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Supplementary appendix

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Supplementary Materials

1-year outcomes in hospital survivors with COVID-19: a longitudinal cohort study

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Contents

Methods supplement

a. Data collection of COVID-19 patients at acute phase

We defined the acute phase as the time between symptom onset and hospital discharge. Clinical data for acute phase were retrieved from electronic medical records, including demographic characteristics (age, sex, education, and cigarette smoking); clinical characteristics (self-reported comorbidities, symptom onset time, and chest images); laboratory test results; and treatment (corticosteroids, intravenous immunoglobulin, antibiotics, thymosin, and antivirals including lopinavir–ritonavir, arbidol, chloroquine phosphate, and hydroxychloroquine). The disease severity was characterised by the highest seven-category scale during the hospital stay (termed the severity scale), which consisted of the following categories: 1, not admitted to hospital with resumption of normal activities; 2, not admitted to hospital, but unable to resume normal activities; 3, admitted to hospital but not requiring supplemental oxygen; 4, admitted to hospital but requiring supplemental oxygen; 5, admitted to hospital requiring high-flow nasal cannula (HFNC), non-invasive mechanical ventilation (NIV), or both; 6, admitted to hospital requiring extracorporeal membrane oxygenation, invasive mechanical ventilation (IMV), or both; and 7, death.

b. Inclusion and exclusion criteria of community-dwelling non-COVID-19 participants

Inclusion criteria:

1. At least 20 years of age

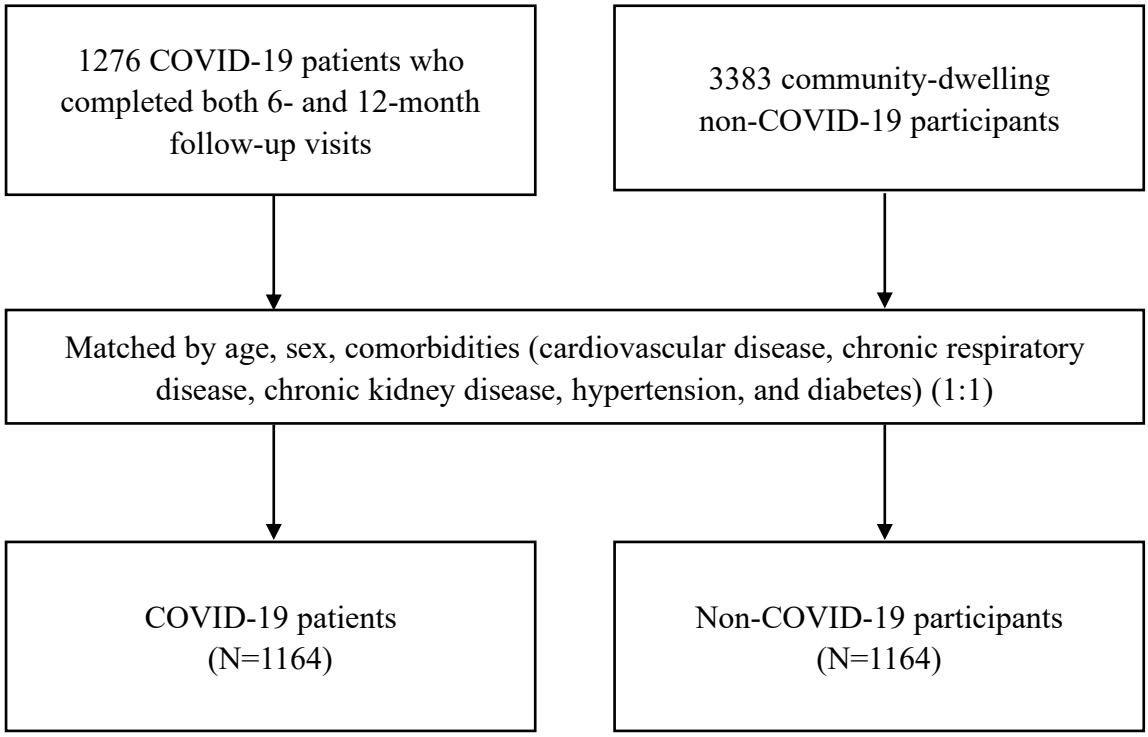
Exclusion criteria:

1. History of laboratory confirmed SARS-CoV-2 infection
2. Unable to complete the associated questionnaires, such as dementia and psychotic disease
3. Inability to move autonomously

c. Recruitment of community-dwelling non-COVID-19 participants

A 4-stage stratified sampling method was used to select non-COVID study participants as controls from Wuhan. In the first stage, two districts were selected from 13 districts of Wuhan stratified by geographical region and economic development level. One of the district (Jiangan District) is located at the center of Wuhan and the gross domestic product of which was high. The other district (Dongxihu District) is located relatively far away from the center of Wuhan and the gross domestic product of which was not that high. In the second stage, one sub-district each (Jinqiao sub-district and Jiangjunlu sub-district) was respectively selected from Jiangan District and Dongxihu District. In the third stage, 6 of 11 communities from Jinqiao sub-district and 6 of 11 communities from Jiangjunlu sub-district, the directors of which agreed the survey to be conducted in their communities, were selected. In the final stage, the grid administrators (each of whom is responsible for contacting some of the residents in the community and sending notification) from each community were contacted to recruit study population. The community members who were eligible and finished the survey were finally included. The selection of districts and sub-districts was not at random.

d. Matching of COVID-19 patients and community-dwelling non-COVID-19 participants



e. Study procedures

Time and Events schedule				
	COVID-19 patients			Community non-COVD-19 participants
	Data collection at acute phase	6-month visit	12-month visit	
Eligibility screening		X	X	X
Informed consent		X	X	X
Demographic data	X	X	X	X
Medical history	X	X	X	X
Clinical and Laboratory data during hospitalization	X			
Treatment during hospitalization	X			
Physical examination	X	X	X	X
Questionnaire on symptom		X[a]	X[a]	X[b]
mMRC dyspnoea scale		X	X	X
EQ-5D-5L Questionnaire		X	X	X
EQ-VAS		X	X	X
Ischaemic stroke and cardiovascular event registration form		X	X	
Blood specimen for complete blood count	X	X	X	X
Blood specimen for renal function*	X	X	X	X
Blood specimen for liver function†	X		X	X
Blood specimen for HbA1C	X	X	X	X
Blood specimen for lipid‡	X		X	X
Blood specimen for antibody testing	X	X[c]	X	
Blood specimen for cytokine testing	X[d]	X[d]	X[d]	
Routine urine	X		X	X
6-min walking test		X	X	
Pulmonary function tests		X[e]	X[f]	
Lung HRCT		X[e]	X[g]	
Ultrasonography		X[e]		

mMRC=modified British Medical Research Council. EQ-5D-5L=EuroQol five-dimension five-level questionnaire. EQ-VAS=EuroQol Visual Analogue Scale. HbA1C= glycated hemoglobin A1C. HRCT=high resolution computed tomography.

a: Symptom was further divided into prevalent symptom and sequelae symptom

b: Only record the prevalent symptom during follow-up

c: Antibody test only for those who had previously been enrolled in LOTUS China trial and attended 6-month visit.

d: Cytokine test only for those who had plasma at each time period including at acute phase, discharge, 6- and 12-month visits.

e: At 6-month visit, a stratified disproportional random sampling procedure according to severity scale was

used to select patients to undergo these tests. Patients requiring HFNC, NIV, or IMV (severity scale≥5) during hospitalization were all invited to receive the pulmonary function test and HRCT of chest. The ratio used to select patients not requiring supplemental oxygen (severity scale 3) and those requiring supplemental oxygen (severity scale 4) was 1:2. Finally, 349 patients completed the pulmonary function test and 353 completed chest HRCT at 6-month visit.

f: 349 patients who had completed the pulmonary function test at 6 months were all invited to administer the test at the 12-month visit.

g: Of 353 patients who had completed chest HRCT at 6 months, 186 presented with abnormal CT were invited to receive the test at the 12-month visit.

* Renal function includes creatine, estimate glomerular filtration rate (eGFR), and cystatin C.

† Liver function includes alanine aminotransferase (ALT), aspartate aminotransferase(AST), albumin, total protein, total bilrubin and direct bilrubin.

‡ Serum lipid includes total cholesterol, triglyceride, low density lipoprotein cholesterol and high density lipoprotein cholesterol.

f. Outcome measures

Outcome measures in COVID-19 survivors:

- Prevalent and sequelae symptoms, including fatigue or muscle weakness (composite outcome), sleep difficulties, hair loss, smell disorder, palpitations, joint pain, decreased appetite, taste disorder, dizziness, nausea or vomiting (composite outcome), chest pain, sore throat or difficult to swallow (composite outcome), skin rash, myalgia, headache, and cough.
- mMRC dyspnoea score.
- Health-related quality of life, including pain or discomfort (composite outcome), anxiety or depression (composite outcome), mobility, personal care, usual activity, and score of EuroQol Visual Analogue Scale.
- Distance walked in 6 minutes expressed as metres and percentage of predicted values
- New onset ischemic stroke and cardiovascular event (composite outcome) after discharge. Cardiovascular event includes stable angina pectoris, unstable angina pectoris, and myocardial infarction.
- Outpatient visit, hospital readmission, and work status after discharge.
- Lung function parameters include forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), total lung capacity (TLC), functional residual capacity (FRC), residual volume (RV), and diffusion capacity for carbon monoxide (DLCO).
- Lung imaging includes abnormal CT, ground glass opacity, irregular lines, subpleural line, interlobular septal thickening, reticular pattern, and consolidation.
- Laboratory tests results include complete blood count, creatine, estimate glomerular filtration rate (eGFR), and cystatin C, alanine aminotransferase (ALT), aspartate aminotransferase(AST), albumin, total protein, total bilrubin and direct bilrubin, total cholesterol, triglyceride, low density lipoprotein cholesterol, high density lipoprotein cholesterol, and cytokines.

