Health outcomes one year after Omicron infection among 12,789 adults: a community-based cross-sectional study

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Summary

Background Characterizing the paradigm and impact of long COVID is crucial for addressing this worldwide health challenge. This study aimed to investigate the prevalence of long COVID one year after primary Omicron infection and characterize differences in long-term health consequence between participants with persistent long COVID and those who fully recovered.

Methods This a community-based cross-sectional study conducted from December 2023 to March 2024 at the China-Japan Friendship Hospital and 16 administrative districts in Beijing. 12,789 participants infected with Omicron between December 2022 and January 2023 were recruited through stratified multistage random sampling and included in the final analysis. Of them, 376 participants with persistent long COVID and 229 without long COVID were matched for further physical examinations. The primary outcome was the prevalence of long COVID one year after infection. Secondary outcomes included muscle strength, exercise capacity, health-related quality of life (HRQoL), mental health, work status, laboratory tests, and examinations.

Findings Among 12,789 participants (media [IQR] age, 48.4 [37.3 to 61.4] years; 7817 females [61.1%]), 995 of them (7.8%) experienced long COVID within one year, with 651 (5.1%) having persistent symptoms. Fatigue (598/995 [60.1%]) and post-exertional malaise (367/995 [36.9%]) were the most common symptoms. Brain fog had the lowest resolution proportion as 4.2% within one year. The odds of long COVID increased with reinfections (odds ratios for one reinfection 2.592 [95% CI: 2.188 to 3.061]; two or more: 6.171 [3.227 to 11.557]; all $p < 0.001$). Participants with persistent long COVID had markedly lower muscle strength (upper-limb: 26.9 ± 12.4 vs. 29.1 ± 14.5 Kg; lower-limb: 40.0 [27.0 to 62.0] vs. 43.0 [28.0 to 59.0] s), worse exercise capacity and poorer HRQoL, and meaningful difference in laboratory tests results compared to those without long COVID. They also exhibited significantly higher proportions

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of abnormal lung function (FEV_1 %pred<80%: 13.0% vs. 2.0%; DLco %pred<80%: 32.7% vs. 19.9%) and lung imaging abnormalities (23.5% vs. 13.6%).

Interpretation The considerable health burden of long COVID and the progression of neurological symptoms following Omicron infection warrant close monitoring. Utilizing professional questionnaires and developing reliable diagnostic tools are necessary for improving diagnosis and treatment of long COVID.

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Keywords: Long covid; COVID-19; Health outcomes; Lung function; Neurological

Research in context

Evidence before this study

Omicron has become the most prevalent strain globally, with 4.2–18.2% of individuals who were infected experienced long COVID. Several risk factors for the development of long COVID have been identified. However, as of September 21, 2023, a PubMed search indicated that data on the prevalence of long COVID after primary Omicron infection in representative populations, as well as the factors contributing to its persistence, remained scarce. The diagnosis of long COVID, which primarily depends on patient-reported symptoms, continues to be challenging, with no universally accepted objective diagnostic tools available.

Added value of this study

This community-based cross-sectional study included 12,789 highly vaccinated adults primarily infected with Omicron, with 7.8% of them developed long COVID within one year, and 5.1% had persistent long COVID (LC) at 1-year after infection. The risk of long COVID increased with reinfection in a dose-dependent manner. While risk factors for long COVID were identified, they did not further contribute to its persistence. The highest rate of symptom recovery occurring within 6 months after infection, except for brain fog and cognitive impairment. Compared to participants without long COVID, those with persistent LC exhibited higher levels of leukocytes, triglycerides, fibrinogen, and myoglobin. They also had significantly higher proportions of abnormal lung function, and lung imaging abnormalities.

Implications of all the available evidence

Nearly 5% of highly vaccinated adults experienced persistent LC one year after primary Omicron infection. Reinfection increased the risk for the development of long COVID. Participants with persistent LC displayed higher levels in several laboratory tests parameters, alongside more prevalent abnormal lung function, all of which could serve as diagnostic indicators for long COVID. The findings of this study underscore the significant long-term health impacts of long COVID on multiple organ systems and emphasize the necessity of ongoing monitoring and targeted interventions to address the persistent symptoms experienced by suffered individuals.

Introduction

There were more than 700 million individuals infected with SARS-CoV-2 have been documented worldwide,[1] though the actual number is likely underestimated. Numerous studies indicated that a substantial proportion of COVID-19 patients still enduring symptoms, which can last from 4 weeks to 12 weeks or even extend to several months or years post-infection.[2–5] This chronic condition was named post-COVID-19 condition by the WHO,[6] also known as long COVID, which is an umbrella term that has been well known and used in many researches and media.[7,8] Post-exertional malaise (PEM), fatigue or muscle weakness, sleep difficult, dyspnea, brain fog, and palpitations were the common symptoms.[5,9,10] Individuals with long COVID displayed impaired lung function,[4,11,12] and had a higher risk of extrapulmonary organ disease burden compared to those without COVID-19.[13–19] This condition can persist for up to two to three years after infection.[5,20–22] Given annual SARS-CoV-2 infection estimates, the proportion of symptomatic cases, global incidence, and the reduced risk of long COVID over time, the cumulative incidence of long COVID is estimated at around 400 million worldwide.[23] This highlights the immense scale of the issue and the significant challenge it poses to global health system.

At the end of 2022, the Omicron BA.5 and BF.7 caused an outbreak in Beijing, China.[24,25] Several studies focused on different study populations reported the prevalence of long COVID decreased in Omicron-

infected patients compared to those infected with alpha and delta variants.[26–28] However, there is a paucity of data on the prevalence of long COVID after Omicron infection based on a representative population, and there is a lack of clinical measurements to distinguish long COVID patients.

Thus, we conducted this study to investigate the prevalence of long COVID in a large, community-based population of highly vaccinated Chinese adults one year after primary Omicron infection. We also assessed the health consequences between participants with persistent long COVID symptoms and those without long COVID.

Methods

Study design and participants recruitment

This was a community-based cross-sectional study conducted in Beijing, China. The target populations were individuals aged≥18 years who reported positive result for SARS-CoV-2, including antigen or RT-PCR tests, between 1st December, 2022 and 31st January, 2023 (the peak period).[29] Individuals meeting any of the following criteria were excluded: unable to cooperate with investigators due to severe mental disorder or dementia; limited mobility due to severe osteoarticular diseases, stroke and other reasons; non-permanent residents of Beijing city; refused to participate due to other reasons. A stratified multistage random sampling method was utilized to recruit participants from 16 administrative districts in Beijing, for more details please see Appendix pp 3. All participants included in this study had no prior history of SARS-CoV-2 infection before contracting the Omicron variant, as confirmed by the Epidemiological Investigation System for COVID-19 in Beijing.

