Auditorium "A. Comelli"
Palazzo della Regione Autonoma
Friuli Venezia Giulia
via Sabbadini 31, Udine
Martedì 12 dicembre 2023, ore 08.45 - 17.30

RETE CURE SICURE FVG

ASU FC
Azienda sanitaria universitaria Friuli Centrale

REGIONE AUTONOMA FRIULI VENEZIA GIULIA

Seminario

GIORNATA REGIONALE DELLA SICUREZZA E QUALITÀ DELLE CURE 2023

Codice evento ASUFC_23603

EFFETTI DEL LONG-COVID IN MEDICINA PRIMARIA

Stefano Celotto - SIMG, Udine

SIMG SOCIETÀ ITALIANA DI MEDICINA GENERALE E DELLE CURE PRIMARIE

DISCLOSURES

In qualità di RELATORE, ai sensi dell'art.76 sul Conflitto di Interessi dell'Accordo StatoRegioni del 2 febbraio 2017, dichiaro che negli ultimi due anni ho avuto i seguenti rapporti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario:

Angelini, Pfizer

Dichiaro, inoltre, che i contenuti formativi esposti sono indipendenti da interessi commerciali.

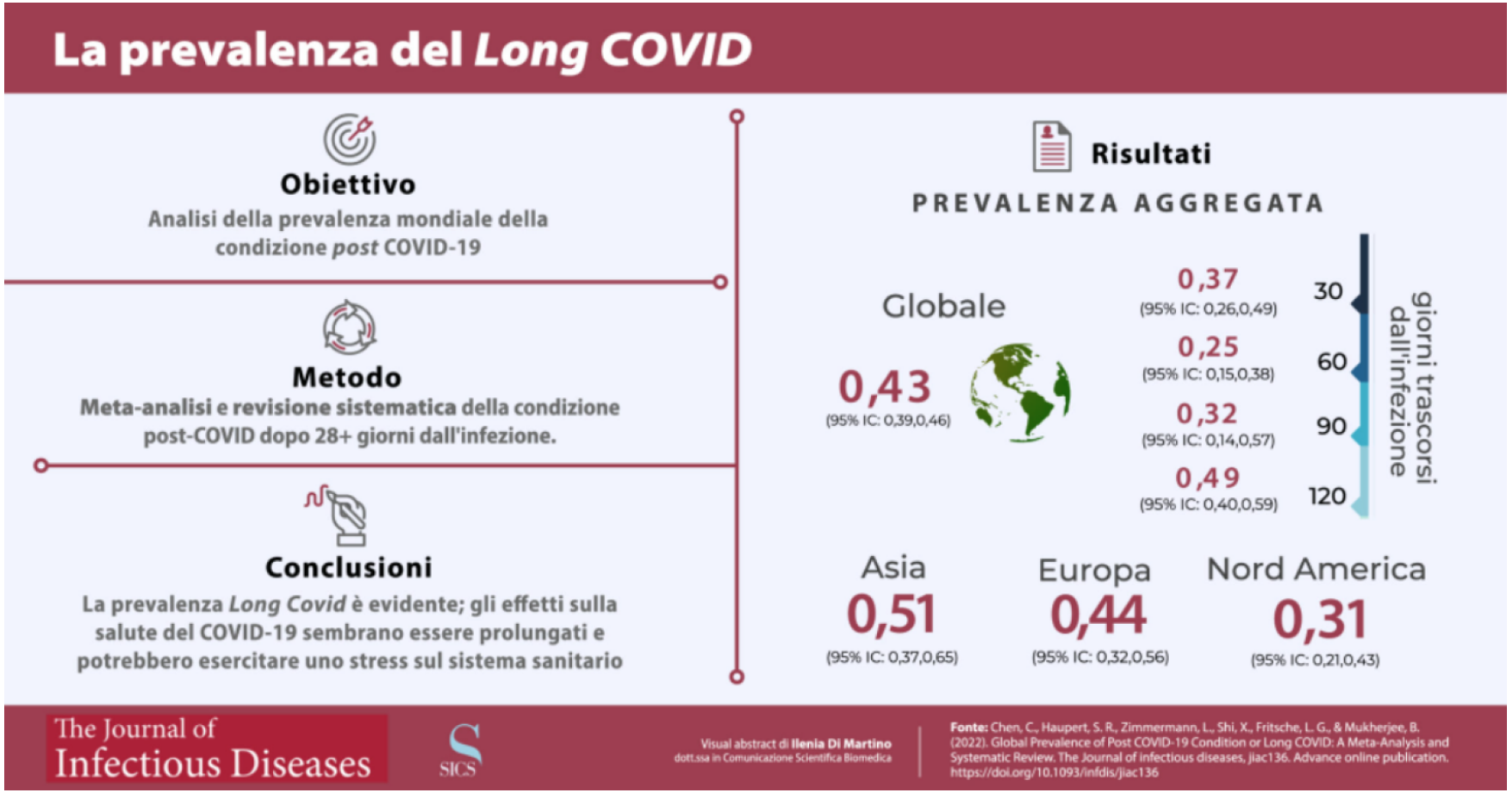
LONG COVID: DEFINIZIONI

- Malattia COVID-19 acuta: segni e sintomi attribuibili alla COVID-19 di durata fino a 4 settimane

LONG COVID

- Malattia COVID-19 sintomatica persistente: segni e sintomi attribuibili alla COVID-19 di durata compresa tra 4 e 12 settimane
- Sindrome post-COVID-19: segni e sintomi sviluppati durante o dopo un'infezione compatibile con la COVID-19, presenti per più di 12 settimane e non spiegabili con diagnosi alternative.

PREVALENZA


La prevalenza del Long COVID
Obiettivo
Analisi della prevalenza mondiale della condizione post COVID-19
Metodo
Meta-analisi e revisione sistematica della condizione post-COVID dopo 28+ giorni dall'infezione.
Conclusioni
La prevalenza Long Covid è evidente; gli effetti sulla salute del COVID-19 sembrano essere prolungati e potrebbero esercitare uno stress sul sistema sanitario
Risultati
PREVALENZA AGGREGATA
Globale
0,43
(95% IC: 0,39,0,46)
0,37
(95% IC: 0,26,0,49)
0,25
(95% IC: 0,15,0,38)
0,32
(95% IC: 0,14,0,57)
0,49
(95% IC: 0,40,0,59)
30
60
90
120
giorni trascorsi dall'infezione
Asia
0,51
(95% IC: 0,37,0,65)
Europa
0,44
(95% IC: 0,32,0,56)
Nord America
0,31
(95% IC: 0,21,0,43)
The Journal of Infectious Diseases
SIGS
Visual abstract di Ilenia Di Martino
dott.ssa in Comunicazione Scientifica Biomedica
Fonte: Chen, C., Haupert, S. R., Zimmermann, L., Shi, X., Fritsche, L. G., & Mukherjee, B. (2022). Global Prevalence of Post COVID-19 Condition or Long COVID: A Meta-Analysis and Systematic Review. The Journal of infectious diseases, jiac136. Advance online publication. https://doi.org/10.1093/infdis/jiac136

