

# **GIORNATA REGIONALE DELLA SICUREZZA E QUALITÀ DELLE CURE – EDIZIONE 2023**

## **Il Long-COVID nelle diverse ondate epidemiche**

Prof Carlo Tascini

Direttore Clinica Malattie Infettive

Università di Udine – ASUFC

[c.tascini@gmail.com](mailto:c.tascini@gmail.com)

## Conflict of interest Disclosure

**prof. Carlo Tascini has received in the last two years grants as a speaker at symposia from:**

- AstraZeneca
- AVIR Pharma
- Merck
- Pfizer
- Astellas
- Angelini
- Gilead
- Novartis
- Biotest
- Thermofischer
- Correvio/Advanz Pharma
- Basilea
- Glaxo
- Biomerieux
- Hikma
- Zambon

# Profiling post-COVID-19 condition across different variants of SARS-CoV-2: a prospective longitudinal study in unvaccinated wild-type, unvaccinated alpha-variant, and vaccinated delta-variant populations



Liane S Canas, Frika Molteni, Jie Deng, Carole H Sudre, Benjamin Murray, Eric Kerfoot, Michela Antonelli, Khaled Rjoob, Joan Capdevila Pujol, Lorenzo Polidori, Anna May, Marc F Österdahl, Ronan Whiston, Nathan J Cheetham, Vicky Bowyer, Tim D Spector, Alexander Hammers, Emma L Duncan, Sébastien Ourselin, Claire J Steves, Marc Modat



## Summary

**Background** Self-reported symptom studies rapidly increased understanding of SARS-CoV-2 during the COVID-19 pandemic and enabled monitoring of long-term effects of COVID-19 outside hospital settings. Post-COVID-19 condition presents as heterogeneous profiles, which need characterisation to enable personalised patient care. We aimed to describe post-COVID-19 condition profiles by viral variant and vaccination status.

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# Studio Cormor

- Studio prospettico dei pazienti positivi della prima ondata (marzo-Maggio 2020) diagnosticati ad Udine
- Tutti i pazienti da asintomatici ad intubati

We performed a bidirectional cohort study design in a tertiary care teaching hospital (Udine, Italy, 1000 beds) designated as a regional centre for COVID-19 patients and serving approximately 350 000 citizens. The reference Ethics Committee (CEUR-2020-OS-219 and CEUR-2020-OS-205) approved the study and all procedures were in accordance with the ethical standards of the Health Care Trust.

A cohort of all consecutive adult in- and out-patients ( $\geq 18$  years) attending the Infectious Disease Department with a diagnosis of COVID-19 from 1 March to 30 May 2020 were eligible. Patients who were willing to participate were included and a database concerning their demographic, clinical and laboratory data was populated. Six

# Studio Cormor

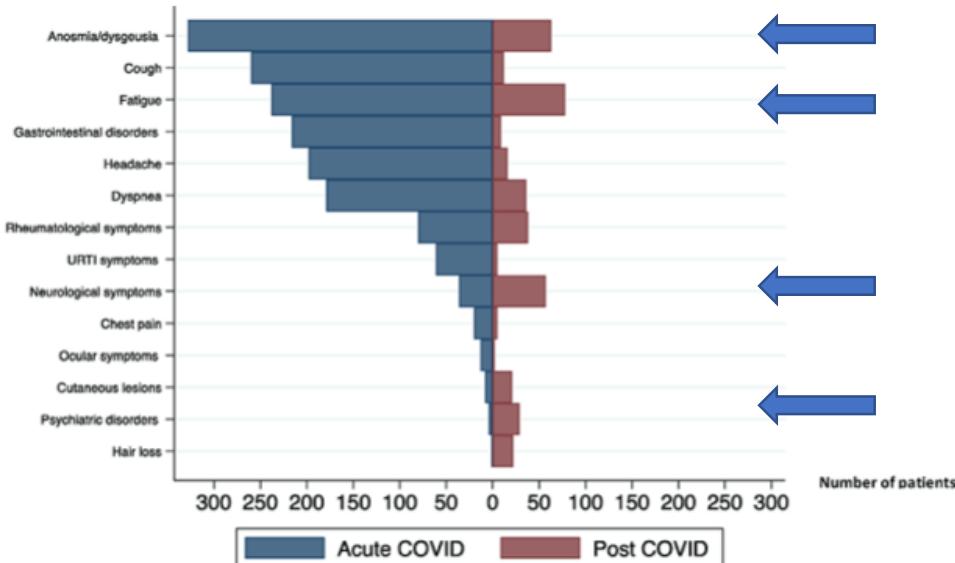
- Circa 1000 pazienti con Covid-19 nella prima ondata ad Udine
- 599 pazienti sono stati arruolati, 241 con sintomi long covid e 358 no
- Sierologia che identificava solo anticorpi anti-spike prodotti durante l'infezione



## Original article

## Post-COVID-19 symptoms 6 months after acute infection among hospitalized and non-hospitalized patients

Maddalena Peghin <sup>1,\*</sup>, Alvisa Palese <sup>2</sup>, Margherita Venturini <sup>2</sup>, Maria De Martino <sup>3</sup>,  
 Valentina Gerussi <sup>1</sup>, Elena Graziano <sup>1</sup>, Giulia Bontempo <sup>1</sup>, Francesco Marrella <sup>1</sup>,  
 Alberto Tommasini <sup>4,5</sup>, Martina Fabris <sup>6,7</sup>, Francesco Curcio <sup>6,7</sup>, Miriam Isola <sup>3</sup>,  
 Carlo Tascini <sup>1</sup>

**Table 4**Multivariable analysis of risk factors associated with post-COVID-19 syndrome ( $n = 599$ )

Risk factors	OR	95% CI	p
<b>Gender</b>			
Female	0.025	1.05–2.27	
<b>Age group</b>			
41–60 vs. 18–40	1.00	0.61–1.62	0.99
>60 vs. 18–40	1.03	0.62–1.74	0.90
>60 vs. 41–60	1.04	0.67–1.60	0.87
<b>Symptoms of acute COVID-19 at the onset, number</b>	1.81	1.59–2.05	<0.001
<b>Management</b>			
Ward vs. outpatients	1.87	1.19–2.94	0.007
ICU vs. outpatients	3.10	1.18–8.11	0.021
ICU vs. ward	1.65	0.61–4.46	0.32

CI, confidence of interval; Ct, cycle threshold; ICU, intensive care unit; OR, odds ratio.



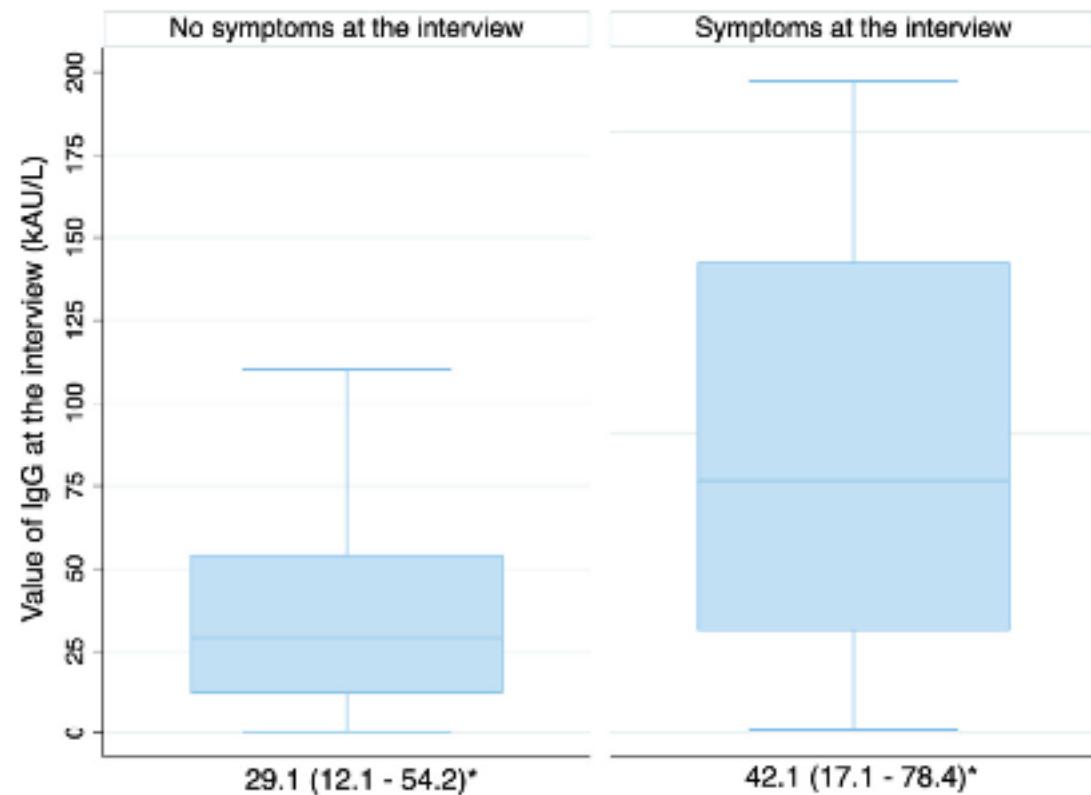
Original article

## Post-COVID-19 symptoms 6 months after acute infection among hospitalized and non-hospitalized patients

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 Carlo Tascini <sup>1</sup>

obtained using iFlash-SARS-CoV-2 (Yhlo), a paramagnetic particle based chemiluminescence immunoassay (CLIA). According to the manufacturer's information, the IgM and IgG cut-off is 10.0 kAU/L. Ct, IgG and IgM were considered in order to identify associations, if any, between the anti-SARS-CoV-2 and post-COVID syndrome. Further test procedures are summarized in [Table S2](#).

# Studio Cormor: Post-COVID dopo 6 mesi



**Fig. 3.** Serological response against SARS-CoV-2 in patients with or without post-COVID-19 syndrome at 6 months. \*median (IQR).

# Long Covid

- Qualsiasi cosa sia, è correlata **alla gravità dell'infezione**
- Qui non c'erano ancora le varianti differenti
- Non c'era il vaccino
- Anche gli asintomatici potevano avere long Covid



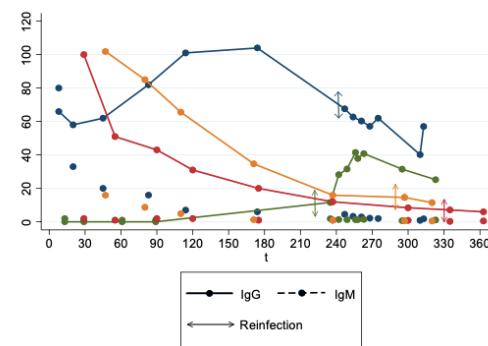
## Low risk of reinfections and relation with serological response after recovery from the first wave of COVID-19

Maddalena Peghin<sup>1</sup> · Emilio Bouza<sup>2,3,4,5</sup> · Martina Fabris<sup>6,7</sup> · Maria De Martino<sup>8</sup> · Alvisa Palese<sup>9</sup> · Giulia Bontempo<sup>1</sup> · Elena Graziano<sup>1</sup> · Valentina Gerussi<sup>1</sup> · Valentina Bressan<sup>9</sup> · Assunta Sartor<sup>6</sup> · Miriam Isola<sup>8</sup> · Carlo Tascini<sup>1</sup> · Francesco Curcio<sup>6</sup>

(2/137, 1.5%), or seropositive (2/353, 0.6%) ( $p=0.085$ ). All reinfections were mild ( $n=5$ ) or asymptomatic ( $n=1$ ). After reinfection, none of patients developed IgM response and only two had a transitory boosted IgG immunization response. In an unselected population after the first wave of COVID-19, after a prolonged observation period (mean 10 months), reinfection was very uncommon; occurred in patients with a previous history of mild infection, mostly with weak or absent serological response; and manifested with mild or asymptomatic clinical presentation.

**Table 2** Demographic, clinical, and laboratory characteristics of patients with possible SARS-CoV-2 reinfections

	Gender, age, occupation setting	Comorbidities	First positive and first negative NAAT Ct values	First episode Disease severity	IgM/IgG seroconversion after first episode	Serological response at time of reinfection *	Reinfection Positive NAAT No. of days to reinfection Ct values	Reinfection Disease severity
Patient 1 Blue line	F, 33 y HCW in a disability center	No	31/03/2020 08/04/2020 35	Mild (cough, fever, anosmia/ageusia)	Yes	21/09/2020 Seropositive IgG 104 IgM 6	27/11/2020 241 days	Mild (fatigue)
Patient 2 Green line	F, 28 y HCW in a nursing home	No	16/04/2020 24/04/2020 34	Mild (fatigue, cough, fever, myalgia)	No	14/07/2020 Seronegative IgG 0 IgM 1	24/11/2020 222 days	Mild (fatigue, cough, fever, myalgia)
Patient 3 Yellow line	M, 55y HCW in a nursing home	No	28/03/2020 13/04/2020 NA	Mild (cough, fever)	Yes	20/11/2020 Seropositive IgG 15.9 IgM 1	11/01/2021 289 days	Asymptomatic
Patient 4 Red line	F 49 y HCW in a nursing home	No	10/03/2020 08/04/2020 NA	Mild (cough, nausea/vomit fatigue, myalgia, anosmia/ageusia)	Yes	04/01/2021 Seroreverted Seronegative IgG 8.4 IgM 0.9	03/02/2021 323 days	Mild (headache)
Patient 5	F 44y HCW in non COVID-19 hospital ward	Migraine	14/04/2020 24/04/2020 36	Mild (nose cold, odynophagia, chest pain)	No	Seronegative IgG 0 IgM 1	15/12/2020 251 days NA	Mild (nose cold, sneezing, odynophagia)
Patient 6	F 45y HCW in a nursing home	No	17/03/2020 07/04/2020 30	Mild (cough, diarrhea, fatigue, myalgia, anosmia/ageusia)	Yes	14/01/2021 Seroreverted Seronegative IgG 6.8 IgM 3.9	21/01/2021 310 days 34	Mild (odynophagia)





## The Fall in Antibody Response to SARS-CoV-2: a Longitudinal Study of Asymptomatic to Critically Ill Patients Up to 10 Months after Recovery

Maddalena Peghin,<sup>a</sup> Maria De Martino,<sup>b</sup> Martina Fabris,<sup>c</sup> Alvisa Palese,<sup>d</sup> Erica Visintini,<sup>d</sup> Elena Graziano,<sup>b,e</sup> Valentina Gerussi,<sup>b,e</sup> Giulia Bontempo,<sup>a,e</sup> Federica D'Aurizio,<sup>c</sup> Alessia Biasotto,<sup>c</sup> Assunta Sartor,<sup>c</sup> Corrado Pipan,<sup>c,e</sup> Stefania Marzinotto,<sup>c</sup> Francesco Curcio,<sup>c,e</sup> Emilio Bouza,<sup>f,g,h,i</sup> Miriam Isola,<sup>b,e</sup> Carlo Tascini<sup>a,e</sup>

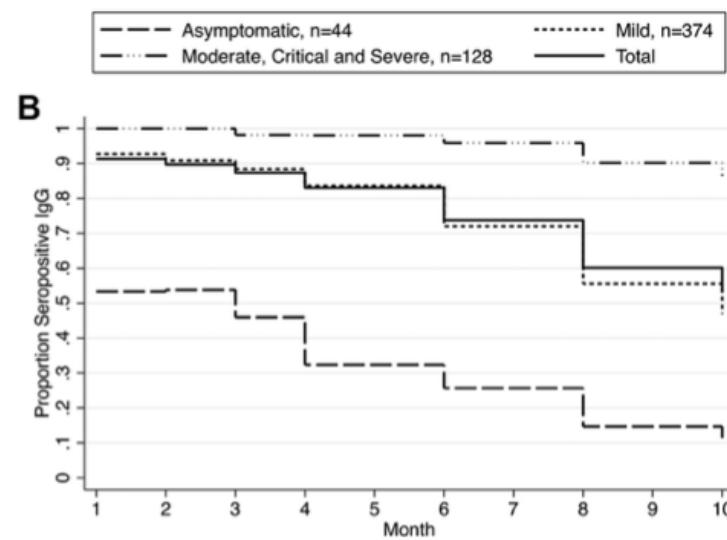


FIG 2 (A and B) Longitudinal assessment of anti-SARS-CoV-2 IgM (A) and IgG (B) in patients who recovered from COVID-19, according to the grade of severity of acute disease.

