Disease Burden from Coronavirus Disease 2019 Symptoms Among Inpatients at the Temporary Military Hospitals in Wuhan: A Retrospective Multi-Center Cross-Sectional Study

Mai-hong He
The No.900 Hospital of Joint Logistics Support Troop of PLA
Xiao-xiao Li (shawnleemm@gmail.com)
Fuzhou University https://orcid.org/0000-0002-8359-3897
Qing Tan
The No.923 Hospital of PLA
Chen Yong
Chinese PLA Center for Disease Control and Prevention
Kong Yue
The No.900 Hospital of Joint Logistics Support Troops of PLA
Jian-ping You
The First Affiliated Hospital of Army Medical University
Xian Lin
The No.900 Hospital of Joint Logistics Support Troop of PLA
Ying Lin
The No.900 Hosptial of Joint Logistics Support Troop of PLA
Zheng Qing
The No.900 Hospital of Joint Logistics Support Troop of PlA

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Abstract

Background: Since the advent of the coronavirus disease 2019 (COVID-19) pandemic, in most parts of the world, people are still at risk of the disease. 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: The symptoms were identified by literature review and medical staff questionnaire. DWs of COVID-19 symptoms were determined by the person-trade-off approach proposed by the World Health Organization. The extracted medical records data of 2,702 randomly selected inpatients with COVID-19 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 by analysis of variance. Multiple line regression models were used to determine the relationship between DALY and age, gender, body mass index, length of stay, symptom duration before admission, and native place.

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: COVID-19 and its symptoms could cause heavy disease burden. Although the disease burden was higher among females than in the males; however, their daily disease burdens were similar. Life value differs for different age groups; taking the changing life value with age into account; the disease burden in the younger population was higher than that in the older population. Besides, treatment at the hospitals relieved the disease burden efficiently, while delay in hospitalization could worsen it. Therefore, deployment of adequate medical resources for early hospitalization of patients with moderate or severe symptoms is needed by the public health authority.

Background

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

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

Since the 1990s, the World Health Organization (WHO) and the World Bank have proposed indicators to evaluate the BOD, that is, the disability-adjusted life years (DALY) measure. This single-utility measure used to determine the burden attributable to a specific disease is calculated using the standard method proposed by Murray and Lopez [10]. The DALY is a summary measure of population health that accounts for both the years of life lost (YLLs) and years lost due to disability (YLDs). The DALY was first developed for the primary purpose of quantifying the global burden of disease (GBD), expressed in terms of the relative magnitude of losses of healthy life associated with different causes of disease and injury [11]. Since then, the DALY has been widely used globally to estimate the BOD at the national, international, and regional levels.

In recent years, the DALY has been used to evaluate the BOD caused by some specific diseases. Qi et al. comprehensively evaluated the direct and indirect BOD caused by Asian Lineage Avian Influenza A (H7N9) public health emergencies [12]. Zhang et al. evaluated and analyzed the BOD and related factors in hospitalized patients with coal workers' pneumoconiosis and provided the basis for improving relevant medical policy [13]. Bacellar et al. used similar method to assess the BOD in hospitalized elderly patients with neurological disorders in Brazil, and recommended measures to improve the treatment plan [14]. Adopting the WHO approach, Pei and Li et al. formulated the disability weights (DWs) for chronic mountain disease, which was used to calculate the BOD among soldiers stationed at Tibet, and provided an important basis for evaluating the ability of troops to carry out tasks [15].

The DALY method could provide important insights into public health studies and practice regarding COVID-19. This year, series of researches were conducted worldwide to estimate the BOD of COVID-19 in different regions, from multiple perspectives, and using different methods. Jo et al. adopted DW from previous similar causes to calculate the BOD due to COVID-19 in Korea including YLDs and YLLs [16]. Oh et al. estimated the YLLs due to COVID-19 in 30 high-incidence countries using the WHO-provided data [17]. To assess the socio-economic burden of COVID-19 pandemic in Italy, Nurchis et al. estimated YLLs and YLDs along with the productive YLL and the comparable DW of lower respiratory tract infection was adopted to estimate the YLDs [18]. Mohanty et al. examined COVID-19 impact in the USA, Italy, Germany, and Sweden’s longevity, years of potential life lost, and DALY, and also adopted similar diseases DW as proxy [19]. Furthermore, Ortiz-Prado et al. also assessed the BOD caused by COVID-19 in Ecuador by adopted other similar diseases DW [20].

These researches not only contributed greatly to the understanding of COVID-19 BOD, but also provided the basis for the global COVID-19 public health services and related policy-making. However, in recent reports, the assessment of COVID-19 BOD remained at the macro level and relatively unclear. The challenge here relates to the fact that only the DWs from similar diseases were adopted, leaving COVID-19 with a singular DW, which ignored the complexity of COVID-19 symptoms. Until now, limited reports exist on China's COVID-19 BOD, especially BOD based on each COVID-19 symptom, in detail. Thus, this study aimed to establish the DW for COVID-19 symptoms, to estimate the BOD among inpatients in Wuhan, China, and to analyze the characteristics and potential influencing factors. To design this technical approach, in this study we referred to the previous studies' methods to design this technical approach. The BOD caused by COVID-19 symptoms was evaluated according to the data from existing medical records.

Method

Study design and Ethics statement

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 design did not violate any ethical principle, the research ethics committee of the No. 900 Hospital of Joint Logistics Troop of PLA gave a written ethical approval (approval number: 2020-001).