Outcome measures in non-COVID-19 participants:

- Prevalent symptoms, including fatigue or muscle weakness (composite outcome), sleep difficulties, hair loss, smell disorder, palpitations, joint pain, decreased

appetite, taste disorder, dizziness, nausea or vomiting (composite outcome), chest pain, sore throat or difficult to swallow (composite outcome), skin rash, myalgia, headache, and cough.

- mMRC dyspnoea score.
- Health-related quality of life, including pain or discomfort (composite outcome), anxiety or depression (composite outcome), mobility, personal care, usual activity, and score of EuroQol Visual Analogue Scale.
- Laboratory tests results include complete blood count, creatine, eGFR, and cystatin C, ALT, AST, albumin, total protein, total bilrubin and direct bilrubin, total cholesterol, triglyceride, low density lipoprotein cholesterol and high density lipoprotein cholesterol.

Outcomes definition

- **Sequelae symptom:**

  For COVID-19 patients at both 6- and 12-month follow-up visits, sequelae symptoms are defined as those which are newly occurring and persistent, or worse than the status before COVID-19.
- **Prevalent symptom:**

  Prevalent symptom is defined as the existing symptom at follow-up.
- **Abnormal lung CT:**

  Abnormal lung CT is defined as the presence of at least one abnormal radiographic pattern on lung HRCT at follow-up.

Outcome assessment tool

- Symptom questionnaire for COVID-19 patients at 6-month visit is shown in our previous paper. [1]
- The symptom questionnaire for COVID-19 patients at 12-month visit is shown in the Supplementary.
- The symptom questionnaire for non-COVID-19 participants is shown in the Supplementary.

- The mMRC dyspnoea scale to record the level of dyspnoea with physical activity.[2] Details of this scoring system are: 0, no breathlessness except on strenuous exercise; 1, shortness of breath when hurrying on the level or walking up a slight hill; 2, walks slower than people of the same age on the level because of breathlessness or has to stop to catch breath when walking at their own pace on the level; 3, stops for breath after walking approximately 100 m or after a few minutes on the level; and 4, too breathless to leave the house, or breathless when dressing or undressing.
- The EQ-5D-5L questionnaire[3] and the EQ-VAS[4] to evaluate the health-related quality of life. The EQ-5D-5L is a validated questionnaire to evaluate patient quality of life by assessment of the following five factors: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Categorisation within each factor is divided into five levels that range from no problems to extreme problems. The EQ-VAS is a patient's subjective assessment of generic health ranging from 0 to 100, with higher scores representing better subjective health experience.
- 6-min walking test was done according to the ATS practical guidelines.[5] Each follow-up patient walked on the flat ground as fast as possible without oxygen inhalation and completed the 6MWD test independently.
- An ischaemic stroke and cardiovascular event registration form to record the event of ischemic stroke and cardiovascular event. [6]
- A questionnaire was used to record the self-reported outpatient visit, hospital readmission, and work status after discharge from COVID-19.
- The pulmonary function test was done in the Lung Function Laboratory of Jin Yin-tan Hospital using the Master Screen PFT (Vyaire Medical GmbH, Hoechberg, Germany) according to American Thoracic Society guidelines.[7]
- Chest HRCT was in the supine position during end-inspiration (SIEMENS SOMATOM PERSPECTIVE 64 CT scanner). Images were reconstructed at 1 mm slice thickness, with 1 mm increment, 512 mm × 512 mm. The CT features were evaluated by one experienced radiologist and one pulmonologist.

- Cytokines levels were tested using the Bio-Plex Pro™ Human Cytokine Screening Panel 27-plex (Bio-rad, USA) in Bio-Plex 200 System (Bio-rad, USA) at Key Laboratory of Respiratory Disease Pathogenomics, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China.
- All laboratory tests except for cytokines were performed in clinical laboratory of Wuhan Jin Yin-tan Hospital, China.

1.Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet 2021; 397(10270): 220-32.

2. Mahler DA, Wells CK. Evaluation of clinical methods for rating dyspnea. Chest 1988; 93: 580–86.

3. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res 2011; 20: 1727–36.

4. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med 2001; 33: 337–43.

5. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002; 166: 111–17.

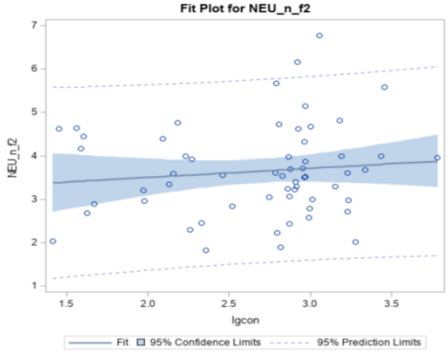
6. Xie W, Wu Y, Wang W, et al. A longitudinal study of carotid plaque and risk of ischemic cardiovascular disease in the Chinese population. J Am Soc Echocardiogr 2011; 24: 729–37.

7. American Thoracic Society. Standardization of spirometry, 1994 update. Am J Respir Crit Care Med 1995; 152: 1107–36.

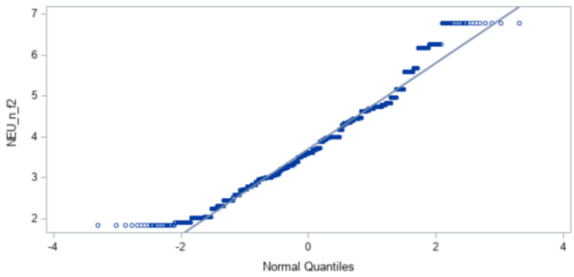
g. Testing for assumption of linear regression

Assumptions of linear regression were tested when exploring association of cytokine level with continuous outcome (neutrophil number, lymphocyte number, and monocyte number). The key assumption checked included linear relationship (age, cytokine level and outcome), normality, no or little multicollinearity, no auto-correlation, and homoscedasticity. No obvious violation of assumptions was observed. As an example, for association of IL-1ra with neutrophil number, we listed the results for checking assumption of this linear regression analysis.

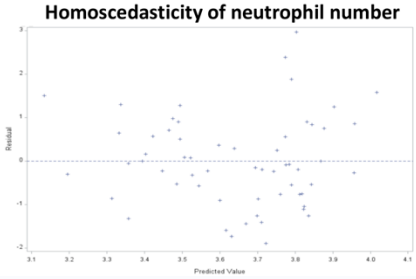
Linearity-Fit plot for neutrophil number



Normality of neutrophil number



Homoscedasticity of neutrophil number



Multicollinearity of neutrophil number

Parameter Estimates							
Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|	Variance Inflation
Intercept	Intercept	1	2.63778	0.93101	2.83	0.0065	0
age	age	1	0.00622	0.01210	0.51	0.6096	1.06268
gender	gender	1	0.03565	0.29186	0.12	0.9032	1.09393
corti		1	-0.36717	0.36136	-1.02	0.3141	1.11267
lgcon1		1	0.18895	0.18974	1.00	0.3238	1.07532

Auto-correlation of neutrophil number

Dependent Variable: NEU_n_f2

cytokine=d_IL_1ra

Durbin-Watson D	2.019
Number of Observations	59
1st Order Autocorrelation	-0.015

Heteroscedasticity Test					
Equation	Test	Statistic	DF	Pr > ChiSq	Variables
NEU_n_f2	White's Test	6.11	12	0.9104	Cross of all vars
	Breusch-Pagan	3.04	4	0.5518	1, age, gender, corti, lgcon1

Symptom questionnaire for COVID-19 survivors at 12-month visit

1. Have you experienced fatigue now?

□ No (go Q2) □ Yes (go Q1.1)

1.1 Is it newly onset post COVID-19?

□ No (go Q1.2) □ Yes (go Q2)

1.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

2. Have you experienced muscle weakness now?

□ No (go Q3) □ Yes (go Q2.1)

2.1 Is it newly onset post COVID-19?

□ No (go Q2.2) □ Yes (go Q3)

2.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

3. Have you experienced sleep difficulty now?

□ No (go Q4) □ Yes (go Q3.1)

3.1 Is it newly onset post COVID-19?

□ No (go Q3.2) □ Yes (go Q4)

3.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

4. Have you experienced hair loss now?

□ No (go Q5) □ Yes (go Q4.1)

4.1 Is it newly onset post COVID-19?

□ No (go Q4.2) □ Yes (go Q5)

4.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

5. Have you experienced smell disorder now?

□ No (go Q6) □ Yes (go Q5.1)

5.1 Is it newly onset post COVID-19?

□ No (go Q5.2) □ Yes (go Q6)

5.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

6. Have you experienced palpitations now?

□ No (go Q7) □ Yes (go Q6.1)

6.1 Is it newly onset post COVID-19?

□ No (go Q6.2) □ Yes (go Q7)

6.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

7. Have you experienced decreased appetite now?

□ No (go Q8) □ Yes (go Q7.1)

7.1 Is it newly onset post COVID-19?

□ No (go Q7.2) □ Yes (go Q8)

7.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

8. Have you experienced taste disorder now?

□ No (go Q9) □ Yes (go Q8.1)

8.1 Is it newly onset post COVID-19?

□ No (go Q8.2) □ Yes (go Q9)

8.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

9. Have you experienced dizziness now?

□ No (go Q10) □ Yes (go Q9.1)

9.1 Is it newly onset post COVID-19?

□ No (go Q9.2) □ Yes (go Q10)

9.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

10. Have you experienced nausea or vomiting now?

□ No (go Q11) □ Yes (go Q10.1)

10.1 Is it newly onset post COVID-19?

□ No (go Q10.2) □ Yes (go Q11)

10.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

11. Have you experienced chest pain now?

□ No (go Q12) □ Yes (go Q11.1)

11.1 Is it newly onset post COVID-19?

□ No (go Q11.2) □ Yes (go Q12)

11.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

12. Have you experienced sore throat or difficult to swallow now?

□ No (go Q13) □ Yes (go Q12.1)

12.1 Is it newly onset post COVID-19?

□ No (go Q12.2) □ Yes (go Q13)