90% of patients for IgM at 4 months and in 47% for IgG at 10 months. Older age, number of symptoms at acute onset, and severity of acute COVID-19 were all independent predictors of long-term immunity both for IgM ( $\beta$ , linear regression coefficient, 1.10,  $P = 0.001$ ;  $\beta$  5.15  $P = 0.014$ ;  $\beta$  43.84  $P = 0.021$ , respectively) and for IgG ( $\beta$  1.43  $P < 0.001$ ;  $\beta$  10.46  $P < 0.001$ ;  $\beta$  46.79  $P < 0.001$ , respectively), whereas the initial IgG peak was associated only with IgG duration ( $\beta$  1.12,  $P < 0.001$ ). IgM antibodies disap-



Original article

Post-COVID-19 syndrome and humoral response association after 1 year in vaccinated and unvaccinated patients

Maddalena Peghin <sup>1,2,\*</sup>, Maria De Martino <sup>3</sup>, Alvisa Palese <sup>4</sup>, Valentina Gerussi <sup>1</sup>,  
Giulia Bontempo <sup>1</sup>, Elena Graziano <sup>1,2</sup>, Erica Visintini <sup>4</sup>, Denise D'Elia <sup>1</sup>, Fabiana Dellai <sup>1</sup>,  
Francesco Marrella <sup>1</sup>, Martina Fabris <sup>5</sup>, Francesco Curcio <sup>5</sup>, Assunta Sartor <sup>5</sup>, Miriam Isola <sup>3</sup>,  
Carlo Tascini <sup>1</sup>

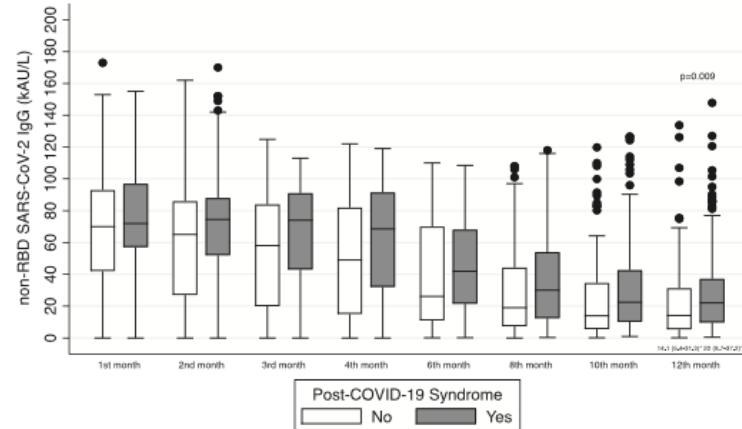
479 pazienti furono intervistati 13 mesi dopo infezione acuta, long COVID 47%

Misura di anticorpi anti RBD e non-RDB.

Titolo degli Ab non-RDB era correlato al long covid

Titolo degli Ab RDB non correllava con long-Covid, pertanto la vaccinazione non correllava con long-COVID

**Results:** A total of 479 patients (52.6% female; mean age: 53 years) were interviewed 13.5 months (standard deviation: 0.6 months) after acute infection. Post-COVID-19 syndrome was observed in 47.2% of patients ( $n = 226$ ) after 1 year. There were no significant differences in the worsening of post-COVID-19 symptoms (22.7% vs. 15.8%;  $p = 0.209$ ) among vaccinated ( $n = 132$ ) and unvaccinated ( $n = 347$ ) patients. The presence of non-RBD SARS-CoV-2 IgG induced by natural infection showed a significant association with post-COVID-19 syndrome (OR: 1.35; 95% CI, 1.11–1.64;  $p = 0.003$ ), and median non-RBD SARS-CoV-2 IgG titres were significantly higher in long haulers than in patients without symptoms (22 kAU/L (interquartile range, 9.7–37.2 kAU/L) vs. 14.1 kAU/L (interquartile range, 5.4–31.3 kAU/L);  $p = 0.009$ ) after 1 year. In contrast, the presence of RBD SARS-CoV-2 IgG was not associated with the occurrence of post-COVID-19 syndrome (>2500 U/mL vs. 0.9–2500 U/mL; OR: 1.36; 95% CI, 0.62–3.00;  $p = 0.441$ ), and RBD SARS-CoV-2 IgG titres were similar in long haulers as in patients without symptoms (50% values > 2500 U/mL vs. 55.6% values > 2500 U/mL;  $p = 0.451$ ).



**Fig. 3.** Serological evolution against SARS-CoV-2 measured with non-RBD SARS-CoV-2 IgG in patients with or without post-COVID-19 syndrome at 12 months. COVID-19, Coronavirus Disease 2019; RBD, receptor binding domain; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2.

**Table 4**

SARS coronavirus type 2 RBD IgG and non-RBD IgG antibodies after natural infection and vaccination in patients with or without post-COVID-19 syndrome

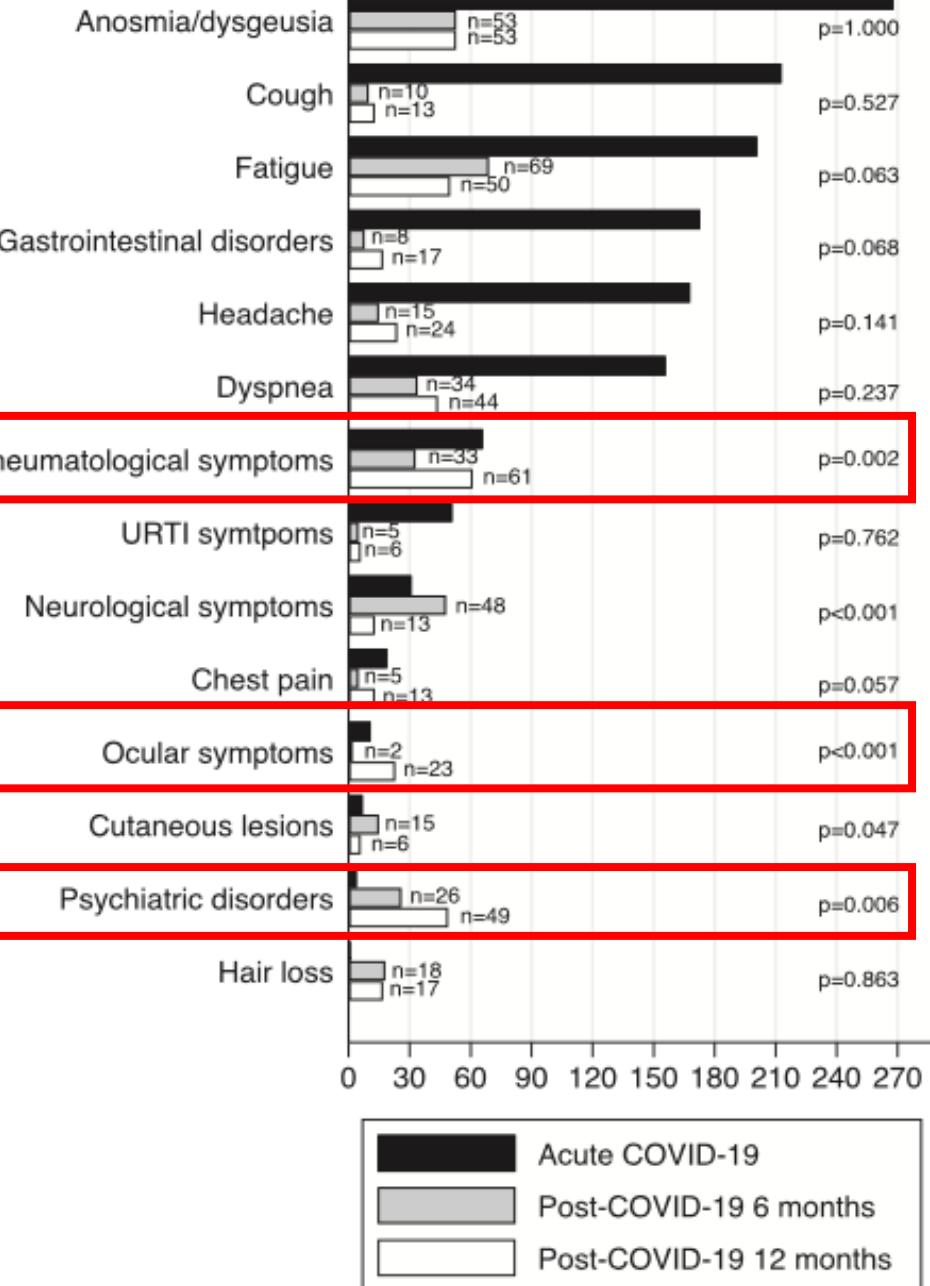
	Post-COVID-19 syndrome				p-value <sup>a</sup>
	Yes (n = 153)	No (n = 122)	Vaccinated	Unvaccinated	
Non-RBD IgG at 12 months <sup>b</sup> , median (interquartile range)	22 (9.7–37.2)	14.1 (5.4–31.3)			<b>0.009</b>
RBD IgG at 12 months <sup>c</sup> , n/N (%)					0.451
<0.9	0/31 (0.0)	2/23 (8.7)	0/27 (0.0)	0/21 (0.0)	
0.9–2500	3/31 (9.7)	19/23 (82.6)	3/27 (11.1)	21/21 (100)	
>2500	28/31 (90.3)	2/23 (8.7)	24/27 (88.9)	0/21 (0)	

RBD, receptor binding domain.

<sup>a</sup> Comparison between post-COVID-19 syndrome (yes/no).

<sup>b</sup> Value available for 275 patients.

<sup>c</sup> Value available for 102 patients.



**Fig. 2.** Acute- and post-COVID-19 related symptoms at 6 and 12 months. \* p refers to post-COVID-19 symptoms at 6 and 12 months. COVID-19, Coronavirus Disease 2019; upper respiratory tract infection.

Communication

## COVID-19 Survivors Are Still in Need of Neuropsychiatric Support Two Years after Infection

Marco Colizzi <sup>1,2,\*</sup>, Maddalena Peghin <sup>3,4</sup>, Maria De Martino <sup>5</sup>, Giulia Bontempo <sup>3</sup>, Stefania Chiappinotto <sup>6</sup>, Federico Fonda <sup>6</sup>, Miriam Isola <sup>5</sup>, Carlo Tascini <sup>3</sup>, Matteo Balestrieri <sup>1</sup> and Alvisa Palese <sup>6</sup>

La gravità della dispnea ed in numero dei sintomi correlavano con i **sintomi psichiatrici a 24 mesi**, specie la perdita di concentrazione

**Table 4.** Lack of concentration and focus at the 24-month follow-up.

Risk Factors at Onset	OR	Multivariable Analysis	
		95% CI	p-Value
Co-morbidities, number	1.52	1.12, 2.08	0.008
Overall symptoms, number	1.09	0.87, 1.38	0.456
Fatigue	1.43	0.62, 3.27	0.398
Dyspnoea	3.17	1.40, 7.16	0.005
Management			
Outpatient	1		
Ward	0.74	0.33, 1.68	0.469
Intensive care unit	1.21	0.31, 4.77	0.783

URTI, upper respiratory tract infection.

Dyspnea at the onset predicted both symptoms of psychiatric disorders ( $OR = 3.26$ , 95% CI = 1.22–8.70, and  $p = 0.019$ ) and a lack of concentration and focus ( $OR = 3.17$ , 95% CI = 1.40–7.16, and  $p = 0.005$ ) 24 months post-infection, with the number of comorbidities at the onset also predicting the occurrence of a lack of concentration and focus ( $OR = 1.52$ , 95% CI = 1.12–2.08, and  $p = 0.008$ ). The findings of this study may have important public health implications, as they underlie the fact that COVID-19 survivors are still in need of neuropsychiatric support two years after infection.

# Post-COVID-19 Syndrome 2 Years After the First Wave: The Role of Humoral Response, Vaccination and Reinfection

Maddalena Peghin,<sup>1,a,✉</sup> Maria De Martino,<sup>2,a</sup> Alvisa Palese,<sup>3</sup> Stefania Chiappinotto,<sup>3</sup> Federico Fonda,<sup>3</sup> Valentina Gerussi,<sup>4</sup> Assunta Sartor,<sup>5,b</sup> Francesco Curcio,<sup>5</sup> Paolo Antonio Grossi,<sup>1</sup> Miriam Isola,<sup>2,a</sup> and Carlo Tascini<sup>4,a</sup>

<sup>1</sup>Infectious and Tropical Diseases Unit, Department of Medicine and Surgery, University of Insubria-ASST Sette Laghi, Varese, Italy, <sup>2</sup>Division of Medical Statistic, Department of Medicine, University of Udine, Udine, Italy, <sup>3</sup>Department of Medicine, University of Udine, Udine, Italy, <sup>4</sup>Infectious Diseases Division, Department of Medicine, University of Udine and Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), 33100 Udine, Italy, <sup>5</sup>Institute of Clinical Pathology, Department of Laboratory Medicine, University of Udine, ASUFC, Udine, Italy, and <sup>b</sup>Department of Medicine (DAME), University of Udine, Udine, Italy

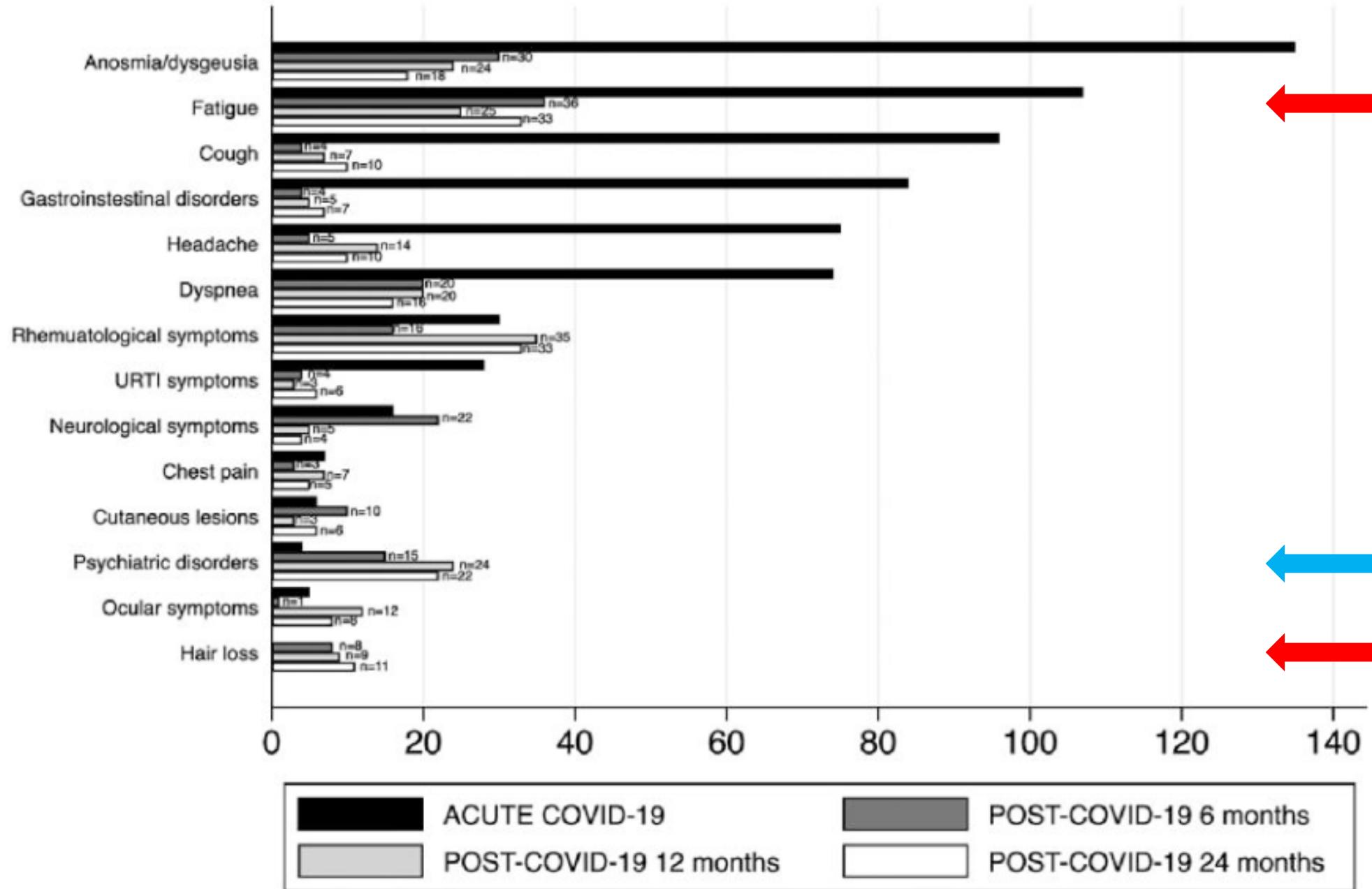
**Background.** The aim of this study was to describe the long-term evolution of post-COVID-19 syndrome over 2 years after the onset of severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) in survivors of the first wave.

**Methods.** This prospective study was based on interviews and investigated post-COVID-19 syndrome 6, 12, and 24 months after the disease onset in all adult in- and outpatients with COVID-19 followed at Udine Hospital (Italy) during the first wave (March–May 2020). Humoral response, vaccination status, and reinfection were assessed.

**Results.** Overall, 230 patients (53.5% female; mean age 54.7 years) were interviewed 2.3 years (standard deviation = 0.11) after acute onset. Post-COVID-19 syndrome was observed in 36.1% of patients ( $n = 83$ ) at 2 years. The most common persistent symptoms were fatigue (14.4%), rheumatological (14.4%), and psychiatric symptoms (9.6%). Overall, 55.4% (46 of 83) of long haulers searched for healthcare system support and 21 (45.7%) were visited by a specialist. Female gender (odds ratio [OR] = 2.50,  $P = .005$ ), a proportional increase in the number of symptoms during acute COVID-19 (OR = 1.40,  $P = .001$ ), and the presence of comorbidities (OR = 1.57,  $P = .004$ ) were all independent risk factors for post-COVID-19 syndrome. Vaccination and reinfection had no impact on post-COVID-19 syndrome dynamics. The presence of receptor-binding domain (RBD) SARS-CoV-2 immunoglobulin G (IgG) and non-RBD SARS-CoV-2 IgG titers were not associated with the occurrence of post-COVID-19 syndrome.

**Conclusions.** Two years after COVID-19, the burden of persistent symptoms remains high among in- and outpatients' population infected during the first wave. Post-COVID-19 dynamic does not seem to be influenced by SARS-CoV-2 immunization status and reinfection.