Selection Of The Population Groups

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

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

The diagnosis and treatment method were according to the "Diagnosis and treatment standard of COVID-19 (7th edition)" published by the PRC central government [21]. All patients were hospitalized before the release of the 7th edition was reconfirmed according to the diagnostic criteria. The inclusion criteria were having been diagnosed of COVID-19 at the hospitals according to the standard guideline and been hospitalized and treated continuously at the hospitals. To determine the BOD caused by COVID-19, inpatients with records of any other morbidity (other infectious disease, other respiratory disease, psychiatric disease, tumor, pregnant and lactating women, chronic cardiac, liver, kidney, and neurological diseases) were excluded from the study. We also excluded cases of COVID-19 inpatient deaths, due to the reluctance of their family members to allow the use of their family members' data for a public study. Similarly, cases with incomplete medical records were also excluded.

Establishment Of The Disability Weights For Covid-19 Symptoms

DW is a key component of BOD analysis that represents the severity of an illness. DW ranges from 0 to 1, where 0 represents healthy life and 1 represents death [4]. The WHO has been conducting GBD studies for several years, with series of DWs derived for different health states that are the outcomes of different diseases [22–26].

Because COVID-19 is a new infectious disease, no DWs existed for COVID-19 symptoms in the WHO's DWs' list; thus, we attempted to establish customized DWs for COVID-19 symptoms. First, COVID-19 symptoms were listed following the literature review of a series of newly published COVID-19 clinical reports. Based on these, three rounds of questionnaires were completed by front-line medical staffs in the three military field hospitals in Wuhan to derive a raw list of COVID-19 symptoms for DWs establishment (questionnaire sample is shown in Additional file 1).

Then, we convened a nine-expert panel composed of three senior respiratory physicians, two senior infectious disease physicians, one epidemiologist, one public health management expert, and two nursing experts. Based on the raw list of COVID-19 symptoms, the panel performed Delphi process to finally determine the symptom list for DWs creation [27].

Then, the panel members performed the Person-Trade-Off (PTO) exercise to derive each symptom's DW by three levels of severities (health stages) [15, 28, 29]. The health stages were described on an A4-sized vignette that contained disease-specific information in simple terminologies. As a reference framework for this task, the panel members were provided with a WHO-GBD framework table, which displayed 7 disability classes and 22 anchoring example conditions. The coefficient of variation (CV) was calculated to determine the need for additional rounds of discussion and reassignment of values.

Data Extraction

Basic information for the confirmed cases included the identification number (ID), age, gender, weight, height, native place, date of onset reported by patient, diagnostic conclusion, all the symptoms recorded by the medical staff, and inpatient and outpatient time. Nine age groups were created: <10, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and > 80 years. Body mass index (BMI) was calculated from each patient's weight and height, while duration of symptoms was determined as the length of stay + symptom duration before hospitalization (by self-report in the medical record).

To accurately extract the medical data from the records, we trained six staffs to standardize the criteria of how to judge an inpatient with one or more symptoms in a day and how severe the symptoms were according to the medical records. During the data extraction, the six staffs were divided into three groups of two in each group and a cross-check was conducted when data were extracted from the records. The extraction process was conducted from May 29 to August 7, 2020.

Calculation Of Daly For Covid-19 Symptoms

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

$$\mathrm{DALY} = \int_{x=\alpha}^{x=\alpha+L} DCxe^{-\beta x}\, e^{-\gamma(x-\alpha)}dx \qquad (1.0)$$

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

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

$$\mathrm{DALY} = DCxe^{-\beta x} \qquad (2.0)$$

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

In this study, a person's DALY was calculated as follows: 1) the cumulative duration (in days) of each health condition (a health condition is one type of symptom severity); 2) the health condition's duration was multiplied by the corresponding DW to get the DALY of each health condition; 3) all the health conditions' DALY was summed up into an inpatient's synthetic DALY for COVID-19; 4) the synthetic DALY was divided by the patient's length of stay to get an inpatient's daily DALY. Considering that the inpatient's length of stay was relatively short, the unit of DALY was set as days.

Statistical analysis

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

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

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	Proportion
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%

Duration Of Symptoms

Table 2 shows the means for the inpatients age, BMI, symptoms duration before hospitalization, length of stay, and overall duration of symptoms by hospital, gender, and age group. There were no significant differences in age, symptoms duration before hospitalization, length of stay, and overall duration of symptoms among the three hospitals according to the ANOVA test ($P > 0.05$). The inpatients' age ranged 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 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 self-reported symptom duration before hospitalization ranged from 2 to 72 days, with a mean of 24.11 ± 15.66 days. By combining the duration of inpatient and self-reported symptom duration before hospitalization, we obtained the duration of the symptoms, which ranged from 7 to 94 days, with a mean of 41.99 ± 16.37 days.

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

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

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

Table 3
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)

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

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 symptoms' list with six categories. Each symptom included three levels of severity (mild, moderate, and severe), thereby representing 27 health stages. Based on these, we derived the DWs for each health stage by the PTO exercise; along with the expert panel, a consensus was reached at the fifth round of the Delphi process (CV < 0.5). Thus, the DWs of 27 COVID-19 health stages were derived; severe expiratory dyspnea had the highest weight of 0.399, while mild cough and sore throat had the lowest weight of 0.004, as shown in Table 3.