12.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

13. Have you experienced skin rash now?

□ No (go Q14) □ Yes (go Q13.1)

13.1 Is it newly onset post COVID-19?

□ No (go Q13.2) □ Yes (go Q14)

13.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

14. Have you experienced myalgia now?

□ No (go Q15) □ Yes (go Q14.1)

14.1 Is it newly onset post COVID-19?

□ No (go Q14.2) □ Yes (go Q15)

14.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

15. Have you experienced headache now?

□ No (go Q16) □ Yes (go Q15.1)

15.1 Is it newly onset post COVID-19?

□ No (go Q15.2) □ Yes (go Q16)

15.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

16. Have you experienced cough now?

□ No (go Q17) □ Yes (go Q16.1)

16.1 Is it newly onset post COVID-19?

□ No (go Q16.2) □ Yes (go Q17)

16.2 Is it worse than the status prior to COVID-19?

□ No □ Yes

17. Have you experienced joint pain now?

□ No □ Yes (fill in the table below) If other joints, please specify_____

Joints	Hand	Foot	Wrist	Ankle	Jaw	Elbow	Shoulder	Neck	Hip	Knee
Tenderness										
Swollen										
Pain scale (0-10)										
Newly onset post COVID-19 (if no, please fill in the next line)	□ No □ Yes	□ No □ Yes	□ No □ Yes	□ No □ Yes	□ No □ Yes	□ No □ Yes	□ No □ Yes	□ No □ Yes	□ No □ Yes	□ No □ Yes
Worse than the status prior to COVID-19										

0 (no pain) ⟶ 10(Intolerable pain)

Symptom questionnaire for non-COVID-19 participants

1. Have you experienced fatigue now?

□ No □ Yes

2. Have you experienced muscle weakness now?

□ No □ Yes

3. Have you experienced sleep difficulty now?

□ No □ Yes

4. Have you experienced hair loss now?

□ No □ Yes

5. Have you experienced smell disorder now?

□ No □ Yes

6. Have you experienced palpitations now?

□ No □ Yes

7. Have you experienced decreased appetite now?

□ No □ Yes

8. Have you experienced taste disorder now?

□ No □ Yes

9. Have you experienced dizziness now?

□ No □ Yes

10. Have you experienced nausea or vomiting now?

□ No □ Yes

11. Have you experienced chest pain now?

□ No □ Yes

12. Have you experienced sore throat or difficult to swallow now?

□ No □ Yes

13. Have you experienced skin rash now?

□ No □ Yes

14. Have you experienced myalgia now?

□ No □ Yes

15. Have you experienced headache now?

□ No □ Yes

16. Have you experienced cough now?

□ No □ Yes

17. Have you experienced joint pain now?

□ No □ Yes (fill in the table below) If other joints, please specify_____

Joints	Hand	Foot	Wrist	Ankle	Jaw	Elbow	Shoulder	Neck	Hip	Knee
Tenderness										
Swollen										
Pain scale (0-10)										

0 (no pain) ⟶ 10(Intolerable pain)

Table S1. Baseline characteristics of study participants included and not included in final analysis

Characteristics	Study participants finally included in analysis (n=1276)	Study participants not included in analysis (n=937)*	*p* value
Age, years	58.0 (48.0-66.0)	57.0 (47.0-67.0)	0.32
Sex			0.018
Men	681 (53%)	452/936 (48%)	
Women	595 (47%)	484/936 (52%)	
Cigarette smoking			0.09
Never-smoker	1156/1274 (91%)	849/916 (93%)	
Current smoker	85/1274 (7%)	41/916 (4%)	
Former smoker	33/1274 (3%)	26/916 (3%)	
Comorbidity			
Hypertension	358/1275 (28%)	284/914 (31%)	0.13
Diabetes	152/1274 (12%)	125/914 (14%)	0.23
Coronary heart diseases	87/1274 (7%)	76/914 (8%)	0.19
Cerebrovascular diseases	36/1275 (3%)	26/914 (3%)	0.98
Malignancy	35 (3%)	29/914 (3%)	0.56
Chronic obstructive pulmonary disease	19/1275 (1%)	21/914 (2%)	0.16
Chronic kidney disease	16 (1%)	19/914 (2%)	0.13
Highest seven-category scale during hospital stay			0.0031
3: hospitalization, not requiring supplemental oxygen	318 (25%)	288 (31%)	
4: hospitalization, requiring supplemental oxygen	864 (68%)	599 (64%)	
5: hospitalization, requiring HFNC or non-IMV, or both	86 (7%)	42 (4%)	
6: hospitalization, requiring ECMO or IMV, or both	8 (1%)	9 (1%)	
Length of hospital stay, days	14.0 (10.0-20.0)	13.0 (9.0-18.0)	0.0004
ICU admission	54 (4%)	49/916 (5%)	0.22
Length of ICU stay, days	18.0 (7.0-30.0)	11.0 (7.0-15.0)	0.10

Data are n (%), n/N(%), or median (IQR). The differing denominators used indicate missing data. Because only the information extracted from electronic medical record was available for nearly all of the study participant not included in analysis, the results shown in this table are all calculated according to the information collected at acute phase to make comparison.

* Study participants who were not included in analysis included 906 who were lost to 12-month follow-up and 31 patients who only participated 12-month follow-up.

Table S2. Health-related quality of life of 1276 COVID-19 patients who completed both 6- and 12-month follow-up

	Total COVID-19 (N=1276)		Scale 3: Not requiring supplemental oxygen (N=318)		Scale 4：Requiring supplemental oxygen (N=864)		Scale 5-6：Requiring HFNC, NIV or IMV (N=94)	
	6-month	**12-month**	**6-month**	**12-month**	**6-month**	**12-month**	**6-month**	**12-month**
Mobility								
No problems with walking around	1115/1191 (94%)	1156/1271 (91%)	293/310 (95%)	293/317 (92%)	751/796 (94%)	777/860 (90%)	71/85 (84%)	86 (91%)
Slight problems with walking around	71/1191 (6%)	96/1271 (8%)	15/310 (5%)	22/317 (7%)	44/796 (6%)	68/860 (8%)	12/85 (14%)	6 (6%)
Moderate problems with walking around	4/1191 (0%)	14/1271 (1%)	1/310 (0%)	1/317 (0%)	1/796 (0%)	13/860 (2%)	2/85 (2%)	0 (0%)
Severe problems with walking around	1/1191 (0%)	4/1271 (0%)	1/310 (0%)	1/317 (0%)	0/796 (0%)	1/860 (0%)	0/85 (0%)	2 (2%)
Unable to walk around	0/1191 (0%)	1/1271 (0%)	0/310 (0%)	0/317 (0%)	0/796 (0%)	1/860 (0%)	0/85 (0%)	0 (0%)
Personal care								
No problems with washing or dishing	1182/1191 (99%)	1251/1271 (98%)	310/310 (100%)	314/317 (99%)	788/796 (99%)	847/860 (98%)	84/85 (99%)	90 (96%)
Slight problems with washing or dishing	8/1191 (1%)	7/1271 (1%)	0/310 (0%)	0/317 (0%)	7/796 (1%)	5/860 (1%)	1/85 (1%)	2 (2%)
Moderate problems with washing or dishing	1/1191 (0%)	6/1271 (0%)	0/310 (0%)	2/317 (1%)	1/796 (0%)	4/860 (0%)	0/85 (0%)	0 (0%)
Severe problems with washing or dishing	0/1191 (0%)	4/1271 (0%)	0/310 (0%)	1/317 (0%)	0/796 (0%)	2/860 (0%)	0/85 (0%)	1 (1%)
Unable to wash or dish	0/1191 (0%)	3/1271 (0%)	0/310 (0%)	0/317 (0%)	0/796 (0%)	2/860 (0%)	0/85 (0%)	1 (1%)
Usual activities(e.g. work, study, housework, family or leisure activities)								
No problems with usual activities	1164/1182 (98%)	1253/1271 (99%)	306/309 (99%)	315/317 (99%)	778/789 (99%)	847/860 (98%)	80/84 (95%)	91 (97%)
Slight problems with usual activities	14/1182 (1%)	9/1271 (1%)	3/309 (1%)	1/317 (0%)	8/789 (1%)	6/860 (1%)	3/84 (4%)	2 (2%)
Moderate problems with usual activities	3/1182 (0%)	5/1271 (0%)	0/309 (0%)	1/317 (0%)	3/789 (0%)	3/860 (0%)	0/84 (0%)	1 (1%)

Severe problems with usual activities	1/1182 (0%)	3/1271 (0%)	0/309 (0%)	0/317 (0%)	0/789 (0%)	3/860 (0%)	1/84 (1%)	0 (0%)
Unable to do usual activities	0/1182 (0%)	1/1271 (0%)	0/310 (0%)	0/317 (0%)	0/796 (0%)	1/860 (0%)	0/85 (0%)	0 (0%)
Pain/discomfort								
No pain/discomfort	865/1186 (73%)	900/1271 (71%)	223/307 (73%)	233/317 (74%)	593/794 (75%)	605/860 (70%)	49/85 (58%)	62 (66%)
Slight pain/discomfort	273/1186 (23%)	296/1271 (23%)	71/307 (23%)	71/317 (22%)	168/794 (21%)	200/860 (23%)	34/85 (40%)	25 (27%)
Moderate pain/discomfort	42/1186 (4%)	63/1271 (5%)	11/307 (4%)	11/317 (3%)	29/794 (4%)	47/860 (5%)	2/85 (2%)	5 (5%)
Severe pain/discomfort	6/1186 (1%)	10/1271 (1%)	2/307 (1%)	2/317 (1%)	4/794 (1%)	7/860 (1%)	0/85 (0%)	1 (1%)
Extreme pain/discomfort	0/1186 (0%)	2/1271 (0%)	0/310 (0%)	0/317 (0%)	0/796 (0%)	1/860 (0%)	0/85 (0%)	1 (1%)
Anxiety/depression								
No anxiety/depression	913/1187 (77%)	940/1271 (74%)	235/309 (76%)	239/317 (75%)	624/794 (79%)	634/860 (74%)	54/84 (64%)	67 (71%)
Slight anxiety/depression	238/1187 (20%)	280/1271 (22%)	67/309 (22%)	62/317 (20%)	145/794 (18%)	194/860 (23%)	26/84 (31%)	24 (26%)
Moderate anxiety/depression	30/1187 (3%)	47/1271 (4%)	5/309 (2%)	15/317 (5%)	21/794 (3%)	29/860 (3%)	4/84 (5%)	3 (3%)
Severe anxiety/depression	6/1187 (1%)	4/1271 (0%)	2/309 (1%)	1/317 (0%)	4/794 (1%)	3/860 (0%)	0/84 (0%)	0 (0%)
Extreme anxiety/depression	0/1187 (0%)	0/1271 (0%)	0/309 (0%)	0/317 (0%)	0/794 (0%)	0/860 (0%)	0/84 (0%)	0 (0%)

Data are n (%) or n/N(%).The differing denominators used indicate missing data. HFNC=high-flow nasal cannula for oxygen therapy. NIV=non-invasive ventilation. IMV=invasive mechanical ventilation.