**Keywords.** COVID-19; long COVID; post-COVID-19 syndrome; SARS-CoV-2 antibodies.



**Table 4. Univariable and Multivariable Analysis of Risk Factors Associated With Post-COVID-19 Syndrome at 24 Months**

Risk Factors	OR	Univariable 95% CI	P Value	OR	Multivariable 95% CI	P Value
<b>Gender</b>						
Female	2.10	1.21–3.67	.009	2.50	1.32–4.76	.005
<b>Age Group</b>						
41–60 vs 18–40	1.57	0.71–3.49	.269	1.04	0.44–2.47	.921
>60 vs 18–40	2.33	1.04–5.19	.039	1.37	0.52–3.58	.524
>60 vs 41–60	1.48	0.82–2.68	.193	1.31	0.64–2.69	.464
<b>Ethnicity</b>						
European vs Native Italian	3.26	0.92–11.50	.067	...	...	
<b>Smoking Habits</b>						
Smoker vs nonsmoker	1.01	0.44–2.36	.976	...	...	
Ex-smoker vs nonsmoker	1.09	0.58–2.07	0.783	...	...	
Ex-smoker vs smoker	1.08	0.42–2.77	.873	...	...	
<b>Alcohol Habits</b>						
Drinker vs nondrinker	0.47	0.27–0.81	.007	...	...	
Alcohol use disorder + vs nondrinker	1.22	0.07–20.08	.887	...	...	
Alcohol use disorder r + vs drinker	2.63	0.16–43.23	.500	...	...	
<b>Comorbidities, number</b>	1.60	1.24–2.05	<.001	1.57	1.15–2.13	.004
<b>Symptoms of acute COVID-19 at the onset, number</b>	1.40	1.18–1.67	<.001	1.40	1.16–1.70	.001
<b>Management</b>						
Ward vs outpatients	1.72	0.92–3.23	.090	1.28	0.61–2.70	.513
ICU vs outpatients	3.02	0.91–9.95	.070	3.24	0.84–12.58	.089
ICU vs ward	1.75	0.49–6.21	.387	2.53	0.63–10.16	.191
<b>Hospitalization, days</b>	1.04	0.98–1.12	.243	...	...	
<b>Viral shedding, days</b>	1.05	1.02–1.08	.003	...	...	
<b>Non-RBD SARS-CoV-2 IgG<sup>c,b</sup></b>	0.99	0.98–1.01	.312	...	...	
<b>Positive non-RBD SARS-CoV-2 IgG<sup>c</sup></b>	1.38	0.74–2.56	.316	...	...	
<b>Reinfection</b>	1.19	0.58–2.43	.634	...	...	
<b>Number of doses of vaccine</b>	1.03	0.72–1.47	.891	...	...	

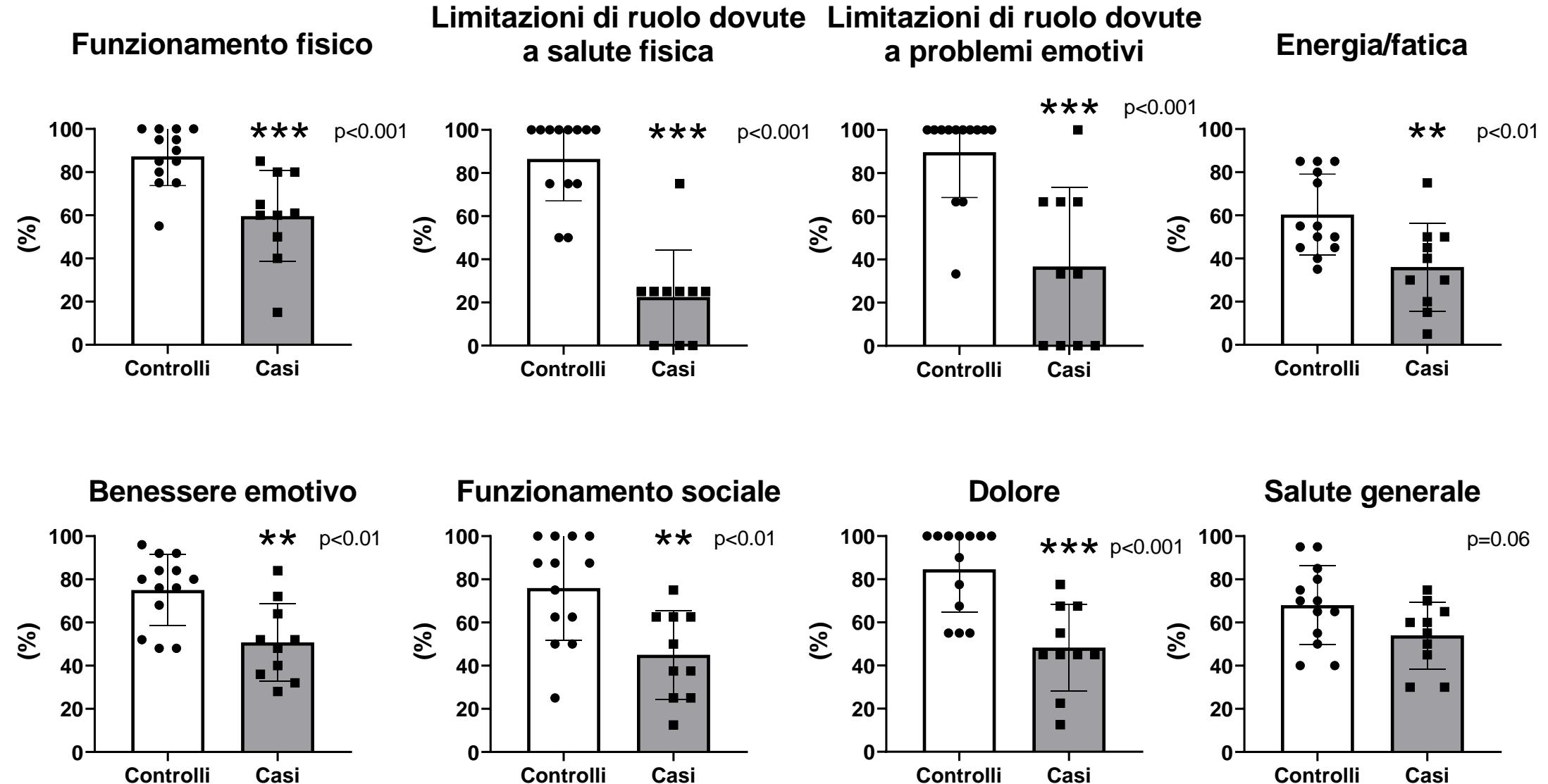
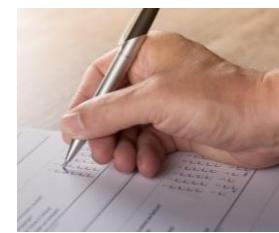
# Fisiologia Università di Udine (Prof Grassi)

- Test attivi e passivi in pazienti long Covid con astenia

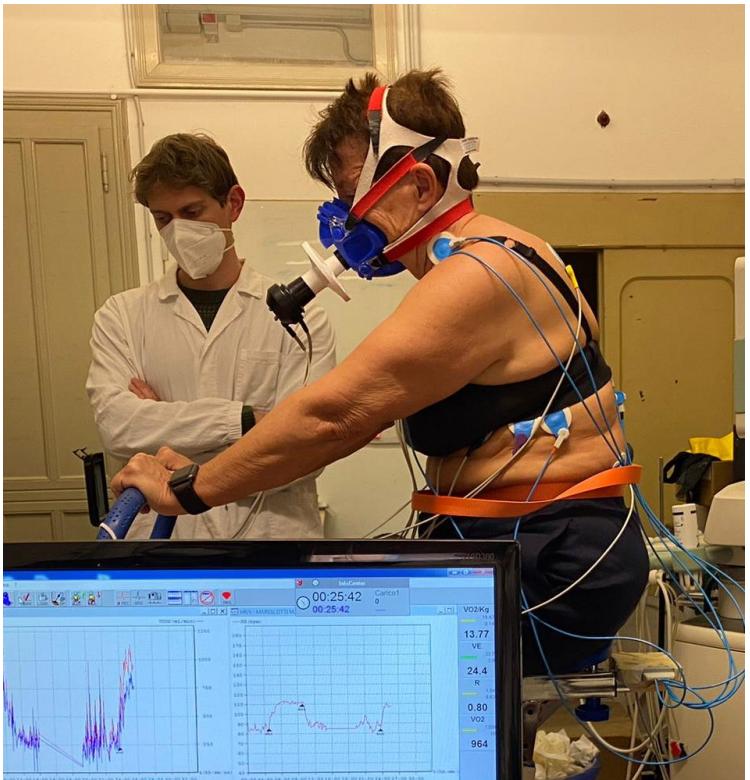
	<b>Controlli</b>	<b>Casi*</b>	<b>p-value</b>
<b>Soggetti (n)</b>	15 (7F, 8M)	11 (5F, 6M)	-
<b>Age (years)</b>	57 ± 7	57 ± 6	0.92
<b>Height (m)</b>	1.70 ± 0.08	1.75 ± 0.10	0.16
<b>Body mass (kg)</b>	73.3 ± 14.1	78.8 ± 10.5	0.29
<b>BMI (kg·m<sup>-2</sup>)</b>	25.1 ± 3.5	25.6 ± 2.3	0.72
<b>Periodo infezione</b>	Mar 2020 (14), Apr 2020 (1)	Mar 2020 (9), Apr 2020 (1), Feb 2021 (1)	-
<b>Ricoveri (TI)</b>	5	2	-
<b>Mesi intercorsi</b>	26 ± 4	28 ± 6	0.24

\*Sintomi: astenia (stanchezza, affaticabilità precoce, dolore muscolare e/o articolare) (10), dispnea o tosse (4)

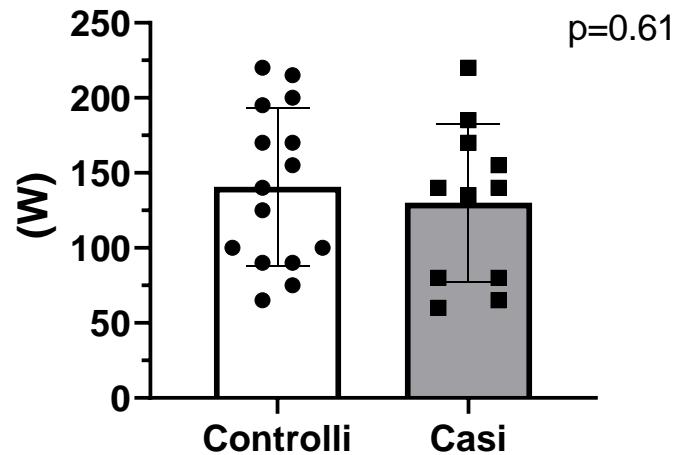
# Questionario di valutazione della qualità della vita (SF-36)



