you for your support and cooperation.

The Research Group on COVID-19 Burden of Disease

Date: _____

Table1: COVID-19 inpatient’s symptom list for the burden of disease evaluation (Template)

| Category (Code) | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Symptom | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Should it be moved to another category? If yes, type the code |
|------------------------------|-------------------------------|-------------------------------|---|---------------------------------|-------------------------------|-------------------------------|---|---|
| Systemic symptoms (01) | | | | Fever and fatigue * | | | | |
| | | | | Muscular soreness * | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Neurological symptoms (02) | | | | Headache | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Respiratory symptoms (03) | | | | Expiratory dyspnea | | | | |
| | | | | Cough | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Cardiovascular symptoms (04) | | | | Palpitations | | | | |
| | | | | Chest tightness * | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |

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| Category (Code) | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Symptom | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Should it be moved to another category? If yes, type the code |
|-------------------------------------|-------------------------------|-------------------------------|---|---------------------------------|-------------------------------|-------------------------------|---|---|
| | | | | | | | | |
| Gastrointestinal symptoms (05) | | | | Diarrhea | | | | |
| | | | | Vomiting * | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Psychological symptoms * (06) | | | | Anxiety and depression * | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Other category (07) (if necessary): | | | | Other symptom 1 (if necessary): | | | | |
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* Newly proposed or adjusted item.

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BMJ Open

Disease burden from COVID-19 symptoms among inpatients at the temporary military hospitals in Wuhan: A retrospective multi-center cross-sectional study

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|---------------------------------|--|
| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2021-048822.R2 |
| Article Type: | Original research |
| Date Submitted by the Author: | 03-Apr-2021 |
| Complete List of Authors: | <p>He, Maihong; The No.900 Hospital of Joint Logistics Support Troop of PLA, Department of Disease Prevention and Control; Clinical College in Fuzhou General Hospital of Fujian Medical University</p> <p>Li, Xiaoxiao; Fuzhou University, Department of National Defense Education and Research Xueyuan Road No.2, University Town, Fuzhou 350108, Fujian, China</p> <p>Tan, Qing; The No.923 Hospital of PLA, Department of Disease Prevention and Control</p> <p>Chen, Yong; Chinese PLA Center for Disease Control and Prevention</p> <p>Kong, Yue; The No.900 Hospital of Joint Logistics Support Troop of PLA, Department of Education</p> <p>You, Jianping; The First Affiliated Hospital of Army Medical University of PLA, Department of Infectious Diseases</p> <p>Lin, Xian; The No.900 Hospital of Joint Logistics Support Troop of PLA, Department of Disease Prevention and Control</p> <p>Lin, Ying; The No.900 Hospital of Joint Logistics Support Troop of PLA, Department of Disease Prevention and Control</p> <p>Zheng, Qing; The No.900 Hospital of Joint Logistics Support Troop of PLA, Meifeng Branch</p> |
| Primary Subject Heading: | Public health |
| Secondary Subject Heading: | Health economics |
| Keywords: | PUBLIC HEALTH, HEALTH ECONOMICS, HEALTH SERVICES ADMINISTRATION & MANAGEMENT |
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3 1 **Disease burden from COVID-19 symptoms among inpatients at the**
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5 2 **temporary military hospitals in Wuhan: A retrospective multi-center**
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7 **cross-sectional study**
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13 5 Maihong He ^{b1,c,(1),†}, Xiaoxiao Li ^{a,*,†}, Qing Tan^{d,(2)}, Yong Chen ^e, Yue Kong ^{b2,(3)}, Jianping You ^f, Xian Lin ^{b1},
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28 District, Wuhan, Hubei, China 430070

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30 **Word count (excluding title page, abstract, references, figures, and tables): 5292 words**

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3 31 **ABSTRACT:**
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6 32 **Objectives:** We aimed to establish a set of disability weights (DWs) for COVID-19 symptoms, evaluate the
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8 33 disease burden of inpatients, and analyze the characteristics and influencing factors of the disease.
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10 34 **Design:** This was a multi-center retrospective cross-sectional descriptive study.
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13 35 **Setting:** The medical records generated in three temporary military hospitals in Wuhan.
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16 36 **Participants:** Medical records of 2,702 inpatients generated from February 5 to April 5, 2020, were randomly
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18 37 selected for this study.
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21 38 **Primary and secondary outcome measures:** DWs of COVID-19 symptoms were determined by the
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23 39 person-trade-off approach. The inpatients' medical records were analyzed and used to calculate the
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25 40 disability-adjusted life years (DALY). The mean DALY was evaluated across sex and age groups. The
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27 41 relationship between DALY and age, sex, body mass index, length of hospital stay, symptom duration before
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29 42 admission, and native place was determined by multiple linear regression.
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34 43 **Results:** For the DALY of each inpatient, severe expiratory dyspnea, mild cough, and sore throat had the highest
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36 44 (0.399) and lowest (0.004) weights, respectively. The average synthetic DALY and daily DALY were 2.29 ± 1.33
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38 45 and 0.18 ± 0.15 days, respectively. Fever and fatigue contributed the most DALY at 31.36%, whereas nausea and
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40 46 vomiting and anxiety and depression contributed the least at 7.05%. There were significant differences between
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42 47 sex and age groups in both synthetic and daily DALY. Age, body mass index, length of hospital stay, and
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44 48 symptom duration before admission were strongly related to both synthetic and daily DALY.
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49 49 **Conclusions:** Although the disease burden was higher among women than men, their daily disease burdens were
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51 50 similar. The disease burden in the younger population was higher than that in the older population. Treatment at
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53 51 the hospitals relieved the disease burden efficiently, while a delay in hospitalization worsened it.
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57 52 **Keywords:** COVID-19; Wuhan; Burden of disease; Bio-security; Symptom; Inpatient; Disability-adjusted life years
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3 **53 Strengths and limitations of this study**
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5 54 The validity of the large sampled medical records from the military medical units was high.
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8 55 To determine the pure burden of COVID-19 symptoms, comorbidity and mortality cases were excluded.
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10 56 Self-reported bias of symptom duration prior to hospital admission may be high.
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13 57 Cultural and ethnic differences and virus variation over time may have affected data comparison.
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58 BACKGROUND

59 The coronavirus disease (COVID-19) pandemic is both a global public health emergency and a major
60 bio-security event; it brings pain and loss to individuals and families and a heavy burden to countries and
61 societies.^[1,2] Scientific evaluation of the social and economic impact of the public health incident provides an
62 important way to determine the therapeutic effectiveness in medical institutions and an important basis for the
63 government to formulate relevant rescue policies and recovery measures. The economic burden of disease
64 (BOD) and injury include treatment costs and various forms of losses in life (e.g., death and poor quality of
65 life due to a temporary or sustained decline in the quality of life).^[3,4]

66 There are several new features of COVID-19 compared with severe acute respiratory syndrome (SARS)
67 and the Middle East respiratory syndrome (MERS).^[5] The severe acute respiratory syndrome coronavirus 2
68 (SARS-CoV-2) infection can cause symptoms such as fever, fatigue, cough, dyspnea, headache, nausea,
69 vomiting, abdominal pain, and diarrhea, and in severe cases, severe acute respiratory syndrome, multiple
70 organ failure, and even death.^[6-9] As it is an emerging disease, the BOD caused by COVID-19 remains
71 unclear. Studying the BOD and symptoms of COVID-19 will help to deepen our understanding of the
72 disease, its harm, and severity and to predict the developing trend of the disease. Thus, public health
73 authorities could improve the treatment and rehabilitation programs, renew relief measures, and adjust
74 public health policies appropriately.

75 Since the 1990s, the World Health Organization (WHO) and the World Bank have proposed indicators
76 to evaluate the BOD, which is a measure of the disability-adjusted life years (DALY). This single-utility
77 measure used to determine the burden attributable to a specific disease is calculated using the standard
78 method proposed by Murray and Lopez.^[10] The DALY is a summary measure of population health
79 accounting for both the years of life lost (YLLs) and years lost due to disability (YLDs). The DALY was first
80 developed for quantifying the global burden of disease (GBD), expressed as the relative magnitude of losses

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3 81 of healthy life associated with different causes of disease and injury.^[11] Since then, the DALY has been
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5 82 widely used globally to estimate the BOD at the national, international, and regional levels.
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8 83 Recently, DALY has been used to evaluate the BOD of some specific diseases. Qi et al.
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10 84 comprehensively evaluated the direct and indirect BOD of public emergencies caused by Asian Lineage
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12 85 Avian Influenza A (H7N9) infection.^[12] Zhang et al. evaluated the BOD and related factors in hospitalized
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14 86 patients with coal workers' pneumoconiosis and provided the basis for improving relevant medical
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16 87 policies.^[13] Bacellar et al. assessed BOD in hospitalized elderly patients with neurological disorders in
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18 88 Brazil and recommended measures to improve the treatment plan.^[14] Adopting the WHO approach, Pei and
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20 89 Li et al. formulated the disability weights (DWs) for chronic mountain disease, which was used to calculate
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22 90 the BOD among soldiers stationed in Tibet and helped evaluate the ability of troops to perform tasks.^[15]
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29 91 The DALY method could provide important insights into public health studies and practice regarding
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31 92 COVID-19. This year, a series of research studies were conducted worldwide to estimate the BOD of
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33 93 COVID-19 in different regions, from multiple perspectives, and using different methods. Jo et al. adopted
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35 94 DWs from previous similar causes to calculate the BOD of COVID-19 in Korea, including YLDs and
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37 95 YLLs.^[16] Oh et al. estimated the YLLs due to COVID-19 in 30 high-incidence countries using the
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39 96 WHO-provided data.^[17] To assess the socio-economic burden of the COVID-19 pandemic in Italy, Nurchis et
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41 97 al. estimated YLLs and YLDs along with the productive YLLs, and the comparable DW of lower respiratory
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43 98 tract infection as adopted to estimate the YLDs.^[18] Mohanty et al. examined the impact of COVID-19 on the
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45 99 longevity, years of potential life lost, and DALY in the USA, Italy, Germany, and Sweden, and adopted DWs
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47 100 of similar diseases as proxy.^[19] Furthermore, Ortiz-Prado et al. assessed the BOD of COVID-19 in Ecuador
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49 101 by adopting the DWs of other similar diseases.^[20]
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57 102 These studies not only contributed greatly to the understanding of BOD of COVID-19 but also provided
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59 103 the basis for global COVID-19 public health services and related policy-making. However, in recent reports,
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3 104 BOD assessment of COVID-19 remained at the macro level and relatively unclear, mainly because, only the
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5 105 DWs from similar diseases were adopted, leaving COVID-19 with a singular DW, which ignored the
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8 106 complexity of COVID-19 symptoms. Until now, limited reports exist on China's COVID-19 BOD, especially
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11 107 based on each COVID-19. Thus, we aimed to establish the DW for COVID-19 symptoms, to estimate the
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13 108 BOD among inpatients in Wuhan, China, and to analyze the characteristics and potential influencing factors.
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16 109 To design this technical approach, we design a technical approach based on previous studies. The BOD of
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18 110 COVID-19 symptoms was evaluated from existing medical records.
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21 111 **METHOD**

22 112 **Selection of the population groups**

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26 113 To counter the public health disaster and bio-security crisis caused by COVID-19 in Wuhan, People's
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29 114 Liberation Army (PLA) performed a series of non-combat military operations, including the deployment of
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31 115 three temporary military hospitals (Huoshenshan Hospital [from March 2 to April 15, 2020],
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34 116 Taikang-Tongji Hospital [March 13 to April 16, 2020], and Guanggu Woman and Child Hospital [March
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36 117 13 to April 16, 2020]). The first hospital was a newly built one, while the other two were civil medical
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39 118 facilities temporarily utilized by the PLA medical staff. While in operation, all the hospitals were
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42 119 designated as specialized COVID-19 hospitals.