Table S3. Characteristics of matched COVID-19 survivors and non-COVID-19 participants

Characteristics	Matched Non-COVID-19 participants (n=1164)	Matched COVID-19 patients at12-month follow-up visit (n=1164)	*P* value
Age, years	58.0 (49.0-66.0)	59.0 (49.0-67.0)	0.85
Sex			1.00
Men	623 (54%)	623 (54%)	
Women	541 (46%)	541 (46%)	
Education			0.0057
College or higher	259/1163 (22%)	316/1161 (27%)	
Middle school or lower	904/1163 (78%)	845/1161 (73%)	
Cigarette smoking			<0.0001
Never-smoker	773 (66%)	957 (82%)	
Current smoker	327 (28%)	83 (7%)	
Former smoker	64 (5%)	124 (11%)	
Comorbidity			
Hypertension	400 (34%)	400 (34%)	1.00
Diabetes	157 (13%)	157 (13%)	1.00
Cardiovascular diseases	82 (7%)	81 (7%)	0.94
Cerebrovascular diseases	45 (4%)	38 (3%)	0.43
Malignancy	25 (2%)	32 (3%)	0.35
Chronic obstructive pulmonary disease	6 (1%)	10 (1%)	0.32
Chronic kidney disease	18 (2%)	18 (2%)	1.00

Data are n (%), n/N(%), or median (IQR). The differing denominators used indicate missing data.

Table S4. Comparison of prevalent symptom and health-related quality of life at 12-month follow-up between matched COVID-19 survivors and non-COVID-19 participants

	Matched Non-COVID-19 participants (n=1164)	Matched COVID-19 patients at 12-month follow-up visit (n=1164)	*P* value
Prevalent symptom			
Any one of the following symptoms	383 (33%)	764 (66%)	<0.0001
Fatigue or muscle weakness	75 (6%)	254 (22%)	<0.0001
Sleep difficulties	156 (13%)	291 (25%)	<0.0001
Hair loss	107 (9%)	266 (23%)	<0.0001
Smell disorder	1 (0%)	70 (6%)	<0.0001
Palpitations	53 (5%)	147 (13%)	<0.0001
Joint pain	86 (7%)	296 (25%)	<0.0001
Decreased appetite	11 (1%)	34 (3%)	0.0005
Taste disorder	5 (0%)	38 (3%)	<0.0001
Dizziness	69 (6%)	113 (10%)	0.0007
Nausea or vomiting	5 (0%)	16 (1%)	0.016
Chest pain	22 (2%)	110 (9%)	<0.0001
Sore throat or difficult to swallow	7 (1%)	61 (5%)	<0.0001
Skin rash	10 (1%)	88 (8%)	<0.0001
Myalgia	4 (0%)	62 (5%)	<0.0001
Headache	30 (3%)	93 (8%)	<0.0001
Cough	36 (3%)	117 (10%)	<0.0001
mMRC score			<0.0001
0	941 (81%)	834/1163 (72%)	
≥1	223 (19%)	329/1163 (28%)	
EQ-5D-5L questionnaire *			
Mobility: Problems with walking around	41 (4%)	103 (9%)	<0.0001
Personal care: Problems with washing or dishing	6 (1%)	16 (1%)	0.032
Usual activity: Problems with usual activity	11 (1%)	12 (1%)	0.83
Pain or discomfort	53 (5%)	337 (29%)	<0.0001
Anxiety or depression	59 (5%)	300 (26%)	<0.0001
Quality of life †	85.0 (80.0-90.0)	80.0 (75.0-90.0)	<0.0001

Data are n/N(%) or median (IQR). mMRC=modified British Medical Research Council. EQ-5D-5L=EuroQol five-dimension five-level questionnaire. *Detailed results of EQ-5D-5L questionnaire are shown in Table S6. † Quality of life was assessed using the EuroQol Visual Analogue Scale, ranging from 0 (worst imaginable health) to 100 (best imaginable health).

Table S5. Comparison of laboratory findings at 12-month follow-up between matched COVID-19 survivors and non-COVID-19 participants

Laboratory tests	Matched Non-COVID-19 participants (n=1164)	Matched COVID-19 patients at 12-month follow-up visit (n=1164)	*P* value
Leukocyte count, × 10^9 per L	6.4 (5.4-7.6)	6.1 (5.1-7.3)	<0.0001
<4	33/1091 (3%)	62/1160 (5%)	0.023
Lymphocyte count, × 10^9 per L	2.1 (1.7-2.5)	2.0 (1.6-2.4)	0.0012
<0.8	3/1091 (0%)	9/1160 (1%)	0.10
Haemoglobin, g/dL	141.0 (131.0-152.0)	143.0 (134.0-155.0)	<0.0001
Anemia	28/1091 (3%)	12/1160 (1%)	0.0060
Platelet count, × 10^9 per L	231.0 (194.0-271.0)	219.0 (185.5-254.0)	<0.0001
<100	9/1091 (1%)	14/1160 (1%)	0.37
Albumin, g/L	44.9 (43.2-46.6)	45.9 (44.2-47.6)	<0.0001
Alanine aminotransferase, U/L	21.0 (16.0-29.0)	20.0 (14.0-29.0)	0.033
>40	109/1091 (10%)	136/1159 (12%)	0.18
Aspartate aminotransferase, U/L	27.0 (23.0-31.0)	26.0 (22.0-31.0)	0.06
>40	78/1091 (7%)	93/1159 (8%)	0.43
Creatinine, μmol/L	67.4 (55.4-80.3)	71.9 (59.2-84.1)	<0.0001
Creatinine > 133μmol/L	11/1092 (1%)	13/1159 (1%)	0.79
eGFR, ml/min	100.9 (89.0-110.8)	97.4 (85.0-107.6)	<0.0001
≥90	807/1092 (74%)	770/1159 (66%)	0.0003
60-89	250/1092 (23%)	351/1159 (30%)	
< 60	35/1092 (3%)	38/1159 (3%)	
HbA1C, %	5.4 (5.1-5.9)	5.4 (5.1-5.8)	0.012
≥6.5%	147/1088 (14%)	106/1106 (10%)	0.0040

Data are n (%), n/N(%), or median (IQR). The differing denominators used indicate missing data. Estimate glomerular filtration rate=eGFR. HbA1C= glycated hemoglobin A1C.

Table S6. Detailed results of EQ-5D-5L questionnaire of matched COVID-19 patients and non-COVID-19 participants

	Matched Non-COVID-19 participants (n=1164)	Matched COVID-19 patients at 12-month follow-up visit (n=1164)
Mobility		
No problems with walking around	1123 (96%)	1061 (91%)
Slight problems with walking around	29 (2%)	90 (8%)
Moderate problems with walking around	12 (1%)	10 (1%)
Severe problems with walking around	0	2 (0%)
Unable to walk around	0	1 (0%)
Personal care		
No problems with washing or dishing	1158 (99%)	1148 (99%)
Slight problems with washing or dishing	3 (0%)	5 (0%)
Moderate problems with washing or dishing	1 (0%)	6 (1%)
Severe problems with washing or dishing	2 (0%)	3 (0%)
Unable to wash or dish	0	2 (0%)
Usual activities (e.g. work, study, housework, family or leisure activities)		
No problems with usual activities	1153 (99%)	1152 (99%)
Slight problems with usual activities	8 (1%)	5 (0%)
Moderate problems with usual activities	0	3 (0%)
Severe problems with usual activities	3 (0%)	3 (0%)
Unable to do usual activities	0	1 (0%)
Pain/discomfort		
No pain/discomfort	1111 (95%)	827 (71%)
Slight pain/discomfort	45 (4%)	270 (23%)
Moderate pain/discomfort	7 (1%)	57 (5%)
Severe pain/discomfort	1 (0%)	9 (1%)
Extreme pain/discomfort	0	1 (0%)
Anxiety/depression		
No anxiety/depression	1105 (95%)	864 (74%)
Slight anxiety/depression	55 (5%)	253 (22%)
Moderate anxiety/depression	2 (0%)	43 (4%)
Severe anxiety/depression	2 (0%)	4 (0%)
Extreme anxiety/depression	0	0

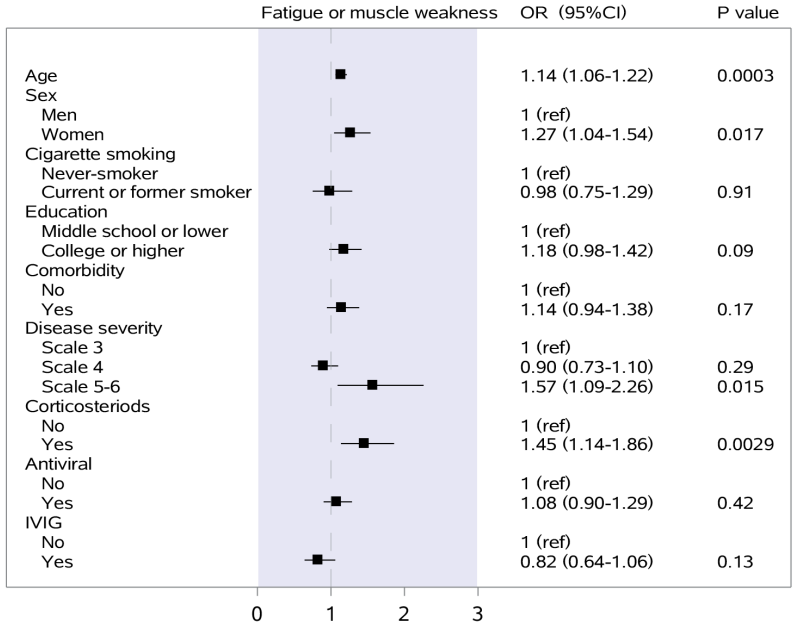
Data are n/N(%). EQ-5D-5L=EuroQol five-dimension five-level questionnaire.