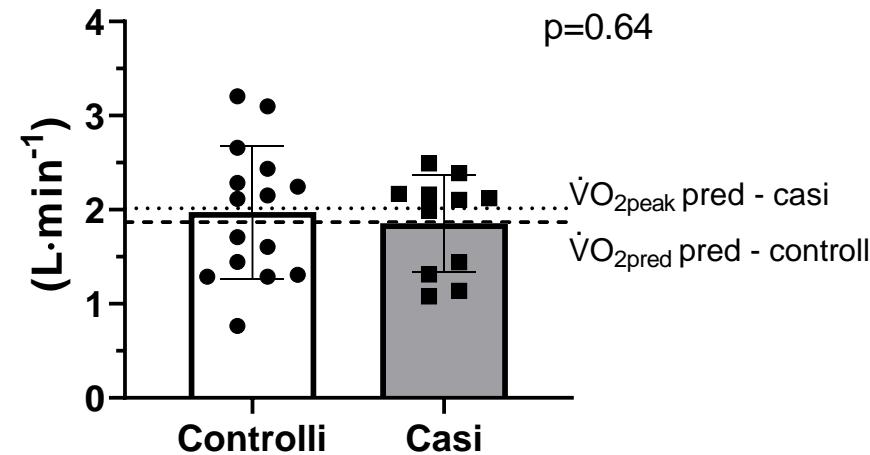
# Test incrementale al cicloergometro



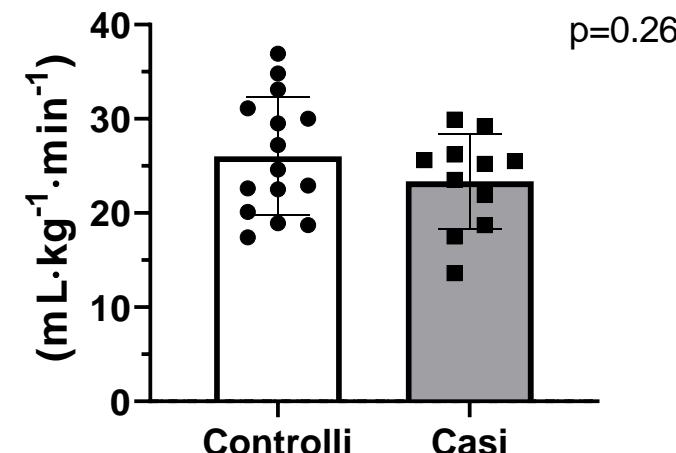
Work rate<sub>peak</sub>



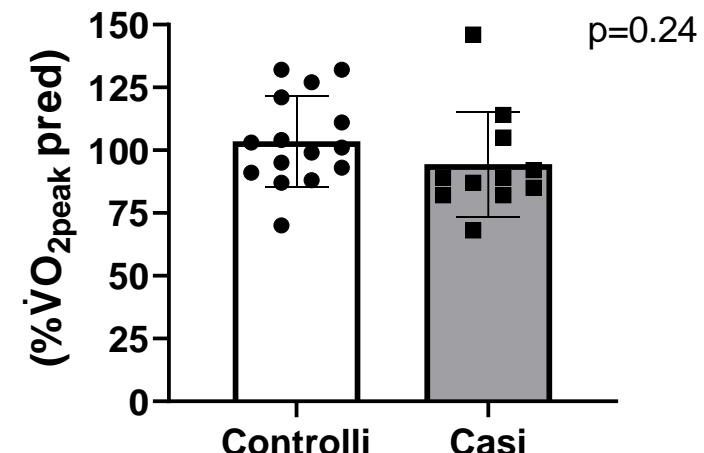
$\dot{V}O_{2\text{peak}}$



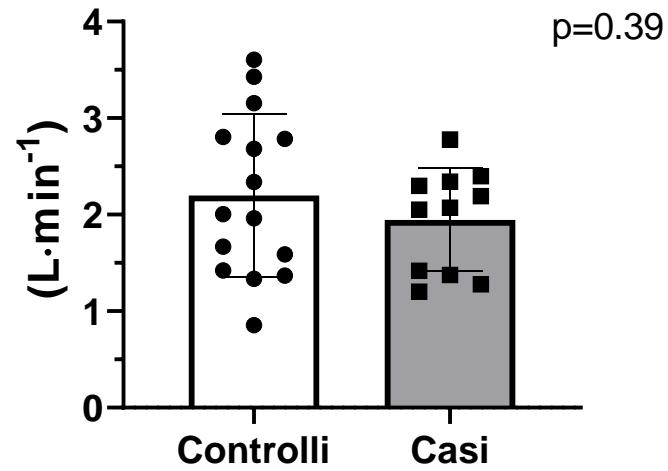
$\dot{V}O_{2\text{peak}}$



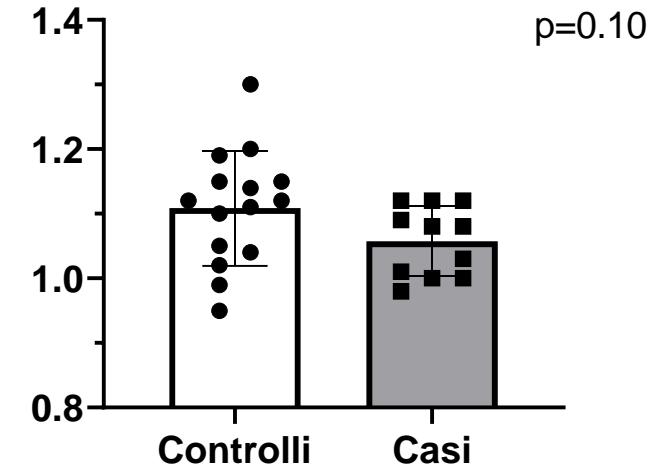
$\dot{V}O_{2\text{peak}}$



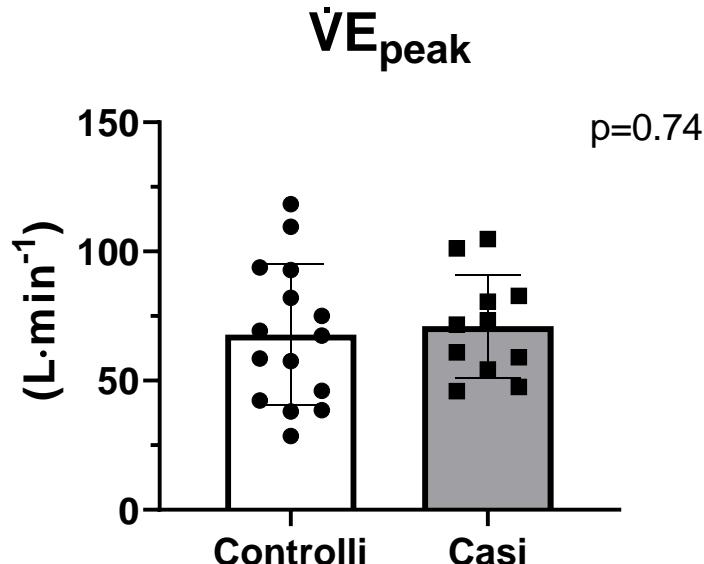
$\dot{V}CO_2$ peak



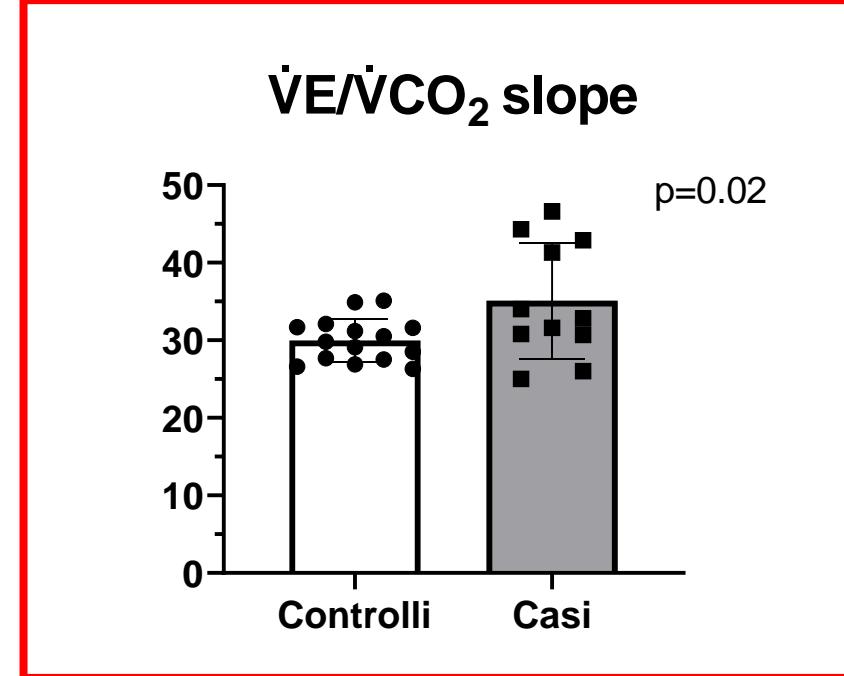
R<sub>peak</sub>

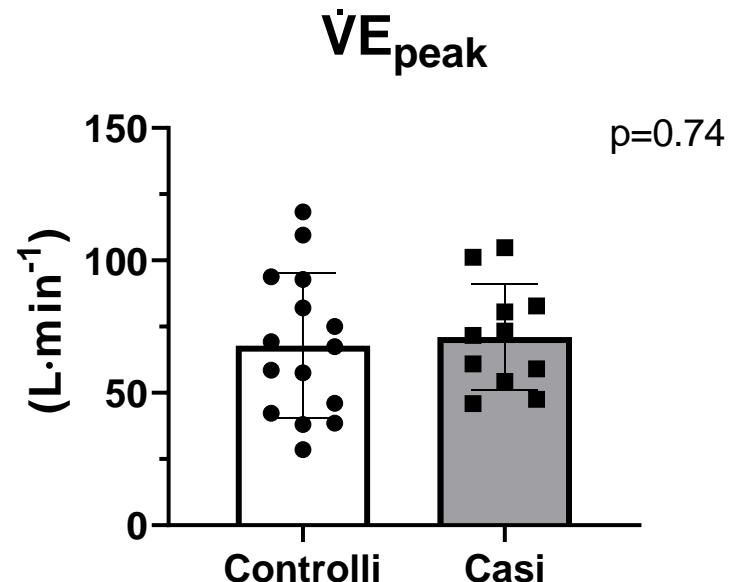
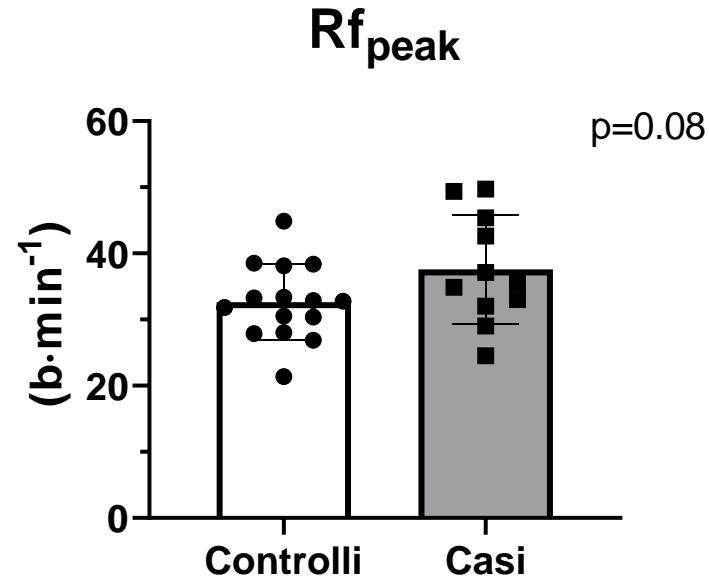
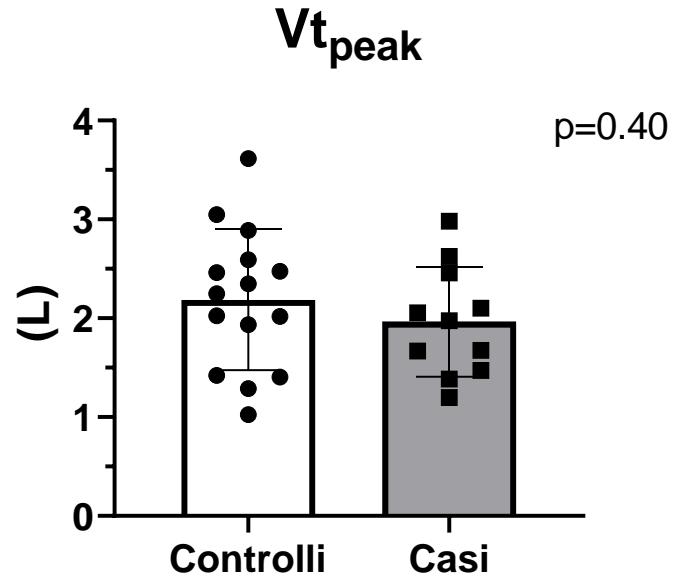


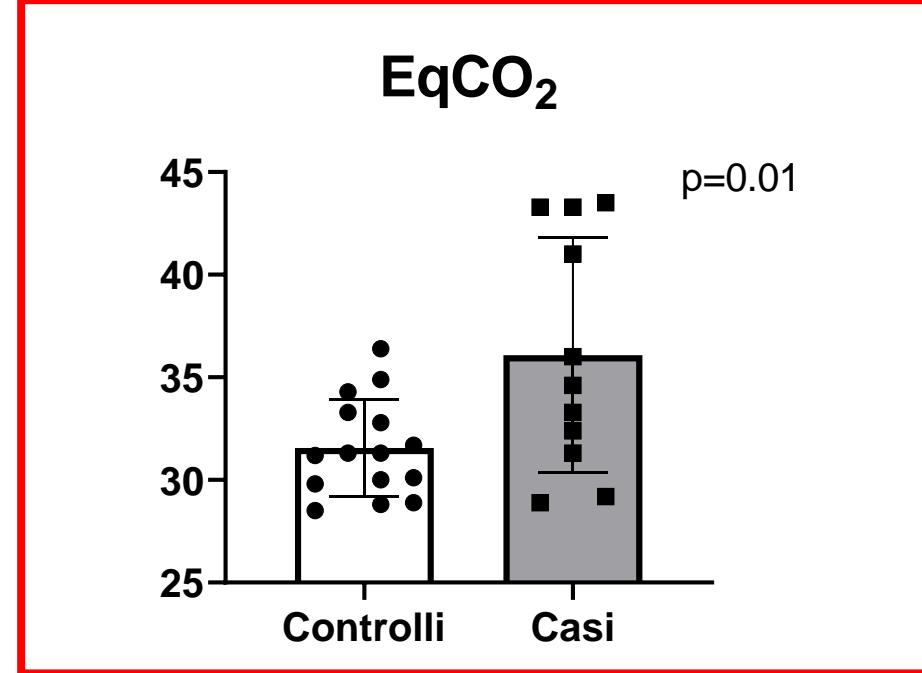
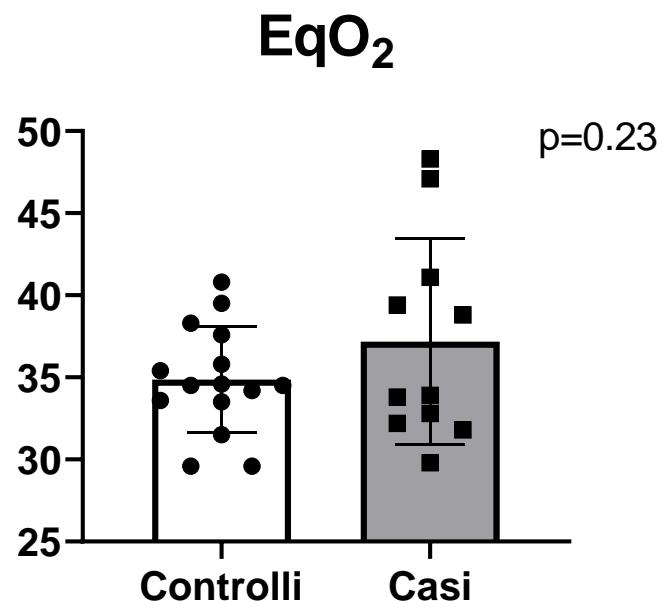
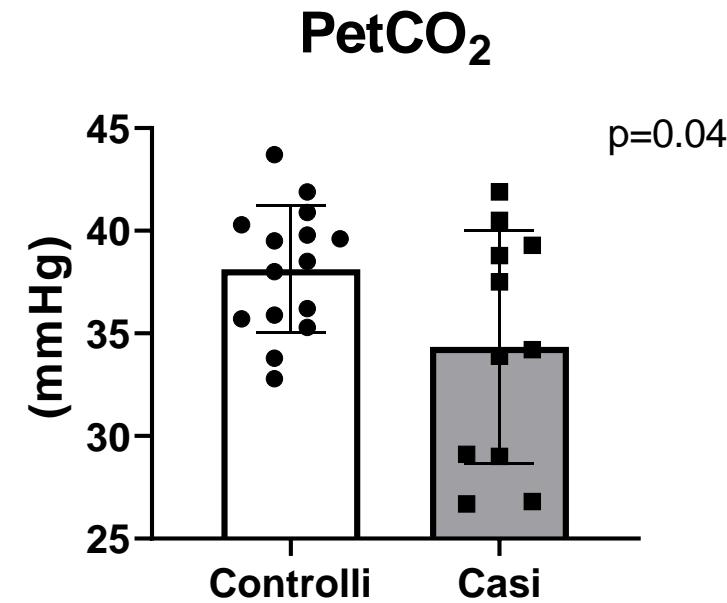
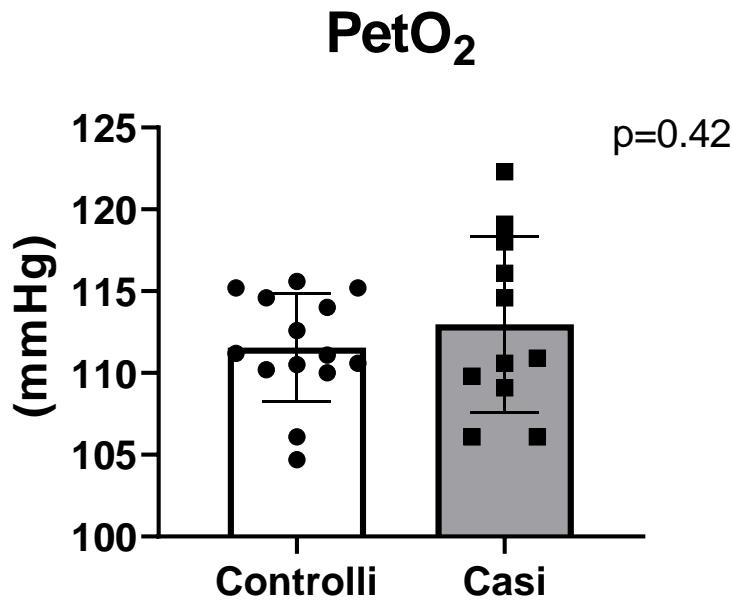
$\dot{V}E$ peak