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44 120 All the analyzed inpatient data were randomly selected from the three temporary military hospitals'
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47 121 medical records using the same recording standard. The included inpatients' hospitalization period ranged
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50 122 from February 5 to April 5, 2020. The selection process was conducted from May 25 to June 5, 2020, after
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52 123 the closure of the temporary hospitals (Fig. 1). Data for 2,702 inpatients were included in this study. All the
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55 124 inpatients treated by the military medical staff were from the military hospitals affiliated to the PLA.

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57 125 <Insert Fig. 1 here>
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60 126 The diagnosis and treatment method were based on the "Diagnosis and treatment standard of

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3 127 COVID-19 (7th edition)” published by the People’s Republic of China’s (PRC) central government.^[21] The
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5 128 standard detailed laboratory tests for COVID-19, with pathogenic, serological, and chest image criteria,
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8 129 were included. All patients were hospitalized before the release of the 7th edition and were reconfirmed
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10 130 according to the diagnostic criteria. The inclusion criteria were COVID-19 diagnosis at the hospitals
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12 131 according to the standard guideline and continuous treatment at these hospitals. To determine the BOD of
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14 132 COVID-19, inpatients with any other morbidity (other infectious diseases, other respiratory diseases,
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16 133 psychiatric disease, tumor, pregnancy and lactation, and chronic cardiac, liver, kidney, and neurological
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18 134 diseases) were excluded. We also excluded COVID-19 inpatient deaths due to the reluctance of their family
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20 135 members to allow the use of their data for a public study. Similarly, cases with incomplete medical records
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22 136 were excluded.
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29 137 **Establishment of the disability weights for COVID-19 symptoms**

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31 138 DW is a key component of BOD analysis that represents disease severity. It ranges from 0 to 1, where 0
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33 139 represents healthy life, and 1 represents death.^[4] WHO has been conducting GBD studies for several years,
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35 140 with series of DWs derived for different health states that are the outcomes of different diseases.^[22-26]
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39 141 Because COVID-19 is a new infectious disease, no DWs exist for COVID-19 symptoms in the
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41 142 WHO’s DW list; thus, we attempted to establish customized DWs for COVID-19 symptoms. First,
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43 143 COVID-19 symptoms were listed following a literature review of newly published clinical reports on
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45 144 COVID-19. Three rounds of questionnaires were completed by front-line medical staff in the three military
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47 145 field hospitals in Wuhan to derive a raw list of COVID-19 symptoms for establishing DWs (questionnaire
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49 146 sample is shown in Additional file 1).
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55 147 Then, we convened a nine-expert panel composed of three senior respiratory physicians, two senior
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57 148 infectious disease physicians, one epidemiologist, one public health management expert, and two nursing
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59 149 experts. Based on the raw list of COVID-19 symptoms, the panel performed the Delphi process to
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3 150 determine the final symptom list for creation of DWs.^[27]
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5 151 Then, the panel members performed the Person-Trade-Off (PTO) exercise to derive each symptom's
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8 152 DWs by three levels of severities (health stages).^[15, 28, 29] The health stages were described on an A4-sized
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10 153 vignette that contained disease-specific information in simple terminologies. As a reference framework for
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13 154 this task, the panel members were provided with a WHO-GBD framework table, which displayed seven
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16 155 disability classes and 22 anchoring example conditions. The coefficient of variation (CV) was calculated to
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18 156 determine the need for additional rounds of discussion and reassignment of values.
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20 157 **Data extraction**

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22 158 Basic information for the confirmed cases included the identification number (ID), age, sex, weight, height,
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25 159 native place, date of onset reported by the patient, diagnostic conclusion, symptoms recorded by the
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28 160 medical staff, and inpatient and outpatient time. Nine age groups were created: <10, 10-19, 20-29, 30-39,
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30 161 40-49, 50-59, 60-69, 70-79, and >80 years. Body mass index (BMI) was calculated, while the duration of
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33 162 symptoms was determined as the length of stay + symptom duration before hospitalization (self-reported in
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36 163 the medical record).
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38 164 To accurately extract the medical data from the records, we trained 6 staffs by same criteria. During
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41 165 the data extraction, the six staff members were divided into three groups of two, and when data were
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44 166 extracted from the records, these were cross-checked. The extraction process was conducted from May 29
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46 167 to August 7, 2020.
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48 168 49 169 **Calculation of DALY for COVID-19 symptoms**

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51 170 The DALY was used to estimate the disease burden of COVID-19 symptoms. The DALY is calculated as
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54 171 the sum of the YLLs due to premature mortality in the population and the equivalent 'healthy' YLDs for
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56 172 incident cases of the health condition.^[4,11,30] However, we did not consider COVID-19-related deaths.
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59 173 Therefore, the DALY due to COVID-19 was equal to the YLDs. Thus, a patient's individual DALY was
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3 174 calculated using the following formula^[15]:

$$4 \quad 5 \quad 6 \quad 7 \quad 175 \quad \text{DALY} = \int_{x=\alpha}^{x=\alpha+L} DC x e^{-\beta x} e^{-r(x-\alpha)} dx \quad (1.0)$$

8 176 where D represents DW, K is an age weighting factor, C is a constant, r is the discount rate, a is the
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10 177 age at onset, β is a parameter from the age weighting function, and L is lifetime with disability. We used the
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13 178 base case recommended by Murray and Lopez, with $C = 0.1658$, $r = 0.03$, $K = 1$, and $\beta = 0.04$.^[15,31]

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16 179 Considering that the COVID-19 inpatient hospitalization time was relatively short, L in the formula
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18 180 (1.0) is shorter than 1 year; thus, the age of each inpatient was treated as fixed. Accordingly, the formula
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21 181 was simplified as follows:

$$22 \quad 23 \quad 24 \quad 25 \quad 182 \quad \text{DALY} = DC x e^{-\beta x} \quad (2.0)$$

26 183 In formula 2.0, $C x e^{-\beta x}$ reflects the life value discounted by age. This function is based on the
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28 184 hypothesis that life value is different for different age groups: a person's life value increases after they are
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31 185 born and reaches the peak in their youth; next, the life value declines with age (Fig.2). Hence, in
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34 186 calculating the DALY, DALY will differ for different age groups despite identical symptoms.

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37 187 <Insert Fig. 2 here>

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39 188 We calculated the DALY as follows: 1) the cumulative duration (in days) of each health condition (a
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42 189 health condition is one type of symptom severity); 2) the duration was multiplied by the corresponding DW to
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45 190 get the DALY of each health condition; 3) all the DALY values were summed up into an inpatient's synthetic
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48 191 DALY for COVID-19; 4) the synthetic DALY was divided by the patient's length of stay to get the daily
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50 192 DALY. Considering that the inpatient's length of stay was relatively short, the unit of DALY was set as days.

51 193 **Statistical analysis**

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53 194 The demographic characteristics of patients such as hospitalization, sex, and native place, were evaluated.
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56 195 The distribution of each symptom according to the hospital, sex, and overall population, was calculated.
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59 196 The mean DALY, synthetic DALY, daily DALY, age, BMI, and symptom course (including symptom
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3 197 duration before hospitalization, length of stay, and overall duration) based on the hospital, sex, and age
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5 198 groups were calculated and compared by analysis of variance (ANOVA) or t-test (for two groups only).
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8 199 The ratio difference of the cumulative duration (in days) of symptom severity levels (mild, moderate, and
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10 200 severe) was tested by a chi-square test. The proportions of BOD for each symptom by sex and age group,
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13 201 and in the entire sample population were computed. DALY per 1,000 capita was also calculated by age
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16 202 group and sex. Each symptom's duration in the whole study population was also calculated.

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18 203 To test the relationship between DALY and age, sex, BMI, and symptom duration, separate linear
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21 204 regression analyses were performed using DALY as the dependent variable and age, sex, BMI, native
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24 205 place, symptom duration before hospitalization, and length of stay as independent variables. In the
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26 206 regression models, sex and native place were set as categorical variables while the others were continuous
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29 207 variables. Synthetic and daily DALY were analyzed, and each hospital's study population and overall study
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31 208 population were analyzed separately. IBM SPSS Statistics for Windows, version 25.0 (IBM Corp.,
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34 209 Armonk, N.Y., USA) was used for statistical analyses. A P -value <0.05 was considered statistically
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37 210 significant.

211 **Patient and public involvement**

212 This was a multi-center retrospective cross-sectional descriptive study of COVID-19 inpatients in Wuhan,
213 PRC. The study was performed after the closure of the three temporary military hospitals. None of the
214 inpatients were involved in any health intervention. All individual data were anonymized prior to retrieval
215 and analysis. Because only patient data were used, no patients were directly involved in the study.

216 **RESULTS**

217 **Patient characteristics**

218 Data of 2,702 inpatients (872, 921, and 909 from Taikang-Tongji, Huoshenshan, and Guanggu Woman and
219 Child Hospitals, respectively) were used. Table 1 shows the inpatients' demographic characteristics.

220 All were Chinese, and 1,326 were female, whereas 1,376 were male; 2,618 were natives of Hubei
 221 Province, while 84 were not. The mean age was 55.52 ± 16.09 years and 54.18 ± 15.85 years for female and
 222 male populations, respectively. The mean age of male patients was significantly lower ($P=0.03$). No
 223 significant difference was found in symptom duration before hospitalization, length of stay, and overall
 224 duration of symptoms between female and male populations.