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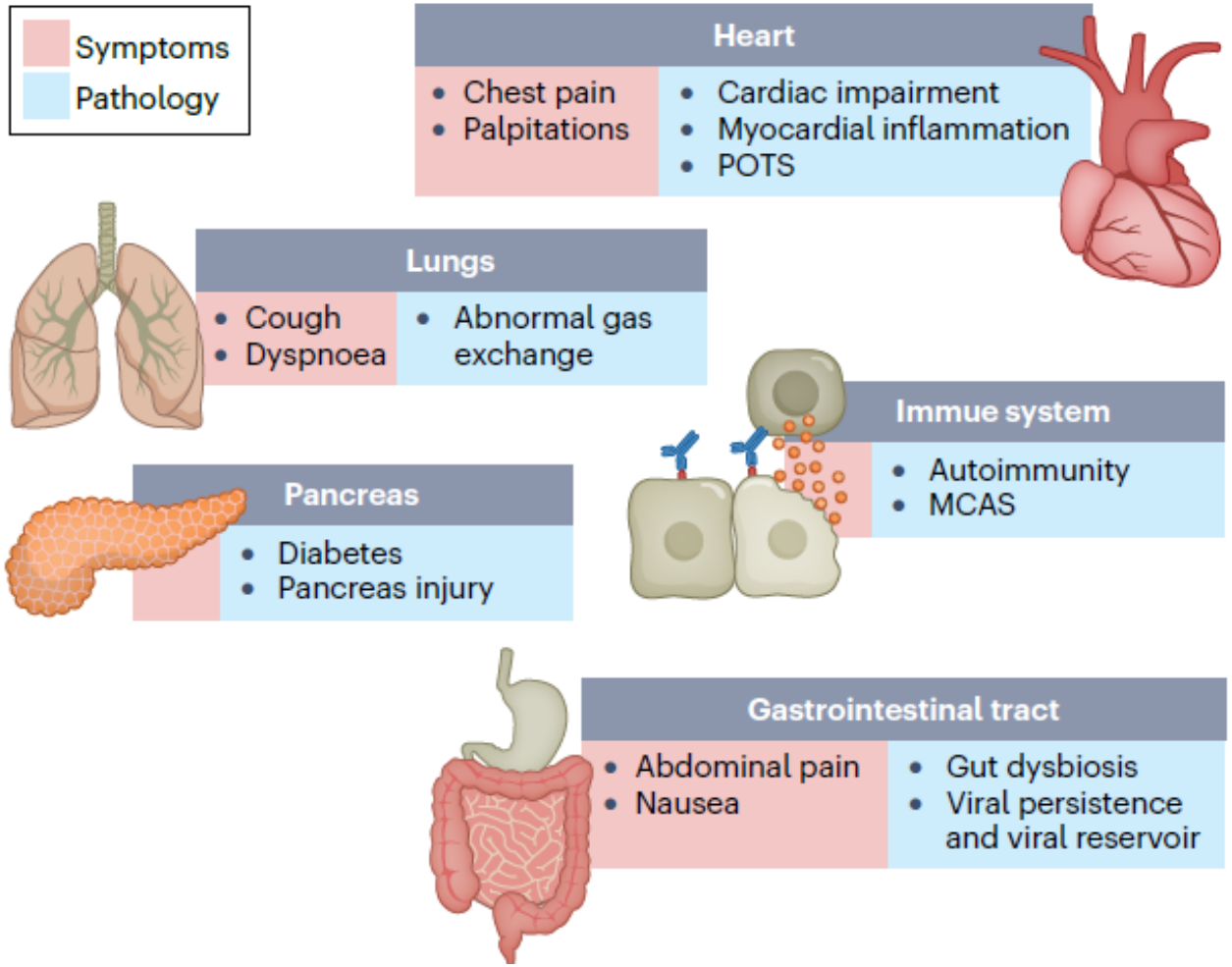

nature reviews microbiology

https://doi.org/10.1038/s41579-022-00846-2

Review article

Check for updates

Long COVID: major findings, mechanisms and recommendations

Hannah E. Davis[1], Lisa McCorkell[2], Julia Moore Vogel[3] & Eric J. Topol[3]

POTS: Postural tachycardia syndrome
MCAS: Mast Cell Activation Syndrome

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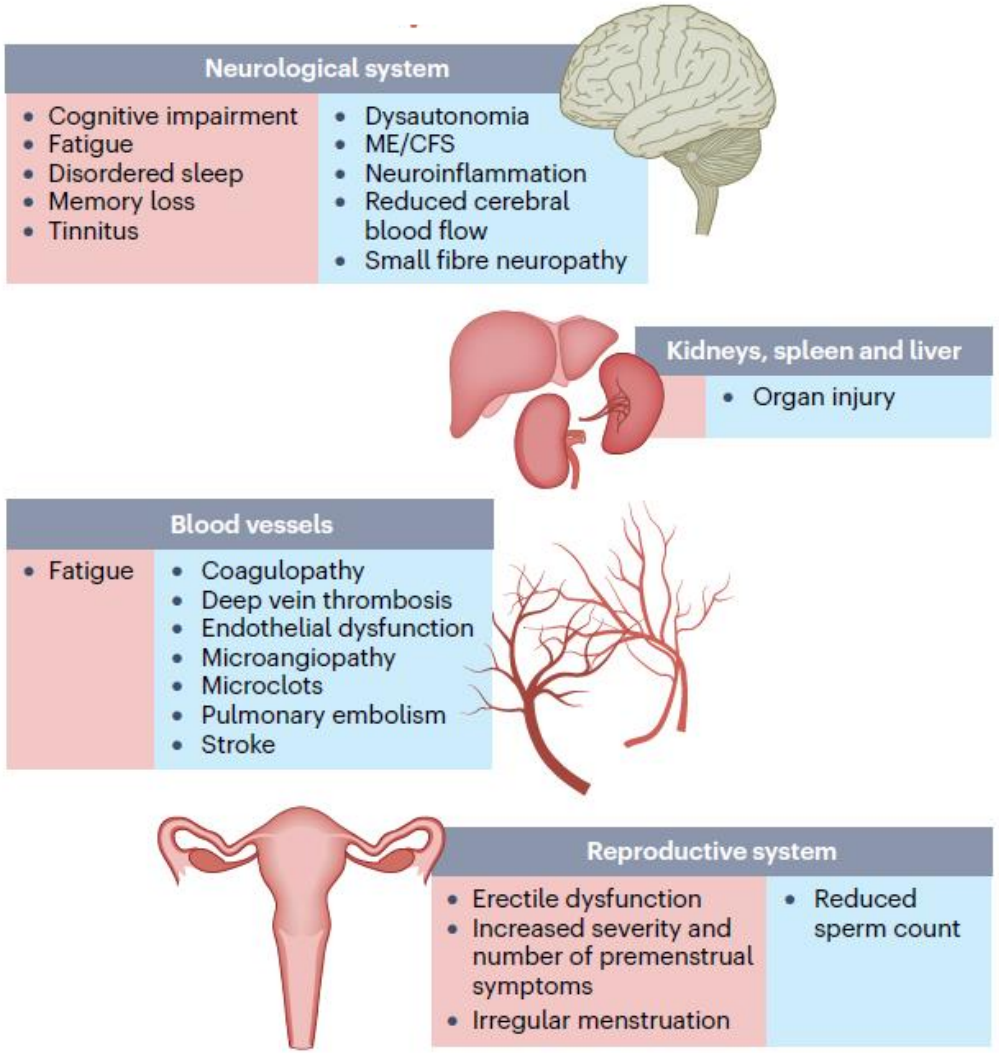