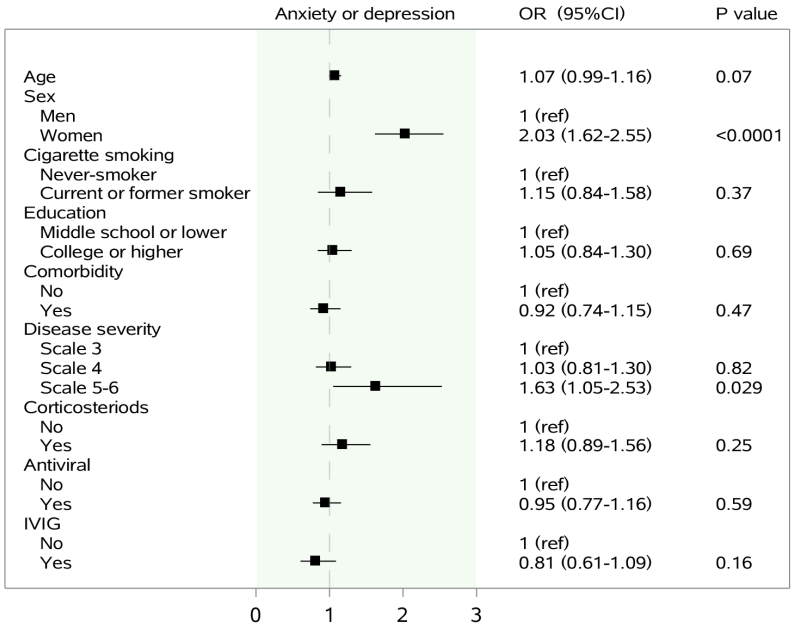
Table S7. Association of lung diffusion impairment and lung radiographic abnormality among COVID-19 survivors at 12 months

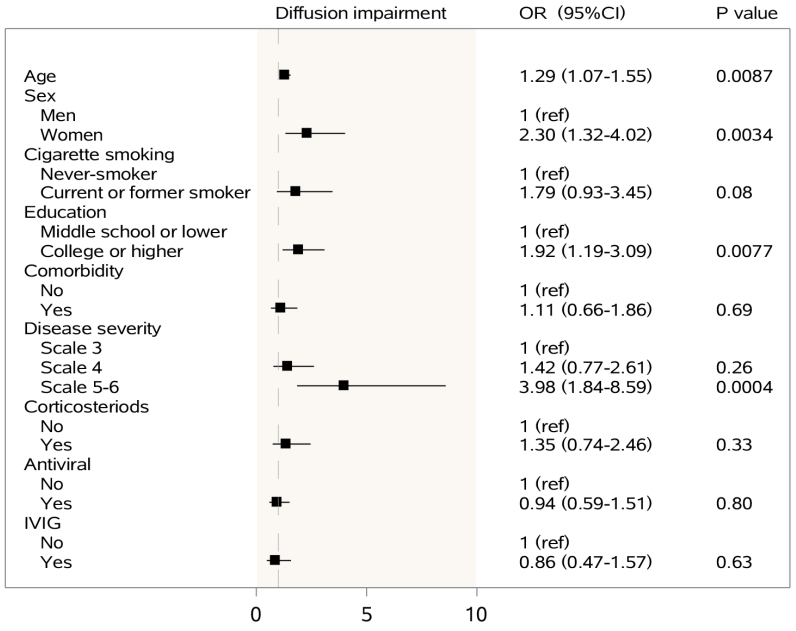
	OR (95% CI)	p value
Model 1		
Abnormal CT	2.59 (0.93-7.19)	0.07
GGO	3.10 (1.10-8.76)	0.033
Irregular lines	2.78 (1.03-7.51)	0.044
Model 2		
Abnormal CT	2.26 (0.73-7.03)	0.16
GGO	2.59 (0.85-7.84)	0.09
Irregular lines	2.87(0.92-8.92)	0.07

GGO=ground glass opacity, CT=computed tomography.
Model 1: Adjusted for age, gender, cigarette smoking, education, comorbidity, disease severity
Model 2: As for model 1 plus corticosteroids, antivirals, and intravenous immunoglobulin

Figure S1. Sensitivity analysis for risk factors associated with fatigue or muscle weakness, anxiety or depression, and diffusion impairment



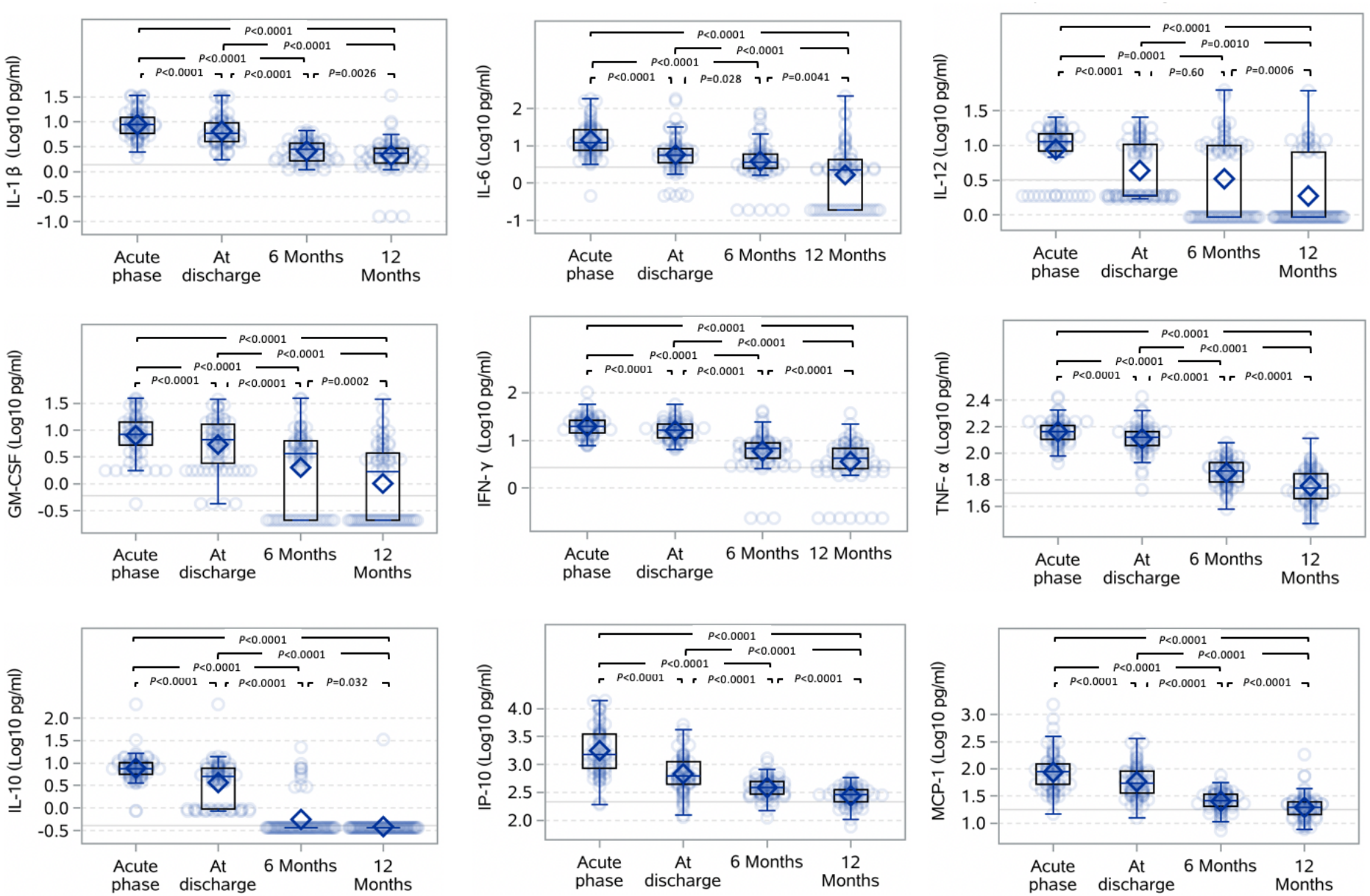


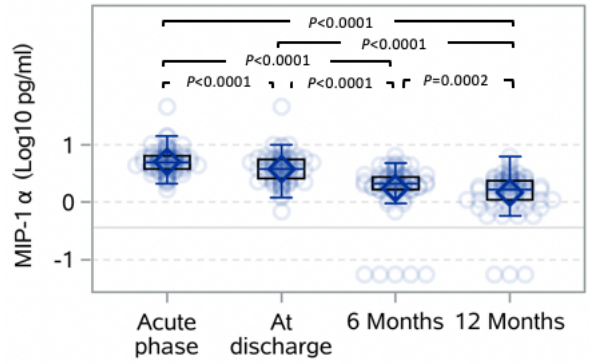


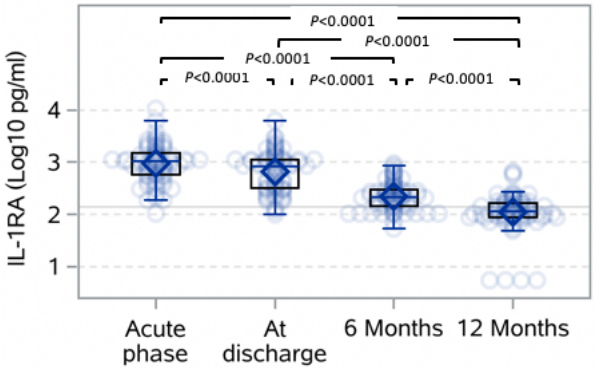
To reduce the effect of bias due to differences between patients who were included in these analyses and those who were not because of lost to follow-up, inverse probability-weighted generalized estimating equations were used as sensitivity analyses for exploring risk factors associated with fatigue or muscle weakness, anxiety or depression, and diffusion impairment.