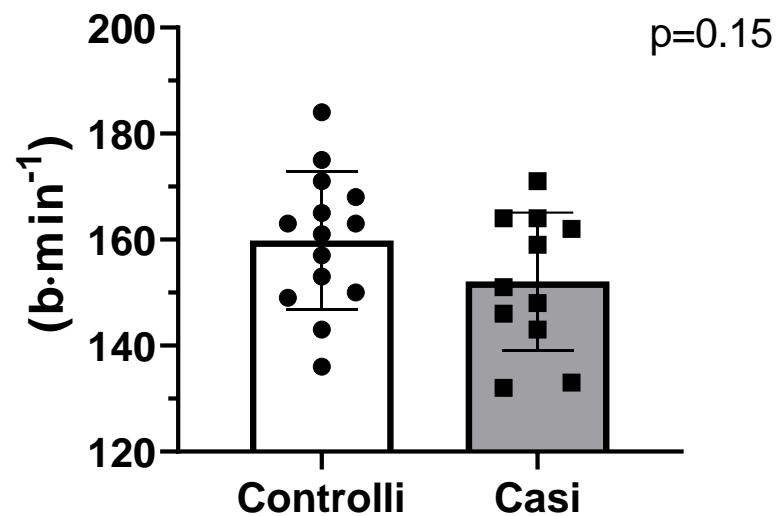
$\dot{V}E/\dot{V}CO_2$  slope



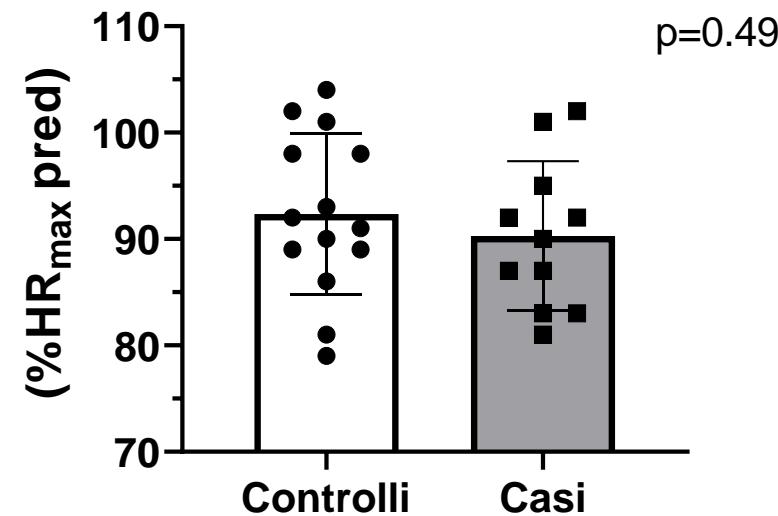




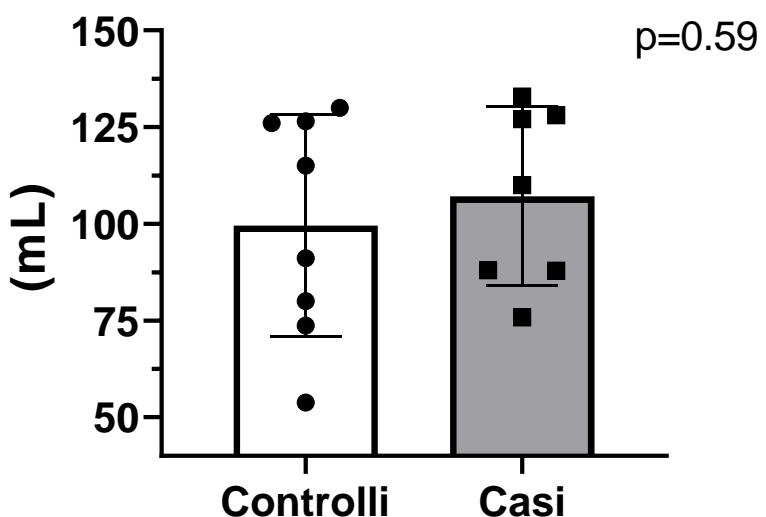
**HR<sub>peak</sub>**



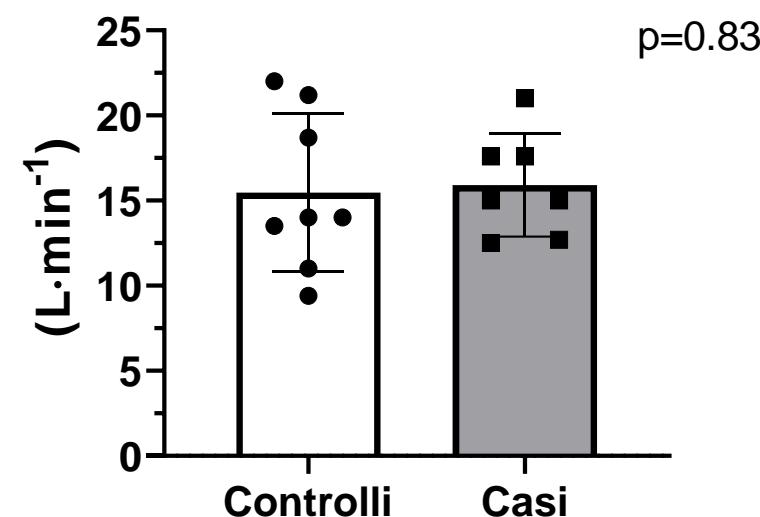
**HR<sub>peak</sub>**



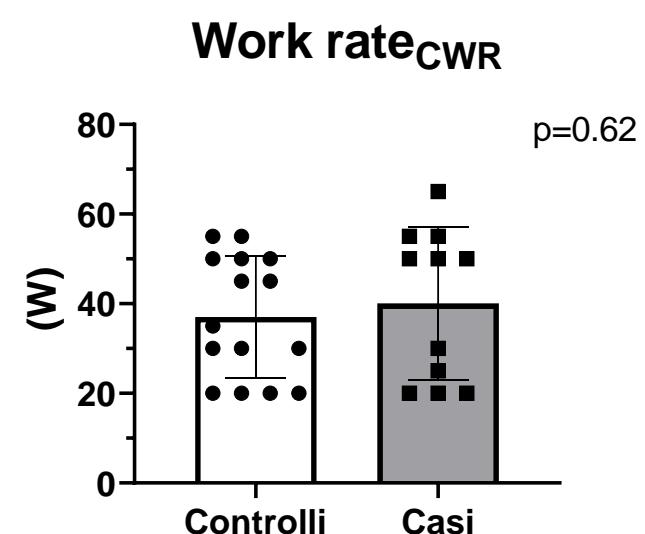
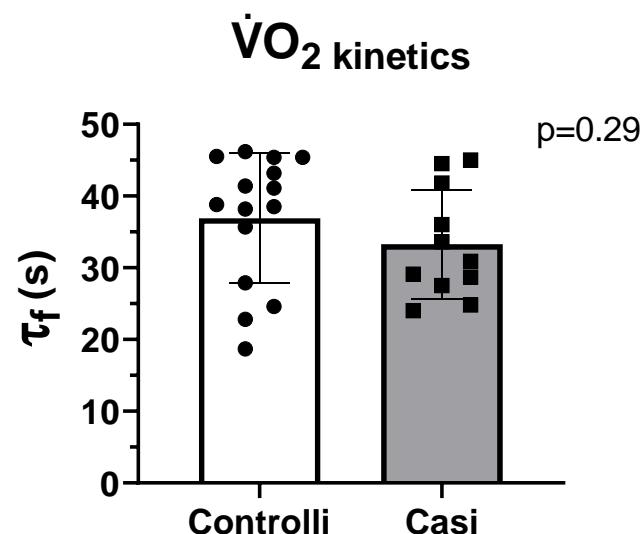
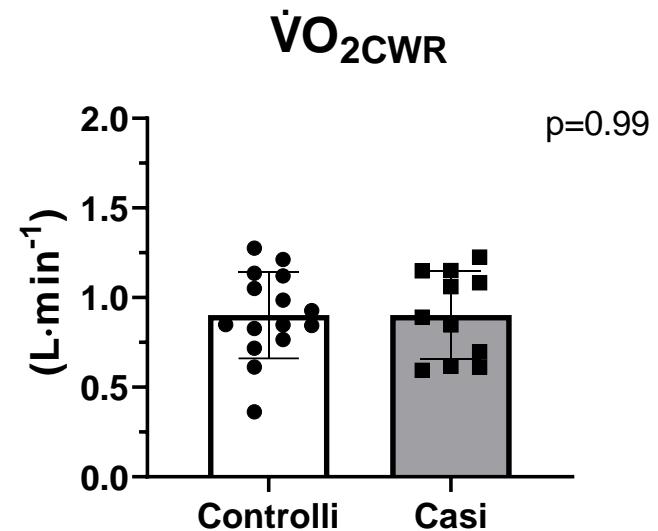
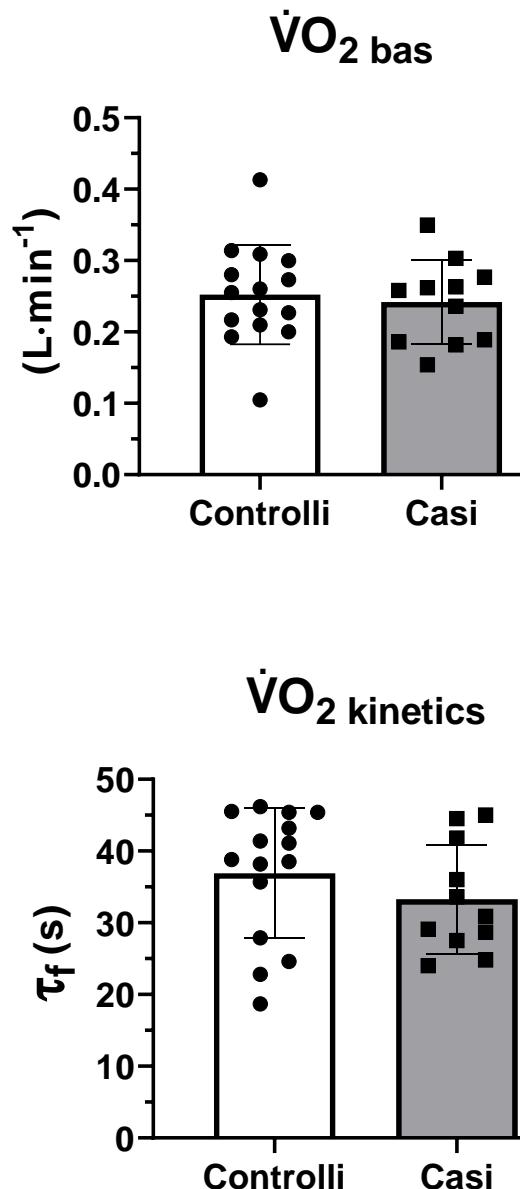
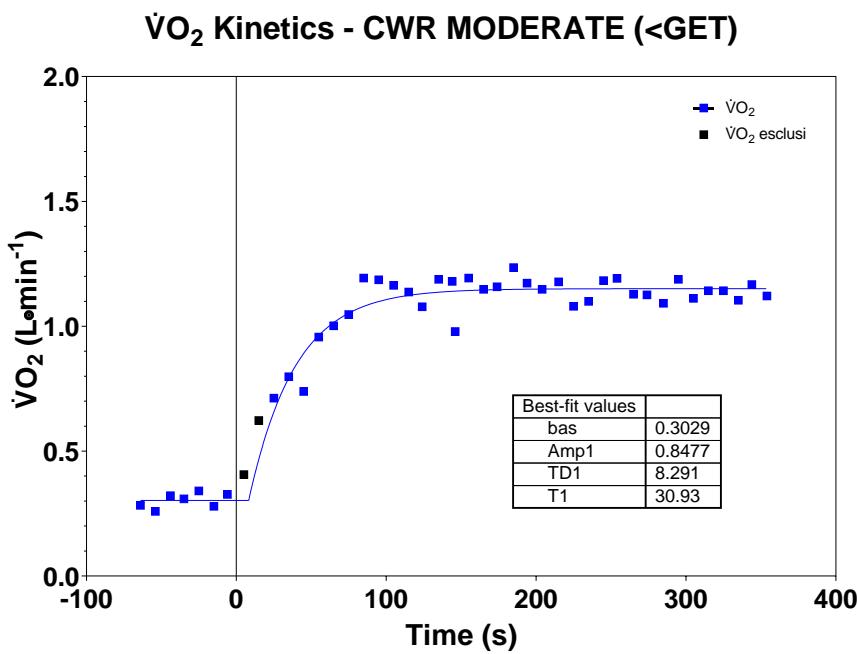
**SV<sub>peak</sub>**



**CO<sub>peak</sub>**



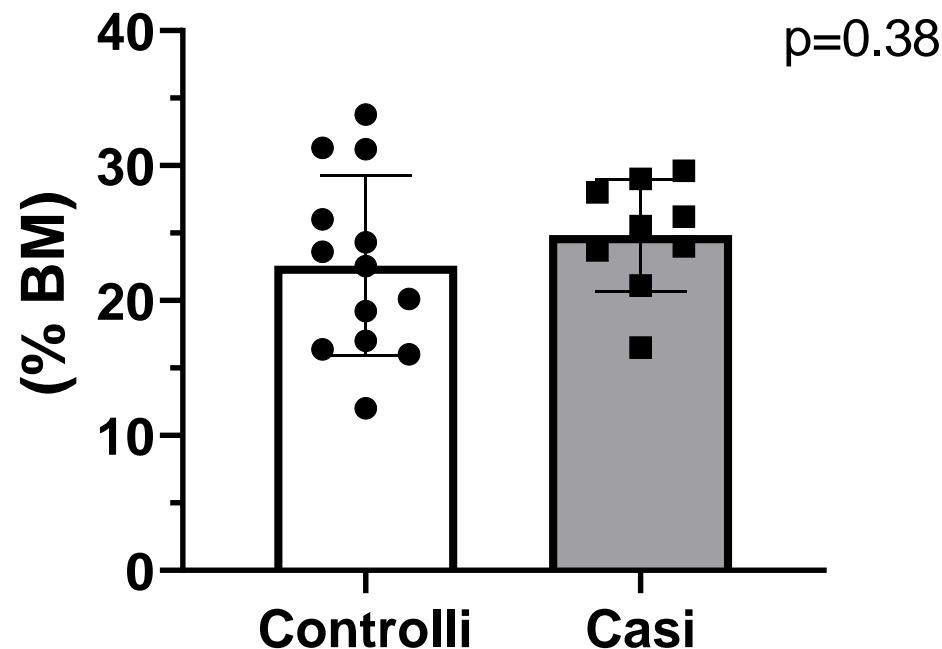
# Esercizio a carico costante di moderata intensità (<GET)



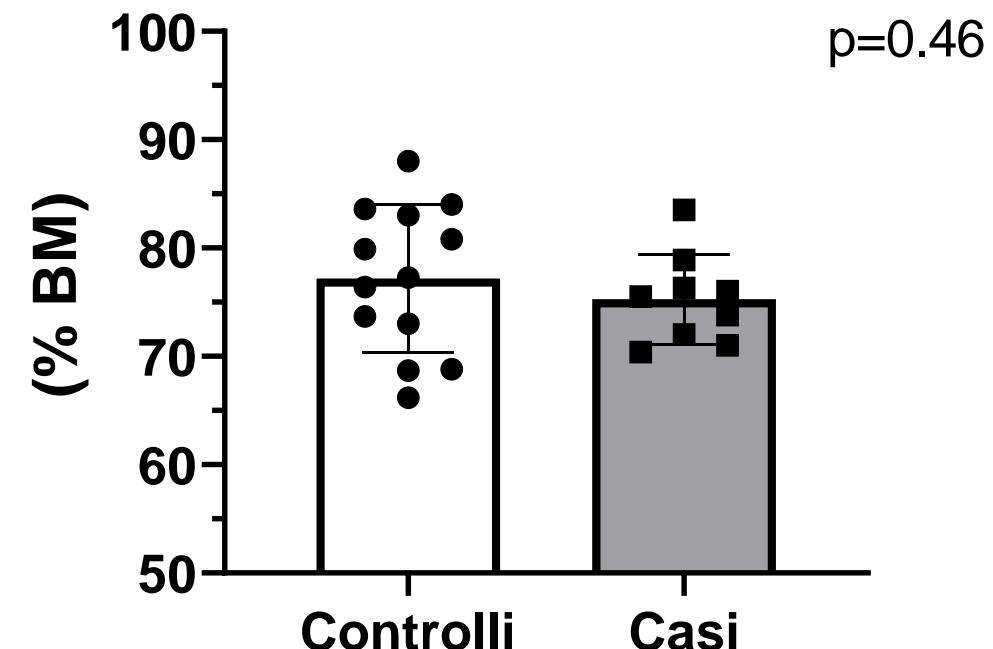
# Bioimpedenziometria (BIA)



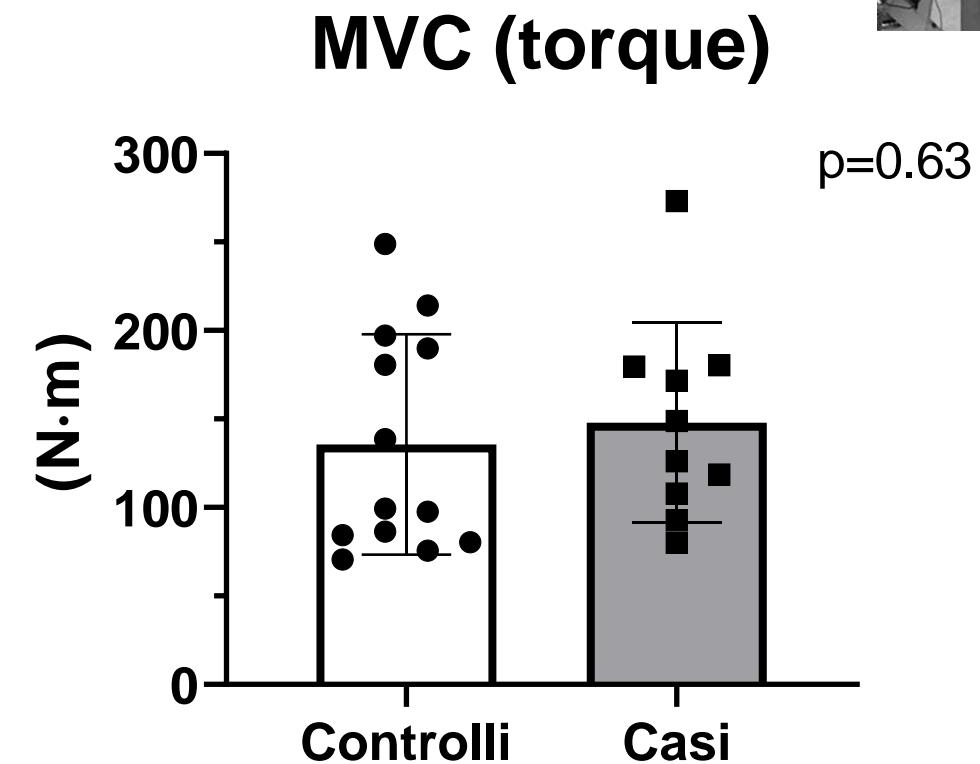
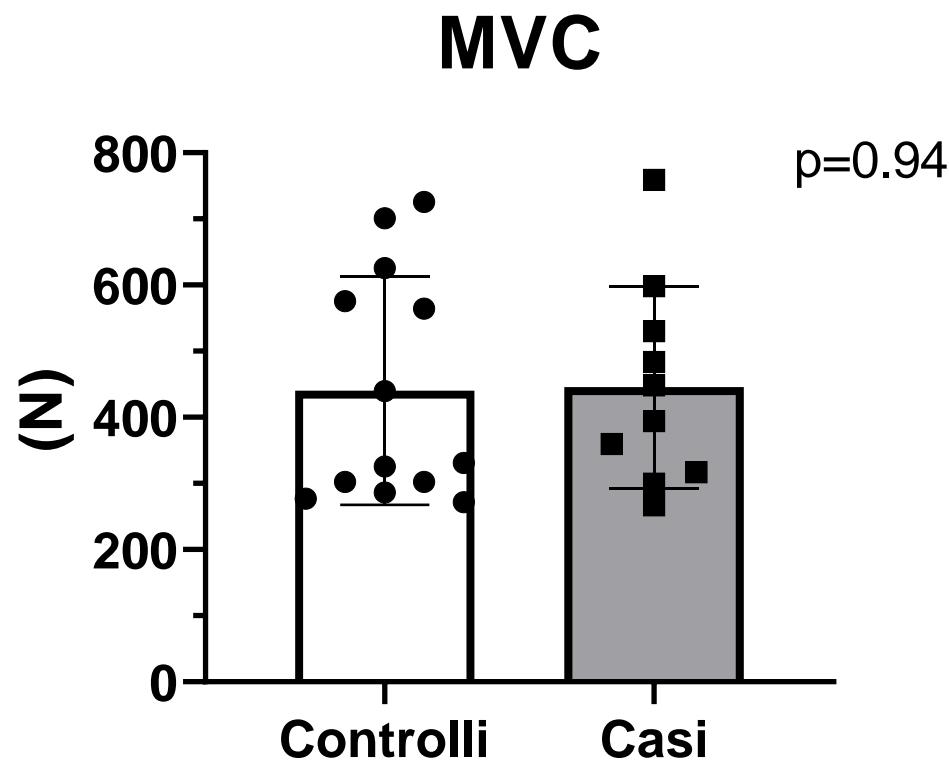
**FM**