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

The mean and standard deviation of DALY by symptom by hospital, gender, and overall study population are shown in Table 4, and those by age group are shown in Table 5. The mean overall DALY in the overall study population was 2.29 ± 1.33 days, whereas the mean DALY per day was 0.18 ± 0.15 days. Among the three hospitals, no significant difference occurred with each symptom's DALY, the synthetic DALY, or the DALY per day in ANOVA test ($P > 0.05$). However, in the LSD test of the ANOVA, synthetic DALY in Huoshenshan Hospital was significantly lower than that in Taikang-Tongji ($P = 0.048$) and Guanggu Woman and Child ($P = 0.031$) Hospitals, respectively. The DALY per day in Huoshenshan Hospital was significantly lower than that in Guanggu Woman and Child Hospital ($P = 0.023$). The DALY for fever and fatigue, muscular soreness, palpitations and chest tightness, nausea and vomiting, and synthetic DALY was significantly lower for the male population than for the female population by t-test ($P > 0.05$). In the inpatient population the overall DALY per 1,000 capita was 6.28, in female and male population the overall DALY per 1,000 capita was 6.07 and 6.51 years respectively.

Table 4
The mean DALY of COVID-19 inpatient by symptoms in each hospital, gender, and overall 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

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

DALY, Disability-adjusted life years.

Table 5
COVID-19 inpatient DALY by symptoms and age group

Symptom	< 20 years (n = 49)	20–29 years (n = 116)	30–39 years (n = 305)	40–49 years (n = 529)	50–59 years (n = 592)	60–69 years (n = 635)	70–79 years (n = 306)	> 79 years (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

COVID-19, coronavirus disease 2019.

DALY, Disability-adjusted life years.

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

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

To visualize each symptom's DALY by age group and gender, we drew a thermal map for each subgroup's DALY per 1,000 capita (in days), as shown in Fig. 10. Fever and fatigue were in the most intense (red) area, while palpitations and chest tightness were the next intense area, for both female and male populations. Female population aged 30–39 years had the highest DALY score of 1,115 DALY (in days) per 1,000 capita. On the contrary, in the female population above 79 years, the lowest DALY temperature of 50 DALY (in days) per 1,000 capita was found.

We also identified the changing curves of the means synthetic DALY, DALY per day and by age groups and gender, as shown in Fig. 11 and Fig. 12. The two-way ANOVA test showed that both age and gender significantly affected synthetic DALY (P< 0.05); and there was a significant interaction effect between the two variables (P= 0.02). However, when DALY per day was the dependent variable, the significant difference with gender was lost (P= 0.08), whereas age remained significant (P< 0.05), and the interaction effect between the two variables was also lost (P= 0.518).

Linear Regression Analyses

The results of the multiple linear models are shown in Table 6. When synthetic DALY was set as the dependent variable, all of the four models were significant (P< 0.05), with R^2 ranging from 0.214 to 0.240. In the four models, symptom duration before hospitalization and length of stay were significantly positively associated with synthetic DALY; while age was significantly negatively associated with the overall synthetic DALY. For gender and BMI, however, the four models showed different results. In the Guanggu Woman and Child Hospital model, gender and BMI were not significant (P = 0.098 and P= 0.146); in contrast, in the other three models, gender and BMI were significant, indicating that the female population had higher DALY than the male population (P< 0.05), and high BMI population had higher DALY (P< 0.05).

When DALY per day was set as the dependent variable, all of the four models were significant (P< 0.05), with R^2 ranging from 0.153 to 0.188. For age and symptom duration before hospitalization, the level of significance was the same as with model type I. Length of stay remained significant; however, the effectiveness was negatively reversed for DALY. For gender, the overall sample and Huoshenshan Hospital models were significant (P= 0.037 and P =0.022, respectively), and for BMI, the overall sample and Taikang-Tongji Hospital models were significant (P< 0.001 and P =0.001, respectively). In all the models, native place was not significant (P> 0.05).

Table 6
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		Guang Woma 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.'
	β	P-value	β	P-value	β	P-value	β	P-value	β	P-value	β	P-value	β	P-value	β
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
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
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
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
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
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

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

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

Discussion

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

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

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

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

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

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

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

Conclusion

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

Abbreviations

BOD
burden of disease
COVID-19

coronavirus disease 2019
DALY
disability-adjusted life years
DW
disability weight
PLA
people's liberation army
GBD
global burden of disease
WHO
World Health Organization
YLDs
years lost due to disability
YLLs
years of life lost

Declarations

Ethics approval and consent to participate

The research ethics committee of the No.900 Hospital of Joint Logistics Troop of PLA gave ethical approval (approval number: 2020-001). None of the inpatients were involved in any health intervention. All the individual data were anonymized prior to retrieval and analysis, and they did not contain any individual's private information.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from Wuhan Huoshenshan Hospital, Tongji Hospital, and Guanggu Womam & Child Hospital. However, restrictions will apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the health service authority of Joint Logistics Troop of PLA.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

XXL and MH conceived and designed the studies; MH and XXL did literature search and review; XXL, JY, and YC conducted questionnaire and PTO processes; XL1, QZ, and XL2 collected and extracted the data; MHe, QT and YK contributed materials; XXL, JY, and YC analyzed and interpreted the data; XXL and MH drafted the article and revised it. All the authors gave approval before submission.