225 By age groups, there were significant differences in the symptom duration before hospitalization, length
 226 of stay, and overall duration of symptoms according to the ANOVA test ($P>0.05$). The least significant
 227 difference (LSD) test showed that the 20-29 years age group had the least symptom duration, whereas the
 228 60-69 years age group had the highest duration, with a significant difference between the groups ($P<0.05$).

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Table 1: Demographic characteristics of inpatients

| Characteristics | Number of patients | Proportio n |
|-------------------------|--------------------|----------------|
| Hospital | | |
| Taikang-Tongji | 872 | 32.27% |
| Huoshenshan | 921 | 34.09% |
| Guanggu Woman and Child | 909 | 33.64% |
| Sex | | |
| Female | 1326 | 49.07% |
| Male | 1376 | 50.93% |
| Native place | | |
| Hubei province | 2618 | 96.89% |

| Characteristics | Number of patients | Proportio n |
|------------------------|--------------------|----------------|
| Outside Hubei province | 84 | 3.11% |

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232 **Duration of symptoms**

233 Table 2 shows the mean age, BMI, symptom duration before hospitalization, length of stay, and overall

234 duration of symptoms according to hospital, sex, and age group. There were no significant differences in

235 age, symptom duration before hospitalization, length of stay, and overall duration of symptoms among the

236 three hospitals according to the ANOVA test ($P>0.05$). The inpatients' age ranged from 11 to 94 years237 (mean, 54.84 ± 15.98 years), while BMI ranged from 16.23 to 28.7 (mean, 22.11 ± 1.94). The length of stay238 ranged from 5 to 50 days (mean, 17.88 ± 7.38 days), whereas the self-reported symptom duration before239 hospitalization ranged from 2 to 72 days (mean, 24.11 ± 15.66 days). By combining the inpatient and

240 self-reported symptom duration before hospitalization, we obtained the total duration of symptoms, which

241 ranged from 7 to 94 days (mean, 41.99 ± 16.37 days).

242

243 **Table 2: Means of age, body mass index, symptom duration before hospitalization, length of stay, and**244 **overall duration of symptoms by hospital, sex, and age group of inpatients**

| | Age | Body mass index | Symptoms duration before hospitalization (days) | Length of stay (days) | Overall duration of symptoms (days) |
|---------------------------------|------------------|--------------------|--|--------------------------|--|
| Hospital | | | | | |
| Taikang-Tongji (n=872) | 54.76 ± 15.75 | 22.25 ± 1.92 | 24.36 ± 15.92 | 17.92 ± 7.42 | 42.28 ± 16.57 |
| Huoshenshan (n=921) | 55.21 ± 15.88 | 22.02 ± 2.00 | 24.65 ± 15.65 | 17.91 ± 7.34 | 42.55 ± 16.33 |
| Guanggu Woman and Child (n=909) | 54.53 ± 16.29 | 22.07 ± 1.90 | 23.34 ± 15.40 | 17.80 ± 7.39 | 41.15 ± 16.21 |
| Sex | | | | | |
| Female (n=1326) | 55.52 ± 16.09 | 22.14 ± 1.92 | 24.11 ± 15.40 | 18.11 ± 7.34 | 42.22 ± 16.04 |
| Male (n=1376) | 54.18 ± 15.85 | 22.08 ± 1.96 | 24.12 ± 15.92 | 17.66 ± 7.41 | 41.77 ± 16.69 |

| | Age | Body mass index | Symptoms duration before hospitalization (days) | Length of stay (days) | Overall duration of symptoms (days) |
|-------------------|-------------|-----------------|---|-----------------------|-------------------------------------|
| Age group (years) | | | | | |
| <20 (n=49) | 15.59±2.53 | 21.79±2.19 | 24.61±14.01 | 13.22±5.67 | 37.84±13.16 |
| 20-29 (n=116) | 25.35±2.53 | 21.95±1.76 | 16.28±12.36 | 14.91±5.69 | 31.20±14.32 |
| 30-39 (n=305) | 34.87±2.84 | 22.21±1.98 | 23.77±16.68 | 15.79±6.71 | 39.56±17.44 |
| 40-49 (n=529) | 44.84±2.96 | 22.10±1.97 | 21.56±14.29 | 17.24±6.93 | 38.80±14.31 |
| 50-59 (n=592) | 54.68±2.80 | 22.13±1.97 | 23.83±15.81 | 17.98±7.20 | 41.81±16.15 |
| 60-69 (n=635) | 64.16±2.72 | 22.2±1.910 | 27.63±16.08 | 18.49±7.12 | 46.12±16.39 |
| 70-79 (n=306) | 73.96±2.88 | 21.99±1.84 | 25.12±15.95 | 20.34±8.09 | 45.46±16.04 |
| >79 (n=170) | 84.49±3.35 | 21.97±2.04 | 23.94±14.37 | 19.86±8.96 | 43.79±17.55 |
| Overall (n=2702) | 54.84±15.98 | 22.11±1.94 | 24.11±15.66 | 17.88±7.38 | 41.99±16.37 |

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246 To further analyze the disease course (duration of symptom before hospitalization, length of stay, and
 247 overall duration of symptom), we drew line diagrams of the means by age group and sex (Figs. 3 to 5). We
 248 also performed a two-way ANOVA to test for the difference in the mean course of the disease by age group
 249 and sex. The results showed that age was significantly associated with the disease variables ($P<0.05$), while
 250 sex was not, and that the two factors had no significant interaction ($P>0.05$).

251 <Insert Fig. 3, 4, and 5 here>

252 We also calculated each symptom's cumulative duration (in days) by three levels of severity in the
 253 overall sample population (Table 3). Fever and fatigue had the longest duration, with a cumulative duration
 254 of 26,863 days. The lowest cumulative duration was for anxiety and depression (4,565 days). By chi-square
 255 test, the proportion of severity differed significantly among different symptoms ($P<0.05$). Anxiety and
 256 depression had the highest proportion of severe conditions (30.54%), whereas cough and sore throat had the

highest proportion of mild conditions (10.63%). The cumulative durations (in days) by symptoms are shown in Fig. 6a. Cough and sore throat contributed the maximum to symptom duration (32.06%), whereas anxiety and depression contributed the least (3.72%).

<Insert Fig. 6 here>

Table 3: Each COVID-19 symptom's cumulative duration (in days) in the study population

| Symptoms | Mild | | Moderate | | Severe | | Overall duration (days) |
|----------------------------------|-------|-------|----------|-------|--------|-------|----------------------------|
| | Day | % | Day | % | Day | % | |
| Fever and fatigue | 2,231 | 8.31 | 20,846 | 77.60 | 3,785 | 14.09 | 26,863 |
| Muscular soreness | 334 | 3.08 | 8,220 | 75.71 | 2,303 | 21.21 | 10,858 |
| Dizziness and headache | 92 | 1.68 | 3,864 | 70.51 | 1,524 | 27.81 | 5,481 |
| Expiratory dyspnea | 104 | 1.83 | 4,096 | 72.23 | 1,471 | 25.94 | 5,672 |
| Cough and sore throat | 4,180 | 10.63 | 30,172 | 76.75 | 4,959 | 12.61 | 39,312 |
| Palpitations and chest tightness | 862 | 5.86 | 11,232 | 76.34 | 2,620 | 17.81 | 14,715 |
| Nausea and vomiting | 387 | 4.40 | 6,434 | 73.19 | 1,970 | 22.41 | 8,792 |
| Abdominal pain and diarrhea | 150 | 2.36 | 4,534 | 71.30 | 1,675 | 26.34 | 6,360 |
| Anxiety and depression | 35 | 0.77 | 3,135 | 68.69 | 1,394 | 30.54 | 4,565 |
| Overall | 8,375 | 6.83 | 92,533 | 75.47 | 21,701 | 17.70 | 122,610 |

COVID-19, coronavirus disease 2019.

DWs of COVID-19 symptoms

After two rounds of the Delphi process by the panel, we developed a 9-item COVID-19 symptom list with six categories. Each symptom included three levels of severity (mild, moderate, and severe), thereby

268 representing 27 health stages. Based on these, we derived the DWs for each health stage by the PTO
 269 exercise; along with the expert panel, a consensus was reached at the fifth round of the Delphi process (CV
 270 <0.5). Thus, the DWs of 27 COVID-19 health stages were derived; severe expiratory dyspnea had the
 271 highest weight of 0.399, while mild cough and sore throat had the lowest weight of 0.004 (Table 4).

Table 4: Disability weights for the symptoms of COVID-19

| Category | Symptom categories | Health stages | DWs | 95% CI |
|-----------------------|------------------------|---------------|-------|---------------|
| Systemic symptoms | Fever and fatigue | Mild | 0.006 | (0.004-0.008) |
| | | Moderate | 0.051 | (0.036-0.066) |
| | | Severe | 0.133 | (0.089-0.177) |
| | Muscular soreness | Mild | 0.015 | (0.012-0.018) |
| | | Moderate | 0.054 | (0.041-0.067) |
| | | Severe | 0.110 | (0.059-0.113) |
| Neurological symptoms | Dizziness and headache | Mild | 0.028 | (0.019-0.037) |
| | | Moderate | 0.083 | (0.055-0.111) |
| | | Severe | 0.163 | (0.109-0.217) |
| Respiratory symptoms | Expiratory dyspnea | Mild | 0.045 | (0.040-0.050) |
| | | Moderate | 0.108 | (0.085-0.131) |
| | | Severe | 0.399 | (0.293-0.505) |
| | Cough and sore throat | Mild | 0.004 | (0.003-0.005) |
| | | Moderate | 0.011 | (0.008-0.014) |
| | | Severe | 0.034 | (0.023-0.045) |

| Category | Symptom categories | Health stages | DWs | 95% CI |
|---------------------------|----------------------------------|---------------|-------|---------------|
| Cardiovascular symptoms | Palpitations and chest tightness | Mild | 0.041 | (0.029-0.053) |
| | | Moderate | 0.072 | (0.048-0.096) |
| | | Severe | 0.179 | (0.120-0.238) |
| Gastrointestinal symptoms | Nausea and vomiting | Mild | 0.009 | (0.006-0.012) |
| | | Moderate | 0.057 | (0.038-0.076) |
| | | Severe | 0.130 | (0.089-0.171) |
| | Abdominal pain and diarrhea | Mild | 0.011 | (0.008-0.014) |
| | | Moderate | 0.091 | (0.062-0.120) |
| | | Severe | 0.194 | (0.128-0.260) |
| Psychological symptoms | Anxiety and depression | Mild | 0.030 | (0.021-0.039) |
| | | Moderate | 0.120 | (0.084-0.156) |
| | | Severe | 0.366 | (0.243-0.489) |

COVID-19, coronavirus disease 2019; DWs, disability weights; CI, confidence interval

DALY of inpatients

According to the formula and DWs, the DALY of each inpatient for each symptom was calculated, as well as their synthetic DALY and daily DALY. The proportion of DALY in the study population is shown in Fig. 6b. Among these, fever and fatigue contributed the most in DALY (31.36%), whereas nausea and vomiting and anxiety and depression contributed the least (7.05%).

