

Long COVID pediatrico



UNIVERSITÀ
DI PARMA

Susanna Esposito

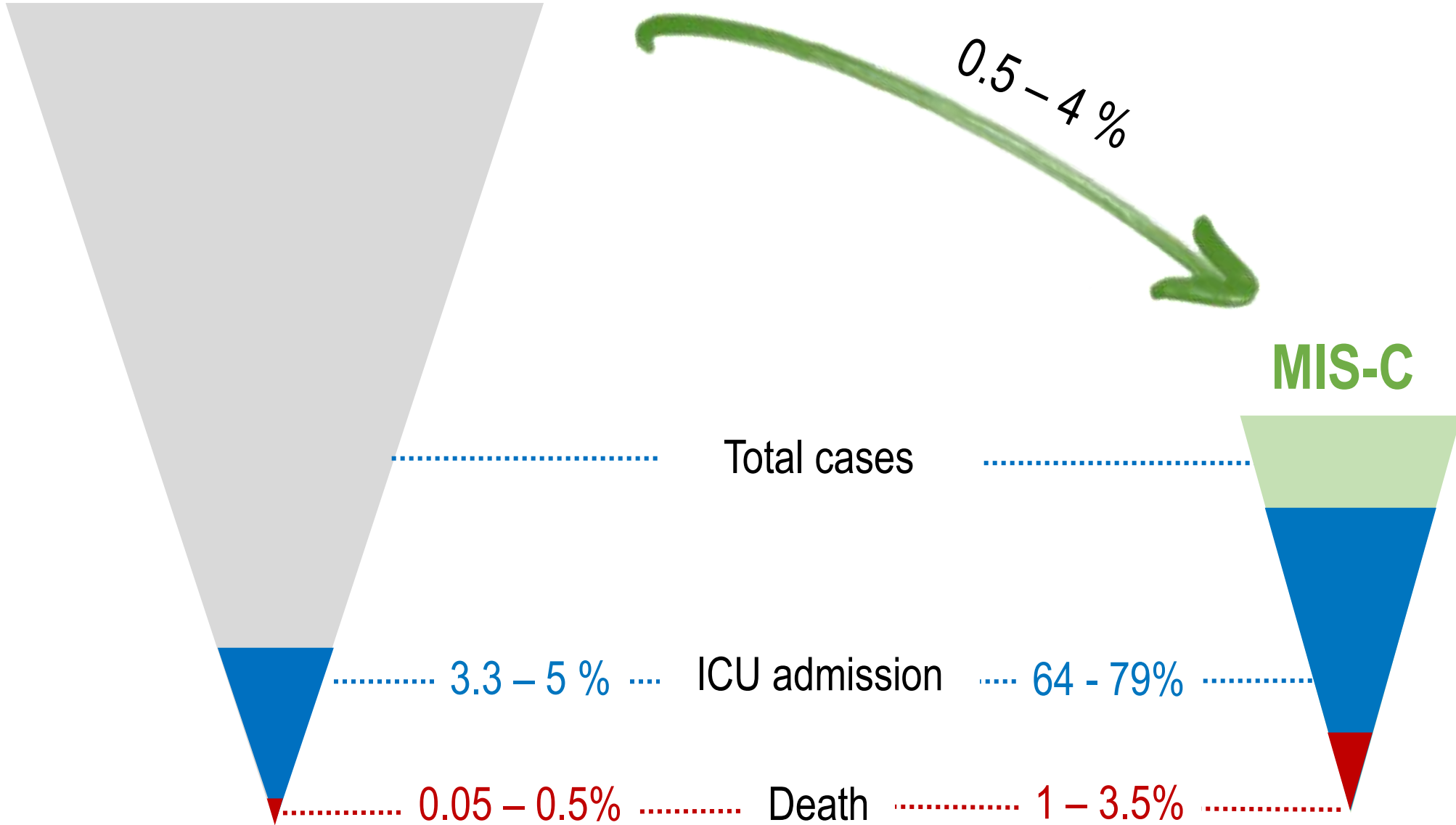
Clinica Pediatrica
Scuola di Specializzazione in Pediatria
Università di Parma, Parma



AGENDA

- **Definizione di long COVID**
- **Epidemiologia del long COVID**
- **Manifestazioni cliniche del long COVID in età pediatrica**
- **Impatto complessivo del COVID in età pediatrica**

Acute infection by SARS-CoV-2 in children



Acute COVID-19: signs and symptoms of COVID-19 for up to 4 weeks.