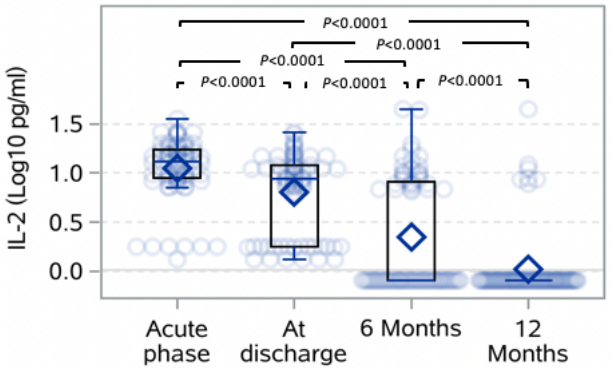
For association of disease severity with outcome, age, sex, cigarette smoking, education, comorbidity, corticosteroids, antivirals, and intravenous immunoglobulin were adjusted. For association of factors including sex, corticosteroid, antiviral, and intravenous immunoglobulin with outcome, the aforementioned variables were all included in the model. When exploring associations of education and smoking with outcome, the aforementioned variables except for comorbidity, and both comorbidity and disease severity (due to the potential mediation) were included, respectively. Only sex, smoking, and education were adjusted for association between age and outcome due to the potential mediation of other factors. For association of comorbidity with outcome, the aforementioned variables except for disease severity were all included. OR (95% CI) for age indicates the risk of fatigue or muscle weakness, anxiety or depression, and diffusion impairment per 10-year age increase. OR=odds ratio.

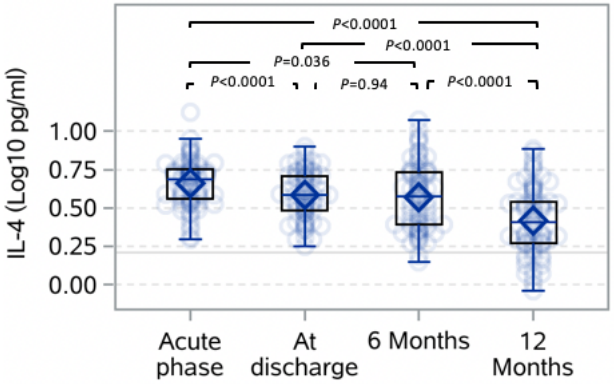
Figure S2. Dynamics of plasma cytokines at varying time periods

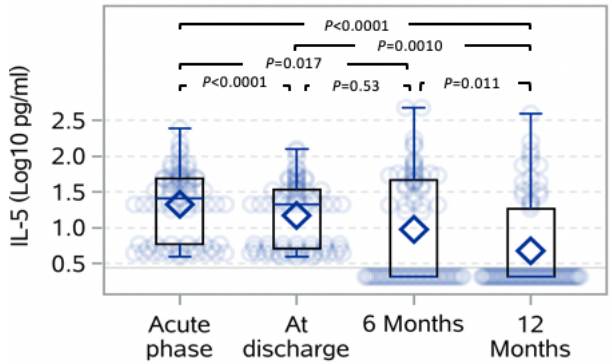


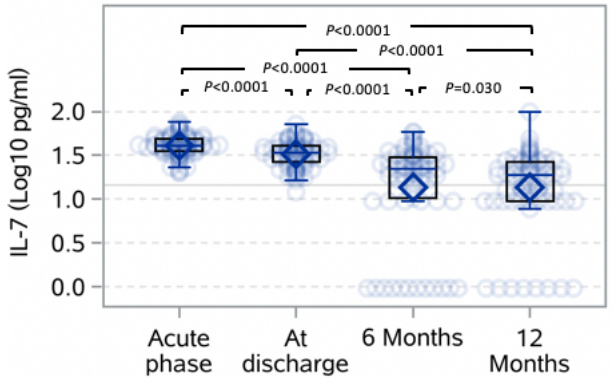

MIP-1 α (Log10 pg/ml)
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P=0.0002
1
0
-1
Acute phase
At discharge
6 Months
12 Months

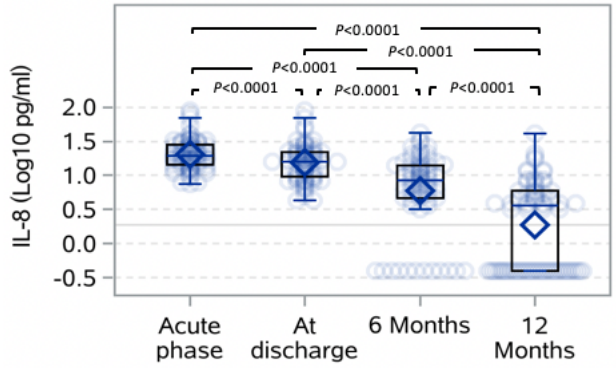

IL-1RA (Log10 pg/ml)
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
4
3
2
1
Acute phase
At discharge
6 Months
12 Months

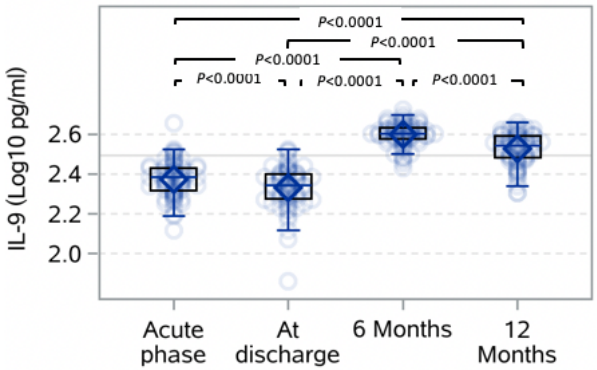

IL-2 (Log10 pg/ml)
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
1.5
1.0
0.5
0.0
Acute phase
At discharge
6 Months
12 Months

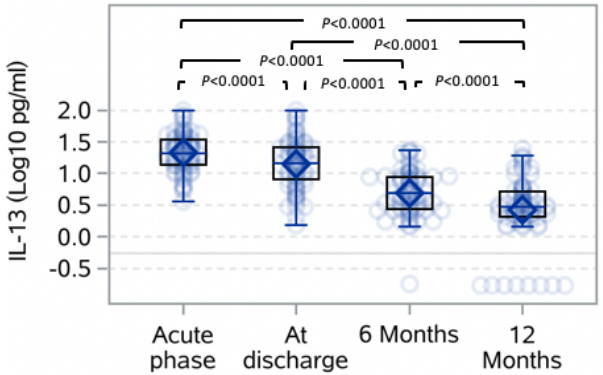

IL-4 (Log10 pg/ml)
P<0.0001
P<0.0001
P=0.036
P<0.0001
P=0.94
P<0.0001
1.00
0.75
0.50
0.25
0.00
Acute phase
At discharge
6 Months
12 Months

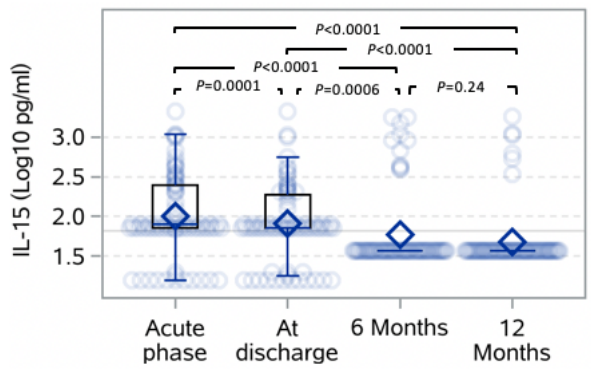

IL-5 (Log10 pg/ml)
P<0.0001
P<0.0001
P=0.0010
P=0.017
P<0.0001
P=0.53
P=0.011
2.5
2.0
1.5
1.0
0.5
Acute phase
At discharge
6 Months
12 Months

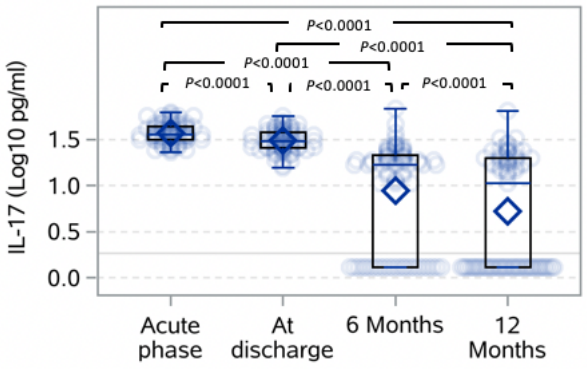

IL-7 (Log10 pg/ml)
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P=0.030
2.0
1.5
1.0
0.5
0.0
Acute phase
At discharge
6 Months
12 Months