The mean and standard deviation of DALY for each symptom by hospital, sex, and overall study population are shown in Table 5, and those by age group are shown in Table 6. The mean overall DALY was 2.29 ± 1.33 days, whereas the mean daily DALY was 0.18 ± 0.15 days. No significant difference was

284 noted in each symptom's DALY, synthetic DALY, or daily DALY among the hospitals ($P>0.05$).

285 However, in the LSD test, synthetic DALY in Huoshenshan Hospital was significantly lower than that in

286 Taikang-Tongji ($P=0.048$) and Guanggu Woman and Child ($P=0.031$) Hospitals. The daily DALY in

287 Huoshenshan Hospital was significantly lower than that in Guanggu Woman and Child Hospital ($P=0.023$).

288 The DALY for fever and fatigue, muscular soreness, palpitations and chest tightness, and nausea and

289 vomiting, and synthetic DALY were significantly lower for male than for female patients ($P>0.05$). In the

290 inpatient population, the overall DALY per 1,000 capita was 6.28, whereas in the female and male

291 populations, the overall DALY per 1,000 capita was 6.07 and 6.51 years, respectively.

292

293 **Table 5: The mean DALY of COVID-19 inpatients or all symptoms, according to hospital, sex, and**

294 **overall study population**

| Symptom | Taikang-Tongji | Huoshenshan | Guanggu Woman and | Woman | Man | Overall |
|----------------------------------|------------------|------------------|------------------------|-----------|------------------------|-----------|
| | Hospital (n=872) | Hospital (n=921) | Child Hospital (n=909) | (n=1326) | (n=1376) | (n=2702) |
| Fever and fatigue | 0.72±0.60 | 0.70±0.59 | 0.73±0.63 | 0.75±0.61 | 0.69±0.60 [‡] | 0.72±0.61 |
| Muscular soreness | 0.19±0.18 | 0.18±0.17 | 0.18±0.17 | 0.19±0.18 | 0.18±0.17 [‡] | 0.18±0.17 |
| Dizziness and headache | 0.14±0.18 | 0.13±0.17 | 0.14±0.20 | 0.13±0.17 | 0.14±0.19 | 0.14±0.18 |
| Expiratory dyspnea | 0.18±0.31 | 0.18±0.32 | 0.21±0.38 | 0.19±0.34 | 0.19±0.33 | 0.19±0.34 |
| Cough and sore throat | 0.18±0.12 | 0.18±0.12 | 0.18±0.13 | 0.18±0.12 | 0.18±0.13 | 0.18±0.12 |
| Palpitations and chest tightness | 0.41±0.45 | 0.37±0.40 | 0.39±0.43 | 0.42±0.44 | 0.36±0.41 [‡] | 0.39±0.43 |
| Nausea and vomiting | 0.16±0.24 | 0.16±0.23 | 0.17±0.24 | 0.17±0.25 | 0.15±0.23 [‡] | 0.16±0.24 |
| Abdominal pain and diarrhea | 0.18±0.30 | 0.16±0.26 | 0.17±0.24 | 0.17±0.26 | 0.16±0.28 | 0.17±0.27 |
| Anxiety and depression | 0.16±0.23 | 0.15±0.21 | 0.17±0.24 | 0.16±0.23 | 0.17±0.23 | 0.16±0.23 |

| | | | | | | |
|--------------|-----------|-------------|-----------|-----------|------------|-----------|
| Total DALY | 2.33±1.33 | 2.21±1.26* | 2.34±1.38 | 2.38±1.33 | 2.21±1.32‡ | 2.29±1.33 |
| DALY per day | 0.19±0.14 | 0.18±0.14** | 0.19±0.16 | 0.19±0.14 | 0.18±0.15 | 0.18±0.15 |

295 * $P < 0.05$ vs. Guanggu Woman and Child Hospital; † $P < 0.05$ vs. Taikang-Tongji Hospital; ‡ $P < 0.05$ vs. woman.

296 DALY, Disability-adjusted life years.

297

298 **Table 6: COVID-19 inpatient DALY by symptoms and age group**

| Symptom | <20 years | 20-29 years | 30-39 years | 40-49 years | 50-59 years | 60-69 years | 70-79 years | >79 years |
|----------------------------------|-----------|-------------|-------------|-------------|-------------|-------------|-------------|-----------|
| | (n=49) | (n=116) | (n=305) | (n=529) | (n=592) | (n=635) | (n=306) | (n=170) |
| Fever and fatigue | 0.75±0.58 | 0.79±0.73 | 0.99±0.89 | 0.88±0.70 | 0.73±0.54 | 0.60±0.42 | 0.55±0.38 | 0.39±0.28 |
| Muscular soreness | 0.14±0.12 | 0.16±0.19 | 0.25±0.23 | 0.22±0.20 | 0.19±0.16 | 0.16±0.13 | 0.15±0.12 | 0.11±0.09 |
| Dizziness and headache | 0.15±0.18 | 0.13±0.16 | 0.17±0.22 | 0.16±0.22 | 0.16±0.21 | 0.11±0.13 | 0.10±0.11 | 0.08±0.09 |
| Expiratory dyspnea | 0.19±0.24 | 0.11±0.15 | 0.18±0.28 | 0.21±0.43 | 0.25±0.45 | 0.17±0.24 | 0.13±0.19 | 0.18±0.25 |
| Cough and sore throat | 0.20±0.09 | 0.25±0.13 | 0.26±0.15 | 0.21±0.14 | 0.18±0.12 | 0.15±0.09 | 0.14±0.08 | 0.09±0.06 |
| Palpitations and chest tightness | 0.33±0.43 | 0.54±0.54 | 0.51±0.61 | 0.47±0.5 | 0.37±0.35 | 0.37±0.34 | 0.31±0.33 | 0.17±0.17 |
| Nausea and vomiting | 0.21±0.28 | 0.25±0.36 | 0.21±0.30 | 0.17±0.23 | 0.18±0.25 | 0.15±0.22 | 0.10±0.12 | 0.06±0.07 |
| Abdominal pain and diarrhea | 0.10±0.11 | 0.25±0.31 | 0.22±0.43 | 0.22±0.36 | 0.15±0.20 | 0.13±0.17 | 0.13±0.17 | 0.10±0.16 |
| Anxiety and depression | 0.21±0.25 | 0.18±0.24 | 0.21±0.28 | 0.20±0.28 | 0.19±0.25 | 0.14±0.16 | 0.09±0.12 | 0.06±0.08 |
| Synthetic DALY | 2.28±0.93 | 2.65±1.46 | 2.98±1.87 | 2.74±1.52 | 2.41±1.12 | 1.98±0.92 | 1.70±0.79 | 1.24±0.69 |
| DALY per day | 0.21±0.11 | 0.21±0.15 | 0.25±0.18 | 0.22±0.17 | 0.20±0.16 | 0.15±0.10 | 0.11±0.06 | 0.09±0.06 |

299 COVID-19, coronavirus disease 2019.

300 DALY, Disability-adjusted life years.

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3 302 According to the ANOVA test, the mean DALY by age groups differed significantly for each
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5 303 symptom and for the synthetic DALY and daily DALY ($P<0.05$). The DALY for both single symptoms
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8 304 and synthesized DALY had the tendency of an inverse U-shaped curve. The DALY increased with age,
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10 305 reached a peak in the prime of life, and then slowly decreased with age. In this study, the 40-49 years age
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13 306 group had the highest DALY for expiratory dyspnea, while the 20-29 years age group had the highest
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16 307 DALY for palpitations and chest tightness, nausea and vomiting, and abdominal pain and diarrhea. DALY
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18 308 for the other symptoms, synthetic DALY, and daily DALY peaked in those aged 20-29 years.

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21 309 The composition of synthetic DALY for each symptom by hospital is shown in Fig. 7, and that by sex
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24 310 and age group is shown in Fig. 8 and Fig. 9, respectively.

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26 311 To visualize each symptom's DALY by age group and sex, we drew a thermal map for each subgroup's
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28
29 312 DALY per 1,000 capita (in days; Fig. 10). Fever and fatigue were in the most intense (red) area, while
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31
32 313 palpitations and chest tightness were in the next intense area, for both female and male populations. The
33
34 314 female population aged 30-39 years had the highest DALY score of 1,115 days per 1,000 capita.
35
36
37 315 Contrarily, in the female population above 79 years, the lowest DALY 50 days per 1,000 capita was found.

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39 316 <Insert Fig. 7, 8, 9, and 10 here>

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41
42 317 We also identified the changing curves of the mean synthetic DALY and daily DALY by age group
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44 318 and sex (Fig. 11 and Fig 12). The two-way ANOVA showed that both age and sex significantly affected
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46
47 319 synthetic DALY ($P<0.05$), and there was a significant interaction effect between the two variables
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49
50 320 ($P=0.02$). However, when DALY per day was the dependent variable, the significant difference with sex
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52 321 was lost ($P=0.08$), whereas age remained significant ($P<0.05$), and the interaction effect between the two
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54
55 322 variables was also lost ($P=0.518$).

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57 323 <Insert Fig. 11 and 12 here>

58
59 324 **Linear regression analyses**

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3 325 The results of the multiple linear models are shown in Table 7. When synthetic DALY was set as the
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5 326 dependent variable, all four models were significant ($P<0.05$), with R^2 ranging from 0.214 to 0.240. In the
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7
8 327 four models, symptom duration before hospitalization and length of stay were significantly positively
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10 328 associated with synthetic DALY, while age was significantly negatively associated with the overall
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12
13 329 synthetic DALY. For sex and BMI, however, the four models showed different results. In the Guanggu
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16 330 Woman and Child Hospital model, sex and BMI were not significant ($P=0.098$ and $P=0.146$); in the other
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18
19 331 three models, sex and BMI were significant, indicating that the female population had higher DALY than
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21 332 the male population ($P<0.05$), and that patients with a high BMI had higher DALY ($P<0.05$).