Ethical considerations

The study was approved by the Research Ethics Commission of China-Japan Friendship Hospital (2023-KY-321) and Beijing Center for Disease Prevention and Control (2023–2026). Electronic and written informed consents were obtained from all the participants when they completed community questionnaire and face-to-face interviews at Hospital, separately.

Study procedure and data collection

This study employed a three-tiered survey approach. In the first tier, conducted from 4th December to 8th December 2023, all participants completed the questionnaire through a smartphone App under the guidance of trained investigators. The demographic data, clinical information about Omicron infection, and the presence and duration of long COVID symptoms over the past year were all documented. The definition of long COVID in this study followed the WHO's clinical case definition.[6] The SARS-CoV-2 vaccination status was confirmed using the Immune Planning Information Management System in China.

The second tier conducted via phone interviews from 18th December to 25th December 2023. A structured questionnaire captured the duration and severity of long COVID symptoms, work status, and health-care use after Omicron infection. Participants who experienced long COVID symptom after infection were categorized as ever long COVID (ever LC), consisting of resolved LC and persistent LC. Those who did not develop any long COVID symptom after Omicron infection were classified as no LC.

The third tier took placed in the China-Japan hospital from 27th December 2023 to 31st March 2024. Participants with persistent LC and those no LC, matched by age, sex, smoking status, comorbidity, resident region, and reinfection history on a basis, were invited for a comprehensive face-to-face evaluation. They underwent a series of professional questionnaires to assess corresponded long COVID symptoms, including dyspnea, fatigue, PEM, sleep quality, cough, depression, anxiety, and health-related quality of life (HRQoL). Muscle strength assessment, a 6-min walking test (6MWT), electrocardiograph (ECG) and general laboratory tests were administered. Persistent LC participants were classified into four subgroups: neurological, cardiovascular, respiratory, and musculoskeletal, each undergoing targeted lab tests and clinical examinations. Detailed information was supplemented in the Appendix pp 3–9 and Supplementary Fig. S1.

Outcomes and measurements

The primary outcome was the prevalence of long COVID, including ever LC and persistent LC, one year following primary Omicron infection. The secondary outcomes were physical and mental health conditions, included muscle strength, 6MWD, HRQoL, mental health, work status, laboratory tests and organ function examinations. More details about methods of assessments and definitions please find in the Appendix pp 9–10.

Statistical analysis

Descriptive statistics were used to summarize the data of demographic and clinical characteristics, including mean and standard deviations for normally distributed data, medians with interquartile ranges (IQRs) for non-normally distributed data, and numbers with percentages (n, %) for categorical variables. We compared ever LC with no LC, as well as persistent LC with resolved LC. For the comparison of the characteristics, we used the Wilcoxon test for non-normally distributed data, and the χ^2 test for categorical data. The DAG was utilized to identify the specific covariate sets required for estimating the total effects of each explanatory variable, detailed in Appendix pp 10–11. Multivariable logistic regression was conducted for each explanatory variable, adjusting for its specific covariate set, to investigate the association between potential explanatory variables and the development of ever LC or persistent LC.

Muscle strength, exercise capacity, HRQoL, and laboratory tests were described for study participants with persistent and without long COVID, and for participants with persistent musculoskeletal, respiratory, cardiovascular, and neurological long COVID symptoms, respectively. Coagulation tests and myocardial enzymes were also presented for these groups except for participants with musculoskeletal symptoms. Furthermore, lung function and imaging, electrocardiogram and echocardiogram, were described for participants with persistent respiratory, and cardiovascular symptoms, respectively, and also for those without long COVID. Dyspnea and cough severity were shown for participants with persistent respiratory long COVID symptom, for those with mild and moderate to severe symptom severity, and for those without long COVID. The cognitive capacity was shown for participants with persistent neurological long COVID symptom and for those with mild and moderate to severe symptom severity.

Comparisons between those with persistent and without long COVID symptoms, with the use of propensity scores and inverse probability weighting, were performed for all above clinical indicators shown for these two groups. Propensity scores to estimate the probability of persistent LC were developed with the use of logistic regression to adjust for differences in baseline characteristics between those with persistent and without long COVID symptoms. Age, sex, body mass index (<24, 24–27.9, ≥28 kg/m^2), education (high school or lower, college or higher), income (<5000 RMB/month, ≥5000 RMB/month), smoking status (never smoker, current or former smoker), comorbidity, vaccination (≤1 dose, 2 doses, ≥3 doses), and reinfection were included in the propensity model. Inverse probability weighting based on the propensity score was further used to adjust for differences between those with persistent and without long COVID symptoms.

All p values were based on two-sided statistical tests, with statistical significance defined as a p value < 0.05. All analyses were completed with SAS Version 9.4 and University Edition (SAS Institute, Inc., Cary, NC, USA), and R software Version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, interpretation, and writing of the report. No support from any organization for the submitted work.

Results

Demographic and clinical characteristics of study population

A total of 12,789 adults (median [IQR] age, 48.4 [37.3 to 61.4] years; 7817 females [61.1%]) who were included in the final analysis of this study (Supplementary Fig. S1). 7.8% (995/12,789) of them ever developed LC within one year after Omicron infection, and 5.1% (651/12,789) had persistent LC at 1-year visit (Table 1, Supplementary Fig. S2). 72.8% (9308/12,789) of participants were never-smoker, with hypertension (21.2% [2709/12,789]) being the most common comorbidity, and 83.9% (10,735/12,789) of participants had received three or more doses SARS-CoV-2 vaccine. Fifty-five (0.4%) participants were hospitalized, with a median hospital stay of 12.0 (7.0–15.5) days. Over the past year, 11.1% (1425/12,789) of all participants were reinfected with SARS-CoV-2, and 48 (0.4%) reinfected more than twice. Compared to no LC participants, those with ever LC had significantly higher proportions of females (72.9% vs 60.1%, p < 0.001). Reinfection was more common among ever LC participants (27.3% vs 10.2%, p < 0.001). Except for resident area and personal inclome, other demographic characteristics were comparable between the resolved and persistent LC groups, and more details provided in Table 1.