Ongoing symptomatic COVID-19: signs and symptoms of COVID-19 from 4 to 12 weeks.



Post-COVID-19 syndrome: signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis.

Che cos'è il long Covid ?

?

1. post-intensive care syndrome
2. post-viral fatigue syndrome
3. long-term COVID syndrome

REVIEW

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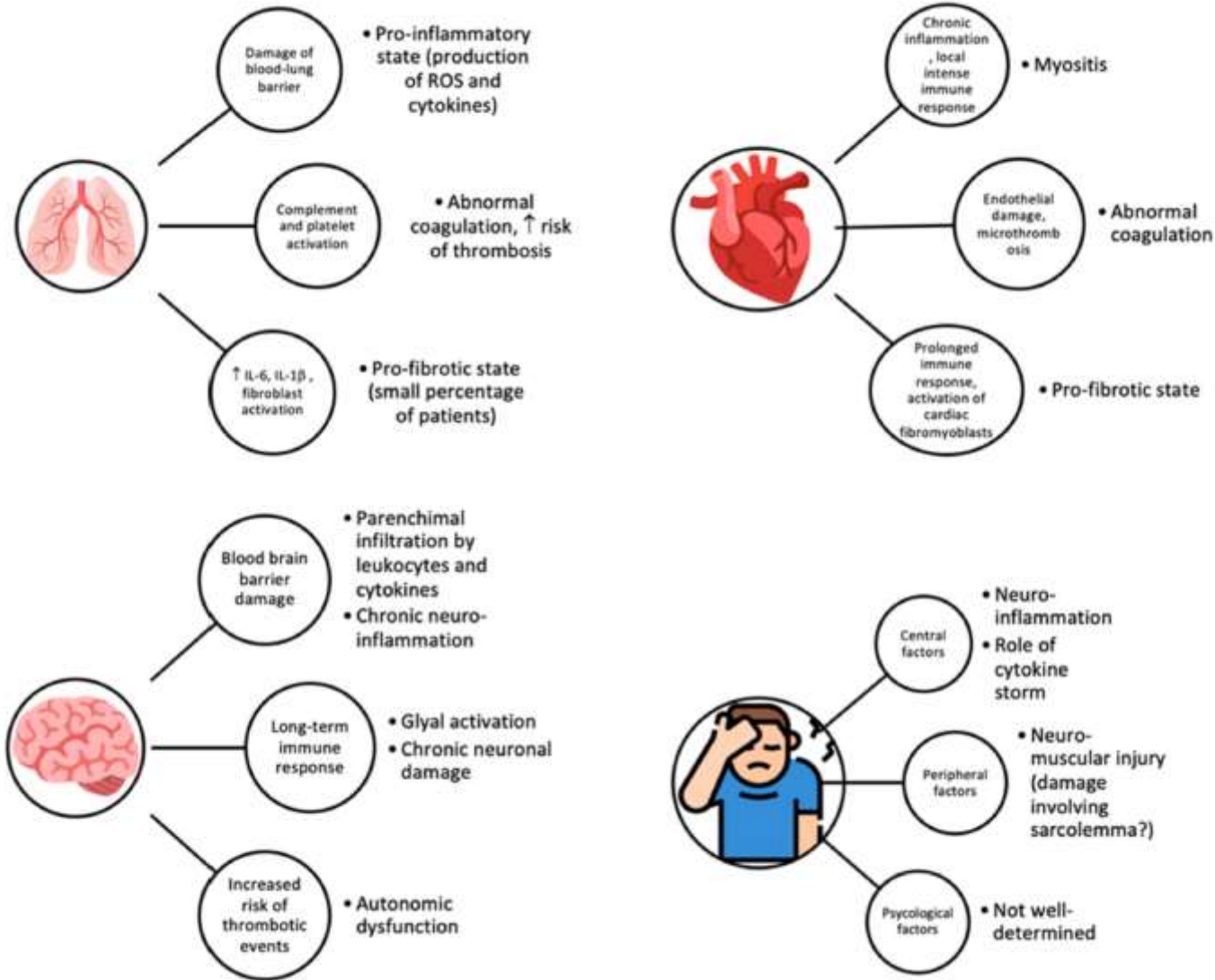
Italian intersociety consensus on management of long covid in children

