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Original Research

An online survey among convalescents 5 months post SARS-CoV-2 infection in China

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ABSTRACT

The effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection persist months and years after recovery. We conducted an online survey to assess the health condition of convalescents approximately 5 months following the primary infection of SARS-CoV-2. The study recruited 5,510 individuals who were primary infected, 626 participants who had experienced reinfection, and 521 participants who were without infective history. The most common disorders after the primary infection group were fatigue (15.18 %), memory issue (13.13 %), post-exertional malaise (PEM, 11.68 %), and brain fog (11.29 %) at the time of survey. In addition, SARS-CoV-2 infection had an impact on the reproductive systems. In stepwise logistic regression analysis, smoking currently, with background diseases, and outpatient visits in the acute phase could be associated with moderate / severe disorders. Further analysis of different background diseases showed that allergic rhinitis, hyperlipidemia, cardiovascular disease, autoimmune diseases, neurological diseases, and asthma likely increased the risk of moderate/severe disorders. The probability of developing disorders of individuals with SARS-CoV-2 reinfection was higher before the secondary infection than uninfected people. Fatigue, PEM, muscle pain/spasms, chills, joint pain, excessive sweating at rest, headache / dizziness, sore throat or foreign body sensation in the throat, cough, expectoration, dry / painful / watery eyes, loss of appetite and constipation were associated with an increased risk of reinfection. It was essential to undertake further research with enhanced randomization in a larger sample in the community, and to strengthen the validation of the research conclusions. The findings of this study contribute to a deeper understanding of the health recovery process among coronavirus disease 2019 (COVID-19) convalescents. Moreover, the findings help identify characteristic health risk factors associated with convalescents and highlight the risk of moderate / severe disorders and reinfection. Furthermore, the findings also provide valuable guidance and reference for SARS-CoV-2 rehabilitation strategies and the prevention of reinfection, offering insights for scientific recommendations.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began spreading across the globe from the end of 2019 and infected billions of people worldwide [1]. The disease caused by SARS-CoV-2 is referred to as coronavirus disease 2019 (COVID-19). For COVID-19, it has been discovered that in addition to clinical outcomes ranging from asymptomatic infection to probably severe pneumonia and even death in the acute phase of the infection, convalescents had certain risks of long-term effects of the infection after recovery, which have been commonly described as post-acute sequelae of COVID-19 (PASC) [2] or long coronavirus disease (COVID) [3]. On December 21, 2021, the World Health Organization (WHO) issued a Delphi consensus on the definition of the post-COVID-19 condition, and this condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the symptom onset, with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis [4]. Since then, the idea of long COVID has been adopted by most domestic and overseas scholars, and it has been reported in scientific research [5–8]. Long COVID is a combination of

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HIGHLIGHTS

Scientific question

Long coronavirus disease (COVID) impacts the daily lives and activities of convalescents. Comprehending its prevalence and risk factors in China is crucial.

Evidence before this study

Individuals with background diseases are at a heightened risk of experiencing long COVID. Those who developed long COVID following their primary infection have a higher likelihood of reinfection.

New findings

The prevalence of long COVID in convalescents at 5 months after primary infection was 6.43 %. Smoking, with background diseases, outpatient visits in the acute phase and existing background diseases were associated with experiencing moderate/severe disorders.

Significance of the study

This study indicates that the risk of experiencing moderate / severe disorders following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection varies among individuals in China. The long-term effects of SARS-CoV-2 infection may increase the likelihood of reinfection.

symptoms that affect a wide range of health outcomes. It is characterized by diverse symptoms involving multiple organ systems, such as the respiratory system, nervous system and cardiovascular system, etc. [9–12]. The symptoms commonly include fatigue, breathlessness, post-exertional malaise (PEM), brain fog, headache, anxiety, depression, rash, joint pain, and palpitations, etc. [13]. Cohort studies and cross-sectional studies involving convalescents from different countries and regions and covering different disease severities showed that the long-term impacts do exist in a certain proportion of the population irrespective the SARS-CoV-2 variants.

It has been demonstrated that some key risk factors can impact the occurrence of long COVID in different populations, such as hospitalized survivors, non-hospitalized adults, adolescents and children, etc. [14–17]. However, most previous studies had simply focused on the risk factors of developing adverse health outcomes after recovery. In fact, convalescents with severe disorders after SARS-CoV-2 infection require longer medical care services and have a stronger demand for and dependence on medical resources. Nevertheless, an investigation of the risk of convalescence in Chinese patients is lacking, and more attention is needed for appropriate health management and intervention.

Since the emergence of the Omicron variant, the risk of reinfection has increased dramatically in convalescents who have recovered from the primary infection [18]. Studies have shown that reinfection contributes to greater risks of hospitalization, a variety of organ and system sequelae, and even death compared with the finding in uninfected people [19,20]. The risk factors of infection mainly involve the immune escape of SARS-CoV-2 variants and decreasing protection efficacy after vaccination [18]. However, the association between primary infection and reinfection is unclear, especially whether incomplete recovery from the primary infection has an impact on the probability of reinfection.

Owing to the nonspecificity of the long COVID and the lack of a definitive diagnosis, establishing a fixed diagnostic criteria can be challenging [21]. Herein, we conducted a cross-sectional study to reveal the health condition of convalescents approximately 5 months following the primary infection and to assess how much of the condition could be attributed to the effects of SARS-CoV-2 infection. Additionally, we explored the risk factors associated with the development of moderate / severe disorders in convalescents. Furthermore, we investigated multiple influencing factors of reinfection to explore the association between the primary infection and reinfection with regard to different health conditions. Out study might provide valuable reference for improving the recovery status after SARS-CoV-2 infection and avoiding reinfection.

2. Materials and methods

2.1. Research design

We conducted an online questionnaire survey to assess the health condition of individuals 5 months after SARS-CoV-2 infection. We distributed the questionnaire over the internet to participants located in China from May 16, 2023, to August 5, 2023. Respondents voluntarily chose to answer the questionnaire, and informed consent was obtained at the beginning. All respondents began answering the questionnaire after providing informed consent. For young children and older people, family members were allowed to assist in responding to the questionnaire. To protect the privacy of all respondents, no personally identifiable information was collected in the questionnaire. Each questionnaire could be answered thrice with the same account. A peak in the number of questionnaire submissions occurred on May 22, 2023. By June 15, 2023, a total of 8,378 questionnaires had been completed. The number of completed questionnaires kept increasing and reached 9,210 by July 2, 2023. Ultimately, the questionnaire collection phase concluded on August 5, 2023. Upon completion of the survey, a total of 9,317 questionnaires were collected. Questionnaires that met the following criteria were excluded from the statistical analysis: (1) Denial of informed consent; (2) Suspected duplication questionnaires, with responses matched according to IP address, age, gender, income, occupation, education, province of residence, urbanicity, number of SARS-CoV-2 infections, and vaccination status; (3) Response time $>$ 24 h or $<$ 1 min; (4) Response by a foreigner; (5) Loss of a large amount of owing to nonhuman factors; (6) Absence of a SARS-CoV-2 nucleic acid swab test result or SARS-CoV-2 antigen rapid diagnostic test result [22]; and (7) Interval between infections $<$90 days in these with reinfection [23].