Influencing factors of long COVID

After multivariable adjustment, participants aged 35–49 and 50–64 years had a higher odd of ever LC compared with participants aged 18–34 years, with odds ratios (OR) of 1.450 (95% CI, 1.194 to 1.770) and 1.237 (1.006–1.528) among all included participants, respectively. However, for those aged 65 years and older, the odds of ever LC did not differ from those aged 18–34 years. Compared to males, females were at higher odds for ever LC (OR 1.777 [1.539 to 2.056]). Participants with at least one comorbidity had 93.3% higher odds of ever LC compared with those without any comorbidity (1.933 [1.647 to 2.268]). Use of corticosteroids during the acute phase was positively associated with ever LC (2.527 [1.573 to 3.965]), while use of antiviral drugs and administration of booster vaccine did not show protection against ever LC. Compared with participants without reinfection, those who were reinfected once and twice or more had higher odds for ever LC with ORs of 2.592 (2.188–3.061) and 6.171 (3.227–11.557), respectively. Hospitalized participants (8.751 [4.632 to 15.977]) and those who visited outpatients or emergency department (2.784 [2.383 to 3.245]) were at much higher odds for ever LC than those who were observed at home. Participants with higher personal income were more likely to develop persistent LC, while no other independent influencing factors for persistent LC were identified (Table 2). The prevalence of various long COVID symptoms was similar between male and female participants with persistent LC, and across different age groups (Supplementary Tables S1 and S2).

Long COVID symptoms, healthcare utilization and work status

Among ever LC participants, fatigue (60.1% [598/995]), PEM (36.9% [367/995]), cough (31.9% [317/995]),

Characteristics	Total, No. (%), N = 12,789	No long COVID, No. (%), N = 11,794	Ever long COVID, No. (%), N = 995	Ever long COVID, No. (%), N = 995		p value[a]	p value[b]
				Resolved long COVID N = 344	Persistent long COVID N = 651		
Age, median (IQR), years	48.4 (37.3–61.4)	48.5 (37.1–61.4)	47.3 (38.4–60.9)	47.8 (38.3–60.1)	46.9 (38.4–61.3)	0.81	0.77
Sex,						<0.001	0.36
Male	4972 (38.9)	4702 (39.9)	270 (27.1)	100 (29.1)	170 (26.1)		
Female	7817 (61.1)	7091 (60.1)	725 (72.9)	244 (70.9)	481 (73.9)		
BMI, median (IQR), kg/m^2	24.2 (22.1–26.7)	24.2 (22.0–26.7)	24.5 (22.4–27.1)	24.3 (22.3–26.8)	24.5 (22.5–27.1)	0.07	0.52
Resident area						<0.001	0.01
Urban	6573 (51.4)	5993 (50.8)	580 (58.3)	181 (52.6)	399 (61.3)		
Suburban	6216 (48.6)	5801 (49.2)	415 (41.7)	163 (47.4)	252 (38.7)		
Education						<0.001	0.44
College or higher	7071 (55.3)	6423 (54.5)	648 (65.1)	218 (63.4)	430 (66.1)		
High school or lower	5718 (44.7)	5371 (45.5)	347 (34.9)	126 (36.6)	221 (34.0)		
Personal income levels (monthly, yuan)						0.02	0.03
≤5000	5874 (45.9)	5453 (46.2)	421 (42.3)	162 (47.1)	259 (39.8)		
>5000	6915 (54.1)	6341 (53.8)	574 (57.7)	182 (52.9)	392 (60.2)		
Cigarette smoking						<0.001	0.89
Never-smoker	9308 (72.8)	8522 (72.3)	786 (79.0)	271 (78.8)	515 (79.1)		
Current smoker	2545 (19.9)	2426 (20.6)	119 (12.0)	40 (11.6)	79 (12.1)		
Former smoker	936 (7.3)	846 (7.2)	90 (9.1)	33 (9.6)	57 (8.8)		
Comorbidities							
Hypertension	2709 (21.2)	2461 (20.9)	248 (24.9)	80 (23.3)	168 (25.8)	0.003	0.42
Diabetes	1296 (10.1)	1177 (10.0)	119 (12.0)	31 (9.0)	88 (13.5)	0.05	0.05
Hyperlipidemia	1005 (7.9)	862 (7.3)	143 (14.4)	46 (13.4)	97 (14.9)	<0.001	0.58
Cerebrovascular and neurological diseases	221 (1.7)	196 (1.7)	25 (2.5)	5 (1.5)	20 (3.1)	0.06	0.18
Cardiovascular diseases	593 (4.6)	510 (4.3)	83 (8.3)	23 (6.7)	60 (9.2)	<0.001	0.21
Chronic Respiratory Diseases	287 (2.2)	228 (1.9)	59 (5.9)	17 (4.9)	42 (6.5)	<0.001	0.41
Chronic kidney diseases	81 (0.6)	64 (0.5)	17 (1.7)	2 (0.6)	15 (2.3)	<0.001	0.08
Chronic liver diseases	55 (0.4)	43 (0.4)	12 (1.2)	1 (0.3)	11 (1.7)	<0.001	0.11
Gastrointestinal diseases	229 (1.8)	189 (1.6)	40 (4.0)	8 (2.3)	32 (4.9)	<0.001	0.07
Malignancy	136 (1.1)	114 (1.0)	22 (2.2)	6 (1.7)	16 (2.5)	<0.001	0.62
Autoimmune diseases	97 (0.7)	79 (0.7)	18 (1.8)	4 (1.2)	14 (2.2)	<0.001	0.39
Anxiety or depression	91 (0.7)	69 (0.6)	22 (2.2)	4 (1.2)	18 (2.8)	<0.001	0.16
SARS-CoV-2 vaccination[c]						0.97	0.51
None or one dose	1055/12,786 (8.3)	975/11,791 (8.3)	80 (8.0)	24 (7.0)	56 (8.6)		
Two doses	996/12,786 (7.8)	919/11,791 (7.8)	77 (7.7)	24 (7.0)	53 (8.1)		
Three doses or more	10,735/12,786 (83.9)	9897/11,791 (83.9)	838 (84.2)	296 (86.1)	542 (83.3)		
Features related with Omicron							
Duration of viral shedding after positive tests[c], median (IQR), days	7.0 (5.0–8.0)	7.0 (5.0–8.0)	7.0 (6.0–10.0)	7.0 (6.0–10.0)	7.0 (7.0–10.0)	<0.001	0.16
Duration of infection related symptoms[d], median (IQR), days	7.0 (5.0–11.0)	7.0 (5.0–10.0)	12.0 (7.0–30.0)	10.0 (7.0–20.0)	14.0 (7.0–30.0)	<0.001	0.02
Pneumonia	279 (2.2)	191 (1.6)	88 (8.8)	14 (4.1)	74 (11.3)	<0.001	<0.001
Treatment location						<0.001	0.07
Home observation	10,898 (85.2)	10,221 (86.7)	677 (68.0)	244 (70.9)	433 (66.5)		
Outpatients or emergency	1836 (14.4)	1540 (13.1)	296 (29.8)	97 (28.2)	199 (30.6)		
Hospitalization	55 (0.4)	33 (0.3)	22 (2.2)	3 (0.9)	19 (2.9)		
Length of hospital stay, median (IQR), days	12.0 (7.0–15.5)	12.0 (6.0–15.0)	12.5 (10.0–16.8)	16.0 (13.5–28.0)	11.0 (10.0–16.0)	0.28	0.19
Oxygen therapy						<0.001	0.13
No Oxygen therapy	12,745 (99.7)	11,771 (99.8)	974 (97.9)	341 (99.1)	633 (97.2)		
Requiring supplemental oxygen	38 (0.3)	19 (0.2)	19 (1.9)	3 (0.9)	16 (2.5)		
Requiring HFNC or NIV, or both	5 (0.04)	3 (0.03)	2 (0.2)	0 (0.0)	2 (0.3)		
Requiring ECMO or IMV, or both	1 (0.01)	1 (0.01)	0 (0.0)	0 (0.0)	0 (0.0)		