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Figures

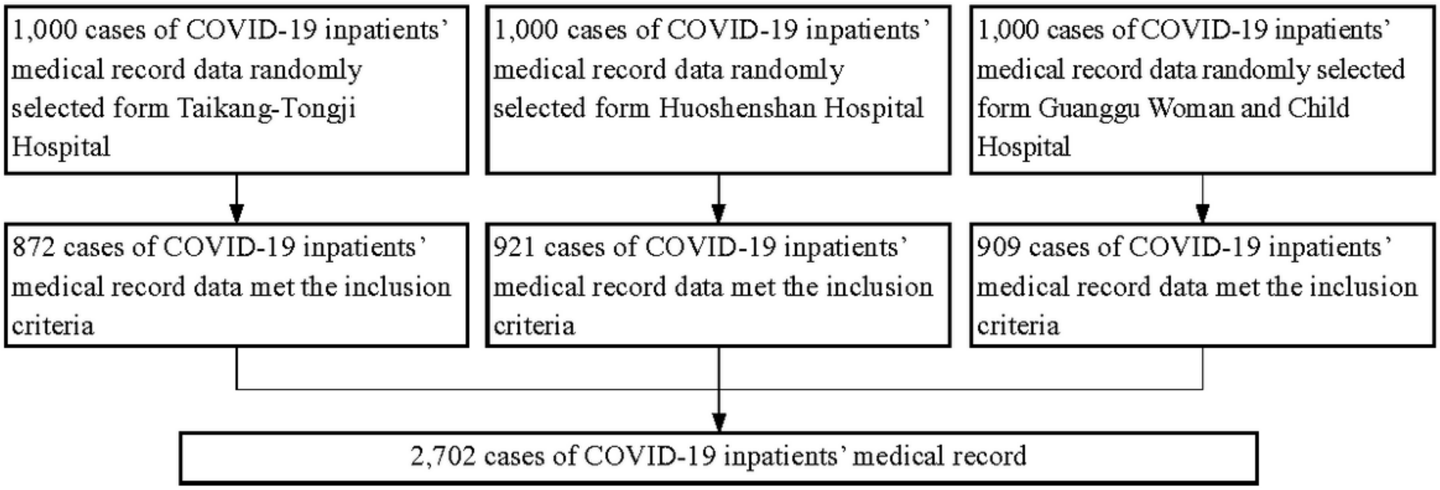

Figure 1

Flow of inpatient selection

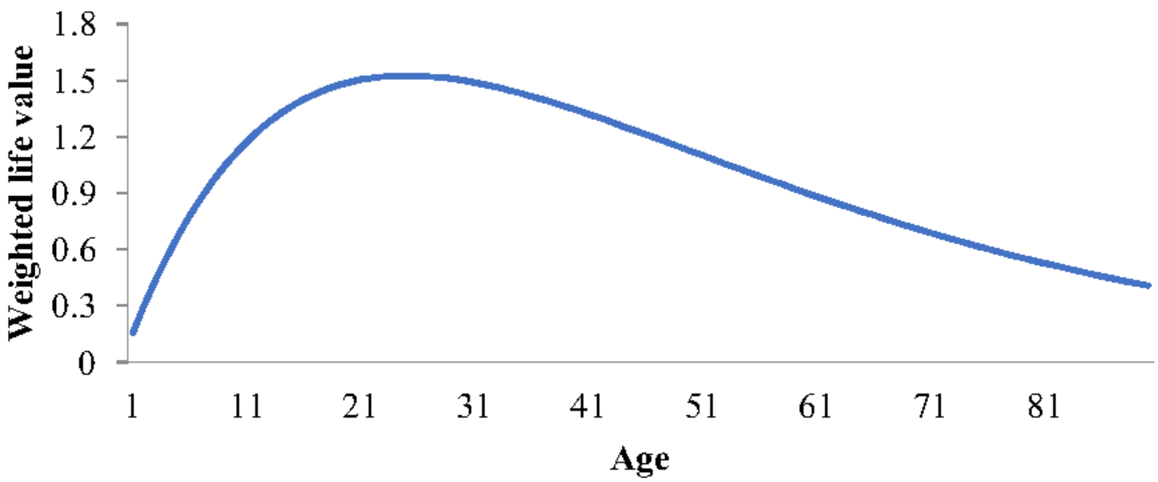

Figure 2

Curve of weighted life value changing with age

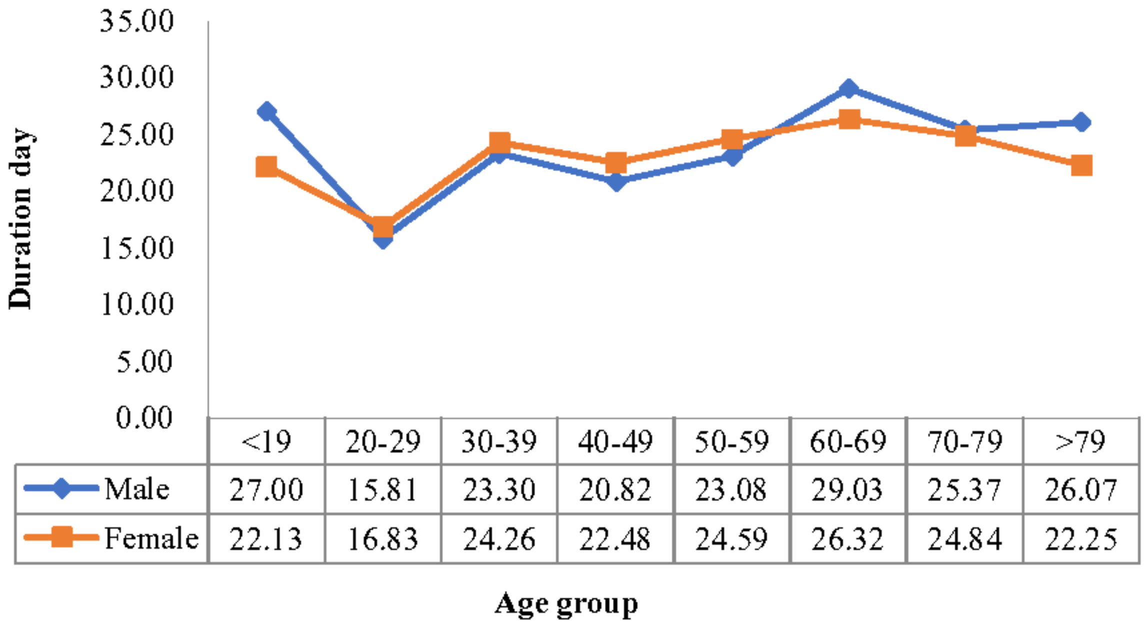

Figure 3

Duration of symptom before hospitalization changes with age group in female and male populations