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Long COVID: major findings, mechanisms and recommendations

Hannah E. Davis[1], Lisa McCorkell[2], Julia Moore Vogel[3] & Eric J. Topol[3]

ME/CFS: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

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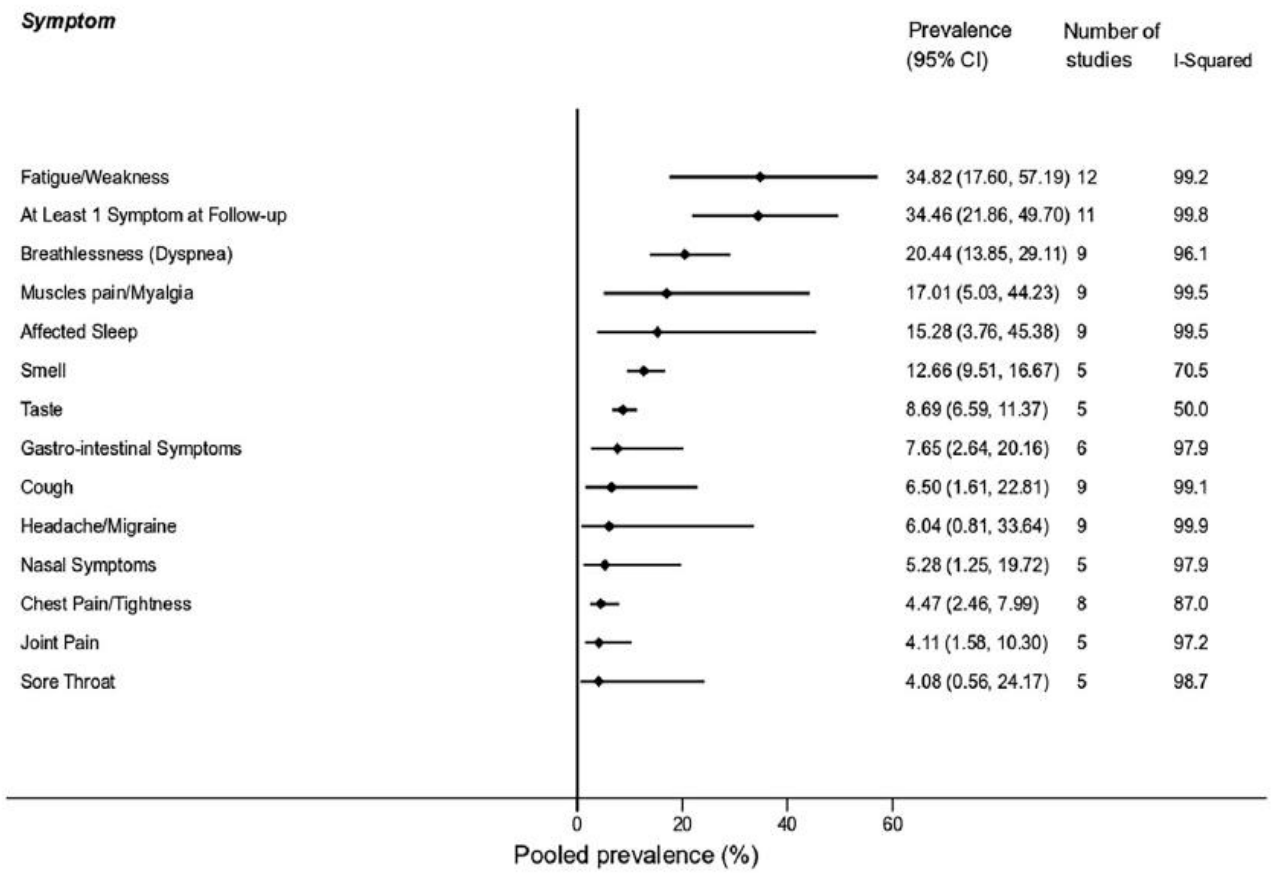

Fig. 3: Prevalence of symptoms (ranked) in the non-hospitalised population. In total 14 symptoms were reported.

The prevalence and long-term health effects of Long Covid among hospitalised and non-hospitalised populations: a systematic review and meta-analysis

Lauren L. O'Mahoney,[a] Ash Routen,[a] Clare Gillies,[a,b] Winifred Ekezie,[a] Anneka Welford,[a] Alexa Zhang,[c] Urvi Karamchandani,[d] Nikita Simms-Williams,[e] Shabana Cassambai,[a] Ashkon Ardavani,[a] Thomas J. Wilkinson,[a] Grace Hawthorne,[a] Ffion Curtis,[a] Andrew P. Kingsnorth,[a] Abdullah Almaqhawi,[f] Thomas Ward,[g] Daniel Ayoubkhani,[b,h] Amitava Banerjee,[i,j] Melanie Calvert,[e,k,l] Roz Shafran,[c] Terence Stephenson,[c] Jonathan Sterne,[m] Helen Ward,[d] Rachael A. Evans,[g,n] Francesco Zaccardi,[a,b] Shaney Wright,[o] and Kamlesh Khunti[a,*]