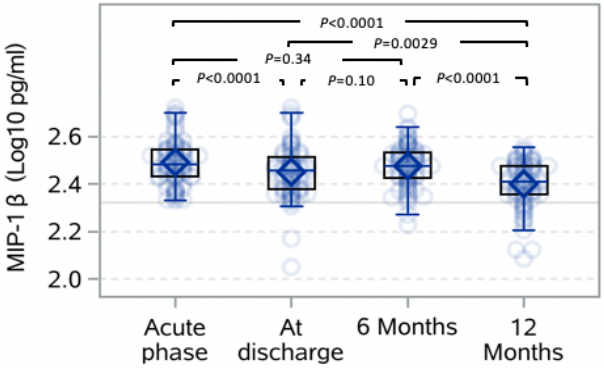

IL-8 (Log10 pg/ml)
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
2.0
1.5
1.0
0.5
0.0
-0.5
Acute phase
At discharge
6 Months
12 Months

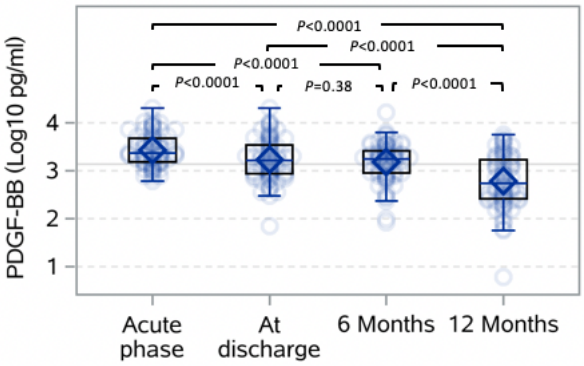

IL-9 (Log10 pg/ml)
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
2.6
2.4
2.2
2.0
Acute phase
At discharge
6 Months
12 Months

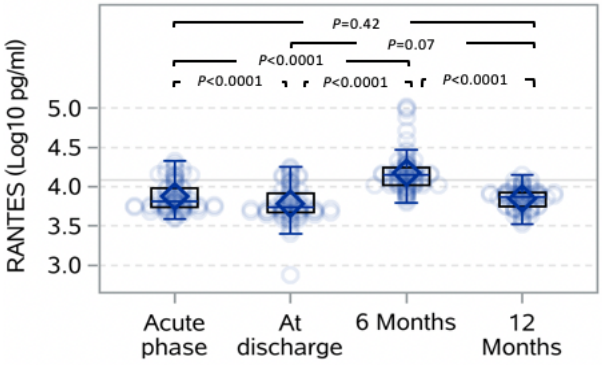

IL-13 (Log10 pg/ml)
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
2.0
1.5
1.0
0.5
0.0
-0.5
Acute phase
At discharge
6 Months
12 Months

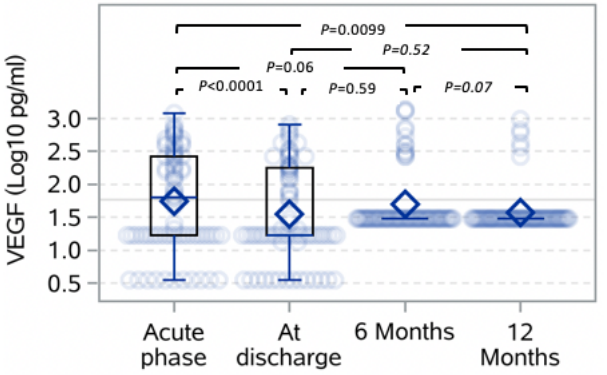

IL-15 (Log10 pg/ml)
P<0.0001
P<0.0001
P<0.0001
P=0.0001
P=0.0006
P=0.24
3.0
2.5
2.0
1.5
Acute phase
At discharge
6 Months
12 Months

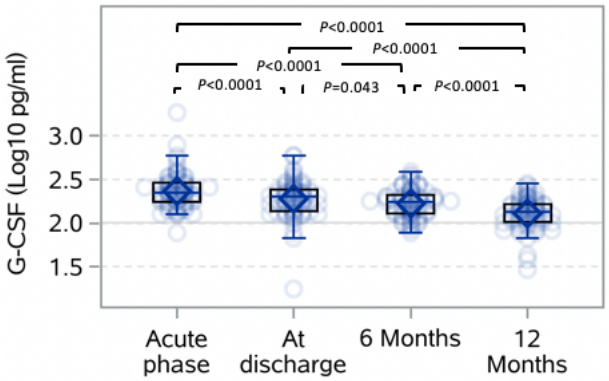

IL-17 (Log10 pg/ml)
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
1.5
1.0
0.5
0.0
Acute phase
At discharge
6 Months
12 Months

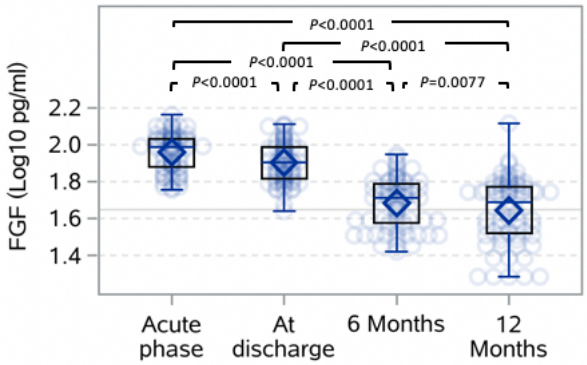

MIP-1 β (Log10 pg/ml)
P<0.0001
P=0.0029
P=0.34
P<0.0001
P=0.10
P<0.0001
2.6
2.4
2.2
2.0
Acute phase
At discharge
6 Months
12 Months

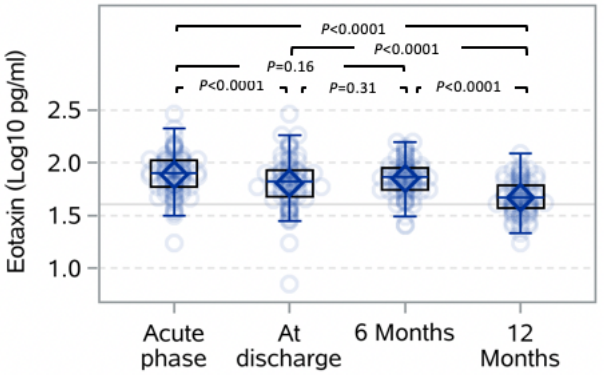

PDGF-BB (Log10 pg/ml)
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P=0.38
P<0.0001
4
3
2
1
Acute phase
At discharge
6 Months
12 Months


RANTES (Log10 pg/ml)
P=0.42
P=0.07
P<0.0001
P<0.0001
P<0.0001
P<0.0001
5.0
4.5
4.0
3.5
3.0
Acute phase
At discharge
6 Months
12 Months


VEGF (Log10 pg/ml)
P=0.0099
P=0.52
P=0.06
P<0.0001
P=0.59
P=0.07
3.0
2.5
2.0
1.5
1.0
0.5
Acute phase
At discharge
6 Months
12 Months

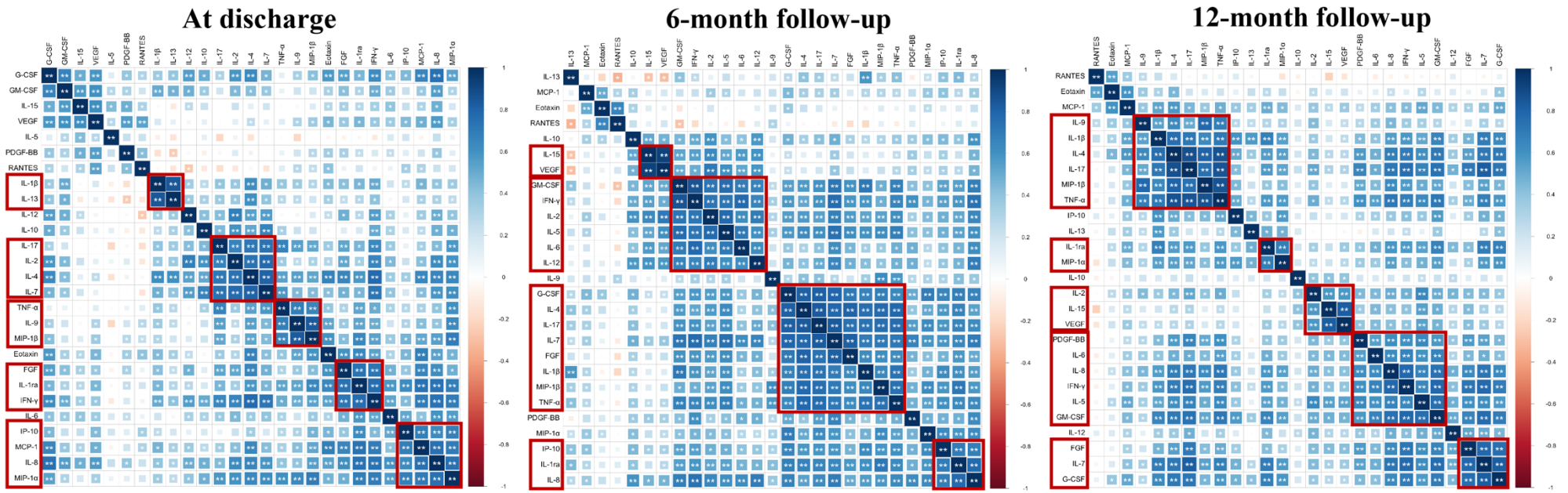

G-CSF (Log10 pg/ml)
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P=0.043
P<0.0001
3.0
2.5
2.0
1.5
Acute phase
At discharge
6 Months
12 Months


FGF (Log10 pg/ml)
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P<0.0001
P=0.0077
2.2
2.0
1.8
1.6
1.4
Acute phase
At discharge
6 Months
12 Months


Eotaxin (Log10 pg/ml)
P<0.0001
P<0.0001
P=0.16
P<0.0001
P=0.31
P<0.0001
2.5
2.0
1.5
1.0
Acute phase
At discharge
6 Months
12 Months