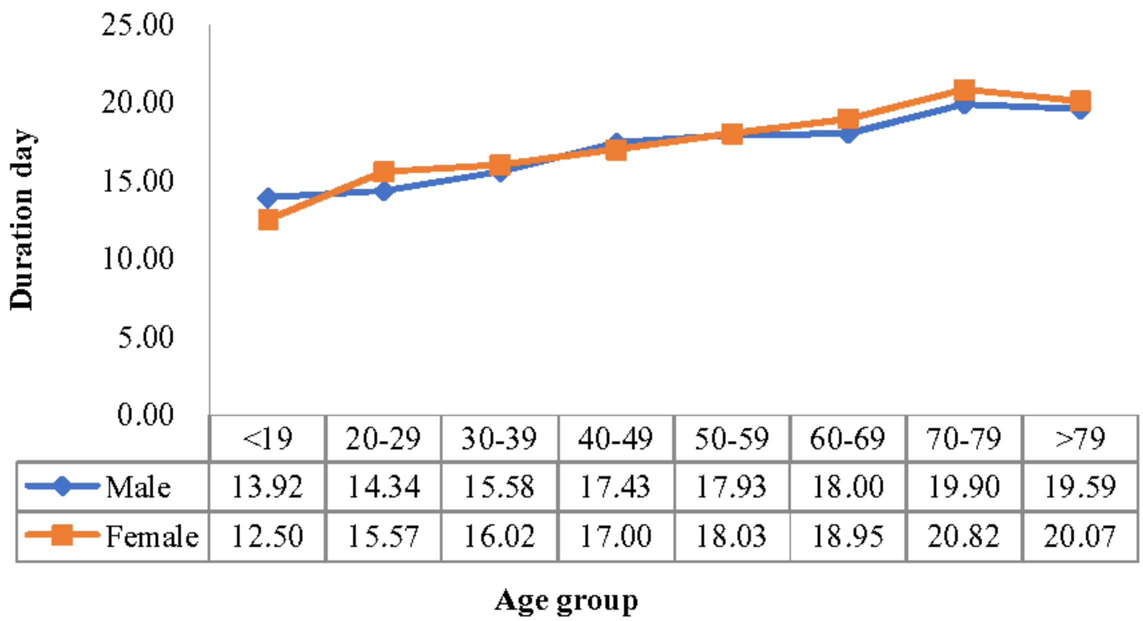

Figure 4

Length of stay changes with age group in female and male populations

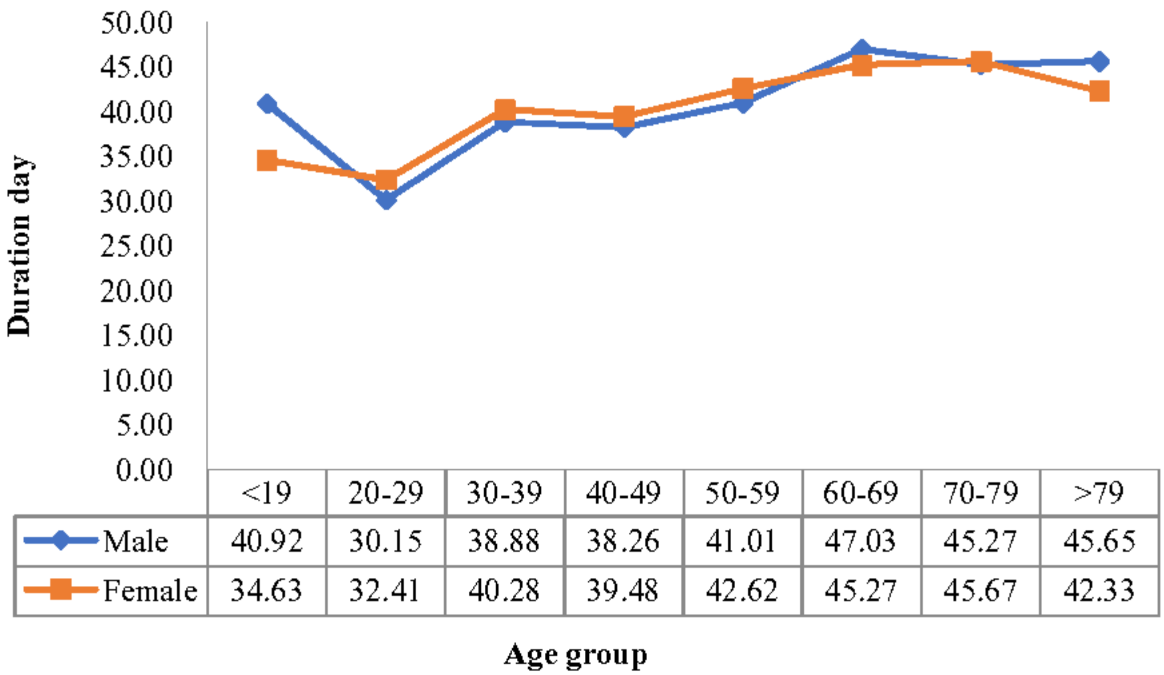

Figure 5

Overall duration of symptom changes with age group in female and male populations