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SINTOMI

www.nature.com/scientificreports

scientific reports

OPEN

Long COVID prevalence and impact on quality of life 2 years after acute COVID-19

Yoonjung Kim, Sohyun Bae, Hyun-Ha Chang & Shin-Woo Kim

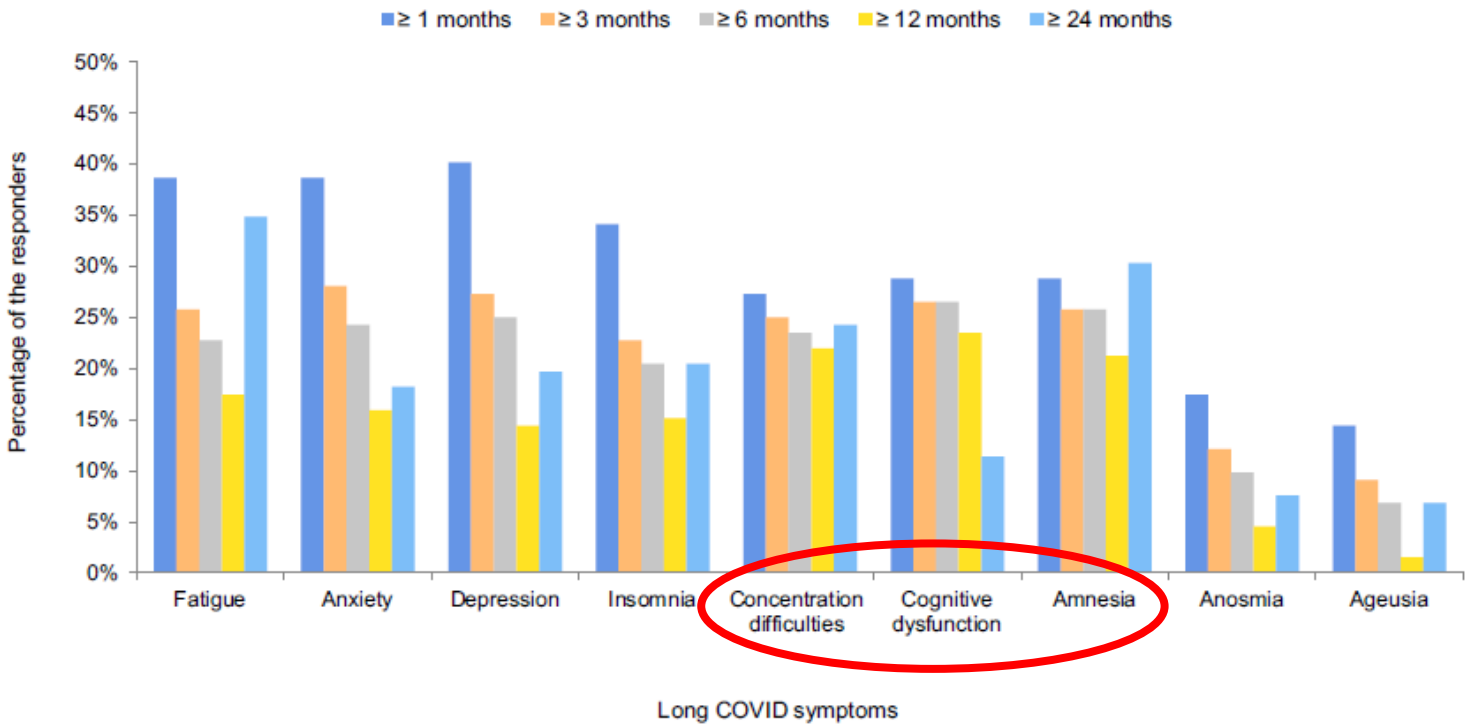

Figure 2. Duration of key long COVID symptoms according to the symptom persistent period at 1, 3, 6, 12, and 24 months after acute COVID-19.

SIMG SOCIETÀ ITALIANA DI MEDICINA GENERALE E DELLE CURE PRIMARIE

SINTOMI

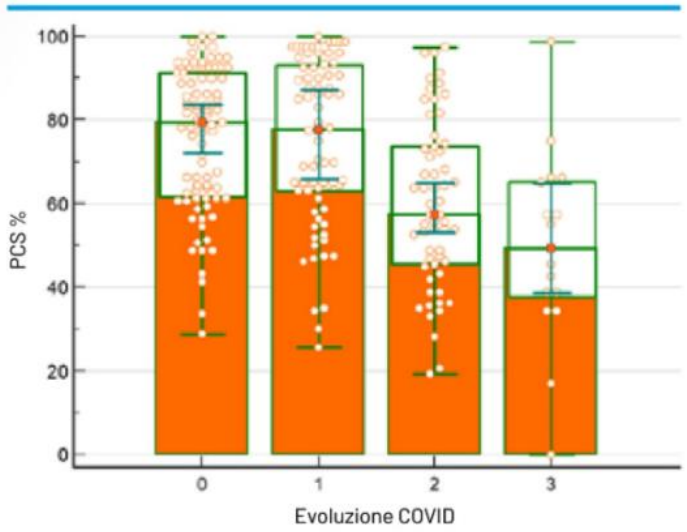

Figura 1 - Distribuzione dei valori di salute fisica (PCS) nei soggetti di controllo e nei pazienti suddivisi per grado di severità di malattia. 0: controlli (n=83), 1: pazienti paucisintomatici a domicilio (n=74), 2: pazienti a domicilio con sintomatologia severa (n=58), 3: pazienti ricoverati in ospedale (n=17). Analisi statistica: ANOVA non parametrica (test di Kruskal-Wallis) p<0.0001, per trend lineare p<0.0001; 0 vs 2/3 p<0.05, 1 vs 2/3 p<0.05

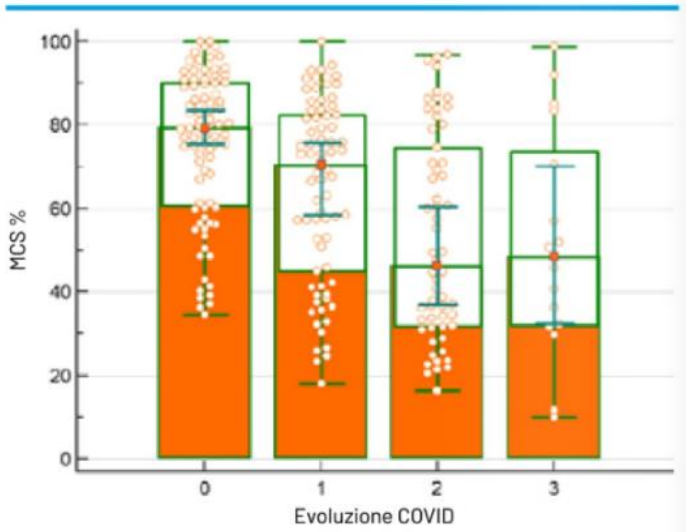

Figura 2 - Distribuzione dei valori di salute mentale (MCS) nei soggetti di controllo e nei pazienti suddivisi per grado di severità di malattia. 0: controlli (n=83), 1: pazienti paucisintomatici a domicilio (n=74), 2: pazienti a domicilio con sintomatologia severa (n=58), 3: pazienti ricoverati in ospedale (n=17). Analisi statistica: ANOVA non parametrica (test di Kruskal-Wallis) p<0.0001, per trend lineare p<0.0001; 0 vs 1/2/3 p<0.05, 1 vs 2 p<0.05

ORIGINAL ARTICLE

Compromessa qualità della vita e disagio psichico perduranti dopo guarigione da Covid-19

Compromised quality of life and continuing mental discomfort after recovery from Covid-19

Carlo Fabris[1], Pamela Marcuzzi[1], Lucia Casatta[1], Denise Sief[1], Alberto Fragali[2], Luigi Canciani[3]

[1]Medico di Medicina Generale - Distretto di Udine; [2]Direttore SOC Area Adulti, Anziani e Cure Primarie - Distretto di Udine; [3]Direttore - Distretto di Udine - Azienda Sanitaria Universitaria Friuli Centrale