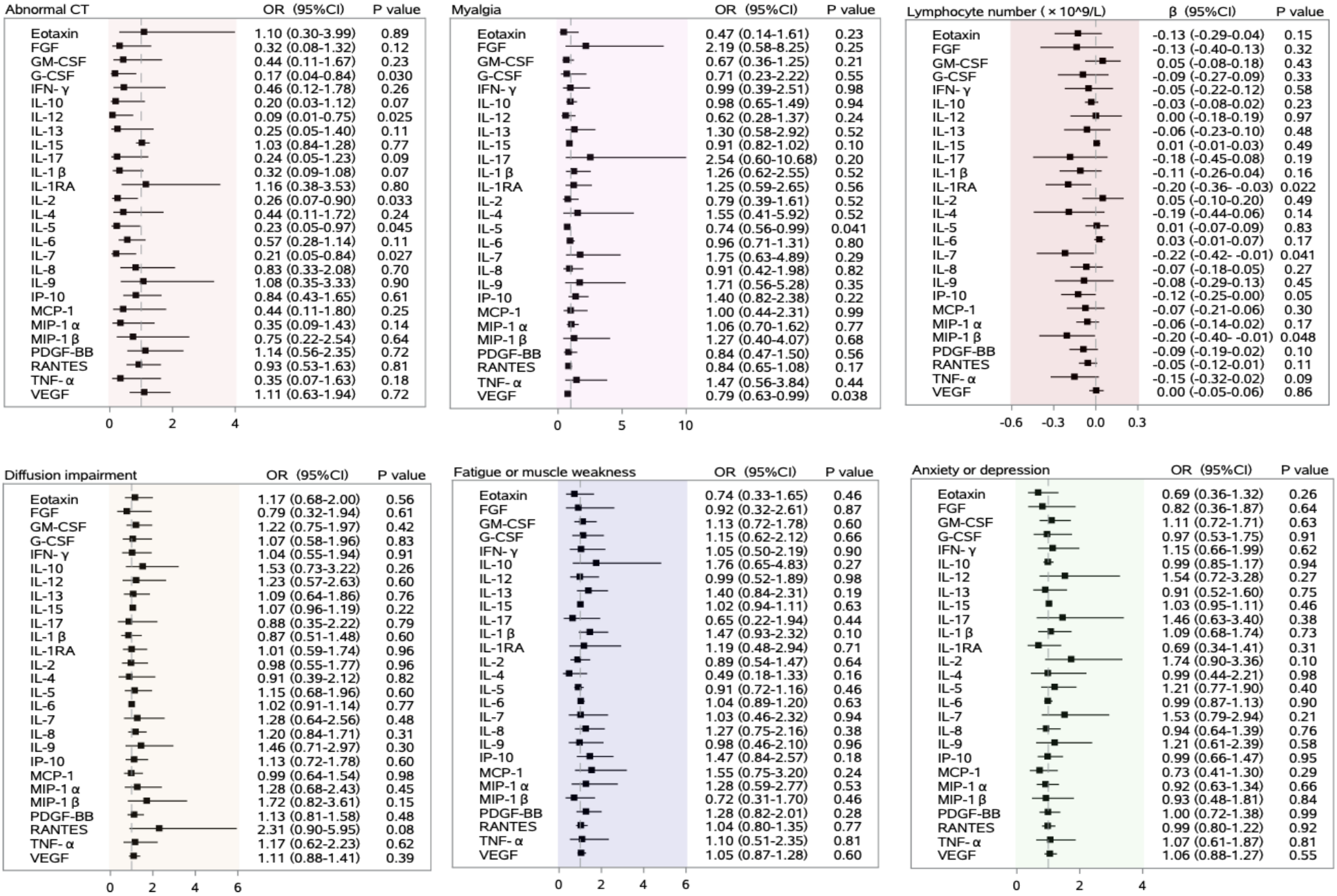
Plasma samples of 73 COVID-19 patients were collected at acute phase, discharge, 6- and 12-month follow-up visit. Solid line indicates the mean value of log_{10}-transformed cytokine in healthy controls. The bottom and top edges of box indicate the 25th and 75th percentiles. The line inside the box indicates the median value. The diamond inside the box indicates the mean value. The whiskers that extend from each box indicate the maximum observation below the value that is 1.5 IQR above 75th percentile.

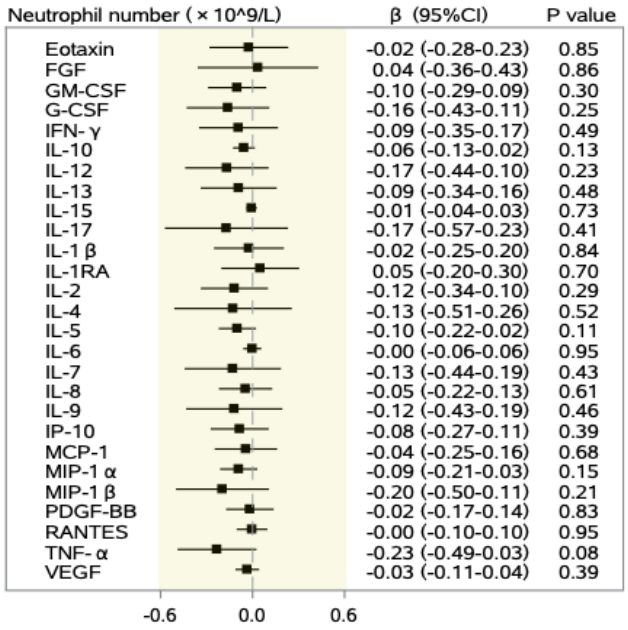
Figure S3. Correlation of plasma cytokines at discharge, 6 and 12 months.

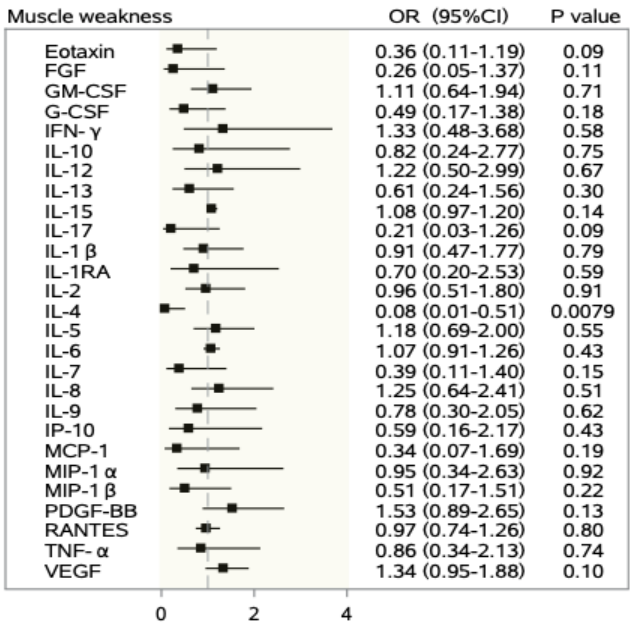


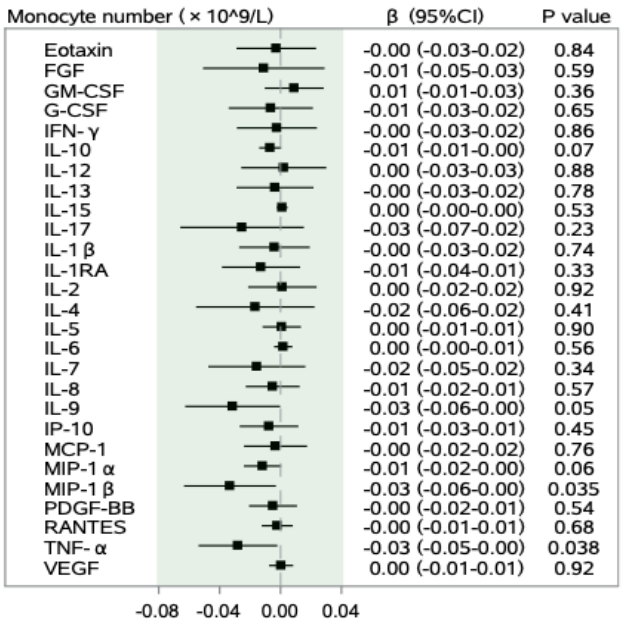
Partial correlation plots adjusted for age, disease severity, and sampling days after symptom onset showing the degree of correlation between every cytokine pair in COVID-19 patients at hospital discharge, 6- and 12-month follow-up. The color and size of square corresponds to the correlation coefficient. The asterisk in colored square indicates the statistical significance of correlation (* $p<0.05$, ** $p<1.4\times10^{-4}$)

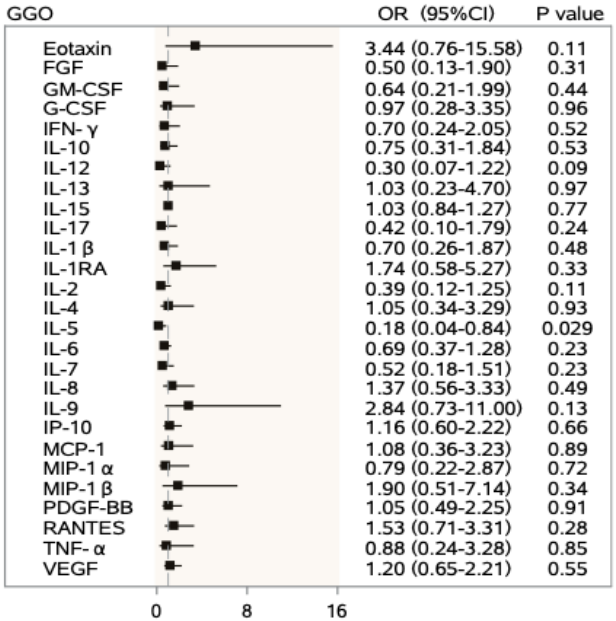
Figure S4. Association of cytokine change (at discharge till 6-month) with 12-month consequence











The change of cytokine was calculated as the value at hospital discharge minus the value at 6-month follow-up. Age, sex, and corticosteroids were adjusted.