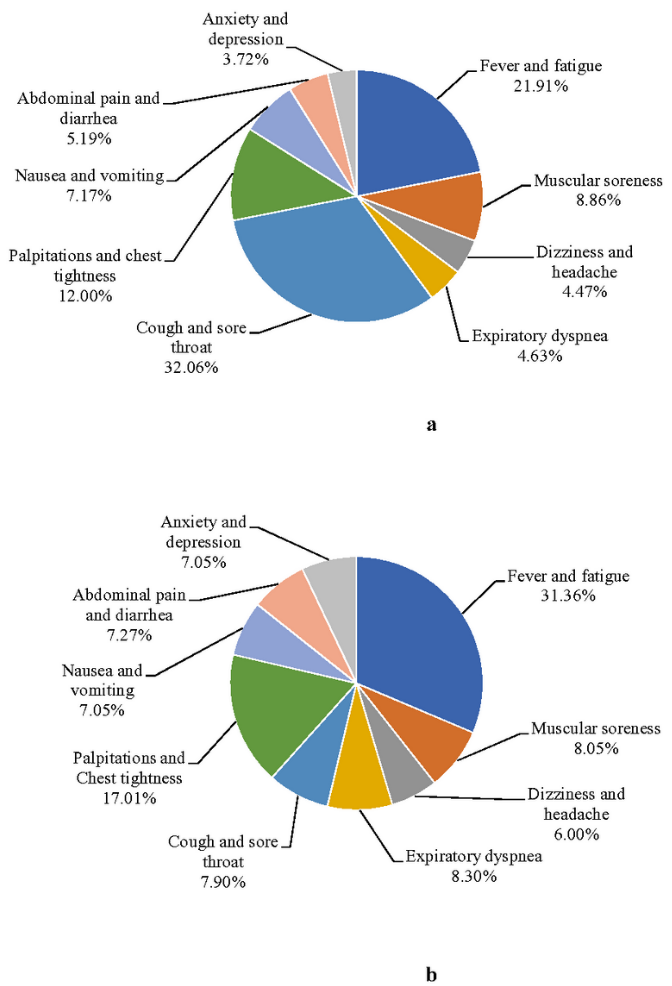

Figure 6

a: The composition proportion of accumulative duration (in day) by symptom in the study population b: The composition proportion of DALY by symptom in the study population