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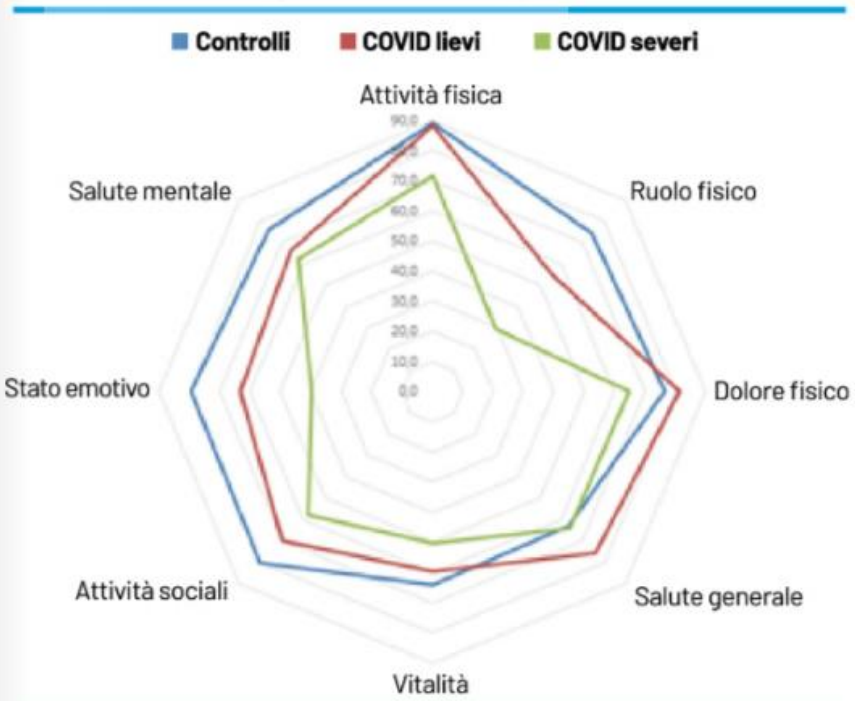

Figura 3 - Grafico radar raffigurante le medie degli otto componenti dello score SF-36 (attività fisica, ruolo e salute fisica, dolore fisico, salute in generale, vitalità, attività sociali, ruolo e stato emotivo, salute mentale) nei soggetti di controllo (n=83), nei pazienti COVId-19 lievi a domicilio (n=74) e nei pazienti con sintomi severi a domicilio-ricoverati in ospedale (n=75)

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SIMG SOCIETÀ ITALIANA DI MEDICINA GENERALE E DELLE CURE PRIMARIE

FATTORI DI RISCHIO

JAMA Network Open

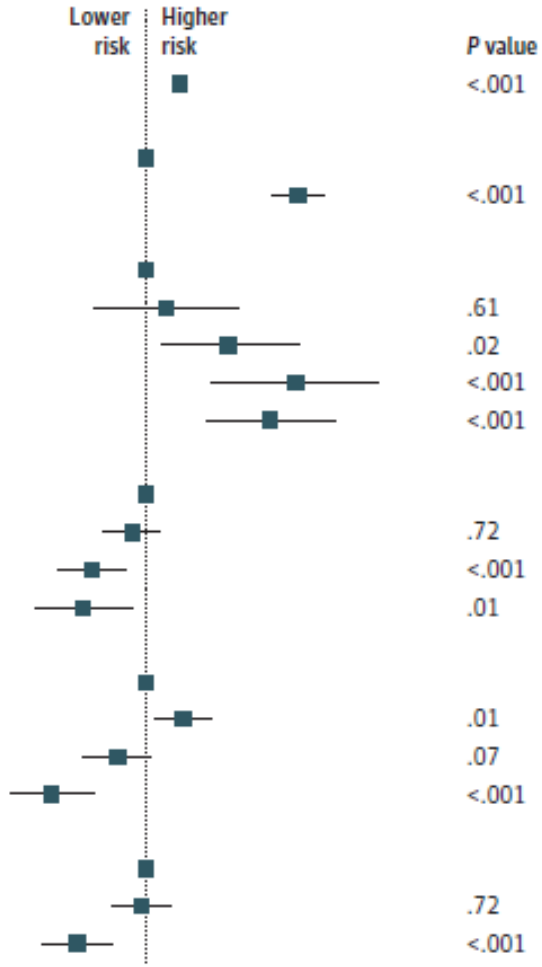
Original Investigation | Infectious Diseases

Prevalence and Correlates of Long COVID Symptoms Among US Adults

Roy H. Perlis, MD, MSc; Mauricio Santillana, PhD; Katherine Ognyanova, PhD; Alauna Safarpour, PhD; Kristin Lunz Trujillo, PhD; Matthew D. Simonson, PhD; Jon Green, PhD; Alexi Quintana, BA; James Druckman, PhD; Matthew A. Baum, PhD; David Lazer, PhD

Figure 1. Logistic Regression Model for Development of Long COVID Among Individuals Testing Positive for COVID-19 by Antigen Test or Polymerase Chain Reaction Test

Variable	No. of respondents	Odds ratio (95% CI)	P value
Age	16091	1.15 (1.12-1.19)	<.001
Gender			
Male	6016	1 [Reference]	
Female	10075	1.91 (1.73-2.13)	<.001
Race			
Asian	817	1 [Reference]	
Black	1546	1.08 (0.80-1.48)	.61
Hispanic	1826	1.42 (1.07-1.91)	.02
Other category	477	1.89 (1.33-2.69)	<.001
White	11425	1.70 (1.32-2.23)	<.001
Income, $			
<25000	3735	1 [Reference]	
25000-74999	6507	0.94 (0.84-1.05)	.72
75000-149999	4404	0.79 (0.69-0.91)	<.001
≥150000	1445	0.76 (0.62-0.93)	.01
Education			
High school or less	3969	1 [Reference]	
Some college	5309	1.17 (1.04-1.31)	.01
Bachelor's degree	4100	0.88 (0.77-1.01)	.07
Graduate degree	2713	0.67 (0.56-0.79)	<.001
Urbanicity			
Rural	2625	1 [Reference]	
Suburban	9044	0.98 (0.87-1.10)	.72
Urban	4422	0.74 (0.64-0.86)	<.001



SIMG SOCIETÀ ITALIANA DI MEDICINA GENERALE E DELLE CURE PRIMARIE

DIFFERENZE DI GENERE

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Original Investigation | Infectious Diseases

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Table 2. Frequency of Current Long COVID Symptoms by Gender