(Table 1 continues on next page)

Characteristics	Total, No. (%), N = 12,789	No long COVID, No. (%), N = 11,794	Ever long COVID, No. (%), N = 995	Ever long COVID, No. (%), N = 995		p value[a]	p value[b]
				Resolved long COVID N = 344	Persistent long COVID N = 651		
(Continued from previous page)							
Use of Corticosteroid	124 (1.0)	87 (0.7)	37 (3.7)	8 (2.3)	29 (4.5)	<0.001	0.13
Use of antiviral drugs[e]	37 (0.3)	24 (0.2)	13 (1.3)	4 (1.2)	9 (1.4)	<0.001	1.00
Reinfection with positive SARS-CoV-2 test[f]						<0.001	0.32
No reinfection	11,316 (88.5)	10,593 (89.8)	723 (72.7)	260 (75.6)	463 (71.1)		
Once reinfection	1425 (11.1)	1173 (10.0)	252 (25.3)	78 (22.7)	174 (26.7)		
Twice or more reinfection	48 (0.4)	28 (0.2)	20 (2.0)	6 (1.7)	14 (2.2)		

Notes: Data are n (%), n/N (%), or median (IQR), unless otherwise indicated. The differing denominators used indicate missing data. All the included participants were Asian. BMI = Body Mass Index. ECMO = extracorporeal membrane oxygenation. HFNC = high-flow nasal cannula for oxygen therapy. IMV = invasive mechanical ventilation. NIV = non-invasive ventilation. [a]P value for the comparison between no long COVID and ever long COVID participants. [b]P value for the comparison between resolved long COVID and persistent long COVID participants. [c]SARS-CoV-2 vaccination was administrated prior to Omicron infection. [d]6002 participants reported duration of viral shedding after positive tests, 10,889 participants reported duration of infection related symptoms. [e]Antiviral drugs including paxlovid, molnupiravir, remdesivir, VV116 and Azvudine. [f]Reinfection was defined as a positive SARS-CoV-2 test, including RT-PCR and antigen tests, after January 2023.

Table 1: **Demographic and clinical characteristics of study population stratified by long COVID categories.**

palpitations (26.6% [265/995]), sleep difficulties (26.3% [262/995]), cognitive impairment (23.7% [236/995]) and brain fog (16.6% [165/995]) were the most common symptoms (Fig. 1a). Brain fog had the lowest resolved proportion as 4.2%, and becoming common in persistent LC participants (Fig. 1b). In resolved LC participants, majority of long COVID symptoms, including cough (75.7%), cough with sputum (69.8%), shortness of breath (66.7%), smell disorder (69.5%) and taste disorder (71.6%), resolved within 6 months after infection (Fig. 1c). However, 63.3% of cognitive impairment and 49.4% of brain fog symptoms resolved within 9–12 months after infection. Among persistent LC participants, over 60% of each long COVID symptoms were new onset after Omicron infection (Fig. 1d), and nearly 90% of each symptoms were mild to moderate (Likert 1–3) severity (Supplementary Fig. S3a).

29.7% (295/995) of ever LC participants required at least one medical visit over the past year, which was markedly higher than 6.9% (69/995) of no LC participants. The proportion of ever LC participants who returned to their original work was significantly lower than that of participants with no LC (96.6% [631/653] vs. 98.9% [633/640]). In addition, only 65.6% (414/631) of ever LC participants returned to their original work efficiency, with 33.9% (214/631) experienced reduced efficiency. These proportions were substantially lower than those of no LC participants, which were 85.6% (542/633) and 13.4% (85/633), respectively. Participants with persistent LC had significantly higher proportions of medical visits (37.5% [244/651] vs 14.8% [51/344]) and reduced work efficiency (46.1% [187/406] vs 12.0% [27/225]) compared to those with resolved LC (Supplementary Table S3).

Muscle strength, exercise capacity and HRQoL

376 of 651 persistent LC and 229 matched no LC participants attended the face-to-face survey (Supplementary Fig. S1). Participants who attended the hospital were younger, had less comorbidities, and exhibited more frequent and severe long COVID symptoms compared to those who did not. Additional comparisons between the groups shown in Supplementary Fig. S3b and c and Tables S4 and S5. Participants with persistent LC had significantly lower muscle strength compared to those without long COVID, including upper-limb (26.9 ± 12.4 vs 29.1 ± 14.5 kg) and lower-limb muscle strength (40.0 [27.0 to 62.0] vs 43.0 [28.0 to 59.0] s), along with a markedly higher proportion of participants with a 6-min walk distance less than the lower limit of normal (35.6% vs 26.6%). Notably, 25.6% of persistent LC participants experienced mobility problem, 9.6% had usual activity problem and 4.2% had personal care problem, all of which were significantly higher than the 7.6%, 0.8% and 1.5% observed in no LC participants, respectively. Participants with persistent LC reported considerably worse HRQoL than those without LC (EQ-VAS 69.3 ± 18.0 vs 77.0 ± 19.6). The proportions of anxiety and depression symptom were statistically higher in persistent LC participants, who also reported noticeably worse sleep quality. 65.7% of persistent LC participants exhibited clinically important fatigue, 34.0% were suggestive of PEM and 5.5% were suggestive of myalgic encephalomyelitis/chronic fatigue syndrome, all of which were nearly twice as high as those in no LC (35.9%, 12.8%, and 1.8%, respectively). These results across different persistent LC subgroups were detailed in Table 3.