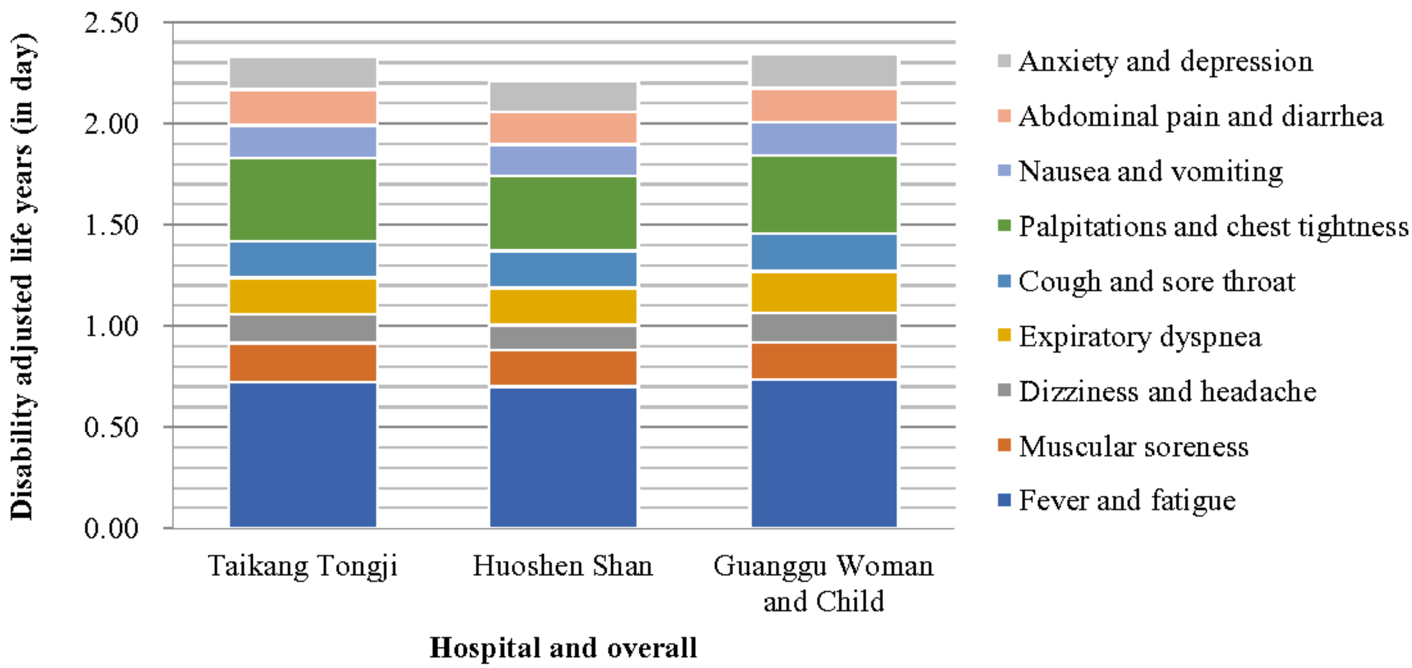

Figure 7

Composition of each military temporary hospital’s synthetic DALY

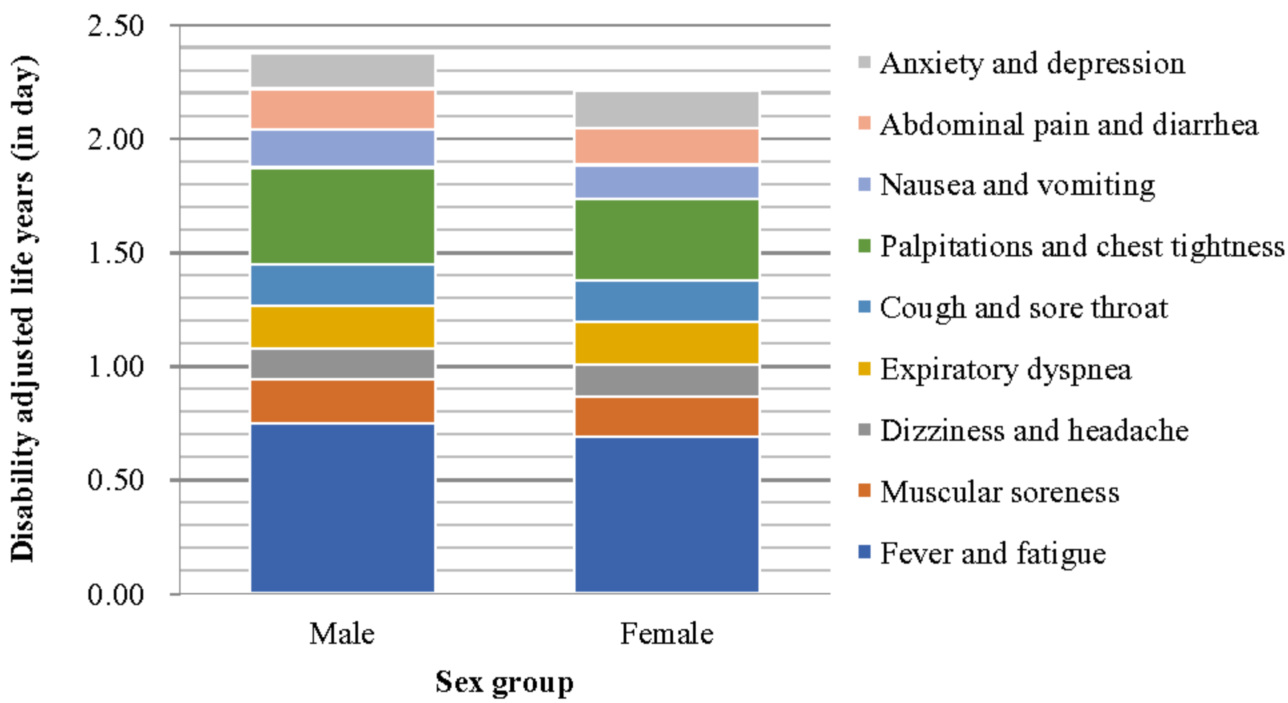

Figure 8

Composition of each gender group’s synthetic DALY

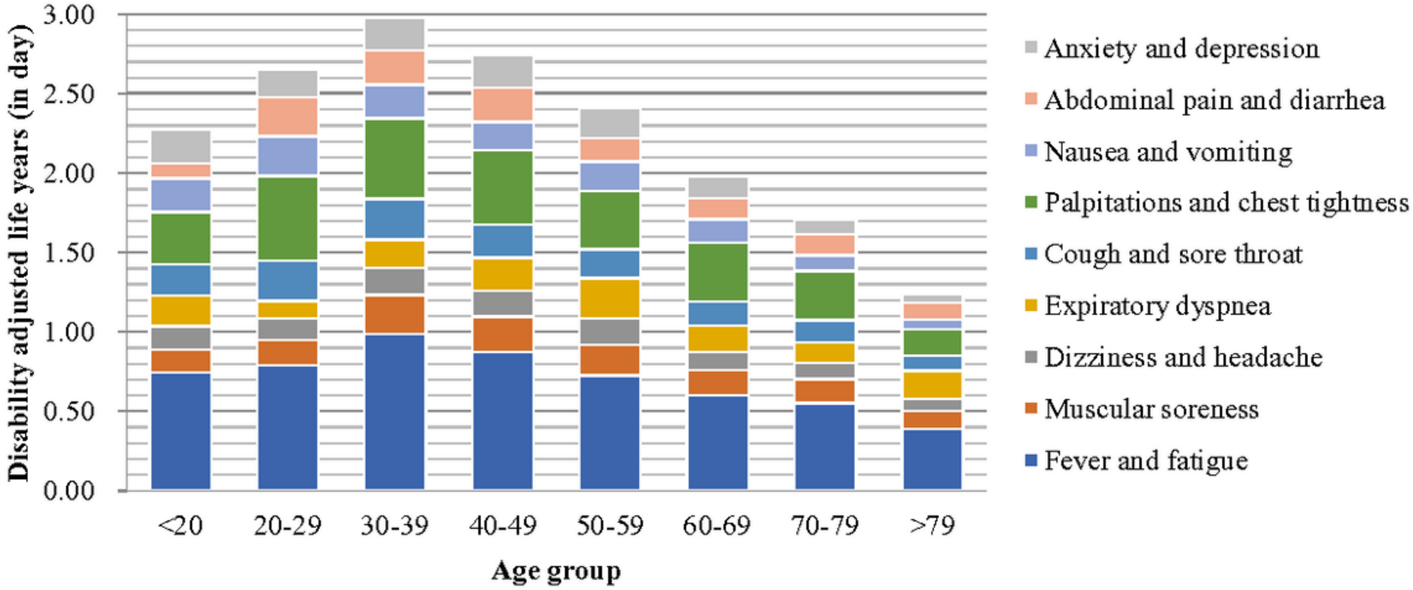

Figure 9

Composition of each age group’s synthetic DALY

Male DALY/1000 captia (in days)									Symptoms	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)		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

Figure 10

Thermal map of COVID-19 inpatient’s DALY by gender and age group (DALY per 1000 capita).