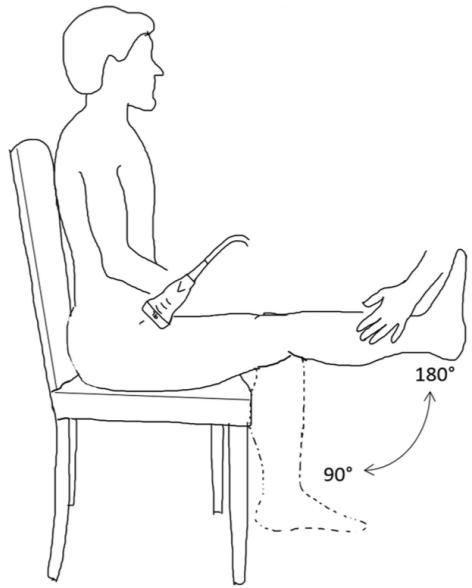
**FFM**



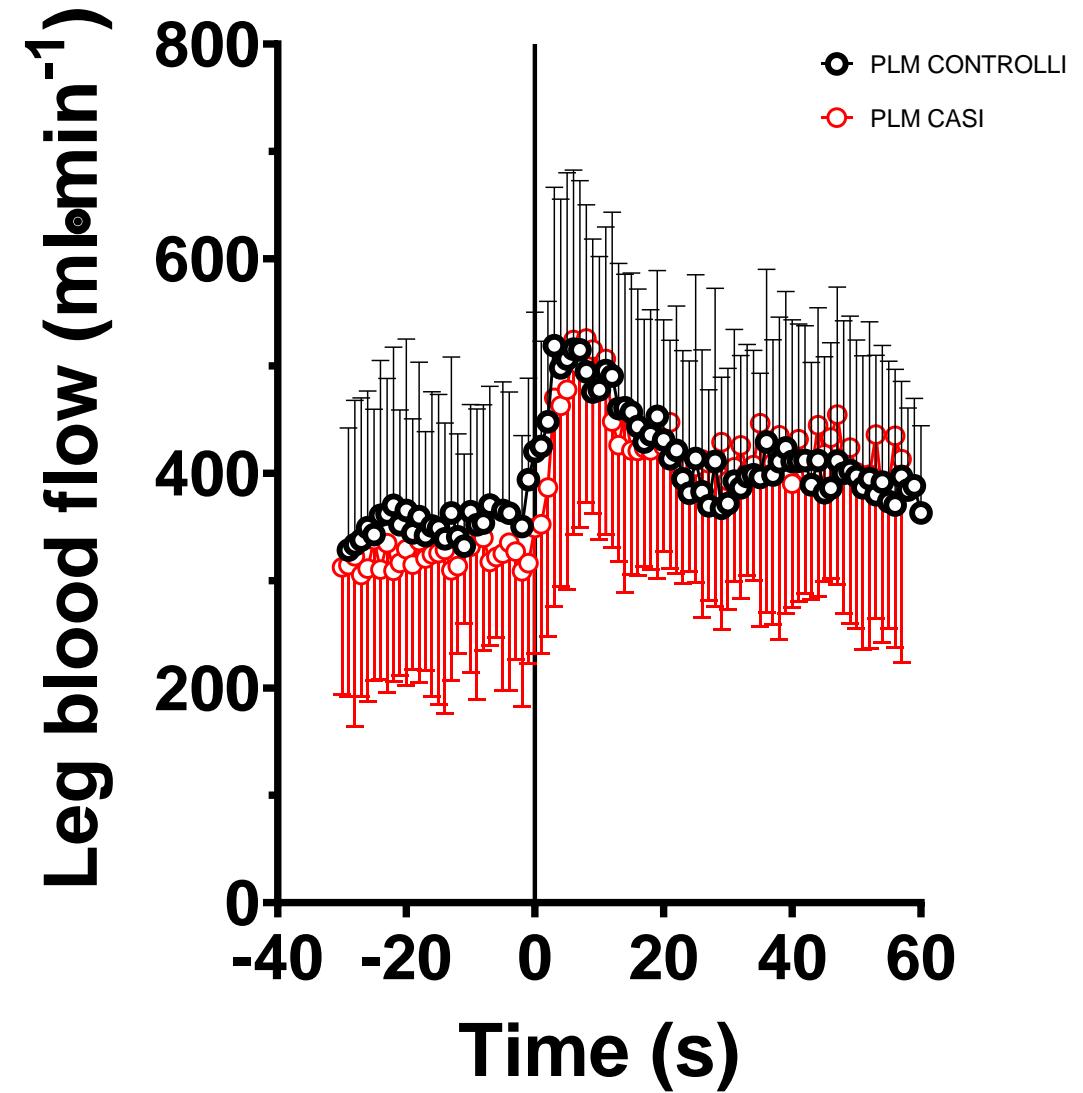
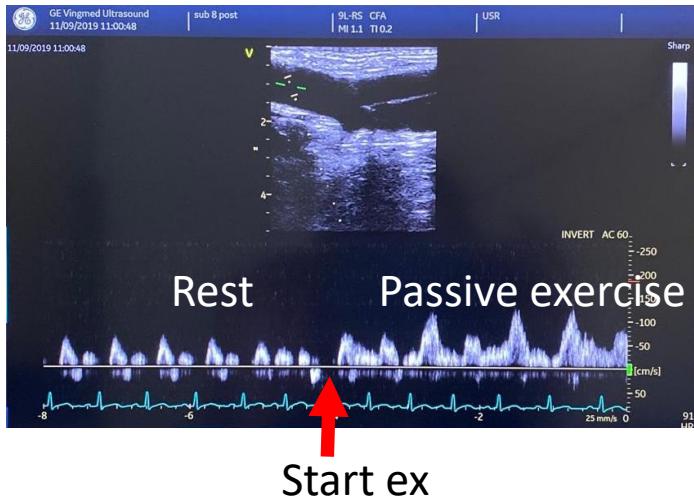
# Massima forza muscolare isometrica



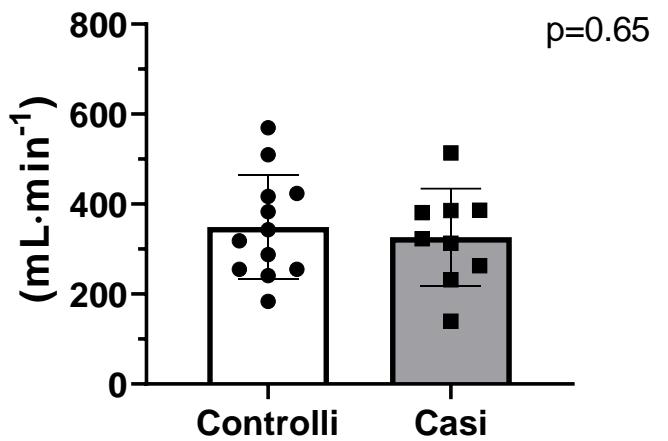
# Passive Leg Movement (PLM)



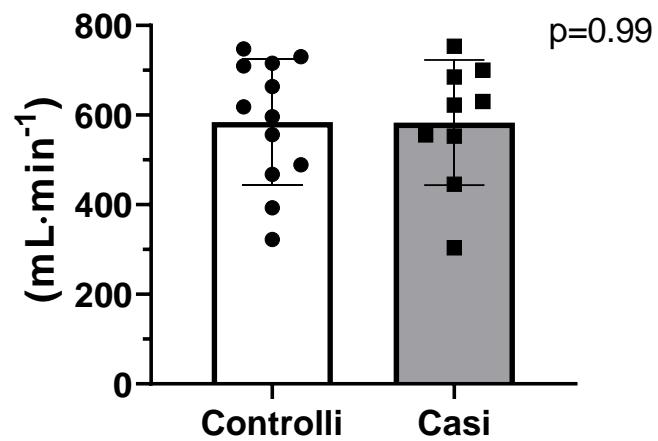
(Gifford & Richardson, 2017)



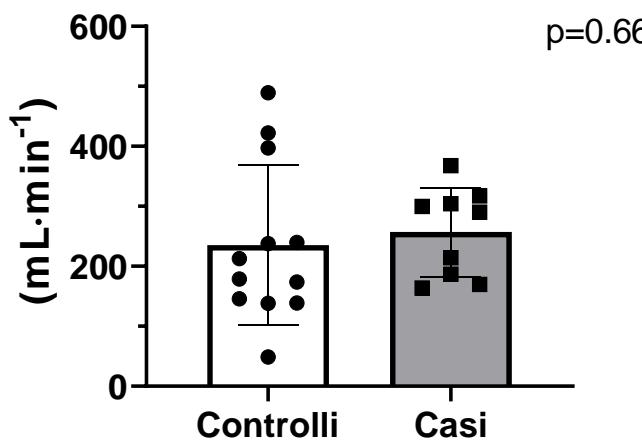
## Baseline



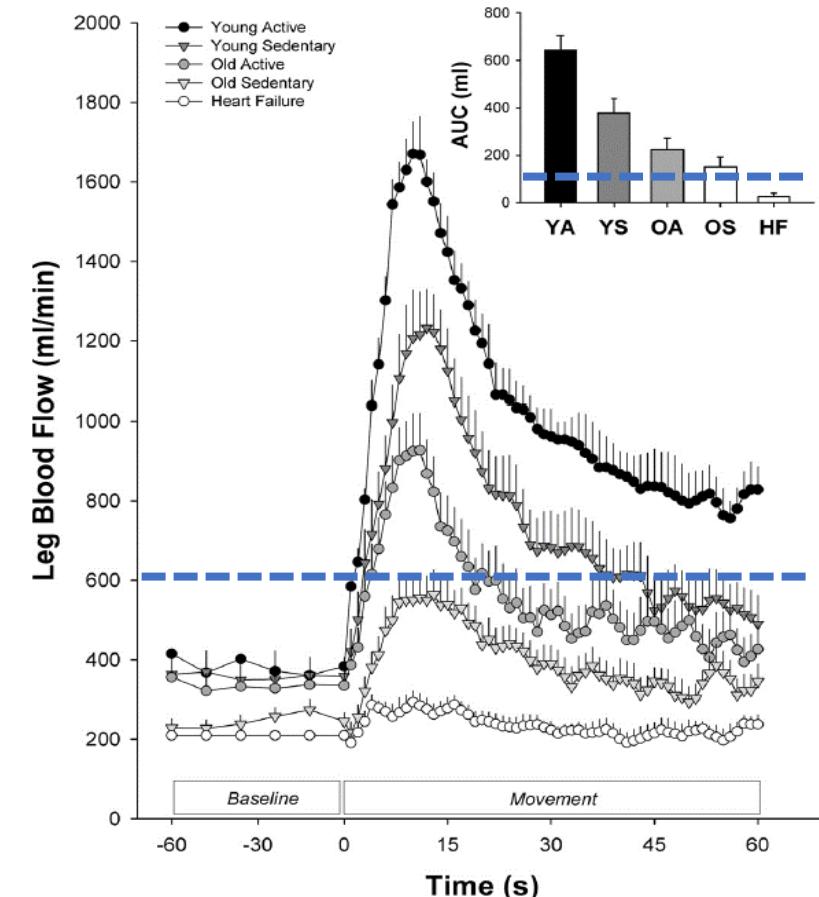
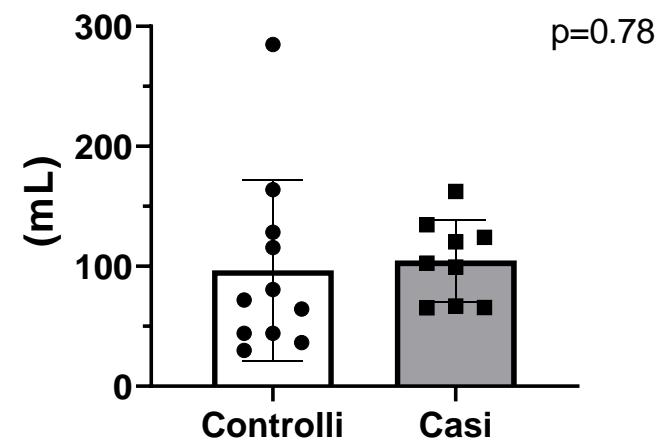
## Peak



## $\Delta$ Peak



## AUC



(Gifford & Richardson, 2017)

## CORRESPONDENCE

## Long-term sequelae of different COVID-19 variants: The original strain versus the Omicron variant

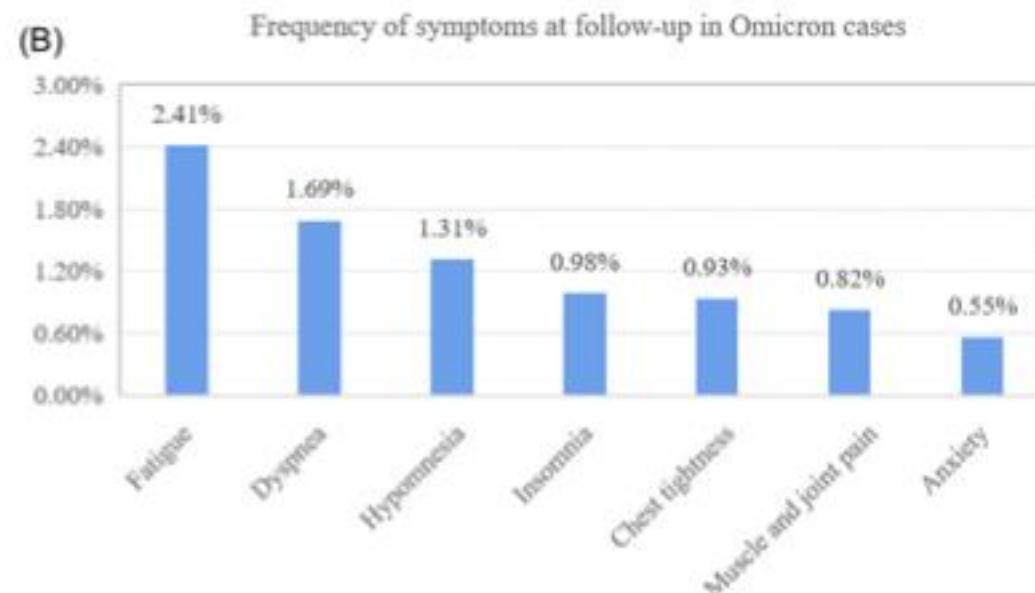
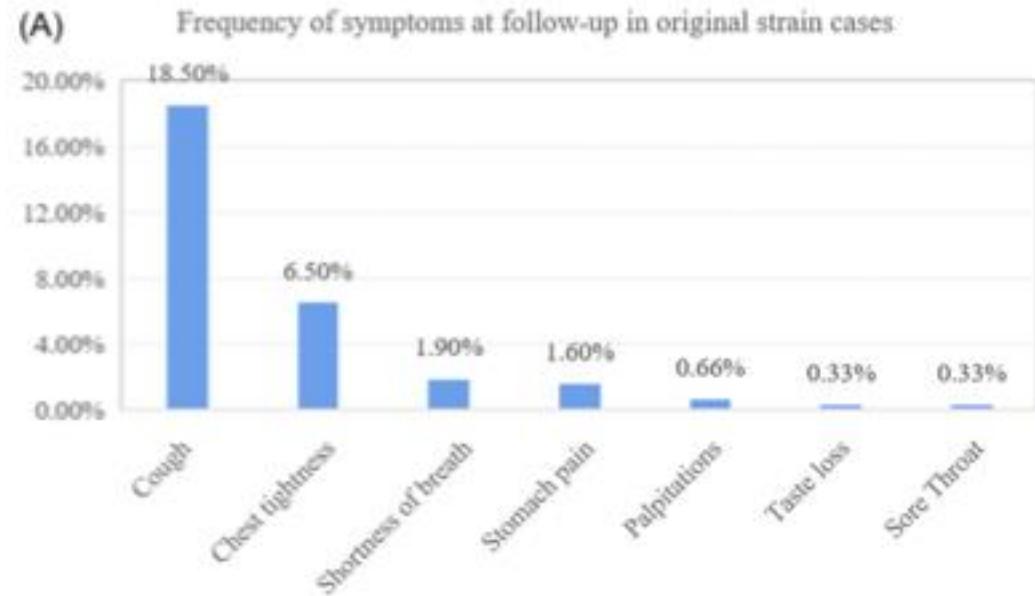
Xuejiao Liao<sup>1,6</sup>, Yuan Guan<sup>1,2,6</sup>, Qibin Liao<sup>1,6</sup>, Zhenghua Ma<sup>1</sup>, Liping Zhang<sup>1</sup>, Jingke Dong<sup>1</sup>, Xiaojuan Lai<sup>1</sup>, Guoqin Zheng<sup>1</sup>, Sumei Yang<sup>1,3</sup>, Cheng Wang<sup>1,3</sup>, Zhonghui Liao<sup>1,3</sup>, Shuo Song<sup>1</sup>, Hongyang Yi<sup>1</sup>, Hongzhou Lu<sup>1,\*</sup>

<sup>1</sup> Institute for Hepatology, Bio-therapeutic Center, National Clinical Research Center for Infectious Disease, Shenzhen Third People's Hospital; The Second Hospital Affiliated with the School of Medicine, Southern University of Science and Technology, Shenzhen, Guangdong, China;

<sup>2</sup> Department of Epidemiology, School of Public Health, Fudan University, Shanghai, China;

<sup>3</sup> Bengbu Medical College, Bengbu, Anhui, China.