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24 333 When DALY per day was set as the dependent variable, all four models were significant ($P<0.05$), with
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26 334 R^2 ranging from 0.153 to 0.188. For age and symptom duration before hospitalization, the level of
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28
29 335 significance was the same as with model I. Length of stay remained significant; however, the effectiveness
30
31
32 336 was negatively reversed for DALY. For sex, the overall sample and Huoshenshan Hospital models were
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34 337 significant ($P=0.037$ and $P=0.022$, respectively), and for BMI, the overall sample and Taikang-Tongji
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37 338 Hospital models were significant ($P<0.001$ and $P=0.001$, respectively). In all the models, native place was
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39 339 not significant ($P>0.05$).

Table 7 Linear regression analyses between COVID-19 inpatient’s DALY and individual variables

| Variable | Model Type I * | | | | | | | | Model Type II ** | | | | | | | |
|---|-----------------------|---------|-----------------------|---------|-----------------------|---------|-------------------------|---------|-----------------------|---------|-----------------------|---------|-----------------------|---------|-------------------------|---------|
| | Overall sample | | Taikang-Tongji | | Huoshenshan | | Guanggu Woman and Child | | Overall sample | | Taikang-Tongji | | Huoshenshan | | Guanggu Woman and Child | |
| | R ² =0.222 | | R ² =0.214 | | R ² =0.224 | | R ² =0.240 | | R ² =0.164 | | R ² =0.188 | | R ² =0.170 | | R ² =0.153 | |
| | β | P-value | β | P-value | β | P-value | β | P-value | β | P-value | β | P-value | β | P-value | β | P-value |
| Age | -0.415 | <0.001 | -0.431 | <0.001 | -0.388 | <0.001 | -0.429 | <0.001 | -0.290 | <0.001 | -0.288 | <0.001 | -0.269 | <0.001 | -0.312 | <0.001 |
| Sex | 0.069 | <0.001 | 0.070 | 0.020 | 0.088 | 0.003 | 0.048 | 0.098 | 0.037 | 0.037 | 0.047 | 0.123 | 0.070 | 0.022 | -0.002 | 0.956 |
| Symptom duration before hospitalization | 0.166 | <0.001 | 0.169 | <0.001 | 0.206 | <0.001 | 0.133 | <0.001 | 0.208 | <0.001 | 0.207 | <0.001 | 0.251 | <0.001 | 0.180 | <0.001 |
| Length of stay | 0.312 | <0.001 | 0.265 | <0.001 | 0.334 | <0.001 | 0.338 | <0.001 | -0.139 | <0.001 | -0.184 | <0.001 | -0.134 | <0.001 | -0.108 | 0.001 |
| Body mass index | 0.048 | 0.005 | 0.090 | 0.003 | 0.011 | 0.719 | 0.042 | 0.146 | 0.062 | <0.001 | 0.101 | 0.001 | 0.030 | 0.331 | 0.056 | 0.068 |
| Native place | 0.015 | 0.365 | 0.000 | 0.987 | -0.017 | 0.549 | 0.030 | 0.303 | 0.003 | 0.856 | -0.005 | 0.882 | -0.002 | 0.951 | 0.024 | 0.437 |

COVID-19, coronavirus disease 2019; DALY, disability-adjusted life years.

* Dependent variable is overall DALY; ** Dependent variable is DALY per day.

340 DISCUSSION

341 Principal findings

342 According to this study, each cured inpatient averagely loses about 2-3 days of healthy life due to
343 COVID-19 symptoms, and discounts almost one-fifth of the daily quality of life. Viewed from the
344 population's perspective, the indirect life loss per 1,000 inpatients was >6 years, even if death was not
345 considered. If we consider the increasing number of COVID-19 inpatients worldwide,^[32] the indirect life
346 loss could be an enormous figure. Considering the pre-hospitalization symptoms and temporary or
347 permanent loss of body function after discharge, the cumulative loss of life would be many-fold higher.
348 The difference in inpatient BOD of each COVID-19 symptom in the three hospitals was relatively small;
349 however, when the BOD was added, inpatients at Huoshenshan Hospital showed a relatively lower overall
350 BOD than the other two hospitals' inpatients. However, the difference was negligible. This can be
351 accounted for by the greater investment of manpower and material resources at Huoshenshan Hospital.

352 Regarding DWs, among the main symptoms of COVID-19, severe expiratory dyspnea accounted for
353 the most serious BOD, followed by negative psychological symptoms such as severe anxiety and
354 depression. In actual cases, however, the prevalence of severe depression and dyspnea among the inpatient
355 population was not high. Although the prevalence and BOD of anxiety and depression were not high, the
356 ratios of their severity were, and these should be considered in medical care. Among the inpatient
357 population, the most common symptoms were cough and sore throat, but these had a low contribution to
358 the BOD. In contrast, fever and fatigue largely contributed to the BOD.

359 Regarding the symptoms of COVID-19, from which the DWs were derived, in addition to fever and
360 dry cough, COVID-19 patients had gastrointestinal symptoms such as nausea and vomiting, diarrhea,
361 abdominal discomfort, and abnormal liver function; and the viral nucleic acid can be detected in the
362 patients' feces.^[33,34] A possible pathogenic mechanism of COVID-19 is as follows^[7,35]: a cytokine storm

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3 363 caused by viral infection leads to an increase in the neutrophil count, which in turn results in the imbalance
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5 364 and excessive activation of the immune response and immune pathology, focal proliferation of lung cells,
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8 365 and accumulation of multinucleated giant cells. These trigger apoptosis of the alveolar epithelial and
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10 366 endothelial cells, and diffuse alveolar injury and interstitial pulmonary fibrosis, resulting in progressive
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13 367 hypoxia and injury to the lungs, heart, liver, and other organs. Moreover, SARS-CoV-2 enters the cells
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16 368 primarily through the angiotensin-converting enzyme 2 (ACE2) receptor.^[36] ACE2 is highly expressed not
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18 369 only in type II alveolar epithelial cells but also in the small intestine, duodenum, colon, and liver,
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20
21 370 suggesting that the virus may invade target organs in the digestive tract via the ACE2 receptor, causing
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24 371 primary injury and digestive symptoms.^[37] Anxiety and depression are also common in hospitalized
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26 372 COVID-19 patients. Anxiety, depression, and other psychological stress responses can stimulate
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29 373 sympathetic nervous system response and increase the systemic arterial pressure and heart rate.^[38]
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31 374 Therefore, the psychological stress due to anxiety and depression may cause tachycardia and increase the
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34 375 left ventricular afterload, thus aggravating pulmonary edema and exacerbating the lung function. The
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36 376 emotional and somatization symptoms caused by the psychological stress may also affect the immune
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39 377 system through neuroendocrine pathways, thereby affecting the patient's rehabilitation process and
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42 378 increasing the BOD.^[39,40]

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44 379 The BOD of female inpatients was higher than that of male inpatients, which is similar to the findings
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47 380 in the Korean report^[16]; however, when the BOD was shared daily between the hospitals, there were no
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50 381 significant differences. This indicated that the symptoms in female inpatients during hospitalization were
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52 382 more severe (i.e., the symptoms fluctuated dramatically during hospitalization). Specific symptoms such as
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55 383 fever, fatigue, muscular soreness, palpitations, chest tightness, nausea, and vomiting could result in a higher
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58 384 BOD in female than in male inpatients. For other symptoms, there was no significant difference between
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60 385 female and male populations in the BOD.

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3 386 Contrary to general thinking, the BOD of the younger population was higher than that of the older
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6 387 population. Both ANOVA and linear models supported this conclusion. The main reason for this trend was
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8 388 that the "value" of life at different age stages was fully accounted for in the BOD evaluation. The illness
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11 389 among youth and middle-aged individuals could bring about greater personal, social, and economic losses.
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13 390 For the synthetic DALY or daily DALY, most linear models indicated that the BOD for obese people was
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16 391 more severe. Obesity affects the immune function of the body, and the burden borne by the organs in obese
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19 392 people is heavier than in non-obese people. Obese people are not only more likely to suffer from various
20
21 393 types of infection, including COVID-19 but also experience more serious complications.^[41, 42] Although
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24 394 synthetic DALY increased with the hospitalization duration, daily DALY decreased significantly. Although
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26 395 the cumulative BOD increased, the BOD shared per day continuously decreased, and the trend of this
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29 396 reduction was very obvious. It indicated that patients received better treatment during hospitalization, and
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31 397 that the symptoms continued to ameliorate with medical care. In contrast, the longer the symptom duration
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34 398 before hospitalization, the heavier the BOD of inpatient duration, indicating that delayed treatment may
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37 399 aggravate the BOD and lead to the consumption of more medical resources. In addition, teenagers and
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39 400 some older age groups, especially those aged above 60 years, exhibited a longer duration of symptoms
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41
42 401 before hospitalization in our study.