2.2. Questionnaire design

The questionnaire included questions on demographic characteristics, living habits, SARS-CoV-2 infection-related situations and healthy symptoms (including symptoms at the time of filling out the questionnaire and a review of prior symptoms up to the last infection). Demographic characteristics included sex, age, minority, region, urbanicity, occupation, income, and education. General conditions included smoking and physical background diseases. SARS-CoV-2 infection-related situations included infection times, vaccination, and outpatient visits in the acute phase. A total of 24 symptoms were assessed, including 8 general physical symptoms (fatigue, PEM, muscle pain or spasms, hair loss, chills, joint pain, excessive sweating at rest and rash) and 16 multisystem symptoms (memory issues, sleep disorder / insomnia, brain fog, headache / dizziness, sore throat or foreign body sensation in the throat, cough, expectoration, chest distress, tachycardia / palpitations, dyspnea, chest pain, dry / painful / watery eyes, blurred vision, loss of appetite, constipation and gingival bleeding). In addition, male respondents were assessed for four types of reproductive disorders (decreased libido, erectile dysfunction, difficulty ejaculating, and orchialgia) and female respondents were assessed for three types of reproductive disorders (menstrual disorders, increased menstrual pain, and irregular uterine bleeding). The severity (mild or moderate / severe) of each symptom was dependent on the subjective perception of the respondents. In addition, the modified British Medical Research

Council (mMRC) dyspnea scale was used to assess functional dyspnea, and to participant recovery was classified according to the score [5,17,24]. Mental health was evaluated using 2 psychiatric questionnaires Generalized Anxiety Disorder seven-item scale (GAD-7) and Patient Health Questionnaire 9 (PHQ-9) [5,17,24]. We used Chinese version of the scales, which are freely accessible via phqscreeners.

2.3. Statistical analysis

Continuous variables related to demographic characteristics and infection periods are presented as median and interquartile range (IQR). Categorical variables are expressed as absolute values along with percentages. The chi-square test (χ^2 test), Fisher's exact test, or Kruskal–Wallis test was used as appropriate for categorical variables and the Mann–Whitney *U* test was used for continuous variables. The Wilcoxon rank sum test was used to assess the composition ratios of different disorders' severity (mild, moderate and severe). Latent class analysis was performed for unsupervised clustering of self-reported symptoms to identify the sequela clusters of the SARS-CoV-2 infection. The final classification method was determined according to the smallest estimated class proportions and statistical model fit indices, such as the Akaike information criterion (AIC), Bayesian information criterion (BIC), adjusted BIC (aBIC), entropy and Lo–Mendell–Rubin (LMR) test [24,25]. A stepwise logistic regression model was used to explore the influencing factors of disorders severity, with adjustment of the variables of age, sex, minority, income, region, urbanicity, smoking status, vaccination statues, background diseases and outpatient visits in the acute phase. Propensity score matching (PSM) was used to match the respondents with reinfection and those without reinfection in a 1:4 ratio. A P value of < 0.05 was considered to indicate statistical significance in two-tailed tests. Statistical processing and analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and IBM SPSS Statistics 27 (IBM, Armonk, NY, USA). Latent class analysis was used by Mplus version 8.3 (Muthen & Muthen, Los Angeles, CA, USA). Results were visualized using GraphPad Prism version 9.5.0 (GraphPad Software, San Diego, CA, USA) and SAS version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

3.1. Participant characteristics

According to the research criteria, 2,660 questionnaires were excluded, and a total of 6,657 valid questionnaires were considered in the statistical analysis (Fig. 1). A total of 5,510 had primary infection with SARS-CoV-2, with a peak time of February 2022. Moreover, 626 participants had reinfection from late January 2020 to late June 2023, and 521 did not report SARS-CoV-2 infection at the time of the survey. The median time for primary infection was 158 (148–169) days, which is about 5 months after infection, and the peak for primary infections was December 2022 (Fig. 2A). According to data from the Global Initiative on Sharing Avian Influenza Data (GISAID), the main endemic strains in China during this period were Omicron variants BF.7.14, BA.5.2, and its subbranches [26]. For the reinfection, the peak was in May 2023 and the median time from the latest infection to the questionnaire survey was 17 (IQR: 8–28) days. The GISAID website showed that the main endemic strains were Omicron variants XXB.1.16, XBB.1.5 and XBB.1.9.1 [26].

The median age of the respondents at the time of the survey was 36 (IQR: 28–45) years. The proportion of female respondents (n = 4,113, 61.78 %) was higher than that of male respondents (n = 2,544, 38.22 %). All respondents were mainly from the northern (n = 2,669, 40.09 %) and eastern (n = 1,221, 18.34 %) regions of China. The respondents in the survey were predominantly urban residents (n = 5,696, 85.56 %), individuals working in a full-time or part-time capacity (n = 5,055, 75.94 %), individuals with a median family income ranging from 30,000 to 100,000 yuan (n = 2,994, 44.98 %), individuals holding a bachelor's degree (n = 4,509, 67.73 %) and nonsmokers (n = 4,127, 61.99 %). The most common background diseases were allergic rhinitis (n = 664, 9.97 %), hypertension (n = 582, 8.74 %) and hyperlipidemia (n = 414, 6.22 %). Among the participants who experienced a primary infection, 406 (7.37 %) received outpatient visits in the acute phase, while among those with reinfections, 45 (7.18 %) received outpatient visits in the acute phase during the last acute phase. However, this difference was not statistically significant (P = 0.8701) (Table 1). The proportion of uninfected individuals was higher among those who received 4 or more vaccine doses (n = 135, 19.76 %) than among those who received 3 doses (n = 306, 6.47 %), 2 doses (n = 66, 6.71 %), or 1 dose (n = 2, 2.25 %) and those without inoculation (n = 12, 6.98 %). Additionally, the rate of reinfection was lower among those who received 4 or more vaccine doses (n = 40, 5.86 %) than among those who received 3 doses (n = 474, 10.02 %) or 2 doses (n = 92, 9.36 %) and those without inoculation (n = 17, 9.88 %) (Fig. 2B).