**Abstract:** Although Omicron appears to cause less severe acute illness than the original strain, the potential for large numbers of patients to experience long COVID is a major concern. Little is known about the recovery phase in cases of Omicron, highlighting the importance of dynamically monitor long COVID in those patients. Subjects of the current study were patients available for a three-month follow-up who were admitted from January 13 to May 22, 2020 (period of the original strain) and from January 1 to May 30, 2022 (period of Omicron). Twenty-eight-point-four percent of patients infected with the original strain had long-term symptoms of COVID-19 and 5.63% of those infected with the





Review

# Comparison of Long COVID-19 Caused by Different SARS-CoV-2 Strains: A Systematic Review and Meta-Analysis

Min Du <sup>1</sup>, Yirui Ma <sup>1</sup>, Jie Deng <sup>1</sup>, Min Liu <sup>1</sup> and Jue Liu <sup>1,2,3,4,\*</sup>

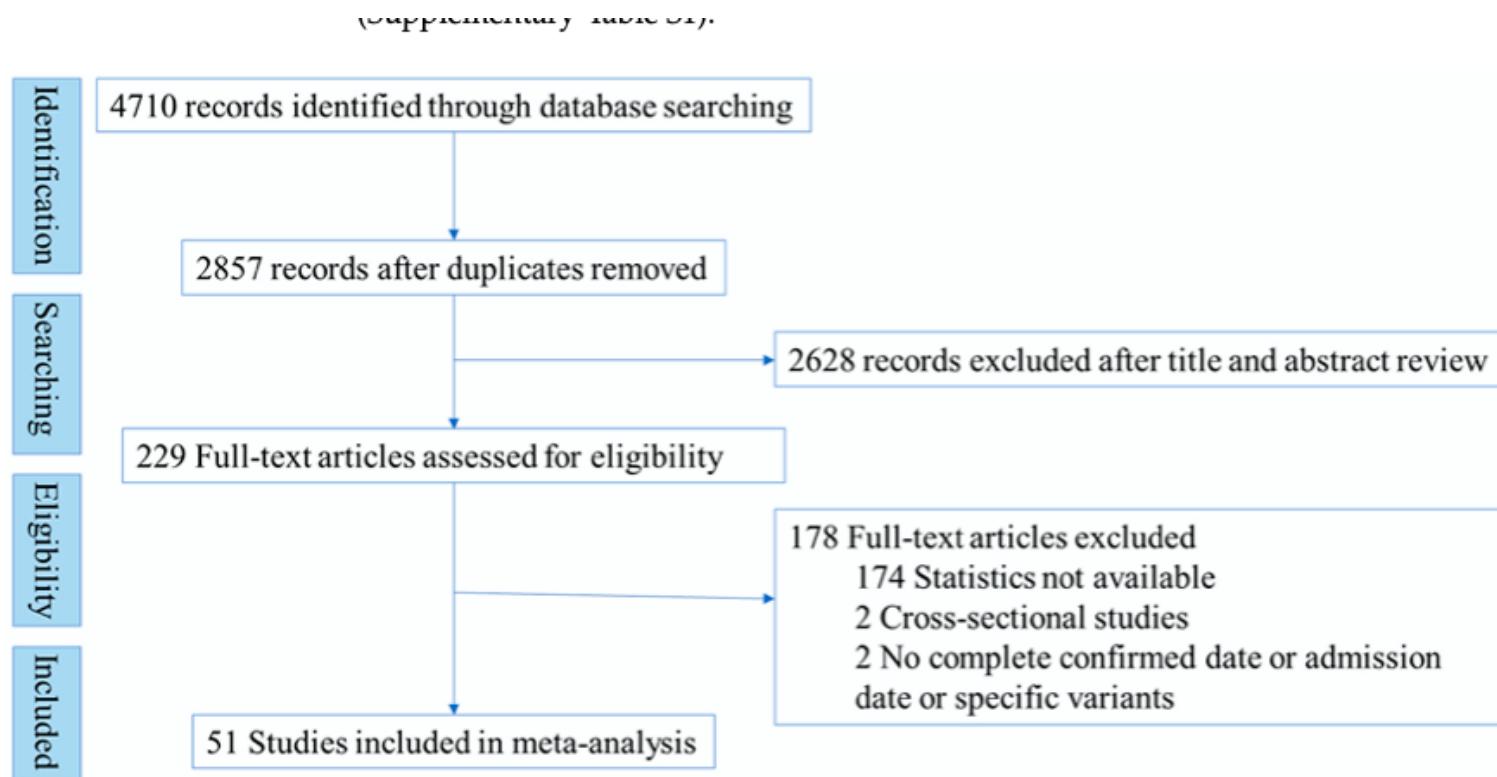


Figure 1. Study flow diagram.

Review

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**Table 1.** Pooled prevalence of long COVID-19 by different strains at 3 months follow-up and above.

Consequences	Number of Studies	Patients n/N	PP (95% CI, %)	p-Value	I <sup>2</sup>
<b>Fatigue</b>					
Alpha	3	494/760	66.1 (42.2, 89.9)	<0.05	98.1%
Beta	1	295/2198	13.4 (12.0, 14.8)	<0.05	-
Delta	1	40/162	24.7 (18.1, 31.3)	<0.05	-
Omicron	2	3457/15,848	18.1 (0.4, 35.8)	<0.05	99.9%
Wild-type	19	1234/6094	26.3 (20.7, 31.9)	<0.05	97.3%
<b>Headache</b>					
Alpha	1	45/324	65.8 (47.7, 83.9)	<0.05	-
Beta	1	8/2198	34.6 (27.2, 41.9)	<0.05	-
Delta	5	32/1516	28.4 (7.9, 49.0)	<0.05	82.1%
Omicron	5	3276/16,157	52.1 (44.0, 60.1)	<0.05	99.9%
Wild-type	1	624/7604	10.0 (7.6, 12.4)	<0.05	95.8%



Review

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Min Du <sup>1</sup>, Yirui Ma <sup>1</sup>, Jie Deng <sup>1</sup>, Min Liu <sup>1</sup> and Jue Liu <sup>1,2,3,4,\*</sup>

**Table 1.** Pooled prevalence of long COVID-19 by different strains at 3 months follow-up and above.

Consequences	Number of Studies	Patients n/N	PP (95% CI, %)	p-Value	I <sup>2</sup>
<b>Olfactory abnormalities</b>					
Omicron	4	2651/16,123	10.2 (-3.2, 23.6)	>0.05	99.8%
Wild-type	4	46/773	7.0 (2.7, 11.4)	<0.05	84.7%
<b>Olfactory loss</b>					
Delta	1	23/1354	1.7 (1.0, 2.4)	<0.05	-
Omicron	1	62/222	27.9 (22.0, 33.8)	<0.05	-
Wild-type	9	418/3725	13.1 (8.5, 17.8)	<0.05	95.1%
<b>Taste abnormalities</b>					
Omicron	4	2030/16,090	8.7 (-2.3, 19.7)	>0.05	99.8%
Wild-type	3	40/703	7.1 (1.0, 13.2)	<0.05	90.9%
<b>Taste loss</b>					
Alpha	1	21/301	7.0 (4.1, 9.9)	<0.05	-
Beta	1	12/2198	0.5 (0.2, 0.9)	<0.05	-
Delta	1	34/1354	2.5 (1.7, 3.3)	<0.05	-
Omicron	1	50/222	22.5 (17.0, 28.0)	<0.05	-
Wild-type	7	328/3515	10.4 (6.1, 14.6)	<0.05	94.4%



Review

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**Table 1.** Pooled prevalence of long COVID-19 by different strains at 3 months follow-up and above.

Consequences	Number of Studies	Patients n/N	PP (95% CI, %)	p-Value	I <sup>2</sup>
<b>Hair loss</b>					
Omicron	2	1572/11,019	18.2 (8.2, 28.2)	<0.05	76.6%
Wild-type	7	209/3018	6.8 (3.4, 10.1)	<0.05	94.2%
<b>Cutaneous or Skin disorders</b>					
Wild-type	6	156/3738	3.9 (2.1, 5.7)	<0.05	88.3%
Rash	5	666/16,548	3.3 (0.4, 6.1)	<0.05	99.3%
Omicron	4	665/16,204	4.2 (0.3, 8.1)	<0.05	99.5%
Wild-type	1	1/344	0.3 (-0.3, 0.9)	>0.05	-
<b>Respiratory symptoms</b>					
<b>Cough</b>					
Alpha	2	87/452	23.7 (2.0, 45.5)	<0.05	95.7%
Delta	1	3/162	1.9 (-0.2, 3.9)	>0.05	-
Gamma	1	34/156	21.8 (15.3, 28.3)	<0.05	-
Omicron	2	1470/15,768	6.8 (-5.1, 18.7)	>0.05	99.9%
Wild-type	21	853/7691	13.4 (10.4, 16.5)	<0.05	97.4%

Review

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Min Du <sup>1</sup>, Yirui Ma <sup>1</sup>, Jie Deng <sup>1</sup>, Min Liu <sup>1</sup>  and Jue Liu <sup>1,2,3,4,\*</sup> 

**Table 1.** Pooled prevalence of long COVID-19 by different strains at 3 months follow-up and above.

Consequences	Number of Studies	Patients n/N	PP (95% CI, %)	p-Value	I <sup>2</sup>
<b>Memory problem</b>					
Omicron	1	1794/11,174	16.1 (15.4, 16.7)	<0.05	-
Wild-type	6	225/1489	17.3 (8.7, 25.9)	<0.05	97.2%
<b>Sleep difficulty</b>					
Alpha	1	151/327	46.2 (40.8, 51.6)	<0.05	-
Delta	2	51/1516	2.5 (0.2, 4.9)	<0.05	82.2%
Omicron	4	3082/16,211	18.7 (1.0, 36.5)	<0.05	99.9%
Wild-type	11	474/3067	24.5 (17.5, 31.5)	<0.05	98.5%
<b>Depression</b>					
Delta	1	1/162	0.6 (-0.6, 1.8)	>0.05	-
Omicron	1	2274/11,149	20.4 (19.6, 21.1)	<0.05	-
Wild-type	9	411/3585	19.7 (10.1, 29.4)	<0.05	99.1%
<b>Anxiety</b>					
Delta	1	1/162	0.6 (-0.6, 1.8)	>0.05	-
Omicron	1	1196/11,174	10.7 (10.1, 11.3)	<0.05	-
Wild-type	11	442/3134	15.3 (9.7, 20.8)	<0.05	96.8%

# Profiling post-COVID-19 condition across different variants of SARS-CoV-2: a prospective longitudinal study in unvaccinated wild-type, unvaccinated alpha-variant, and vaccinated delta-variant populations



Liane S Canas, Frika Molteni, Jie Deng, Carole H Sudre, Benjamin Murray, Eric Kerfont, Michela Antonelli, Khaled Rjoob, Joan Capdevila Pujol, Lorenzo Polidori, Anna May, Marc F Österdahl, Ronan Whiston, Nathan J Cheetham, Vicky Bowyer, Tim D Spector, Alexander Hammers, Emma L Duncan, Sébastien Ourselin, Claire J Steves, Marc Modat



## Summary

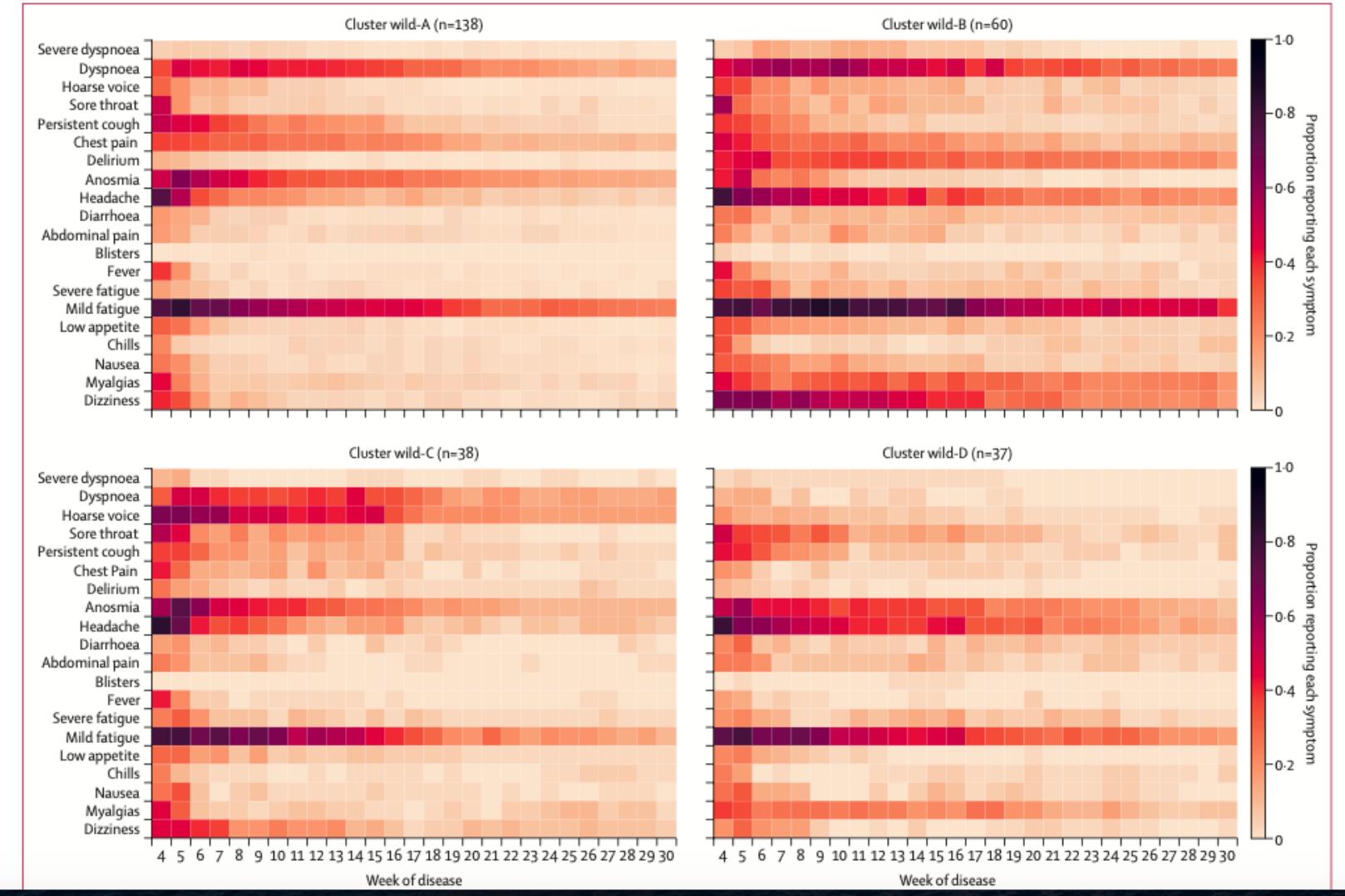
**Background** Self-reported symptom studies rapidly increased understanding of SARS-CoV-2 during the COVID-19 pandemic and enabled monitoring of long-term effects of COVID-19 outside hospital settings. Post-COVID-19 condition presents as heterogeneous profiles, which need characterisation to enable personalised patient care. We aimed to describe post-COVID-19 condition profiles by viral variant and vaccination status.

*Lancet Digit Health* 2023;  
5: e421-34  
Published Online  
May 16, 2023  
<https://doi.org/10.1016/>

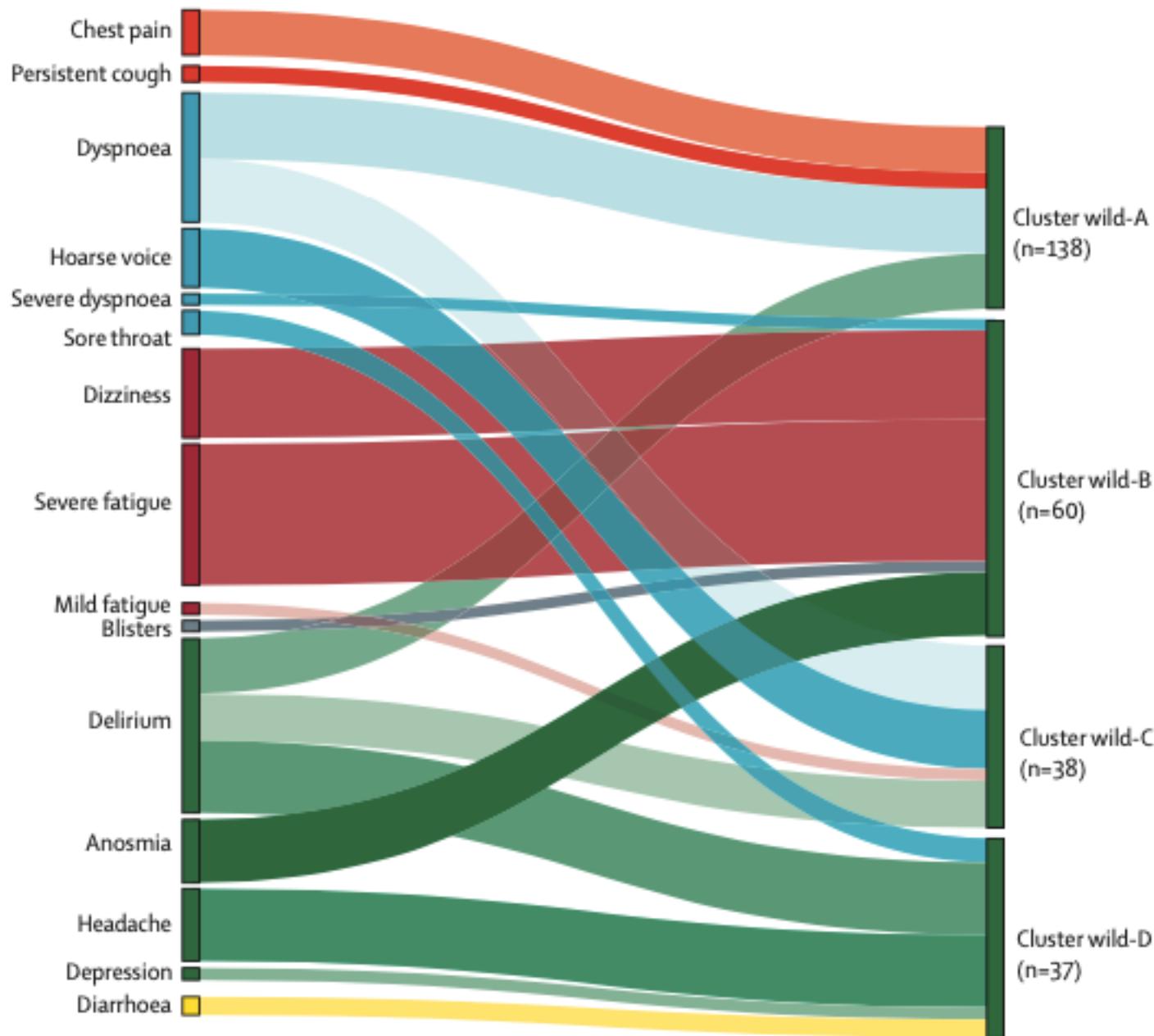
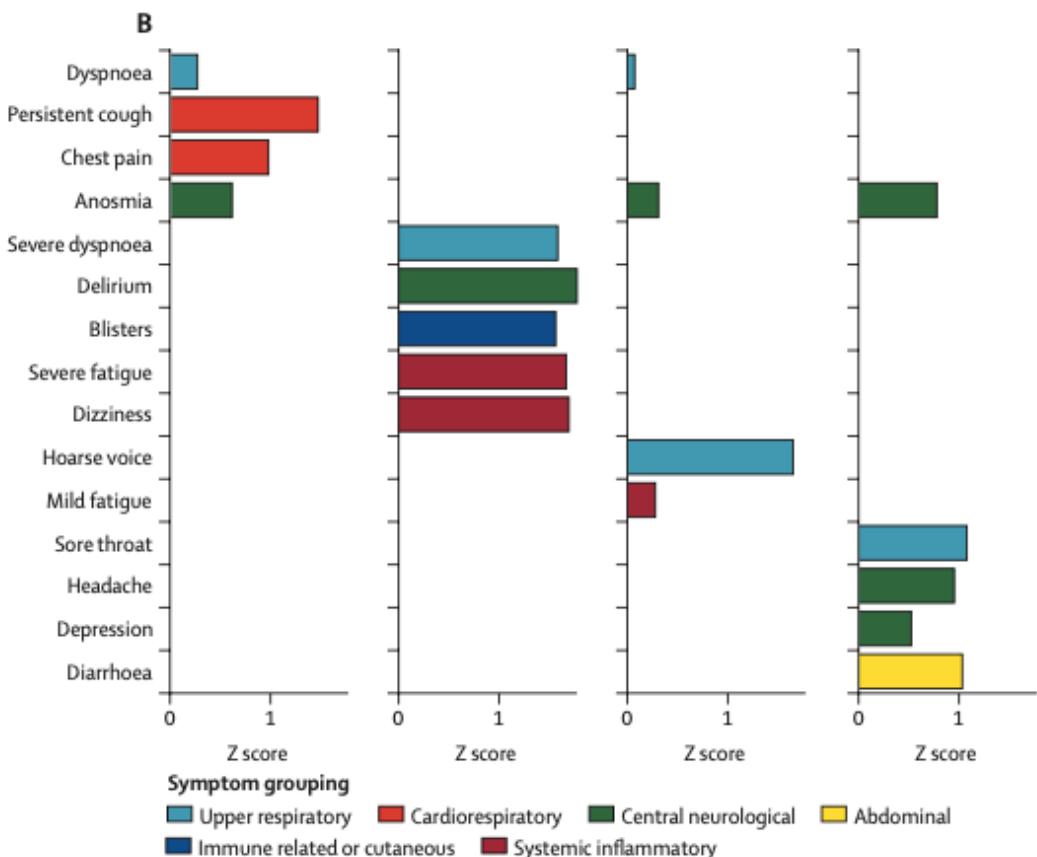
## Procedures