Laboratory tests and examinations

Compared with no LC participants, those with persistent LC had substantially higher average leukocyte counts (6.5 ± 2.1 vs 6.1 ± 2.6 × 10^9/L), triglycerides (1.3 [0.9 to 2.0] vs 1.2 [0.8 to 1.9] mmol/L) and high-density lipoprotein (1.3 ± 0.4 vs 1.2 ± 0.5 mmol/L) than no LC. Participants with persistent LC exhibited significantly

Characteristics	Ever long COVID vs no long COVID		Persistent long COVID vs resolved long COVID	
	OR (95% CI)	p value	OR (95% CI)	p value
Age, years				
18–34	Ref.		Ref.	
35–49	1.450 (1.194–1.770)	<0.001	1.402 (0.945–2.071)	0.0913
50–64	1.237 (1.006–1.528)	0.046	1.159 (0.765–1.751)	0.4837
≥65	1.174 (0.938–1.472)	0.16	1.425 (0.906–2.246)	0.1258
Sex				
Male	Ref.		Ref.	
Female	1.777 (1.539–2.056)	<0.001	1.152 (0.857–1.544)	0.34
Obesity				
No	Ref.		Ref.	
Yes (>28 kg/m^2)	1.252 (1.050–1.487)	0.011	1.217 (0.855–1.748)	0.28
Resident area				
Rural	Ref.		Ref.	
Urban	1.166 (1.014–1.343)	0.032	1.303 (0.981–1.732)	0.07
Education				
High school or lower	Ref.		Ref.	
College or higher	1.816 (1.541–2.143)	<0.001	1.221 (0.877–1.700)	0.24
Personal Income levels (monthly, yuan)				
<5000	Ref.		Ref.	
≥5000	0.966 (0.829–1.127)	0.66	1.372 (1.009–1.868)	0.044
Cigarette smoking				
Never-smoker	Ref.		Ref.	
Current smoker or Former smoker	0.894 (0.723–1.106)	0.30	0.806 (0.513–1.259)	0.35
Comorbidities				
No	Ref.		Ref.	
Yes	1.933 (1.647–2.268)	<0.001	1.078 (0.786–1.483)	0.64
COVID-19 vaccination status				
≤2 dose	Ref.		Ref.	
≥3 doses	1.135 (0.942–1.376)	0.19	0.886 (0.595–1.306)	0.55
Use of corticosteroid				
No	Ref.		Ref.	
Yes	2.527 (1.573–3.965)	<0.001	1.343 (0.580–3.404)	0.51
Use of antiviral drugs[a]				
No	Ref.		Ref.	
Yes	2.253 (0.936–5.116)	0.06	0.457 (0.084–2.278)	0.33
Reinfection with positive SARS-CoV-2 test[b]				
No Reinfection	Ref.		Ref.	
Reinfected Once	2.592 (2.188–3.061)	<0.001	1.174 (0.854–1.623)	0.33
Reinfected twice or more	6.171 (3.227–11.557)	<0.001	1.038 (0.383–3.121)	0.94
Treatment location				
Home observation	Ref.		Ref.	
Outpatients or emergency	2.784 (2.383–3.245)	<0.001	1.167 (0.864–1.581)	0.32
Hospitalization	8.751 (4.632–15.977)	<0.001	2.626 (0.822–11.684)	0.14

Note: Data are odds ratio (95% CI). Odds ratio (OR) for each explanatory variable was obtained from logistic covariate set identified through the DAG. The OR for persistent long COVID among ever long COVID participants were also adjusted by the same factors. [a]Antiviral drugs including paxlovid, molnupiravir, remdesivir, VV116 and Azvudine. [b]Reinfection was defined as a positive SARS-CoV-2 test, including RT-PCR and antigen tests, after January 2023.

Table 2: **Influencing factors for long COVID.**

higher levels of fibrinogen (3.2 ± 0.8 vs 3.0 ± 0.9 g/L), fibrinogen degradation products and D-dimer (all $p < 0.001$) compared to no LC participants, along with statistically higher levels of myoglobin (17.4 [13.7 to 22.0] vs 17.0 [13.7 to 22.3] ug/L) and creatine kinase MB (0.9 [0.6 to 1.3] vs 0.9 [0.6 to 1.2] U/L). For more details among different long COVID subgroups, see Supplementary Tables S6 and S7.

Participants with persistent respiratory long COVID displayed worse lung function, including a markedly