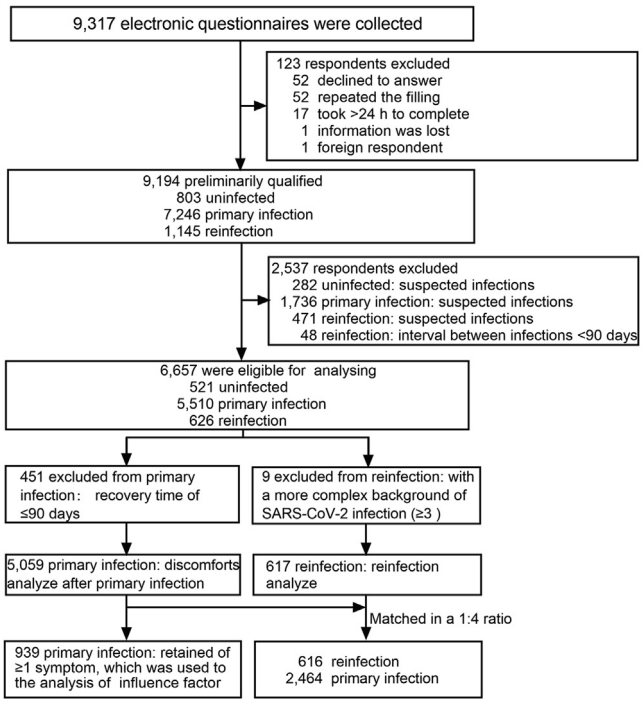
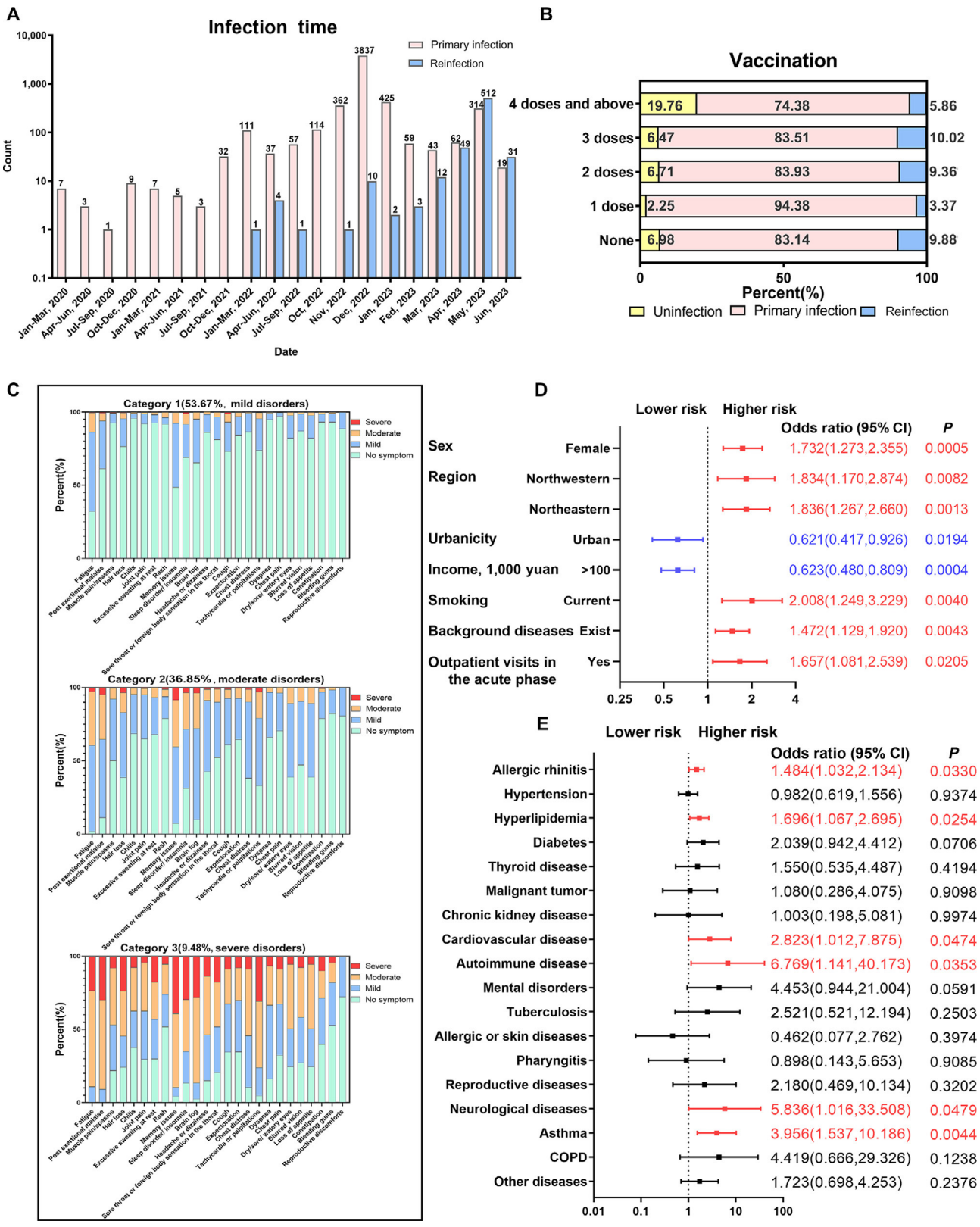


Fig. 1. The flow chart of the study. Only the results of the last response have been included in questionnaires with suspected duplicate responses. One questionnaire is missing owing to improper information preservation during the investigation. Studies support substantial agreement between coronavirus disease 2019 (COVID-19) antigen rapid diagnostic tests (Ag-RDTs) [22] and quantitative reverse transcription polymerase chain reaction for the days of symptom onset. Thus, priority has been given to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid swab test or Ag-RDT results. Current clinical practice for the diagnosis of reinfection emphasizes that the second infection needs to occur more than 90 days after the primary infection. Thus, respondents with a reinfection duration of <90 days have been excluded from the reinfection group. The reinfected group was matched by age, sex, vaccinations, outpatient visits for the first infection and the time of the first infection with primary infected group in a 1:4 ratio.

3.2. Healthy condition of the convalescents after primary infection

To accurately determine the incidence of disorders after recovery from SARS-CoV-2 infection, we selected respondents with primary infection, including 5,059 people with a recovery time of > 90 days (Fig. 1). At a median of 5 months after recovery from the primary


A
Infection time
Primary infection
Reinfection
Count
Date
B
Vaccination
4 doses and above
3 doses
2 doses
1 dose
None
Percent(%)
Uninfection
Primary infection
Reinfection
C
Category 1(53.67%, mild disorders)
Category 2(36.85%, moderate disorders)
Category 3(9.48%, severe disorders)
Severe
Moderate
Mild
No symptom
Percent(%)
D
Lower risk
Higher risk
Odds ratio (95% CI)
P
Sex
Female
1.732(1.273,2.355)
0.0005
Region
Northwestern
1.834(1.170,2.874)
0.0082
Northeastern
1.836(1.267,2.660)
0.0013
Urbanicity
Urban
0.621(0.417,0.926)
0.0194
Income, 1,000 yuan
>100
0.623(0.480,0.809)
0.0004
Smoking
Current
2.008(1.249,3.229)
0.0040
Background diseases
Exist
1.472(1.129,1.920)
0.0043
Outpatient visits in the acute phase
Yes
1.657(1.081,2.539)
0.0205
E
Lower risk
Higher risk
Odds ratio (95% CI)
P
Allergic rhinitis
1.484(1.032,2.134)
0.0330
Hypertension
0.982(0.619,1.556)
0.9374
Hyperlipidemia
1.696(1.067,2.695)
0.0254
Diabetes
2.039(0.942,4.412)
0.0706
Thyroid disease
1.550(0.535,4.487)
0.4194
Malignant tumor
1.080(0.286,4.075)
0.9098
Chronic kidney disease
1.003(0.198,5.081)
0.9974
Cardiovascular disease
2.823(1.012,7.875)
0.0474
Autoimmune disease
6.769(1.141,40.173)
0.0353
Mental disorders
4.453(0.944,21.004)
0.0591
Tuberculosis
2.521(0.521,12.194)
0.2503
Allergic or skin diseases
0.462(0.077,2.762)
0.3974
Pharyngitis
0.898(0.143,5.653)
0.9085
Reproductive diseases
2.180(0.469,10.134)
0.3202
Neurological diseases
5.836(1.016,33.508)
0.0479
Asthma
3.956(1.537,10.186)
0.0044
COPD
4.419(0.666,29.326)
0.1238
Other diseases
1.723(0.698,4.253)
0.2376

infection, the incidence of total disorders in the recovered population was 18.52 %.

Based on a review of the preinfection health condition of respondents with primary infection (12.09 %), the calculated the attributable risk (AR) was 6.43 %. Thus, only 6.43 % of occurrence of disorders were caused by the SARS-CoV-2 infection, and it was often referred to as long COVID. The most common symptoms after primary infection were fatigue (15.18 %), memory issues (13.13 %), PEM (11.68 %), and brain fog (11.29 %). In contrast, these symptoms were significantly less frequent before primary infection, with fatigue (7.31 %), PEM (5.18 %) and sore throat or foreign body sensation in the throat (5.26 %) being the most common. Most of the symptoms were mild. However, ejaculating difficulty among male participants predominated with moderate symptoms after infection (8/16, 50.00 %) but without a significant difference (Table 2).