In this study, we used CSS data reported between March 24, 2020, and Dec 8, 2021, and CSS Biobank data gathered between October, 2020, and April, 2021. We defined people with post-COVID-19 condition as those reporting symptoms for longer than 12 weeks after their first positive PCR or lateral flow test within the study period, as per the UK National Institute for Health and

- Follow-up massimo intorno ai 12-16 mesi
- Hanno identificato differenti cluster di sintomi
- Virus wild-type senza vaccino: 4 clusters, più frequente cardio-polmonare
- Virus alfa senza vaccini: 7 clusters
- Virus delta con vaccino: 5 clusters



# Wild type, no vaccino



# Wild type, no vaccino

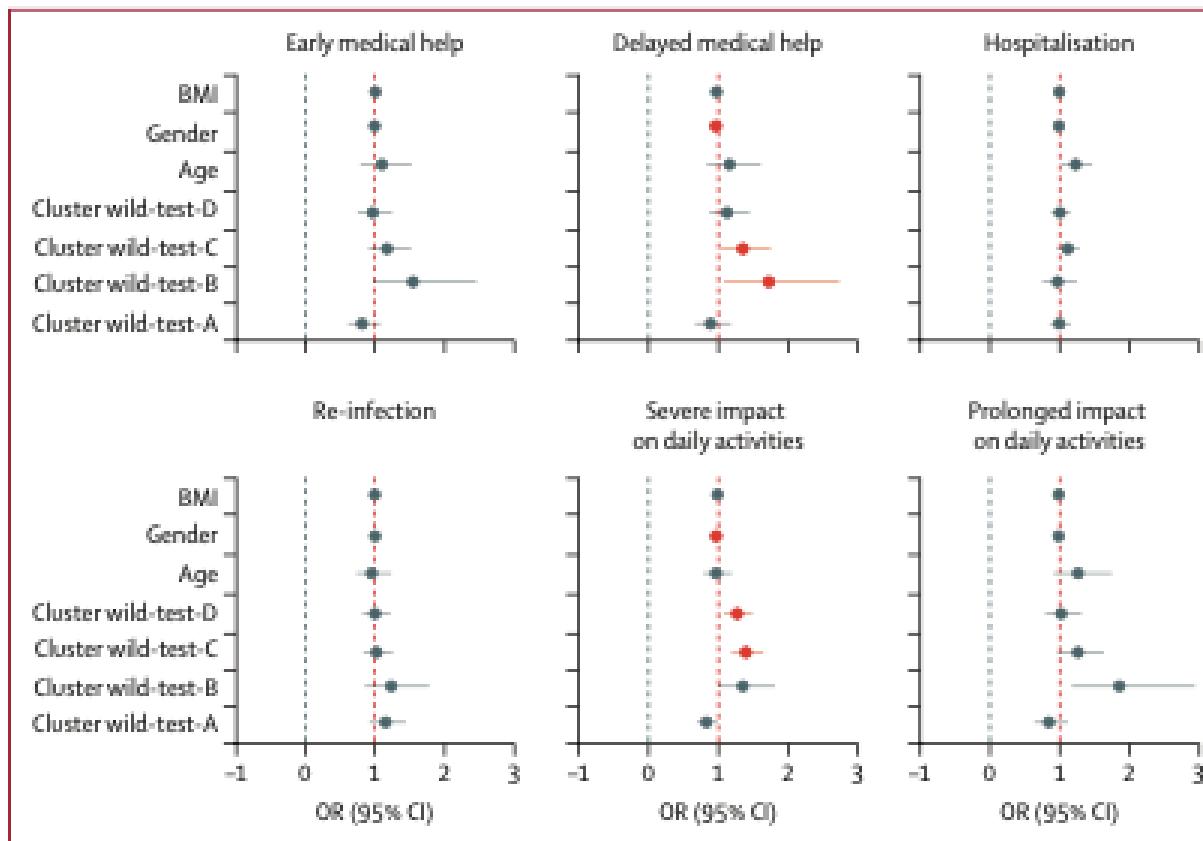
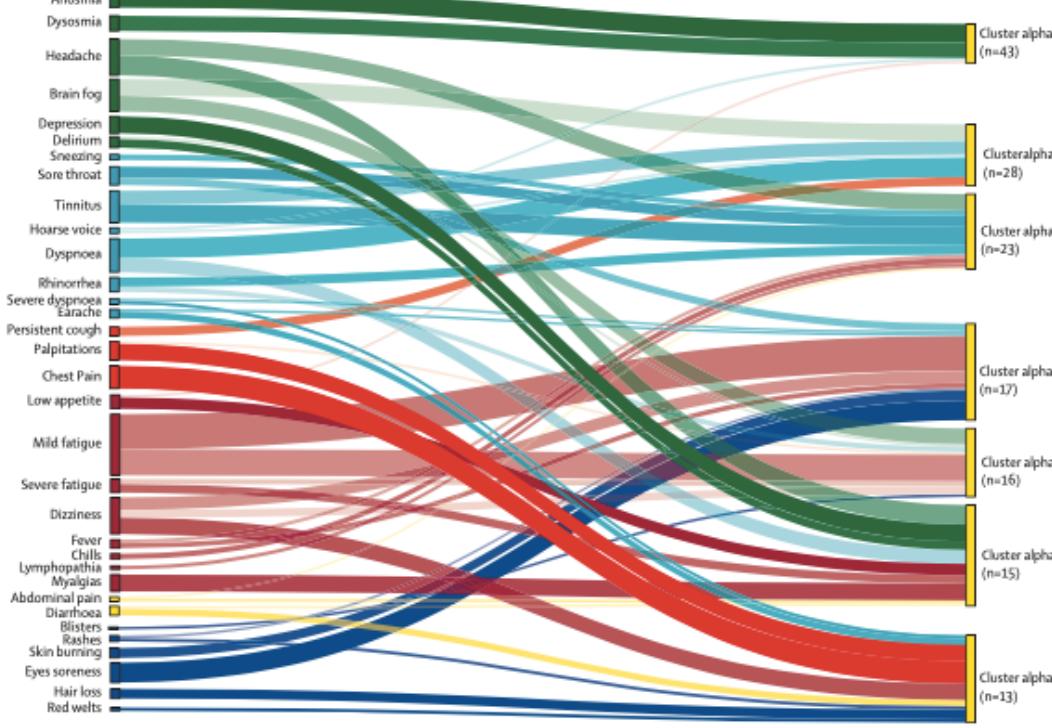


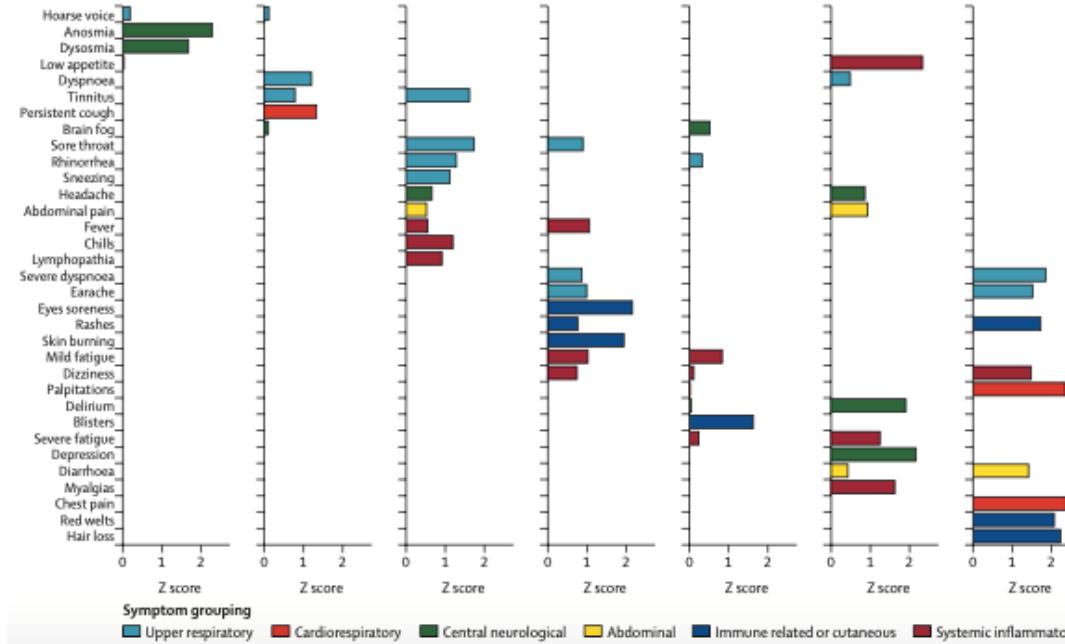
Figure 5: Relation between predicted symptom clusters of post-COVID-19 condition caused by wild-type SARS-CoV-2 and each variable included in the multivariate model

Data points are coloured red to represent significance after false discovery rate correction for  $\alpha=0.05$ . More detail about the questions on which these data were based is in the appendix (p 6).

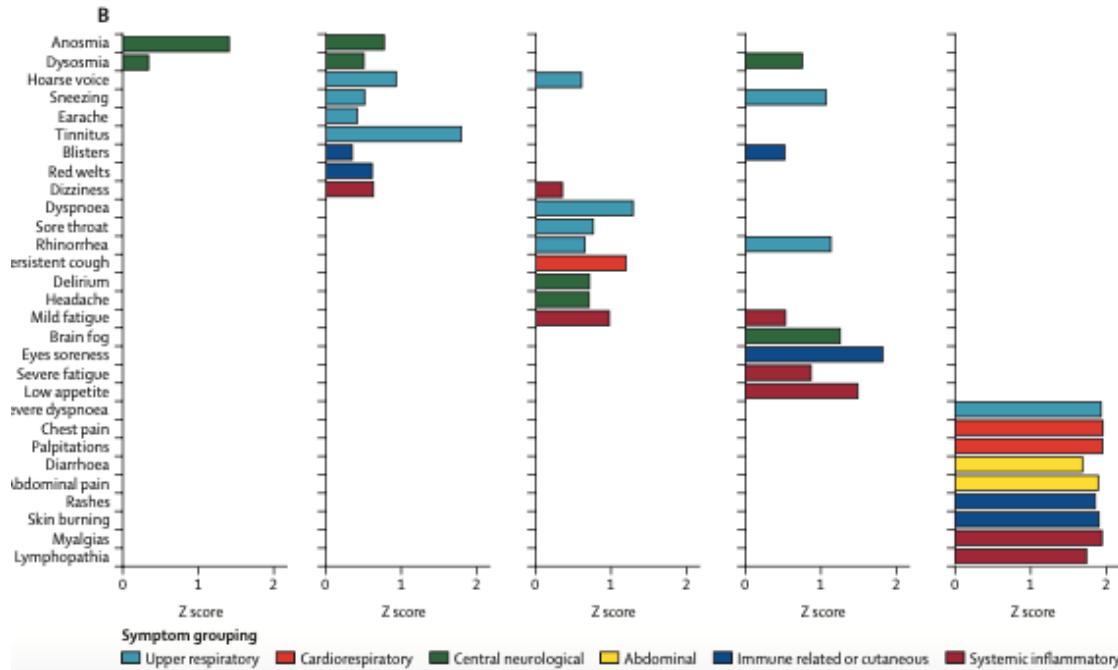
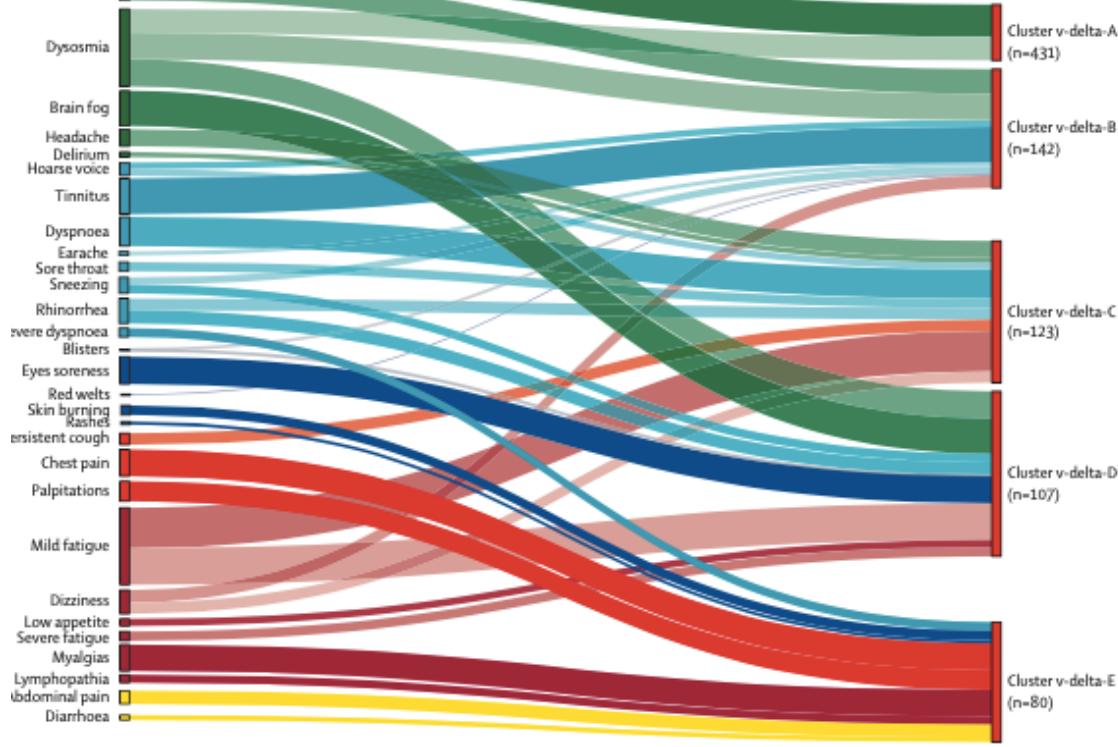
## Virus alfa, no vaccino



B



## Virus delta vaccinati



# Studio Lancet

- Long Covid materia complicatissima
- Necessita di più specialisti
- Organizzazione previdente

# Long COVID

- Malattia riferita, raramente obiettivata
- Definizioni importanti
- Cambia nel tempo, con le varianti virali e con la risposta dell'ospite
- Implementare servizi per la diagnosi e per la cura (coinvolgere differenti specialisti)