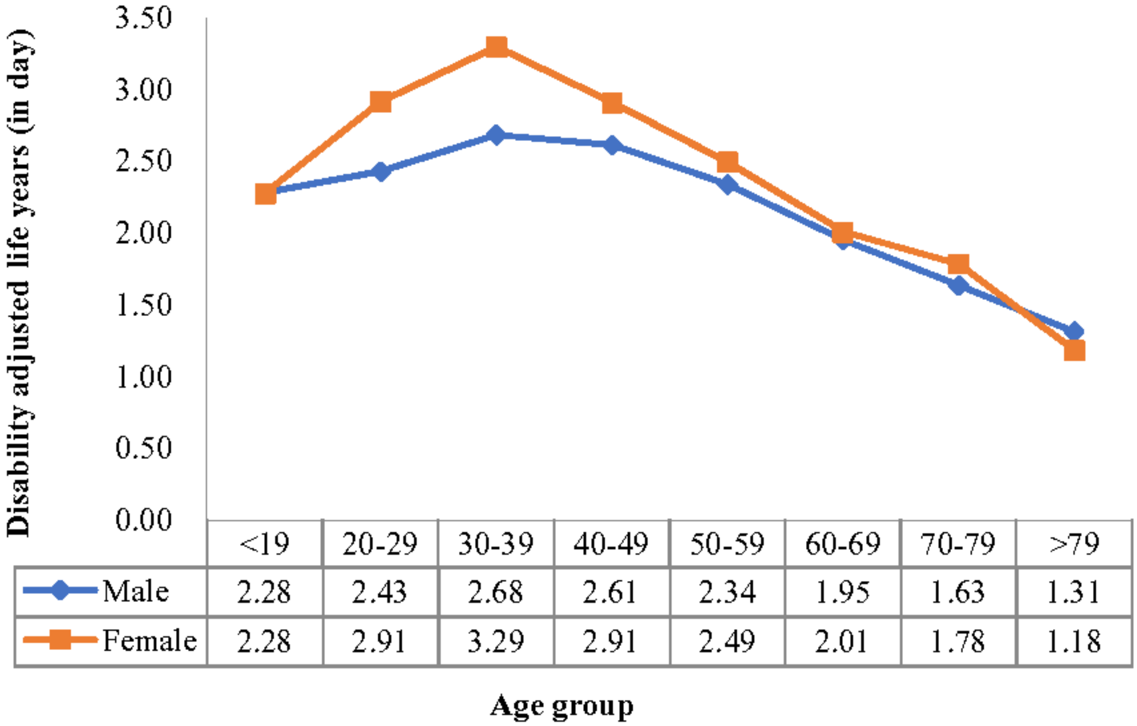

Figure 11

Synthetic DALY changes with age group in female and male populations

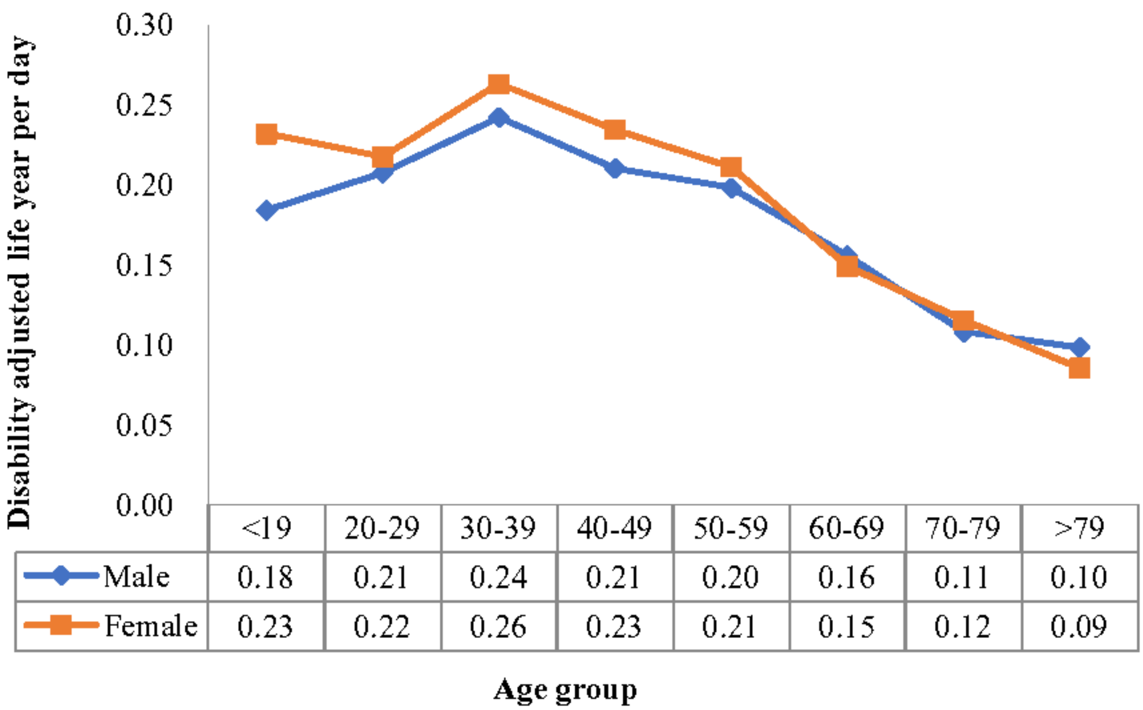

Figure 12

DALY per day changes with age group in female and male populations

Supplementary Files

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- Firstlinemedicalstaffquestionnaire.docx