The frequencies of all general symptoms, except chills and loss of appetite, increased significantly after infection than before infection, and most of the symptoms were mild. In particular, the frequency of mild fatigue increased from 53.24 % to 62.89 % ($P_{composition}$ = 0.0013) and that of mild sore throat or foreign body sensation in the throat increased from 61.69 % to 71.60 % ($P_{composition}$ = 0.0088). Regarding rash, the frequency of moderate symptoms increased from 23.29 % to 34.18 % and that of severe symptoms increased from 1.37 % to 5.70 % ($P_{composition}$ = 0.0188). The proportion of respondents with reproductive symptoms also increased significantly after infection than before infection (increased from 0.89 % to 2.95 %, $P < 0.0001$), among both female participants ($P < 0.0001$) and male participants ($P < 0.0001$). After infection, the frequencies of decreased libido (before vs after infection: 0.32 % vs. 0.96 %, $P < 0.0001$) and erectile dysfunction (0.34 % vs. 0.75 %, $P = 0.0045$) increased significantly among male participants, while the frequencies of menstrual disorder (0.42 % vs. 1.68 %, $P < 0.0001$), increased menstrual pain (0.47 % vs. 0.97 %, $P = 0.0033$) and irregular uterine bleeding (0.14 % vs. 0.45 %, $P = 0.0034$) increased significantly among female participants, and these symptoms were predominantly mild (Table 2).

We assessed the preinfection health status of 5,059 participants against that of uninfected individuals. The findings revealed that although the proportion of respondents with primary infection experiencing disorders before infection was lower than that of uninfected individuals (9.31 % vs. 12.90 %, $P = 0.0398$), severe cases of muscle pain / spasms, excessive sweating at rest, sleep disorders / insomnia, dry / painful / watery eyes, and blurred vision were significantly less frequent among uninfected individuals. This discrepancy could be related to recall bias, which is associated with induced by indistinct recollection of mild to moderate symptoms before infection (Table S1).

Compared with the findings in uninfected people, the frequency of some general disorders still increased after infection, but the difference was not as obvious as it would have been if the comparison had been made on the respondents with primary infection themselves. Moreover, there was no striking increase in issue of the reproductive system either. The number of people with mMRC score of >1 increased significantly after SARS-CoV-2 infection, which indicates that SARS-CoV-2 infection still had some negative effects to some extent on the respiratory system of the population, and the condition continued to recover in the fifth month after infection by halves. The scores of the GAD-7 and PHQ-9 scales after recovery were higher among respondents with primary infection than among those without infection ($P < 0.0001$), which may indicate the long-term adverse effects of SARS-CoV-2 infection on the recovery of anxiety and depression (Table S1).

3.3. Factors that influence the severity of the long-term effects of SARS-CoV-2 infection in responders with the primary infection

To further investigate the factors influencing the severe long-term health effects after SARS-CoV-2 infection, we selected 939 respondents who had at least one symptom at the time of investigation from among 5,059 respondents with primary infected. Laten class analysis was used to assess the all-round severity of all disorders associated with different symptoms in each individual (Fig. 2C). We classified respondents after latent class analysis into the following groups: mild disorders (n = 504, 53.67 %, with a median of 5 symptoms per respondent), moderate disorders (n = 346, 36.85 %, with a median of 12 symptoms per respondent) and severe disorders (n = 89, 9.48 %, with a median of 20 symptoms per respondent), which were based on the assessment of the relevant parameters for latent class analysis (Tables S2 and S3). Smoking currently (odds ratio [OR] = 2.008, 95 % confidence interval [CI]: 1.249–3.229, $P = 0.0040$), having any background disease (OR = 1.472, 95 % CI: 1.129–1.920, $P = 0.0043$) and receiving outpatient visits in the acute phase (OR = 1.657, 95 % CI: 1.081–2.539, $P = 0.0205$) were associated with moderate/severe disorders in the post-COVID-19 condition (Fig. 2D).

In consideration of the complexity of background diseases, we did not strictly separate the specific effects of multiple diseases. For the sake of exploring the specific impact of each disease on disorders, we conducted regression analysis for each disease. The results showed that allergic rhinitis (OR = 1.484, 95 % CI: 1.032–2.134, $P = 0.0330$), hyperlipidemia (OR = 1.696, 95 % CI: 1.067–2.695, $P = 0.0254$), cardiovascular disease (OR = 2.823, 95 % CI: 1.021–7.875, $P = 0.0474$), autoimmune diseases (OR = 6.769, 95 % CI: 1.414–40.173, $P = 0.0353$, neurological diseases (OR = 5.836, 95 % CI: 1.018–33.508, $P = 0.0479$) and asthma (OR = 3.956, 95 % CI: 1.573–1.186, $P = 0.0044$) were significantly associated with the development of moderate/severe disorders. In addition, diabetes and mental disorders had a statistically significant risk for moderate / severe disorders at the test level of 0.1 (Fig. 2E).

As most respondents with reinfection had their last infection less than 90 days from the time of the survey (n = 593, 96.11 %), we were unable to assess the long-term impact of reinfection.

Fig. 2. Time distribution characteristics of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and risk factors for moderate / severe disorders. A) Time distribution of the primary infection and repeat infection (last infection). B) Infection of participants with 5 immunological backgrounds. C) After latent class analysis of 939 respondents who had at least one symptom more than 90 days after SARS-CoV-2 primary infection, the proportions of the severities of 25 symptoms (mild, moderate, and severe) have been determined. As reproductive system symptoms are not uniform in different genders, we have divided the reproductive system symptoms into two categories (with and without), and the category of without reproductive symptoms in the chart has been represented by the color of mild symptoms in the percentile bar chart. D) The risk factors and protective factors of moderate/severe disorders have been screened after logistic regression analysis by the stepwise regression method. Sex, age, ethnicity, income, region, urbanicity, occupation, education, smoking status, vaccination status, background diseases, and outpatient visits in the acute phase have been included in the stepwise logistic regression analysis. E) Analysis of the risk of moderate/severe disorders for each disease alone. Thyroid diseases include hyperthyroidism, hypothyroidism, subacute thyroiditis, thyroid nodules, and Hashimoto's thyroiditis (HT). Malignant tumors include lung cancer, thyroid cancer, and papillary thyroid carcinoma. Autoimmune diseases include rheumatoid arthritis, systemic lupus erythematosus (SLE), inflammatory bowel disease (IBD), and Behcet's disease (BD). Mental disorders include anxiety, depression, and compulsive behavior. Allergies and skin diseases include eczema, psoriasis, and skin allergies. Reproductive diseases include pelvic endometriosis, polycystic ovary syndrome (PCOS), endometrial polyps, and mastitis. Neurological diseases include neural tinnitus, sudden deafness, vegetative system dysfunction, and dysfunction of the autonomic nervous system. Other diseases include joint diseases, oral diseases, digestive diseases, some viral infection or viral carrier, postoperative issues, trauma, etc. There is mutual adjustment for sex, age, ethnicity, income, region, urbanicity, smoking, vaccination, and outpatient visits in the acute phase. Abbreviation: COPD, chronic obstructive pulmonary disease.

Table 1
Baseline characteristics of respondents with different severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection times.