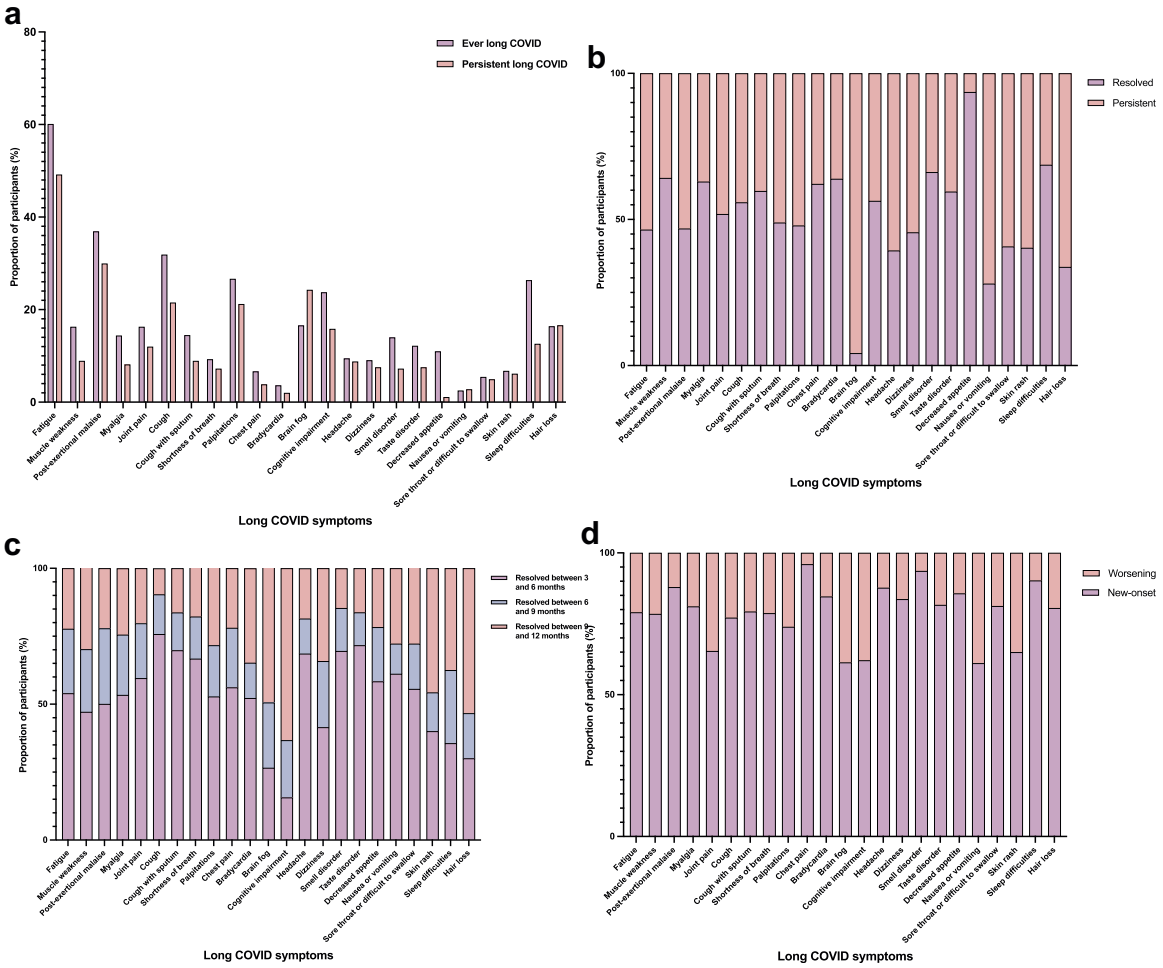

Fig. 1: **Detailed distribution of long COVID symptom among ever long COVID and persistent long COVID participants.** Note: (a) The prevalence of each long COVID symptom in ever long COVID and persistent long COVID participants. (b) The trajectory of each long COVID symptoms in ever long COVID participants. (c) Duration of each long COVID symptoms in resolved long COVID participants. (d) The proportions of new-onset and worsening long COVID symptom in persistent long COVID participants.

higher proportion with abnormal pulmonary ventilation capacity (FEV_1<80% pred, 13.0% vs 2.0%; FVC<80% pred, 2.0% vs 0), diffusion capacity (DLco<80% pred, 32.7% vs 19.9%) and CT abnormalities (23.5% vs 13.6%) compared to those no LC (Fig. 2a and b). 67.4% of participants in respiratory long COVID subgroup experienced dyspnea (mMRC≥1), with a median total Leicester cough questionnaire score of 16.8 (14.2–18.6). Compared with these respiratory long COVID participants, those with no LC had a significantly lower proportion of dyspnea (43.7%) and milder cough (Supplementary Fig. S4a and b). 23.8% of participants with neurological long COVID symptoms demonstrated cognitive impairment (Montreal Cognitive Assessment < 26), with memory being the most affected domain. The proportion of cognitive impairment was 26.5% among participants with moderate to severe neurological long COVID symptoms, and 19.4% among those with mild (Supplementary Fig. S4c). Participants with cardiovascular long COVID had a significantly higher proportion of ischemic abnormalities on ECG compared to no LC, while echocardiography parameters were comparable between the two groups (Supplementary Table S8).

Discussion

7.8% of Chinese adult community dwellers experienced long COVID within one year after primary Omicron infection, and 5.1% had persistent LC at 1-year follow-up. Participants with long COVID symptoms had significantly higher healthcare utilization and reduced work efficacy, resulting in increased health and economic burdens. These findings are crucial for

Characteristics	Persistent long COVID subtypes, No. (%), (N = 376)				Persistent long COVID, No. (%), N = 376[a]	No long COVID, No. (%), N = 229[a]	p value[d]
	Musculoskeletal N = 248	Respiratory N = 127	Cardiovascular N = 108	Neurological N = 161			
Muscle strength							
Grip strength, kg	27.0 (10.4)	28.3 (11.0)	26.3 (9.4)	26.2 (9.4)	26.9 (12.4)	29.1 (14.5)	0.007
Lower-limb muscle strength, median (IQR), s	37.5 (25.0–56.5)	39.0 (25.0–60.0)	38.0 (27.0–65.0)	40.0 (29.0–65.0)	40.0 (27.0–62.0)	43.0 (28.0–59.0)	<0.001
6 MWT							
Distance walked in 6 min, m	484.2 (80.3)	486.6 (83.0)	480.7 (78.6)	496.5 (84.0)	490.0 (101.6)	503.3 (131.1)	0.06
Percentage of predicted value[b]	84.0 (14.9)	83.0 (14.8)	83.8 (14.7)	86.1 (15.1)	83.5 (18.7)	85.5 (23.6)	0.14
Less than LLN[c]	81/236 (34.3)	48/122 (39.3)	36/104 (34.6)	48/152 (31.6)	35.6	26.6	<0.001
EQ-5D-5L							<0.001
Pain or discomfort	148/245 (60.4)	68/126 (54.0)	56/106 (52.8)	90/159 (56.6)	50.7	23.9	<0.001
Anxiety or depression	103/245 (42.0)	44/126 (34.9)	50/106 (47.2)	63/159 (39.6)	38.2	17.2	<0.001
Mobility problem	75/245 (30.6)	34/126 (27.0)	32/106 (30.2)	37/159 (23.3)	25.6	7.6	<0.001
Personal care problem	15/245 (6.1)	4/126 (3.2)	3/106 (2.8)	9/159 (5.7)	4.2	1.5	0.004
Usual activity problem	31/245 (12.7)	8/126 (6.3)	10/106 (9.4)	18/159 (11.3)	9.6	0.8	<0.001
EQ-VAS score	67.3 (14.4)	67.1 (14.3)	66.2 (14.7)	67.2 (14.2)	69.3 (18.0)	77.0 (19.6)	<0.001
Anxiety symptom (GAD7 ≥ 5)	92/246 (37.4)	39/126 (31.0)	50/107 (46.7)	63/160 (39.4)	34.0	17.7	<0.001
Mild (5–9)	55/246 (22.4)	20/126 (15.9)	27/107 (25.2)	40/160 (25.0)	21.1	14.3	<0.001
Moderate (10–14)	25/246 (10.2)	13/126 (10.3)	16/107 (15.0)	16/160 (10.0)	9.0	3.4	
Severe (≥15)	12/246 (4.9)	6/126 (4.8)	7/107 (6.5)	7/160 (4.4)	3.9	0.0	
Depression (PHQ-9 ≥ 5)	132/246 (53.7)	59/126 (46.8)	61/107 (57.0)	82/160 (51.3)	49.0	25.5	<0.001
Mild (5–9)	71/246 (28.9)	36/126 (28.6)	26/107 (24.3)	41/160 (25.6)	28.1	20.4	<0.001
Moderate (10–14)	40/246 (16.3)	16/126 (12.7)	23/107 (21.5)	25/160 (15.6)	13.9	2.7	
Severe (≥15)	21/246 (8.5)	7/126 (5.6)	12/107 (11.2)	16/160 (10.0)	7.0	2.4	
Fatigue severity scale (FSS) ≥ 4	182/246 (74.0)	82/126 (65.1)	86/107 (80.4)	113/160 (70.6)	65.7	35.9	<0.001
10 items the DePaul symptom questionnaire-PEM							
Indicative for PEM	96 (38.7)	52 (40.9)	40 (37.0)	61 (37.9)	34.0	12.8	<0.001
Indicative for ME/CFS	18 (7.3)	6 (4.7)	6 (5.6)	11 (6.8)	5.5	1.8	<0.001
Pittsburgh sleep quality index (PSQI)							
PSQI global score	11.5 (3.8)	10.9 (3.5)	11.9 (4.1)	11.6 (3.7)	11.1 (4.8)	9.0 (5.2)	<0.001
Very good: 0-5	15/244 (6.1)	4/126 (3.2)	4/106 (3.8)	5/159 (3.1)	6.1	14.5	<0.001
Fairly good: 6-10	80/244 (32.8)	60/126 (47.6)	39/106 (36.8)	56/159 (35.2)	38.0	54.1	
Fairly bad: 11-15	105/244 (43.0)	48/126 (38.1)	40/106 (37.7)	69/159 (43.4)	42.2	27.8	
Very bad: 16-21	44/244 (18.0)	14/126 (11.1)	23/106 (21.7)	29/159 (18.2)	13.7	3.6	