	Individuals, No. (%)			
Symptom	Male (n = 564)	Female (n = 1795)	Total (N = 2359)	*P* value
Shortness of breath	230 (40.8)	707 (39.4)	937 (39.7)	.56
Exercise intolerance	161 (28.5)	524 (29.2)	685 (29.0)	.77
Fatigue	267 (47.3)	965 (53.8)	1232 (52.2)	.008
Headache	161 (28.5)	632 (35.2)	793 (33.6)	.003
Loss of smell	199 (35.3)	832 (46.4)	1031 (43.7)	<.001
Brain fog	164 (29.1)	788 (43.9)	952 (40.4)	<.001
Poor memory	120 (21.3)	544 (30.3)	664 (28.1)	<.001
Either brain fog or poor memory	205 (36.3)	874 (48.7)	1079 (45.7)	<.001
Dizziness	92 (16.3)	393 (21.9)	485 (20.6)	.004
Depressed mood	116 (20.6)	434 (24.2)	550 (23.3)	.08
Anxious mood	126 (22.3)	552 (30.8)	678 (28.7)	<.001
Sleep disruption	127 (22.5)	581 (32.4)	708 (30.0)	<.001
Symptom count, mean (SD), No.	3.1 (2.5)	3.9 (2.8)	3.7 (2.7)	<.001

HEALTH SEARCH

Period covered: 2000-2021

~800 GPs, covering 2.1% of the Italian adult population:

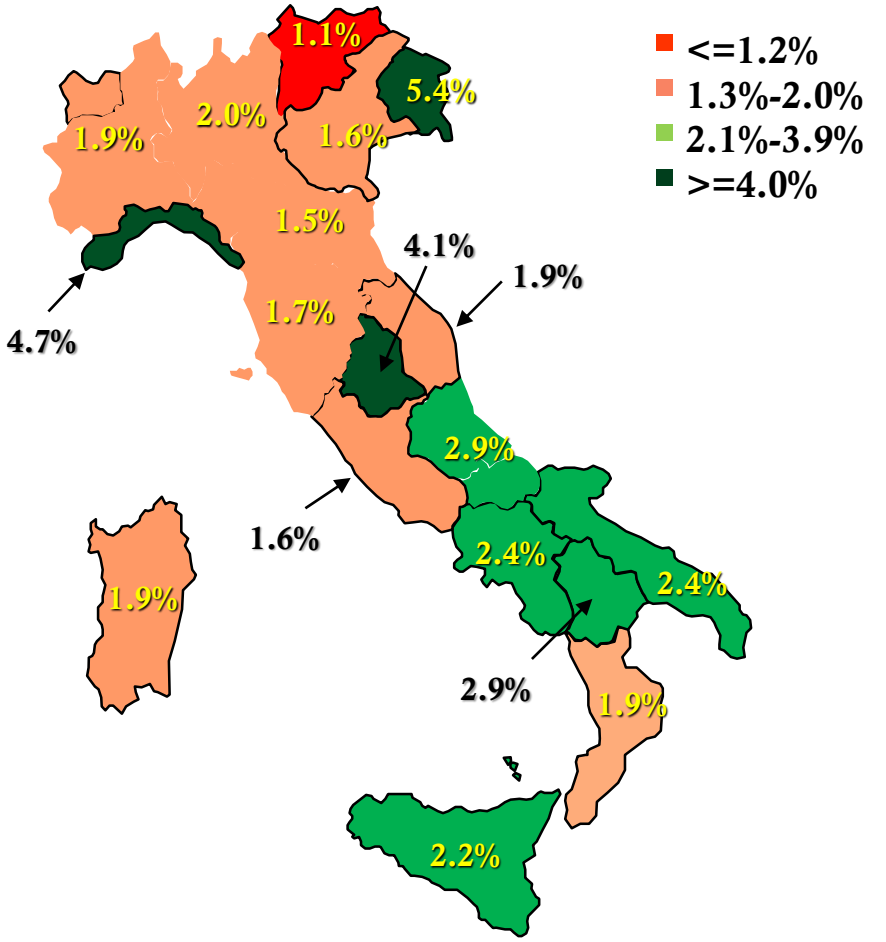
1,6 millions patients (16M PYs)

28 millions diagnoses

330 millions diagnostic procedures

220 millions drug prescriptions

mean follow-up: about 14 years



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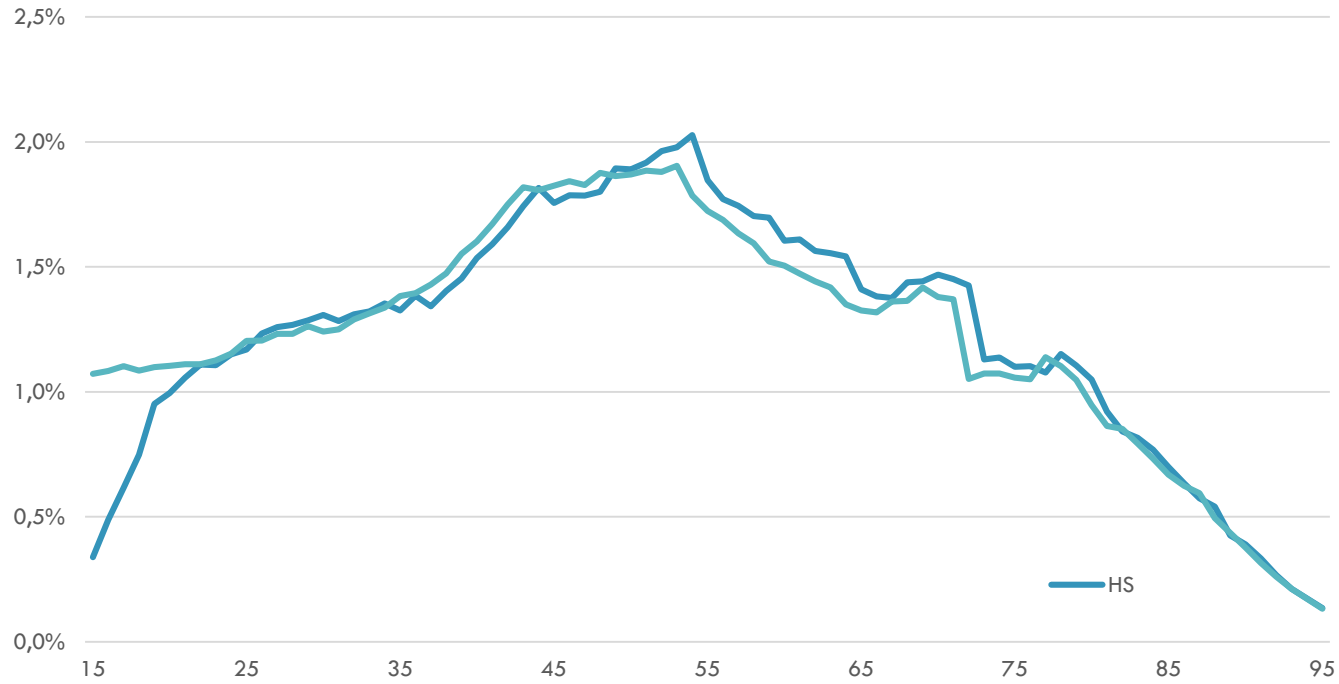
HEALTH SEARCH