Characteristic	Total (n = 6,657)	Uninfected individuals (n = 521)	Primary infection (n = 5,510)	Reinfection (n = 626)
Age, years	36 (28,45)	34 (24,46)	37 (28,45)	35 (28,43)
Sex				
Male	2,544 (38.22)	258 (50.39)	2,072 (37.60)	214 (34.19)
Female	4,113 (61.78)	263 (51.37)	3,438 (62.40)	412 (65.81)
Minority	548 (8.23)	36 (7.03)	466 (8.46)	46 (7.35)
Region				
Northern China	2,669 (40.09)	146 (28.52)	2,298 (41.71)	225 (35.94)
Eastern China	1,221 (18.34)	139 (27.15)	958 (17.39)	124 (19.81)
Northeastern China	999 (15.01)	97 (18.95)	832 (15.10)	70 (11.18)
Southwestern China	573 (8.61)	47 (9.18)	451 (8.19)	75 (11.98)
Northwestern China	511 (7.68)	42 (8.20)	429 (7.79)	40 (6.39)
Southern China	407 (6.11)	30 (5.86)	318 (5.77)	59 (9.42)
Central China	269 (4.04)	18 (3.52)	218 (3.96)	33 (5.27)
Urbanicity				
Rural	459 (6.89)	72 (14.06)	357 (6.48)	30 (4.79)
Suburban	502 (7.54)	51 (9.96)	411 (7.46)	40 (6.39)
Urban	5,696 (85.56)	398 (77.73)	4,742 (86.06)	556 (88.82)
Occupation				
Students	904 (13.58)	140 (27.34)	691 (12.54)	73 (11.66)
Part-Time / full-Time	5,055 (75.94)	312 (60.94)	4,236 (76.88)	507 (80.99)
Retirement / unemployed	291 (4.37)	39 (7.62)	234 (4.25)	18 (2.88)
Freelance	407 (6.11)	30 (5.86)	349 (6.33)	28 (4.47)
Income, 1,000 yuan				
<30	894 (13.43)	117 (22.85)	710 (12.89)	67 (10.70)
30–100	2,994 (44.98)	210 (41.02)	2,522 (45.77)	262 (41.85)
100–500	2,488 (37.37)	165 (32.23)	2,059 (37.37)	264 (42.17)
>500	278 (4.18)	29 (5.66)	216 (3.92)	33 (5.27)
Education				
High School or less	140 (2.10)	32 (6.25)	98 (1.78)	10 (1.60)
Some colleges	427 (6.41)	49 (9.57)	349 (6.33)	29 (4.63)
Bachelor's degree	4,509 (67.73)	341 (66.60)	3,763 (68.29)	405 (64.70)
Graduate degree	1,581 (23.75)	99 (19.34)	1,300 (23.59)	182 (29.07)
Smoking				
Nonsmoker	4,127 (61.99)	298 (58.20)	3,440 (62.43)	389 (62.14)
Current smoker	881 (13.23)	108 (21.09)	712 (12.92)	61 (9.74)
Ex-smoker	249 (3.74)	17 (3.32)	208 (3.77)	24 (3.83)
Passive smoking	1,400 (21.03)	98 (19.14)	1,150 (20.87)	152 (24.28)
Outpatient visits in acute phase	451 (6.77)	–	406 (7.37)	45 (7.18)
Background diseases	1,780 (26.74)	125 (24.41)	1,489 (27.02)	166 (26.52)
Allergic rhinitis	664 (9.97)	52 (10.16)	550 (9.98)	62 (9.90)
Hypertension	582 (8.74)	38 (7.42)	498 (9.04)	46 (7.35)
Hyperlipidemia	414 (6.22)	26 (5.08)	342 (6.21)	46 (7.35)
Diabetes	196 (2.94)	16 (3.13)	160 (2.90)	20 (3.19)
Cardiovascular disease	66 (0.99)	10 (1.95)	48 (0.87)	8 (1.28)
Thyroid disease	59 (0.89)	3 (0.59)	52 (0.94)	4 (0.64)
Malignant tumor	57 (0.86)	2 (0.39)	51 (0.93)	4 (0.64)
Asthma	95 (1.43)	9 (1.76)	75 (1.36)	11 (1.76)
COPD	18 (0.27)	1 (0.20)	16 (0.29)	1 (0.16)
Chronic kidney disease	22 (0.33)		22 (0.40)	
Autoimmune disease	16 (0.24)	2 (0.39)	13 (0.24)	1 (0.16)
Mental disorders	11 (0.17)	0	11 (0.20)	0
Tuberculosis	20 (0.30)	2 (0.39)	16 (0.29)	2 (0.32)
Allergic or skin diseases	13 (0.20)	0	12 (0.22)	1 (0.16)
Pharyngitis	11 (0.17)	0	10 (0.18)	1 (0.16)
Reproductive diseases	13 (0.20)	1 (0.20)	12 (0.22)	0
Neurological diseases	10 (0.15)	0	10 (0.18)	0
Other diseases	129 (1.94)	10 (1.95)	105 (1.91)	14 (2.24)

Age is presented as median (IQR), while other characteristics are presented as n (%). Thyroid diseases include hyperthyroidism, hypothyroidism, subacute thyroiditis, thyroid nodules, and Hashimoto's thyroiditis (HT). Malignant tumors include lung cancer, thyroid cancer, and papillary thyroid carcinoma. Autoimmune diseases include rheumatoid arthritis, systemic lupus erythematosus (SLE), inflammatory bowel disease (IBD), and Behcet's disease (BD). Mental disorders include anxiety, depression, and compulsive behavior. Allergies and skin diseases include eczema, psoriasis, and skin allergies. Reproductive diseases include pelvic endometriosis, polycystic ovary syndrome (PCOS), endometrial polyps, and mastitis. Neurological diseases include neural tinnitus, sudden deafness, vegetative system dysfunction, and dysfunction of the autonomic nervous system. Other diseases include joint diseases, oral diseases, digestive diseases, some viral infection or viral carrier, postoperative issues, trauma, etc. Abbreviation: COPD, chronic obstructive pulmonary disease; -, no data.

3.4. The long-term effects of the primary SARS-CoV-2 infection increase the risk of reinfection

To obtain a clear picture of the long-term symptoms associated with reinfection, we further excluded participants with a more complex background of SARS-CoV-2 infection, including 8 respondents who reported 3 infections and 1 who reported 4 infections. The median time between the first and second infections was 151 (median, IQR: 141–161) days. The frequencies of most symptoms, with the exception of reproductive system symptoms and gingival bleeding, were significantly higher among individuals before reinfection than among individuals without reinfection. The proportion of respondents with reinfection who had any symptoms after the first infection was as high as 29.82 %, which was much higher than the proportion of

Table 2
Self-comparison of disorders before and after the primary infection.