Notes: Data are n (%), n/N (%), mean ± SD, or median (IQR). The differing denominators used indicate missing data. 6MWT = 6-min walk test. LLN = lower limit of normal range. PEM = Post exertional malaise. ME/CFS = Myalgic encephalomyelitis/chronic fatigue syndrome. [a]Adjusted data with the use of inverse probability weighting. [b]Predicted values were calculated according to the method of Enright and Sherrill. [c]The LLN was calculated by subtracting 153 m from the predicted value for men or by subtracting 139 m for women. [d]P value for the comparison between persistent long COVID and no long COVID participants.

Table 3: **Muscle strength, exercise capacity and HRQoL between among persistent long COVID and no long COVID participants.**

enhancing clinical care and public health responses. In Australia, 18% of highly vaccinated individuals with no prior exposure to SARS-CoV-2 reported long COVID at ninety days following the Omicron wave.[30] In the UK, 7.5% of COVID-19 patients reported long COVID, with 5.2% experiencing symptoms lasting one year.[31] 6.9% of American adults ever had long COVID in 2022, with 3.4% still experiencing long COVID at survey.[32] Variations in study design, immunity status, and long COVID definitions hinder comparisons, but evidence suggests long COVID risk is declining,[27,33] underscoring the need for ongoing monitoring of the impact of Omicron on long COVID.

Our results identified female sex, comorbidities, COVID-19 severity, and reinfection as risk factors for long COVID, aligning with previous studies.[2–5,30,32,34–36] Hospitalized patients had a higher risk of long COVID compared to those who were not hospitalized, with impacts lasting up to three years post-infection.[20] Reinfection exhibited a significant dose-response effect on the developing long COVID in our study, which also increased the risk of sequalae and immobility.[37] Besides, long COVID patients were at higher risk for reinfection and more likely to develop pneumonia.[5] This was associated with increased healthcare utilization and reduced work capacity, contributing to a greater health burden

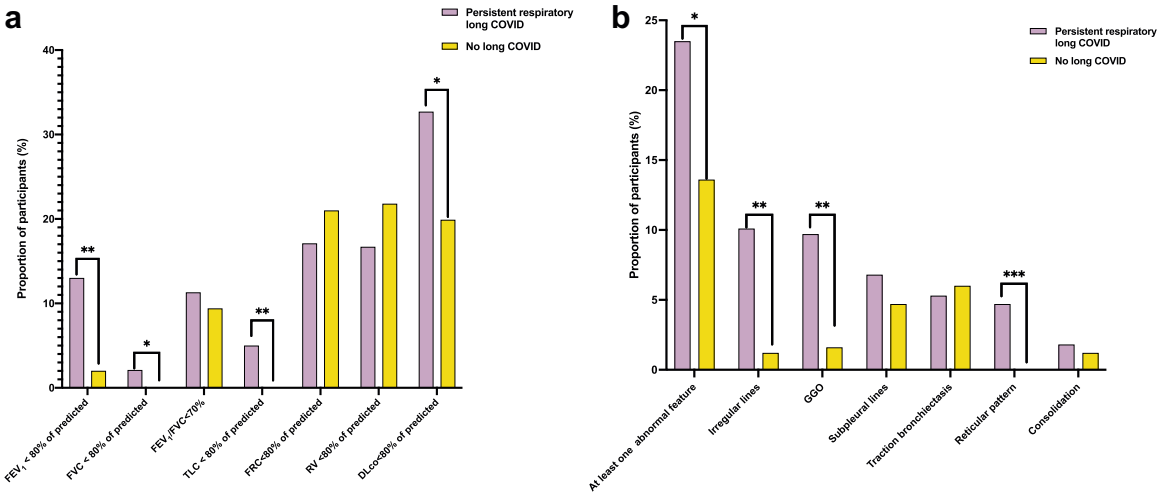

Fig. 2: **Examinations of lung function and imaging between participants with persistent respiratory and their matched no long COVID.** (a) Lung function between participants with persistent respiratory long COVID and those matched no long COVID. (b) CT imaging between participants with persistent respiratory long COVID and those matched no long COVID. Note: Data about the lung function, and CT imaging between participants with persistent long COVID and those without long COVID were adjusted with the use of inverse probability weighting. FEV_1 = forced expiratory volume in 1 s. FVC = forced vital capacity. TLC = total lung capacity. FRC = functional residual capacity. DL_{CO} = diffusion capacity of carbon monoxide. GGO = ground glass opacity. Honeycombing, non-emphysematous cysts, interlobular septal thickening, and crazy paving pattern were also evaluated, but none of the patients presented with these abnormalities. All the data were adjusted with the use of inverse probability weighting. *, p value < 0.05; **, p value < 0.001; ***, p value < 0.0001.

and imposing a substantial economic strain on society. In this study, booster vaccination had no impact on the persistence of long COVID. This finding aligns with another study conducted in a highly vaccinated population infected with Omicron, potentially due to the waning of antibody titers over time.[2,30] Previous studies found that vaccination primarily provides protection against long COVID,[33] and burden of RNA and infectious viral shedding were associated with long COVID.[38] Thus, administrating vaccination, early use of antiviral drugs to control COVID-19 progression, reducing severe illness rates, and preventing reinfection are essential strategies to mitigate the impacts of long COVID, especially for those at risk for severe illness.