Sovrapponibilità con la popolazione generale

HEALTH SEARCH vs. ISTAT (Liste Anagrafiche Comunali: anno 2018

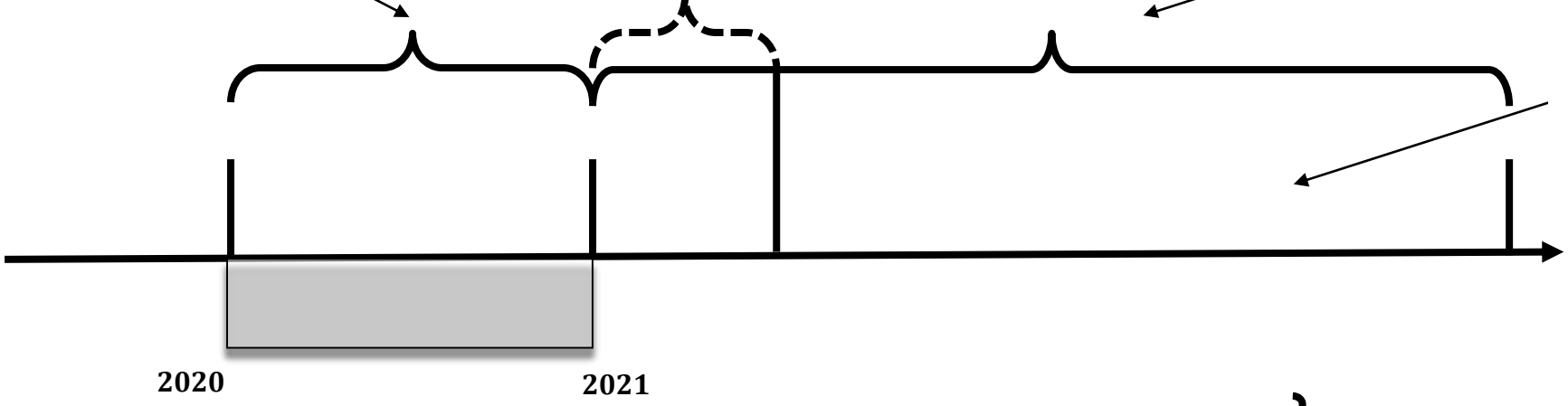


HEALTH SEARCH

T0: ENTRY DATE
Diagnosi di SARS-CoV-2 successivamente neg (T0)

T0-T1: FOLLOW-UP (fino a sei mesi)

almeno 28 giorni



Identificazione eventi riconducibili a long COVID

Definizione dei criteri di matching

Sesso, età e score di co-morbosità
T0-T1: stessa durata del follow-up
T0: stessa data assegnata ai controlli

SIMG SOCIETÀ ITALIANA DI MEDICINA GENERALE E DELLE CURE PRIMARIE

HEALTH SEARCH

Binomial-Gamma distribution

	N=19258		N=52124		N=27588		N=11820	
	I Ondata		II Ondata		III Ondata		VI Ondata	
	IRR (Crude)	(I.C. 95%)	IRR (Crude)	(I.C. 95%)	IRR (Crude)	(I.C. 95%)	IRR (Crude)	(I.C. 95%)
COVID-neg	Rif		Rif		Rif		Rif	
COVID-pos	1,45	[1.36,1.55]	1,28	[1.23,1.33]	1,27	[1.2,1.35]	1,37	[1.18,1.59]

Binomial-Poisson distribution

	N=19258		N=52124		N=27588		N=11820	
	I Ondata		II Ondata		III Ondata		VI Ondata	
	IRR (Crude)	(I.C. 95%)	IRR (Crude)	(I.C. 95%)	IRR (Crude)	(I.C. 95%)	IRR (Crude)	(I.C. 95%)
COVID-neg	Rif		Rif		Rif		Rif	
COVID-pos	2,10	[1.89,2.34]	1,55	[1.46,1.65]	1,54	[1.41,1.68]	1,84	[1.47,2.31]

HEALTH SEARCH

Binomial-Gamma distribution	I Ondata		II Ondata		III Ondata		IV Ondata	
	IRR	(I.C. 95%)	IRR	(I.C. 95%)	IRR	(I.C. 95%)	IRR	(I.C. 95%)
DANNO RENALE								
COVID-neg	Rif		Rif		Rif		Rif	
COVID-pos	1,21	[1.08,1.35]	1,14	[1.06,1.21]	1,16	[1.06,1.27]	1,26	[0.96,1.66]

	I Ondata		II Ondata		III Ondata		IV Ondata	
	IRR	(I.C. 95%)	IRR	(I.C. 95%)	IRR	(I.C. 95%)	IRR	(I.C. 95%)
FEBBRE								
COVID-neg	Rif		Rif		Rif		Rif	
COVID-pos	1,91	[1.43,2.56]	1,58	[1.37,1.82]	1,38	[1.12,1.71]	1,28	[0.83,1.99]

	I Ondata		II Ondata		III Ondata		IV Ondata	
	IRR	(I.C. 95%)	IRR	(I.C. 95%)	IRR	(I.C. 95%)	IRR	(I.C. 95%)
ANSIA/DEPRESSIONE								
COVID-neg	Rif		Rif		Rif		Rif	
COVID-pos	1,52	[1.23,1.88]	1,35	[1.19,1.52]	1,35	[1.19,1.52]	1,29	[0.72,2.31]

COSA PUO' FARE IL TEAM DI CURE PRIMARIE

PRACTICE POINTER

Long covid—an update for primary care

Trisha Greenhalgh,[1] Manoj Sivan,[2] Brendan Delaney,[3] Rachael Evans,[4] Ruairidh Milne[5]

What can primary care teams do?

Diagnosis

- Hear the patient's story
- Diagnose and code 'post covid-19 syndrome'
- Assess for postural tachycardia
- Exclude other diagnoses

Prognosis

- Share uncertainties
- Help set realistic goals
- Monitor progress
- Sickness certification
- Support return to work

Management

- Whole person care and wellbeing
- Manage symptoms and comorbidities
- Encourage self-management

Symptomatic relief, such as antihistamines for urticaria

Offer covid-19 vaccination if not fully up to date

Investigations

Guided by history and examination

POSSIBILI TERAPIE?

nature reviews microbiology

https://doi.org/10.1038/s41579-022-00846-2

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Long COVID: major findings, mechanisms and recommendations

Hannah E. Davis[1], Lisa McCorkell[2], Julia Moore Vogel[3] & Eric J. Topol[3]