Symptoms	The health condition before primary infection (n = 5,059)				The health condition after primary infection (n = 5,059)				*P* value	$P_{composition}$
	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total		
Any symptom				471 (9.31)				937 (18.52)	<0.0001*	
Fatigue	197 (53.24)	148 (40.00)	25 (6.76)	370 (7.31)	483 (62.89)	252 (32.81)	33 (4.30)	768 (15.18)	<0.0001*	0.0013**
PEM	173 (66.03)	78 (29.77)	11 (4.20)	262 (5.18)	357 (60.41)	187 (31.64)	47 (7.95)	591 (11.68)	<0.0001*	0.0689
Muscle pain / spasms	148 (70.14)	54 (25.59)	9 (4.27)	211 (4.17)	205 (73.48)	62 (22.22)	12 (4.30)	279 (5.51)	0.0016*	0.4410
Hair loss	125 (66.49)	51 (27.13)	12 (6.38)	188 (3.72)	268 (67.17)	95 (23.81)	36 (9.02)	399 (7.89)	<0.0001*	0.9532
Chills	111 (71.15)	32 (20.51)	13 (8.33)	156 (3.08)	133 (71.12)	46 (24.60)	8 (4.28)	187 (3.70)	0.0886	0.8188
Joint pain	109 (67.70)	45 (27.95)	7 (4.35)	161 (3.18)	169 (75.11)	49 (21.78)	7 (3.11)	225 (4.45)	0.0009*	0.1089
Excessive sweating at rest	85 (61.15)	41 (29.50)	13 (9.35)	139 (2.75)	141 (66.82)	53 (25.12)	17 (8.06)	211 (4.17)	<0.0001*	0.2893
Rash	55 (75.34)	17 (23.29)	1 (1.37)	73 (1.44)	95 (60.13)	54 (34.18)	9 (5.70)	158 (3.12)	<0.0001*	0.0188**
Memory issues	178 (72.36)	57 (23.17)	11 (4.47)	246 (4.86)	406 (61.14)	192 (28.92)	66 (9.94)	664 (13.13)	<0.0001*	0.0008**
Sleep disorder / insomnia	141 (56.63)	83 (33.33)	25 (10.04)	249 (4.92)	272 (57.75)	156 (33.12)	43 (9.13)	471 (9.31)	<0.0001*	0.7243
Brain fog	166 (70.94)	60 (25.64)	8 (3.42)	234 (4.63)	373 (65.32)	160 (28.02)	38 (6.65)	571 (11.29)	<0.0001*	0.0851
Headache / dizziness	179 (75.85)	50 (21.19)	7 (2.97)	236 (4.66)	256 (74.64)	71 (20.70)	16 (4.66)	343 (6.78)	<0.0001*	0.6666
Sore throat or foreign body sensation in the throat	161 (61.69)	76 (29.12)	24 (9.20)	261 (5.16)	237 (71.60)	75 (22.66)	19 (5.74)	331 (6.54)	0.0030*	0.0088**
Cough	147 (66.22)	59 (26.58)	16 (7.21)	222 (4.39)	239 (72.87)	71 (21.65)	18 (5.49)	328 (6.48)	<0.0001*	0.0932
Expectoration	131 (66.84)	57 (29.08)	8 (4.08)	196 (3.87)	194 (74.33)	58 (22.22)	9 (3.45)	261 (5.16)	0.0019*	0.0867
Chest distress	142 (78.02)	38 (20.88)	2 (1.10)	182 (3.60)	276 (76.03)	75 (20.66)	12 (3.31)	363 (7.18)	<0.0001*	0.5252
Tachycardia or palpitations	140 (72.92)	45 (23.44)	7 (3.65)	192 (3.80)	285 (63.62)	124 (27.68)	39 (8.71)	448 (8.86)	<0.0001*	0.0125
Dyspnea	106 (83.46)	20 (15.75)	1 (0.79)	127 (2.51)	174 (79.45)	38 (17.35)	7 (3.20)	219 (4.33)	<0.0001*	0.3199
Chest pain	90 (84.11)	14 (13.08)	3 (2.80)	107 (2.12)	134 (75.28)	36 (20.22)	8 (4.49)	178 (3.52)	<0.0001*	0.0797
Dry / painful / watery eyes	137 (76.54)	37 (20.67)	5 (2.79)	179 (3.54)	276 (74.80)	88 (23.85)	5 (1.36)	369 (7.29)	<0.0001*	0.7314
Blurred vision	88 (73.33)	26 (21.67)	6 (5.00)	120 (2.37)	236 (75.40)	70 (22.36)	7 (2.24)	313 (6.19)	<0.0001*	0.5649
Loss of appetite	123 (71.93)	37 (21.64)	11 (6.43)	171 (3.38)	155 (77.11)	36 (17.91)	10 (4.98)	201 (3.97)	0.1130	0.2490
Constipation	72 (70.59)	25 (24.51)	5 (4.90)	102 (2.02)	118 (73.29)	32 (19.88)	11 (6.83)	161 (3.18)	0.0002*	0.7274
Gingival bleeding	66 (82.50)	13 (16.25)	1 (1.25)	80 (1.58)	112 (81.16)	22 (15.94)	4 (2.90)	138 (2.73)	<0.0001*	0.7692
Reproductive system symptom				45 (0.89)				149 (2.95)	<0.0001*	
Female				27 (0.53)				96 (1.90)	<0.0001*	
Menstrual disorder	10 (47.62)	9 (42.86)	2 (9.52)	21 (0.42)	49 (57.65)	34 (40.00)	2 (2.35)	85 (1.68)	<0.0001*	0.3002
Increased menstrual pain	17 (70.83)	4 (16.67)	3 (12.50)	24 (0.47)	26 (53.06)	19 (38.78)	4 (8.16)	49 (0.97)	0.0033*	0.2618
Irregular uterine bleeding	5/7	1/7	1/7	7 (0.14)	15 (65.22)	8 (34.78)	0	23 (0.45)	0.0034*	0.9762
Male				18 (0.36)				53 (1.05)	<0.0001*	
Decreased libido	8 (50.00)	4 (25.00)	4 (25.00)	16 (0.32)	26 (55.32)	13 (27.66)	8 (17.02)	47 (0.93)	<0.0001*	0.6062
Erectile dysfunction	10 (58.82)	6 (35.29)	1 (5.88)	17 (0.34)	23 (60.53)	11 (28.95)	4 (10.53)	38 (0.75)	0.0045*	0.9916
Difficulty ejaculating	7/9	2/9	0	9 (0.18)	5 (31.25)	8 (50.00)	3 (18.75)	16 (0.32)	0.1610	0.0248**
Orchialgia	6/7	1/7	0	7 (0.14)	10 (76.92)	1 (7.69)	2 (15.38)	13 (0.26)	0.1793	0.6094

Data are presented as n (%) or n/N. *P* values are reported for the comparisons of the differences in the total composition ratios of the severities of each symptom, and $P_{composition}$ values are reported for the assessment of whether the composition ratios of each symptom with different severities (mild, moderate, and severe) are different. *$P < 0.05$. **$P_{composition} < 0.05$. Abbreviation: PEM, post-exertional malaise

respondents with symptoms before the first infection (29.82 % vs. 18.52 %, $P < 0.0001$). The most common symptom before reinfection was fatigue (24.64 %), followed by sore throat or foreign body sensation in the throat (19.29 %), cough (16.86 %), PEM (16.86 %), brain fog (16.37 %), headache / dizziness (16.21 %), and memory issues (15.88 %) (Table 3). However, there were no significant differences in reproductive system symptoms before reinfection between respondents without reinfection and respondents with reinfection. In brief, respondents with reinfection had a higher probability of disorders before reinfection compared with respondents without reinfection. This meant that the health status of respondents did not return to the level of health of those without infection before the second infection, and this difference was particularly significant for general symptoms, but not for reproductive system symptoms.

Therefore, we speculated whether the health status after recovery from the initial infection of SARS-CoV-2 was related to reinfection. To confirm this hypothesis, we matched respondents who had reinfection with respondents who had only been infected once in a 1:4 ratio to explore the impact of initial SARS-CoV-2 infection on reinfection. A total of 616 respondents who had reinfection and 2,464 respondents who had been infected once were identified (Fig. 1). All symptoms except hair loss, occurred more frequently among respondents with reinfection than among the matched controls (Table S4).

In subsequent analyses, we used a binary logistic regression analysis to evaluate the relationship between the severity of symptoms after recovery from the primary infection and the occurrence of reinfection. The results showed that different disorders severities were associated with the risk of reinfection. The findings were obtained by comparing with respondents who did not have fatigue, PEM, muscle pain / spasms, chills, joint pain, excessive sweating at rest, headache / dizziness, sore throat or foreign body sensation in the throat, cough, expectoration, dry / painful / watery eyes, loss of appetite and constipation. It was noted that respondents with mild or moderate / severe symptoms had an increased risk of repeated SARS-CoV-2 infection. For some symptoms, an increase in the risk of reinfection was found only when the symptoms were mild, such as mild memory issues (OR = 1.380, 95 % CI: 1.029–1.850, $P = 0.0313$), mild brain fog (OR = 1.686, 95 % CI: 1.257–2.261, $P = 0.0050$), mild chest distress (OR = 1.785, 95 % CI: 1.290–2.469, $P = 0.0005$) and mild chest pain (OR = 1.655, 95 % CI: 1.059–2.584, $P = 0.0269$), and when these symptoms were moderate / severe, there was no increase in the risk of reinfection. Conversely, moderate/severe dyspnea significantly increased the risk of reinfection (OR = 2.313, 95 % CI: 1.184–4.518, $P = 0.0141$) (Fig. 3).