Our study provided a detailed trajectory of each long COVID symptom, identifying six months after infection was a key recovery period. In clinical practices, cough is a common symptom following acute respiratory infections and can persist for weeks or months, impacting quality of life and increasing outpatient visits, potentially due to hypersensitivity of the cough reflex.[39] Reduced lung function and abnormal lung imaging in long COVID patients have been reported in several studies.[11,12,40,41] Our study found that abnormal pulmonary ventilation capacity, particularly FEV_1, was prevalent in participants with persistent respiratory LC. FEV_1 is closely associated with chronic pulmonary diseases and increased all-cause mortality.[42] The pathophysiology of respiratory LC involves inflammation, activation and alteration of immune cells, and impaired lung regeneration after infection.[43–47] Pulmonary fibrosis and chronic airway disease after COVID-19 needed to be tracked continuously, as well as further investigation of the mechanisms driving respiratory sequelae following various infections is warranted.

Brain fog and cognitive impairment were difficult to resolve once they occurred, with recovery primarily occurring between 9 and 12 months post-infection, but symptoms could persist for two to three years after infection.[20,48,49] These symptoms potentially increasing the incidence of neurological disorders, similar to what has reported after influenza infection.[50–53] Neurological symptoms are associated with brain structure changes,[54,55] brain hypometabolic,[56] blood–brain barrier dysfunction and systemic inflammation,[57,58] and unrecovered neuroglial injury.[59] One year after acute infection, 9% of patients infected with the original SARS-CoV-2 strain reported palpitations,[3] compared to nearly one in five of Omicron-infected individuals in this study, with symptoms lasting up to one year. The underlying pathophysiology remains unclear, myocardial injury, dysautonomia, arrhythmia, and inflammatory collectively contribute to it.[60,61] Further research is needed to understand the multi-organ impact of long COVID across different variants to address this global challenge.

Several laboratory tests parameters were elevated in persistent LC participants, with previous studies have associated monocyte alterations with lung injury,[45,62] and lung function[63] in long COVID patients, which may also

act as viral reservoirs.[64] Disruptions in lipid metabolism suggest a connection between long COVID and metabolic abnormalities,[65,66] with the observed alterations potentially continuing from acute SARS-CoV-2 infection.[67] A recent study has suggested that coagulopathy contributes to inflammation and neuropathology injury in COVID-19.[68] Elevated coagulation parameters, associated with severe COVID-19 and increased mortality,[69–71] have also been observed in long COVID patients,[72] suggesting a hypercoagulable state that may contribute to prolonged symptoms.[73] These findings highlight the need to focus on vascular disease and thrombotic complications in long COVID patients. A study from the RECOVER Cohort found no significant difference in laboratory tests between individuals with and without long COVID six months after infection.[74] The primary differences between their study and ours stem from variants in timepoints, study populations, and SARS-CoV-2 strains. In our study a substantial number of participants continued to recover between six months and one year, so the discrepancies in findings may be context-specific. Long COVID diagnosis remains challenging due to reliance on subjective complaints and lack of objective tests,[74] making the development of auxiliary diagnostic tools urgent. Although the abnormalities observed in our study have not reached clinical significance, these tests are indicative for diagnosis and essential for differential diagnosis. Clinicians should use validated questionnaires and consider routine clinical tests for accurate diagnosis, management and differentiate long COVID.

This is the first community-based study in China to evaluate long-term health outcomes of individuals with primary Omicron infection. Community recruitment allowed for a representative population, enhancing the generalizability of the findings. Comprehensive examinations providing insights for clinical practice and further research. However, this study has several limitations. Firstly, data of Omicron infection, reinfection and long COVID symptoms were self-reported without medical confirmation. But the diagnosis criteria of Omicron infection or reinfection in this study were based on self-reported positive tests for SARS-CoV-2, and the proportions of self-reported symptoms were similar to that evaluated by the validated questionnaires. All investigators involved received professional training. Secondly, we have to acknowledge that nearly 40% participants with persistent LC did not attend the hospital survey, and a potential selection bias may exist due to more prevalent and severe long COVID symptom among participants who completed the hospital survey. Nevertheless, the other characteristics of attendees and non-attendees were similar. Thirdly, although we adjusted for multiple confounders when comparing clinical examination results between participants with persistent LC and those without LC, we cannot be certain that the abnormalities found in this study are attributable to Omicron infection because we do not have data on their pre-infection period. Fourthly, the small number of participants who completed functional examinations also warrants cautious interpretation of results, which should be validated in larger studies.

In conclusion, 5.1% of Chinese adults with primary Omicron infection had persistent LC at one year after infection. Neurological and respiratory symptoms and function being particularly challenging. Improving clinicians understanding of long COVID and uncovering its mechanisms is essential for address this global challenge.

Contributors

BC, HZ, XG, YeW, QW, PY, YS, and DZ conceived and designed the study. HZ, XG, PY, and YS drafted the paper. XG and YS did the analysis. BC, QW, PY, HZ, YS, XG, RZ, JZ, YeW, CM, ML, JM, AL, YingW, XM, XC, ZL, YiWang, WW, ZZ, YL and JW collected and verified the data. ML evaluated the lung imaging. BC and QW had full access to and verified all of the data in the study, taking responsibility for the integrity of the data and the accuracy of the data analysis. All authors critically revised the manuscript for important intellectual content and agreed to submit the final version for publication. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data sharing statement

Restrictions apply to the availability of these data and they are not publicly available. However, data are available from the corresponding author upon reasonable request and with the permission of the institution. The corresponding authors affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Declaration of interests

All authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2025.101507.

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