Autoimmunity	BC007	Long COVID case report	Neutralizes G protein-coupled receptor autoantibodies
Abnormal clotting	Anticoagulants	Long COVID pilot study	Additional trials in progress
Abnormal clotting	Apheresis	ME/CFS literature, long COVID pilot study	–
Viral persistence and antivirals (COVID-19)	Paxlovid	Long COVID case reports	No active trials, despite strong evidence for viral persistence
Viral persistence and antivirals (reactivations such as of EBV, HCMV and VZV)	Valaciclovir, famciclovir, valganciclovir and other antivirals	ME/CFS literature	–
Endothelial dysfunction	Sulodexide	Long COVID pilot study	–
Gastrointestinal symptoms	Probiotics	Long COVID pilot study	Resolved gastrointestinal and other symptoms
Dysautonomia	Stellate ganglion block	Long COVID case report	Effects may wane over time and require repeated procedures
Endothelial function, microcirculation, inflammatory markers and oxidative stress	Pycnogenol	COVID-19 pilot study	–
MCAS	H_1 and H_2 antihistamines, particularly famotidine	Long COVID case reports, MCAS literature	Expected to treat symptoms, not underlying mechanism
Autonomic dysfunction	Transcutaneous vagal stimulation	Long COVID pilot study	–

EBV, Epstein–Barr virus; HCMV, human cytomegalovirus; MCAS, mast cell activation syndrome; ME/CFS, myalgic encephalomyelitis/chronic fatigue syndrome; POTS, postural orthostatic tachycardia syndrome; VZV, varicella zoster virus.

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Review article

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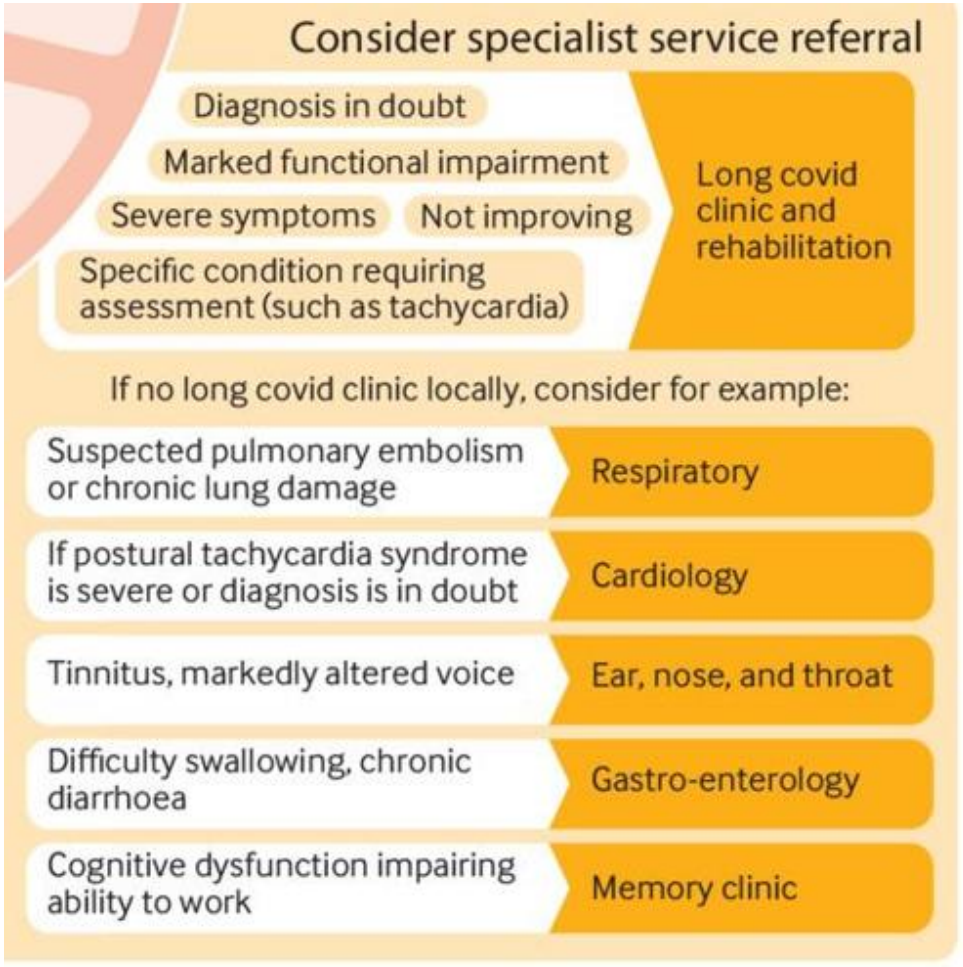
Long COVID: major findings, mechanisms and recommendations

Hannah E. Davis[1], Lisa McCorkell[2], Julia Moore Vogel[3] & Eric J. Topol[3]

Symptoms and/or biological mechanism	Treatments	Supporting evidence	Comments
Postexertional malaise	Pacing	ME/CFS literature	Exercise, cognitive behavioural therapy and graded exercise therapy are contraindicated
POTS	Pharmacological: β-blockers, pyridostigmine, fludrocortisone, midodrine	POTS and ME/CFS literature	Options can be prioritized on the basis of a specific constellation of symptoms
	Non-pharmacological: increase salt and fluid intake, intravenously administered salt, compression stockings	POTS and ME/CFS literature	–
Immune dysfunction	Intravenous immunoglobulin	ME/CFS literature	Consider consulting an immunologist on implementation
Cognitive dysfunction	Cognitive pacing	ME/CFS literature	Consider implementation alongside pacing physical exertion
Cognitive dysfunction	Postconcussion syndrome protocols	ME/CFS and postconcussion syndrome literature	–
Fatigue	Coenzyme Q_{10}, D-ribose	ME/CFS literature	–
Pain, fatigue, neurological symptoms	Low-dose naltrexone	ME/CFS and other literature	Substantial anecdotal reports of success within the patient community
Fatigue, unrefreshing sleep, brain fog	Low-dose aripiprazole	ME/CFS literature	–

QUANDO CONSIDERARE L'INVIO ALLO SPECIALISTA



PRACTICE POINTER

Long covid—an update for primary care

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COSA PUO' FARE IL TEAM DI CURE PRIMARIE

How Primary Care Physicians Can Recognize and Treat Long COVID

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Experts interviewed for this story offered some basic guidance for primary care physicians:

• **Believe the patient**. "Say it out loud. They need to hear it," Palacio said of patients with long COVID symptoms, who are often not believed. If their physician says, "'I believe you, and I will work with you to try to make you better even though I know very little about this,' stress levels go down."

• **Go beyond symptoms**. Physicians are accustomed to checking off symptoms, but it's also important to ask, "'How often do these occur?' and 'How do they affect your ability to carry out normal daily activities?'" Bateman said. "When you can't perform physically and cognitively, it starts to really be disabling."

• **Address fatigue**. "If patients stop overexerting themselves, they start to feel better. It's as simple as that," Brode said. Physicians should discuss with patients "what they can honestly do in their daily activities."

• **Look to familiar conditions**. According to the CDC, long COVID can share symptoms with ME/CFS, fibromyalgia, posttreatment Lyme disease syndrome, dysautonomia, and mast cell activation syndrome. Approaches to managing these conditions can help some patients with long COVID. For example, POTS can be alleviated with fluids, compression garments, and graded horizontal exercise

GRAZIE

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