4. Discussion

Long COVID is a pivotal public health concern that need to be taken seriously in the postpandemic era [27]. We showed that the health statuses of participants were still adversely affected by the SARS-CoV-2 infection 5 months after the spread of the Omicron variant in China. The incidence of long COVID 5 months after the primary infection

Table 3
Disorders before the second severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and general disorders in uninfected respondents.

Symptoms	The health condition of uninfected respondents (n = 521)				The health condition before second infection (n = 617)				*P* value	$P_{composition}$
	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total		
Any symptom				63 (12.09)				184 (29.82)	<0.0001*	
Fatigue	27 (57.45)	19 (40.43)	1(2.13)	47 (9.02)	74 (48.68)	68 (44.74)	10 (6.58)	152 (24.64)	<0.0001*	0.2220
PEM	20 (76.92)	6 (23.08)	0	26 (4.99)	62 (59.62)	34 (32.69)	8 (7.69)	104 (16.86)	<0.0001*	0.0773
Muscle pain / spasms	24 (88.89)	3 (11.11)	0	27 (5.18)	50 (63.29)	24 (30.38)	5 (6.33)	79 (12.80)	<0.0001*	0.0114**
Hair loss	17 (68.00)	6 (24.00)	2(8.00)	25 (4.80)	44 (78.57)	8 (14.29)	4 (7.14)	56 (9.08)	0.0052*	0.3455
Chills	17 (70.83)	6 (25.00)	1(4.17)	24 (4.61)	41 (65.08)	18 (28.57)	4 (6.35)	63 (10.21)	0.0004*	0.5970
Joint pain	18 (78.26)	5 (21.74)	0	23 (4.41)	42 (67.74)	16 (25.81)	4 (6.45)	62 (10.05)	0.0003*	0.2935
Excessive sweating at rest	18 (90.00)	2 (10.00)	0	20 (3.84)	37 (67.27)	11 (20.00)	7 (12.73)	55 (8.91)	0.0006*	0.0419**
Rash	3/9	6/9	0	9 (1.73)	15 (55.56)	8 (29.63)	4 (14.81)	27 (4.38)	0.0110*	0.5575
Memory issues	16 (61.54)	10 (38.46)	0	26 (4.99)	69 (70.41)	25 (25.51)	4 (4.08)	98 (15.88)	<0.0001*	0.4831
Sleep disorder / insomnia	21 (77.78)	5 (18.52)	1(3.70)	27 (5.18)	50 (63.29)	17 (21.52)	12 (15.19)	79 (12.80)	<0.0001*	0.1252
Brain fog	25 (80.65)	6 (19.35)	0	31 (5.95)	72 (71.29)	23 (22.77)	6 (5.94)	101 (16.37)	<0.0001*	0.2527
Headache/dizziness	17 (68.00)	6 (24.00)	2(8.00)	25 (4.80)	63 (63.00)	33 (33.00)	4 (4.00)	100 (16.21)	<0.0001*	0.7635
Sore throat or foreign body sensation in the throat	20 (68.97)	8 (27.59)	1(3.45)	29 (5.57)	65 (54.62)	39 (32.77)	15 (12.61)	119 (19.29)	<0.0001*	0.1152
Cough	26 (74.29)	9 (25.71)	0	35 (6.72)	62 (59.62)	34 (32.69)	8 (7.69)	104 (16.86)	<0.0001*	0.0829
Expectoration	19 (67.86)	9 (32.14)	0	28 (5.37)	58 (65.17)	27 (30.34)	4 (4.49)	89 (14.42)	<0.0001*	0.6940
Chest distress	3 (21.43)	0	14 (2.69)	58 (75.32)	19 (24.68)	0	77 (12.48)	<0.0001*	0.8009	
Tachycardia or palpitations	12 (70.59)	5 (29.41)	0	17 (3.26)	45 (67.16)	22 (32.84)	0	67 (10.86)	<0.0001*	0.7937
Dyspnea	7 (63.64)	4 (36.36)	0	11 (2.11)	30 (68.18)	13 (29.55)	1 (2.27)	44 (7.13)	<0.0001*	0.8266
Chest pain	6/6	0	0	6 (1.15)	29 (78.38)	7 (18.92)	1 (2.70)	37 (6.00)	<0.0001*	0.2229
Dry / painful / watery eyes	23 (95.83)	1 (4.17)	0	24 (4.61)	48 (70.59)	18 (26.47)	2 (2.94)	68 (11.02)	<0.0001*	0.0118**
Blurred vision	17 (94.44)	1 (5.56)	0	18 (3.45)	36 (80.00)	8 (17.78)	1 (2.22)	45 (7.29)	0.0048*	0.1603
Loss of appetite	13 (86.67)	2 (13.33)	0	15 (2.88)	41 (69.49)	16 (27.12)	2 (3.39)	59 (9.56)	<0.0001*	0.1775
Constipation	11 (68.75)	5 (31.25)	0	16 (3.07)	23 (65.71)	10 (28.57)	2 (5.71)	35 (5.67)	0.0346*	0.7478
Gingival bleeding	13 (100)	0	0	13 (2.50)	19 (76.00)	5 (20.00)	1 (4.00)	25 (4.05)	0.1453	0.0613
Reproductive system symptom				5 (0.96)				10 (1.62)	0.3300	
Female				2 (0.38)				4 (0.65)	0.6933	
Menstrual disorder	1/2	0	1/2	2 (0.38)	2/2	0	0	2 (0.32)	0.9999	0.6171
Increased menstrual pain	1/1	0	0	1 (0.19)	1/2	1/2	0	2 (0.32)	0.9999	0.9999
Irregular uterine bleeding	1/1	0	0	1 (0.19)	1/1	0	0	1 (0.16)	0.9999	–
Male				3 (0.58)				6 (0.97)	0.5201	
Decreased libido	0	3/3	0	3 (0.58)	2/4	1/4	1/4	4 (0.65)	0.9999	0.6933
Erectile dysfunction	1/3	2/3	0	3 (0.58)	2/4	1/4	1/4	4 (0.65)	0.9999	0.9999
Difficulty ejaculating	1/1	0	0	1 (0.19)	1/2	0	1/2	2 (0.32)	0.9999	0.9999
Orchialgia	0	0	0	0	1/2	1/2	0	2 (0.32)	0.5031	–

Data are presented as n (%) or n/N. *P* values are reported for the comparisons of the differences in the total composition ratios of the severities of each symptom, and $P_{composition}$ values are reported for the assessment of whether the composition ratios of each symptom with different severities (mild, moderate, and severe) are different. *$P < 0.05$. **$P_{composition} < 0.05$. Abbreviation: PEM, post-exertional malaise.

was 6.43 %. Smoking currently, receiving outpatient visits in the acute phase, and having background diseases probably contributed to the risk of moderate / severe disorders. Notably, our results a mutual association between reinfection and a weak health status from the first infection. Before reinfection, convalescents did not appear to have returned to the general level of health noted in the population without reinfection that is, they had long-term effects of the initial COVID-19 infection. Furthermore, we found that disorders with different severities after recovery from the primary infection could significantly increase the risk of reinfection.

Previous studies have mentioned adverse health effects involving multiple organs and systems in convalescents after a long recovery period from SARS-CoV-2 infection [8,28,29]. Long COVID was shown to be associated with high frequencies of fatigue, dyspnea, muscle ache, and nervous system symptoms (such as memory issues, brain fog, and sleep disorder) at 6 months [8,28,30]. In our study, we found a correlation between SARS-CoV-2 infection and an increase in abnormal symptoms of the respiratory system and reproductive system [31]. Our results showed that convalescents with mild symptoms accounted for the highest proportion of symptomatic respondents. However, convalescents with moderate / severe disorders were also identified, and we found moderate / severe symptoms such as memory issues and rush. Thus, more attention should be paid to convalescents with moderate / severe disorders, which can put greater pressure on the medical system.