43 402 **Strengths and limitations**

45 403 Our work firstly proposed the COVID-19 DWs by each main COVID-19 symptom and calculated the
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48 404 inpatient BOD caused by the symptoms. Although the validity of the large sampled medical records from
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51 405 the military medical units was high, there are some limitations to this study. First, because this was a
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54 406 retrospective rather than prospective study, the data acquired from the medical records may not be fully
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56 407 accurate. The duration of symptoms before admission relied on patients' self-report, which could cause
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59 408 potential self-reported bias. Notwithstanding, considering the relatively large sample, despite adjustment
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3 409 for potential bias, the macroscopic trend could be detected at statistical analysis.
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5 410 Second, the medical records were generated in the early stages of the COVID-19 outbreak when the
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8 411 knowledge about COVID-19 was limited. During that time, the diagnosis and treatment protocol of
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10 412 COVID-19 did not include symptoms such as ageusia and anosmia. Thus, there were only a few records of
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12 413 these symptoms in our data. Consequently, we did not include these as the main symptom in this study.
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14
15 414 However, because inpatients were at the acute stage of the disease, the discomfort from ageusia and
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17 415 anosmia could be clubbed with respiratory and gastrointestinal symptoms. When calculating the disease
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19 416 burden of respiratory and gastrointestinal symptoms, we could make up for the lack of disease burden
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21 417 caused by ageusia and anosmia. Meanwhile, in most cases, ageusia and anosmia were more noticeable after
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23 418 discharge, when other acute symptoms had gradually disappeared. Thus, these symptoms could be treated
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25 419 as sequelae of COVID-19 rather than the main symptoms of inpatients in the acute stage. Third, because
26
27 420 this study is based on Chinese cultural and ethnic backgrounds in the early stage of the COVID-19
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29 421 pandemic, these, combined with the virus strain variations over time, may affect the comparability of the
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31 422 results worldwide. The DWs derived from this study may be limited and should be considered as regional
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33 423 DWs of COVID-19, while the study could be considered a pilot for an international COVID-19 BOD study.
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35 424 Notwithstanding, our primary aim was to focus on the regional disease burden and public health
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37 425 management; the cultural difference may therefore not have had a great impact on our findings.
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46 426 Moreover, to determine BOD caused only by COVID-19 symptoms, this study excluded inpatients
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48 427 with comorbidity. When the COVID-19 symptoms are superimposed on other diseases, the effect might
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50 428 have been complex and may not have been easily evaluated using simple linear summarization function;
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52 429 moreover, quantitative differentiation of BOD purely caused by COVID-19 symptoms would have been
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54 430 challenging. Because the BOD of COVID-19 comorbidities will be helpful for understanding the
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56 431 COVID-19 burden, it should be considered in future studies. Thus, in this study, that inpatients with
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3 432 pre-existing medical conditions were excluded could have affected the findings in the following two ways:
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5 433 a) the severity and disease duration may have been milder and shorter, respectively, and b) the exclusion of
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8 434 patients with a pre-existing psychiatric disease could have explained the short duration of reported anxiety
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11 435 and depression during hospitalization. Besides, deaths were excluded. Thus, this study evaluated DALY in
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14 436 the same way as YLD caused by symptoms during hospitalization.

437 **Implications for health service**

438 The BOD of COVID-19 and its symptoms in the inpatient population are an indirect economic and
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20 439 social burden; however, these are ignored by some public health authorities. This study suggests that to
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23 440 reduce the BOD, symptomatic treatment should focus on symptoms and behaviors that cause a higher BOD
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25 441 and the BOD for vulnerable populations. For example, since cardiovascular and respiratory symptoms in
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28 442 female inpatients were more severe, as were systemic symptoms, focused attention should be on female
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31 443 patients' cardiovascular and respiratory systems during the acute stage. Although the symptoms in elderly
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33 444 people may be slightly more severe, it is more significant to reduce the disease burden in youth and
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36 445 middle-aged inpatients with COVID-19 from a macro-economic perspective, if the medical resources are
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38 446 limited. It is also necessary to reduce the disease burden of obese people by strengthening the intervention
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41 447 in this population during the treatment. Besides, the findings suggest that earlier detection, diagnosis, and
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44 448 treatment of COVID-19 are very important for the healthcare system. However, the findings also suggest
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46 449 that older individuals may have difficulty seeking medical treatment or may lack vigilance of their health,
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49 450 which could result in the consumption of more medical resources. Thus, relevant social service departments
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51 451 should be strengthened to provide help and support for teenagers and elderly people.

52 53 452 **CONCLUSION**

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56 453 COVID-19 symptoms could cause heavy BOD in inpatients. The BOD for the female population was
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59 454 higher than that for the male population; however, the daily BOD between male and female inpatients was
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3 455 similar. When the changing life value with age was considered, the disease burden of the younger
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5 456 population was higher than that of the older population, except for teenagers. The treatment at the three
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8 457 military hospitals efficiently relieved the BOD of the inpatients, despite similar treatment effects. Delay in
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10 458 hospitalization could worsen the BOD for patients with COVID-19. Thus, there is a need for the
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13 459 deployment of adequate medical resources for early hospitalization of patients with moderate or severe
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16 460 symptoms by the public health authority.
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21 462 **List of abbreviations**

23 463 BOD: burden of disease

26 464 COVID-19: coronavirus disease 2019

29 465 DALY: disability-adjusted life years

31 466 DW: disability weight

34 467 PLA: people's liberation army

36 468 GBD: global burden of disease

39 469 WHO: World Health Organization

42 470 YLDs: years lost due to disability

44 471 YLLs: years of life lost

47 472

49 473 **Acknowledgments:** The authors thank the professional guidance and medical staff, including managers,

51 474 physicians, epidemiologists, sanitarians, and nurses in the target wards for their excellent assistance.

53 475 **Authors' contributions:** XXL and MH conceived and designed the studies; MH and XXL did literature

55 476 search and review; XXL, JY, and YC conducted questionnaire and PTO processes; XL, QZ, and YL

57 477 collected and extracted the data; MH, QT, and YK contributed materials; XXL, JY, and YC analyzed and

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2
3 478 interpreted the data; XXL and MH drafted the article and revised it. All the authors gave approval before
4
5 479 submission.

6
7
8 480 **Funding:** This work was funded by the Educational Research Project for Young and Middle-aged Teachers
9
10 481 (supporting XXL) [Funder: Provincial Education Department of Fujian Province, China; Grant No.
11
12 482 JAS19008]; Research Start-up Fund (supporting XXL) [Funder: Fuzhou University, China; Grant
13
14 483 No.CXRC201915]; Soft Science Fund (supporting MH) [Funder: Fujian Province, China; Grant No.
15
16 484 2017R085].

17
18 485 **Disclaimer:** All the funders had no role in the design and conduct of the study; collection, management,
19
20 486 analysis, and interpretation of the data; or preparation, review, and approval of the manuscript. The views
21
22 487 expressed are those of the authors and not necessarily those of the funders.

23
24 488 **Competing interests:** The authors declare that they have no competing interests.

25
26 489 **Patient consent for publication:** Not applicable.

27
28 490 **Availability of data and materials:** The manuscript is based on medical records from PLA military
29
30 491 temporary hospitals specialized for COVID-19 emergency in Wuhan 2020. However, there is no public
31
32 492 data base.

33
34 493 **Ethical Approval Statement:** The Research Ethics Committee of the No.900 Hospital of Joint Logistics
35
36 494 Troop of PLA gave ethical approval (approval number: 2020-001). None of the inpatients were involved in
37
38 495 any health intervention. All the individual data were anonymized prior to retrieval and analysis, and they
39
40 496 did not contain any individual's private information.

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47 499 **REFERENCE**

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603 **Figure legends**

604 **Fig. 1 Flow of inpatient selection**

605 **Fig. 2: Curve of changes in the weighted life value with age**

606 **Fig.3: Duration of symptoms before hospitalization by age group in female and male populations**

607 **Fig.4: Length of hospital stay by age group in female and male populations**

608 **Fig.5: Overall duration of symptom changes with age group in female and male populations**

609 **Fig. 6a: The proportion of accumulative duration (in day) by symptoms in the study population**

610 **Fig. 6b: The proportion of DALY by symptoms in the study population**

611 **Fig. 7: Composition of each military temporary hospital's synthetic DALY**

612 **Fig. 8: Composition of each sex group's synthetic DALY**

613 **Fig. 9: Composition of each age group's synthetic DALY**

614 **Fig. 10: Thermal map of COVID-19 inpatient's DALY by sex and age group (DALY per 1000**
615 **capita).**

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3 616 **Fig. 11: Synthetic DALY changes with age group in female and male populations**

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5 617 **Fig. 12: DALY per day changes with age group in female and male populations**

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10 619 **Additional file**

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13 620 File name: Additional file 1

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15 621 File format: DOC

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17 622 Title of data: questionnaire

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19 623 Description of data: Text/table

1,000 cases of COVID-19 inpatients' medical record data randomly selected from Taikang-Tongji Hospital

1,000 cases of COVID-19 inpatients' medical record data randomly selected from Huoshenshan Hospital

1,000 cases of COVID-19 inpatients' medical record data randomly selected from Guanggu Woman and Child Hospital

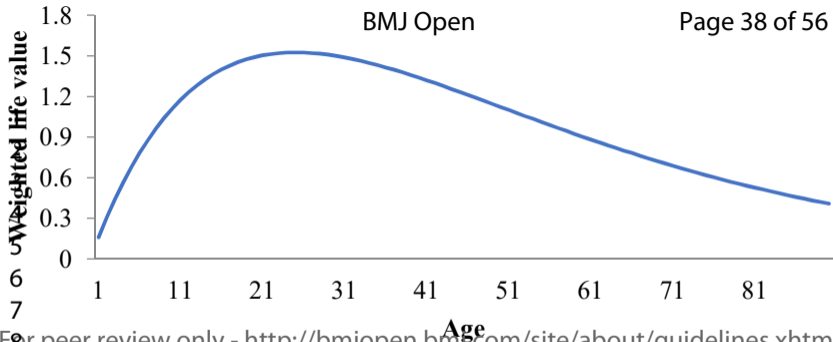
872 cases of COVID-19 inpatients' medical record data met the inclusion criteria

921 cases of COVID-19 inpatients' medical record data met the inclusion criteria

909 cases of COVID-19 inpatients' medical record data met the inclusion criteria

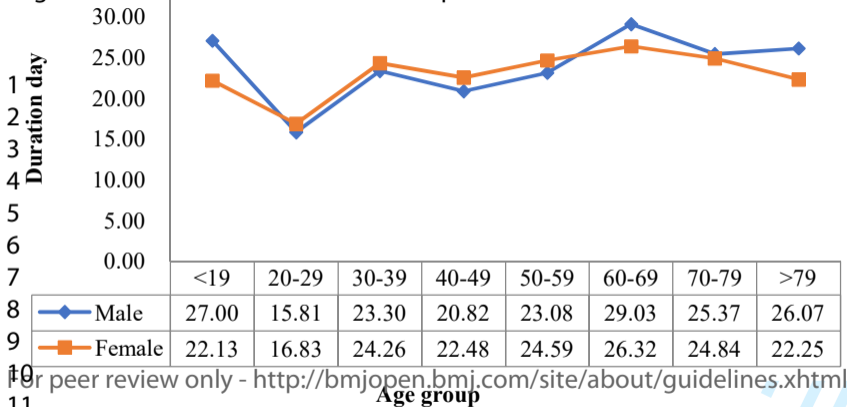
2,702 cases of COVID-19 inpatients' medical record

Fig. 1



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Fig. 2

**Fig. 3**

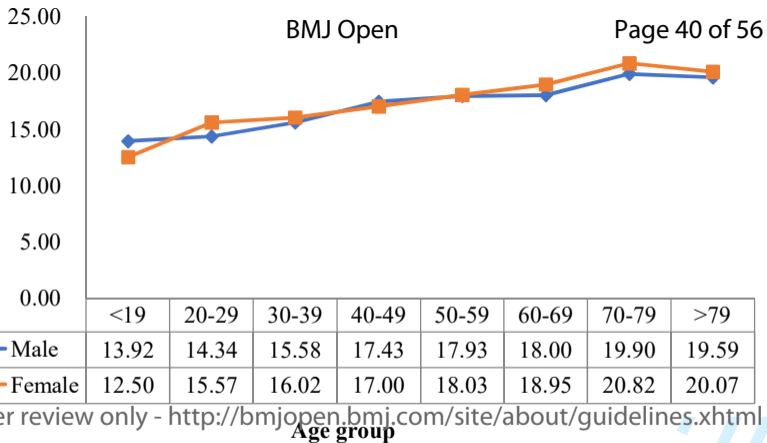
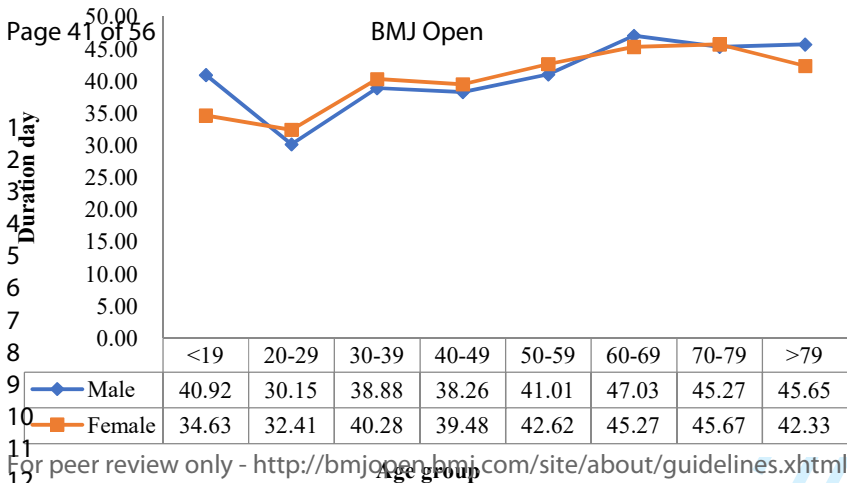


Fig. 4

**Fig. 5**

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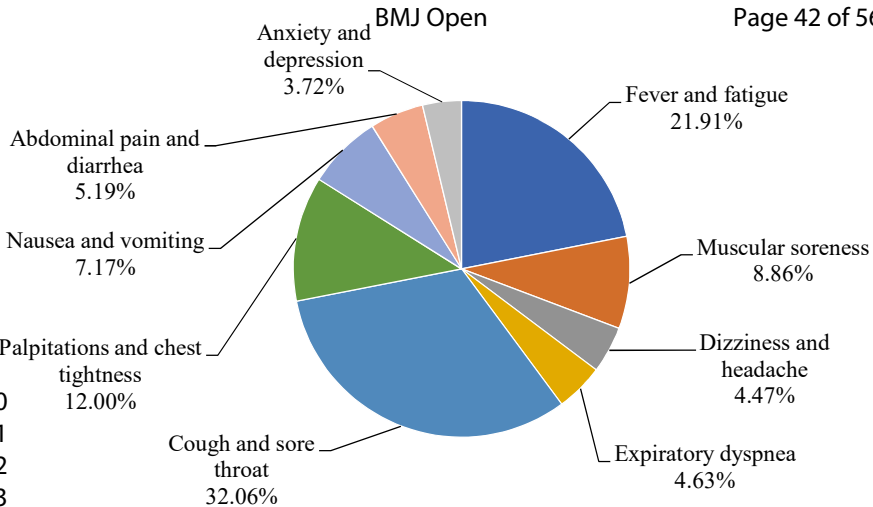


Fig. 6a

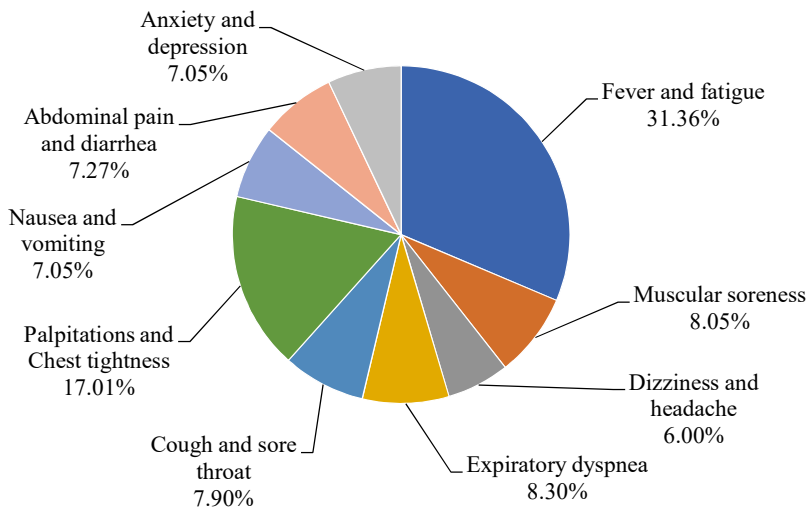


Fig. 6b

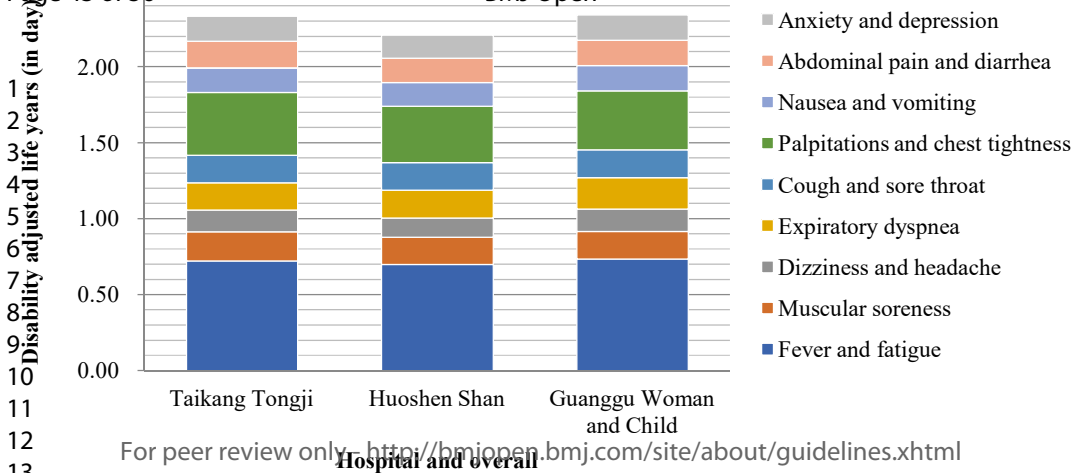


Fig. 7

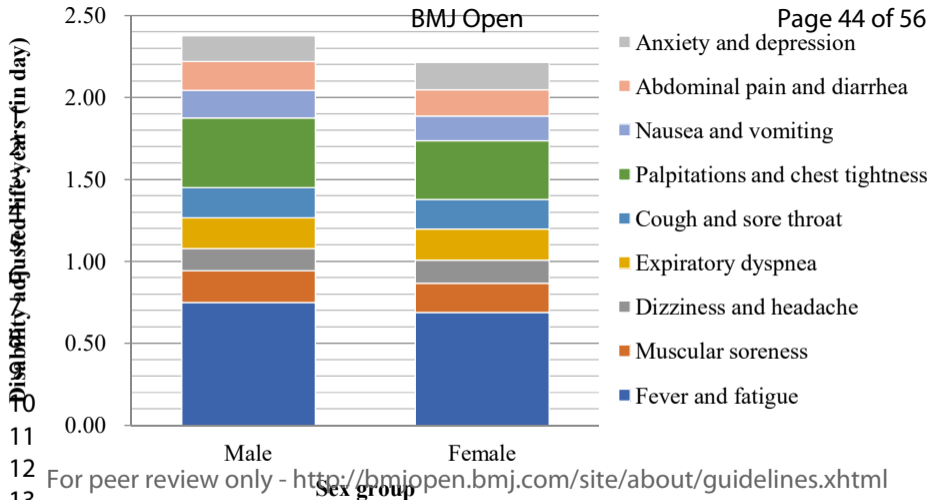


Fig. 8

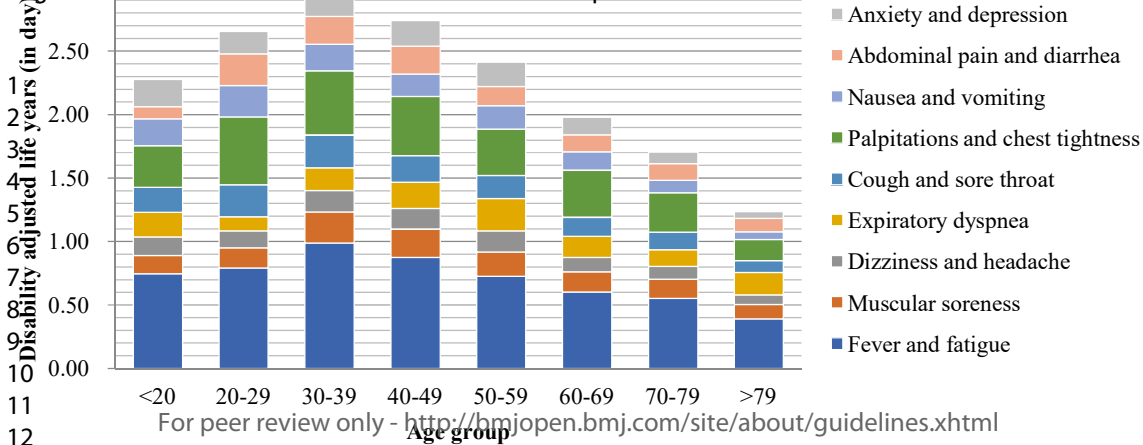
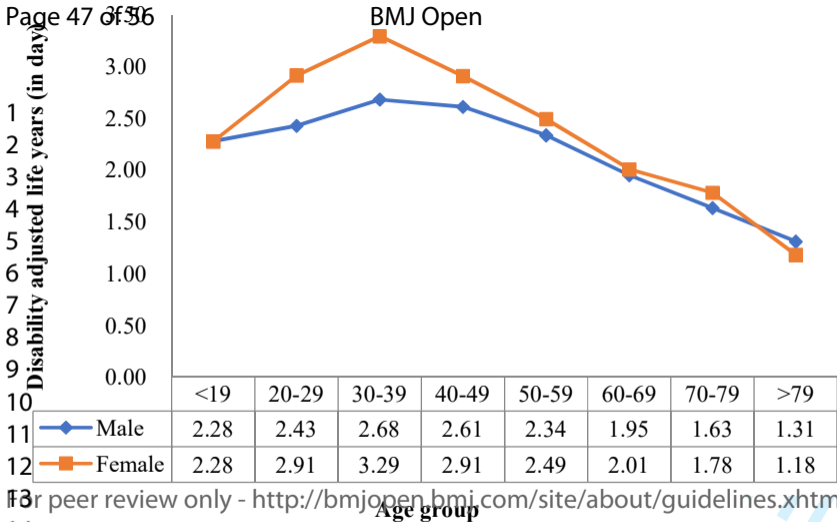