The risk factors associated with COVID-19 outcomes, such as female, smoking, and background diseases, have been demonstrated previously [16,32]. Although we did not use a strict definition of long COVID in our study, smoking and background diseases were likely shown to be risk factors associated with the health of convalescents. Moreover, our study assessed and discussed the correlation of different background diseases with the risk of moderate / severe disorders, among which allergic rhinitis, hyperlipidemia, cardiovascular disease, autoimmune diseases, asthma and neurological diseases had nonnegligible contributions. These results indicated that background diseases contributed to an increase in the risk of a prolonged recovery time from SARS-CoV-2 infection. Besides, previous studies have showed that long COVID is highly associated with obesity or lipid metabolism disorders, asthma or respiratory diseases, and diabetes [2,32–35].

Most studies on reinfection have indicated that prior infection and vaccination mitigate reinfection risk, and initial protection was high but decreased over time [36–38]. Additionally, a study on participants infected with the ancestral strain of SARS-CoV-2 in China showed that individuals who still had long COVID at 2 years after the primary infection had a higher frequency of reinfection [5]. A study using the US Department of Veterans Affairs' national healthcare database reported that those who had reinfection exhibited an increased risk and excess burden of at least one sequelae in the postacute phase of reinfection compared with the findings in those who did not have reinfection [19] However, these studies on reinfection mainly focused on the symptoms of reinfection or the health burden caused by reinfection, and there has been limited assessment of the relevance between the long-term health effects of the first infection and reinfection. A study

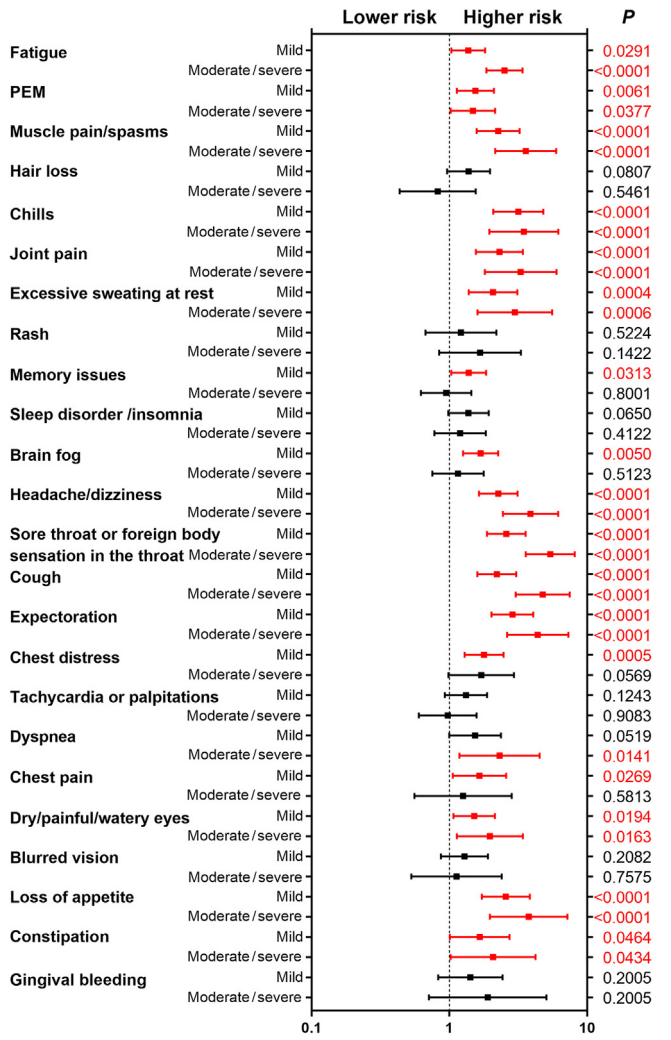


Fig. 3. Disorders after recovery from primary SARS-CoV-2 infection are associated with the risk of reinfection. The symptoms were mainly mild. Owing to the limited number of moderate/severe symptoms, these have been combined for statistical analysis. Each symptom has been referred to without the disorder. There is mutual adjustment for sex, age, vaccination, smoking, region, education, occupation, background diseases, and outpatient visits for the first infection. Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; PEM, post-exertional malaise.

in South Korea showed that long-term care facility residents had a high risk of reinfection [20]. Although SARS-CoV-2 infection mainly depends on the autoimmune response, further investigation is needed on the possible relationship between health characteristics and demographic characteristics. Our data analysis showed that convalescents with disorders in the post-COVID-19 condition had a higher risk of reinfection compared with general recovery respondents. These findings underscore the immense importance of enhancing recovery outcomes for SARS-CoV-2 infection and preventing reinfection and provide valuable insights for future interventions and strategies.

This study has some limitations. First, owing to the disadvantages of online questionnaire delivery, we cannot guarantee the randomness of questionnaire filling. For example, the proportions of female participants, participants from northern regions, urban dwellers, and participants with an undergraduate or graduate educational background were high in the population. The proportion of infection times in the study population may not represent the proportion for the entire Chinese population. Given the potential for considerable volunteer bias among the respondents, the representativeness of the research findings may not be robust. This limitation could, in turn, restrict the generalizability of the conclusions within China. It is essential to exercise caution when extrapolating these results to the broader population, acknowledging the inherent constraints imposed by the sample selection. Furthermore, our survey data were entirely dependent on the self-report of the participants. In addition to the self-detection basis of infection, the severity of each disorder was entirely dependent on the self-assessment and judgment of the participants, and the impact of individual differences on the research results cannot be ignored. Moreover, we did not adopt a strict definition of long COVID and used the disorder instead. In addition, we did not collect relevant information about the SARS-CoV-2 strains in our study, and thus, we could not assess and discuss the roles of the different strains in convalescence progress and repeat infection. Given the limitations of the studies, it was imperative to conduct additional research with improved randomization in a more extensive sample of the community population. This will enable the validation of the research conclusions with a greater abundance of displaying evidence.

Despite these limitations, the present study had some strengths. First, this study conducted a survey on the health conditions about 5 months after recovery from SARS-CoV-2 infection in the Chinese population with a relatively large number of participants and a wide range of subjects. We scientifically assessed the contributions of multiple demographic factors to the risk of developing moderate/severe disorders after SARS-CoV-2 infection using a potential analog model combined with multiple logistic regression models. This approach had a certain scientific significance for predicting the convalescence progress after recovery from SARS-CoV-2 infection. In our innovative analysis of the risk factors for moderate/severe symptoms, we found a high correlation between certain disorders and the occurrence of reinfections.

The findings of this study will help in promoting postacute clinical rehabilitation of COVID-19 infection, constructing post-COVID-19 care strategies, improving health system capacity planning, reducing repeat infections, and addressing the long-term care needs of people with COVID-19.

Ethics statement

The study was approved by the Ethics Committee of the National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention, and informed consent was obtained from the participants (No. IVDC 2023-005).

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Conflict of interest statement

The authors declare that there are no conflicts of interest.

Author contributions

Yalan Wang: Data curation, Formal analysis, Visualization, Writing – original draft. **Maoshun Liu:** Data curation, Investigation, Validation, Writing – original draft. **Yuanyuan Guo:** Formal analysis, Methodology. **Min Li:** Data curation, Formal analysis. **Peipei Guo:** Data curation, Formal analysis. **Wenjun He:** Data curation, Visualization. **Tian Ma:** Data curation, Visualization. **Peipei Liu:** Supervision. **Yaxin Guo:** Writing – review & editing. **Beiwei Ye:** Project adminis-

tration. **Jun Liu:** Conceptualization, Funding acquisition, Project administration, Supervision, Writing – review & editing. **Guizhen Wu:** Conceptualization, Funding acquisition, Project administration, Supervision.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bsheal.2024.06.001.

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