Fig. 9

| Male DALY/1000 captia (in days) | | | | | | | | | BMJ Open | Female DALY/1000 captia (in days) | | | | | | | | |
|---------------------------------|-----------------|------------------|------------------|------------------|------------------|------------------|---------------|---------------------|----------------------------------|-----------------------------------|---------------|------------------|------------------|------------------|------------------|------------------|-----------------|---------------|
| <19 (n=24) | 20-29 (n=54) | 30-39 (n=149) | 40-49 (n=234) | 50-59 (n=295) | 60-69 (n=328) | 70-79 (n=147) | >79 (n=95) | All age (n=1326) | Symptoms | All age (n=1376) | >79 (n=75) | 70-79 (n=159) | 60-69 (n=307) | 50-59 (n=297) | 40-49 (n=295) | 30-39 (n=156) | 20-29 (n=62) | <19 (n=25) |
| 639 | 789 | 1115 | 947 | 776 | 623 | 547 | 379 | 751 | Fever and fatigue | 689 | 412 | 559 | 584 | 677 | 821 | 868 | 796 | 855 |
| 162 | 174 | 276 | 233 | 201 | 163 | 157 | 117 | 193 | Muscular soreness | 177 | 107 | 145 | 154 | 187 | 215 | 217 | 146 | 121 |
| 134 | 150 | 176 | 151 | 159 | 109 | 94 | 83 | 134 | Dizziness and headache | 141 | 65 | 107 | 116 | 169 | 169 | 166 | 117 | 161 |
| 142 | 118 | 181 | 232 | 262 | 160 | 130 | 129 | 190 | Expiratory dyspnea | 191 | 236 | 133 | 177 | 247 | 189 | 175 | 108 | 243 |
| 202 | 275 | 271 | 210 | 183 | 151 | 146 | 87 | 183 | Cough and sore throat | 180 | 101 | 132 | 147 | 182 | 210 | 247 | 229 | 192 |
| 470 | 626 | 614 | 522 | 360 | 383 | 373 | 168 | 423 | Palpitations and Chest tightness | 358 | 162 | 252 | 357 | 373 | 423 | 401 | 457 | 193 |
| 149 | 263 | 238 | 192 | 187 | 151 | 124 | 59 | 171 | Nausea and Vomiting | 153 | 62 | 75 | 142 | 178 | 161 | 180 | 236 | 271 |
| 111 | 316 | 220 | 226 | 179 | 133 | 125 | 108 | 174 | Abdominal pain and Diarrhea | 160 | 100 | 138 | 137 | 126 | 213 | 220 | 187 | 80 |
| 266 | 203 | 202 | 194 | 184 | 135 | 85 | 50 | 157 | Anxiety and Depression | 166 | 63 | 92 | 137 | 197 | 210 | 209 | 153 | 164 |

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Fig. 10

**Fig. 11**

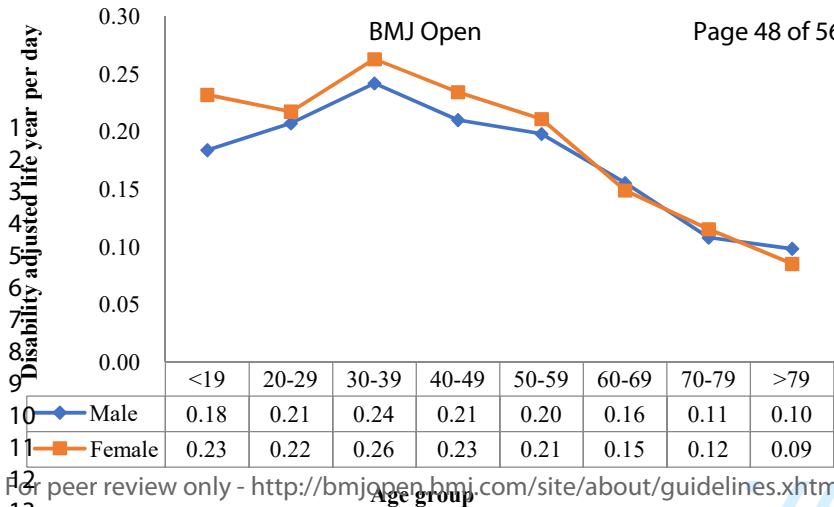


Fig. 12

Additional file 1: Questionnaire

Front-line medical staff questionnaire on symptoms of COVID-19 (The first round)

Dear Sir/Madam:

This is a questionnaire on COVID-19 typical symptom. The aim is to generate a comprehensive list of typical symptoms of inpatient with COVID-19, which can be used to assess the disease burden caused by the symptoms. This study will adopt the method of disability adjusted life years (DALYs) of the World Health Organization (WHO) to evaluate inpatients' burden of disease caused by COVID-19 symptoms.

According to your clinical experience, please judge the raw list of category and symptoms summarized by the literature review (Table 1). The judgment items are included:

For category:

- (1) Whether the category should be included in the list;
- (2) Whether the name of the category is appropriate.

For symptoms:

- (1) Whether the symptom should be listed;
- (2) Whether the symptom should be classified into the current category;
- (3) Whether the name of the symptom is appropriate.

If you think it is necessary, please supplement the symptom list according to your clinical experience. You can add:

- (1) New categories if necessary;
- (2) New symptoms if necessary.

As a front-line clinical expert engaged in COVID-19 treatment, your knowledge about the symptoms of the disease is valuable. Therefore, your opinion is very important for this study. Please try your best to fill the list appropriately. All the information you fill in is for academic research only. We will not analyze your responses individually and will keep them anonymous. Please provide responses to the best of your knowledge.

According to the Delphi process, the opinions of each expert in this round will be anonymously submitted to other experts as reference, in the next round of questionnaire survey. You will also see the anonymous opinions of the other experts. This study is expected to be conducted in 2-3 rounds for a more consistent answer.

Thank you for your support and cooperation.

The Research Group on COVID-19 Burden of Disease

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Table1: COVID-19 inpatient’s symptom list for the burden of disease evaluation (Template)

| Category (Code) | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Symptom | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Should it be moved to another category? If yes, type the code |
|------------------------------|-------------------------------|-------------------------------|---|---------------------------------|-------------------------------|-------------------------------|---|---|
| Systemic symptoms (01) | | | | Fever | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Neurological symptoms (02) | | | | Headache | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Respiratory symptoms (03) | | | | Expiratory dyspnea | | | | |
| | | | | Cough | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Cardiovascular symptoms (04) | | | | Palpitations | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |

| Category (Code) | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Symptom | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Should it be moved to another category? If yes, type the code |
|-------------------------------------|-------------------------------|-------------------------------|---|---------------------------------|-------------------------------|-------------------------------|---|---|
| | | | | Other symptom 2 (if necessary): | | | | |
| Gastrointestinal symptoms (05) | | | | Diarrhea | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Other category (06) (if necessary): | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Other category (07) (if necessary): | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |

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If you have anything else to explain, please write here:

To confirm the above, please sign (or type here): _____

Date: _____

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Front-line medical staff questionnaire on symptoms of COVID-19 (The second/third round)

Dear Sir/Madam:

Thank you for your cooperation and hard work in the last round of the questionnaire survey. The anonymous opinions of other experts in the last round have been sent to you as a reference. We retained all the consensus items in the last round of the expert consultation in the list. We also added the most favorite (approval rate > 50%) new items or the items that were proposed for adjustment (Table 1). Please supplement with the necessary items according to your own clinical experience and the opinions of other experts.

According to your clinical experience, please judge the newly added or adjusted category and symptom items:

For category:

- (1) Whether the category should be included in the list;
- (2) Whether the name of the category is appropriate.

For symptom:

- (1) Whether the symptom should be listed;
- (2) Whether the symptom should be classified into the current category;
- (3) Whether the name of the symptom is appropriate.

Besides, you also can add:

- (1) New categories if necessary;
- (2) New symptoms if necessary.

According to the Delphi process, the opinion of each expert in this round will be anonymous and submitted to other experts as reference, in the next round of the questionnaire survey. You will also see the anonymous opinions of the other experts. This study is expected to be conducted in 2-3 rounds for a more consistent answer.

Thank you for your support and cooperation.

The Research Group on COVID-19 Burden of Disease

Date: _____

Table1: COVID-19 inpatient’s symptom list for the burden of disease evaluation (Template)

| Category (Code) | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Symptom | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Should it be moved to another category? If yes, type the code |
|------------------------------|-------------------------------|-------------------------------|---|---------------------------------|-------------------------------|-------------------------------|---|---|
| Systemic symptoms (01) | | | | Fever and fatigue * | | | | |
| | | | | Muscular soreness * | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Neurological symptoms (02) | | | | Headache | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Respiratory symptoms (03) | | | | Expiratory dyspnea | | | | |
| | | | | Cough | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Cardiovascular symptoms (04) | | | | Palpitations | | | | |
| | | | | Chest tightness * | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |

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| Category (Code) | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Symptom | Include the item or not (Y/N) | Term appropriate or not (Y/N) | If inappropriate, fill in alternative terms | Should it be moved to another category? If yes, type the code |
|-------------------------------------|-------------------------------|-------------------------------|---|---------------------------------|-------------------------------|-------------------------------|---|---|
| | | | | | | | | |
| Gastrointestinal symptoms (05) | | | | Diarrhea | | | | |
| | | | | Vomiting * | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Psychological symptoms * (06) | | | | Anxiety and depression * | | | | |
| | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |
| Other category (07) (if necessary): | | | | Other symptom 1 (if necessary): | | | | |
| | | | | Other symptom 2 (if necessary): | | | | |

* Newly proposed or adjusted item.

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If you have anything else to explain, please write here:

To confirm the above, please sign (or type here): _____

Date: _____

For peer review only