Susanna Esposito^{1*}, Nicola Principi², Chiara Azzari³, Fabio Cardinale⁴, Giuseppe Di Mauro⁵, Luisa Galli⁶, Guido Castelli Gattinara⁷, Valentina Fainardi¹, Alfredo Guarino⁸, Laura Lancellata⁹, Amella Licari¹⁰, Enrica Mancino¹¹, Gian Luigi Marseglia¹⁰, Salvatore Leonardi¹², Raffaella Nenna¹¹, Stefania Zampogna¹³, Stefano Zona¹⁴, Annamaria Staiano⁸ and Fabio Midulla¹²

Main findings: Although the true prevalence of long COVID in pediatrics is not exactly determined, it seems appropriate to recommend evaluating the presence of symptoms suggestive of long COVID near the end of the acute phase of the disease, between 4 and 12 weeks from this. Long COVID in children and adolescents should be suspected in presence of persistent headache and fatigue, sleep disturbance, difficulty in concentrating, abdominal pain, myalgia or arthralgia. Persistent chest pain, stomach pain, diarrhea, heart palpitations, and skin lesions should be considered as possible symptoms of long COVID. It is recommended that the primary care pediatrician visits all subjects with a suspected or a proven diagnosis of SARS-CoV-2 infection after 4 weeks to check for the presence of symptoms of previously unknown disease. In any case, a further check-up by the primary care pediatrician should be scheduled 3 months after the diagnosis of SARS-CoV-2 infection to confirm normality or to address emerging problems. The subjects who present symptoms of any organic problem must undergo a thorough evaluation of the same with a possible request for clinical, laboratory and / or radiological in-depth analysis in case of need. Children and adolescents with clear symptoms of mental stress will need to be followed up by existing local services for problems of this type.

Proposed organ-specific injury in pediatric long Covid

(Fainardi et al., Life 2022)



Long Covid in Children



Epidemiologia – popolazione pediatrica

LANCET
& Adolescent Health

CORRESPONDENCE | VOLUME 5, ISSUE 6, E22-E23, JUNE 01, 2021

Post-acute COVID-19 outcomes in children with mild and asymptomatic disease

Daniela Say • Nigel Crawford • Sarah McNab • Danielle Wurzel • Andrew Steer • Shidan Tosif ✉

(Royal Children's Hospital RCH, Melbourne, Australia)

8% (12/171) ha presentato sintomi LONG COVID

ACTA PÆDIATRICA
NURTURING THE CHILD

BRIEF REPORT

Preliminary evidence on long COVID in children

Daniilo Buonsenso ✉, Daniel Munblit, Cristina De Rose, Dario Sinatti, Antonia Ricchiuto, Angelo Carfi, Piero Valentini

(Policlinico Universitario A. Gemelli, Roma, Italia)

42.6% almeno un sintomo oltre i 60 giorni dopo l'infezione

(anche bambini con infezione paucisintomatica o asintomatica hanno sviluppato sintomi a lungo termine)

Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2

Erika Molteni*, Carole H Sudre*, Liane S Canas, Sunil S Bhopal, Robert C Hughes, Michela Antonelli, Benjamin Murray, Kerstin Kläser, Eric Kerfoot, Liyuan Chen, Jie Deng, Christina Hu, Somesh Selvachandran, Kenneth Read, Joan Capdevila Pujol, Alexander Hammers, Tim D Spector, Sebastien Ourselin, Claire J Steves, Marc Modat, Michael Absoud, Emma L Duncan

(United Kingdom)

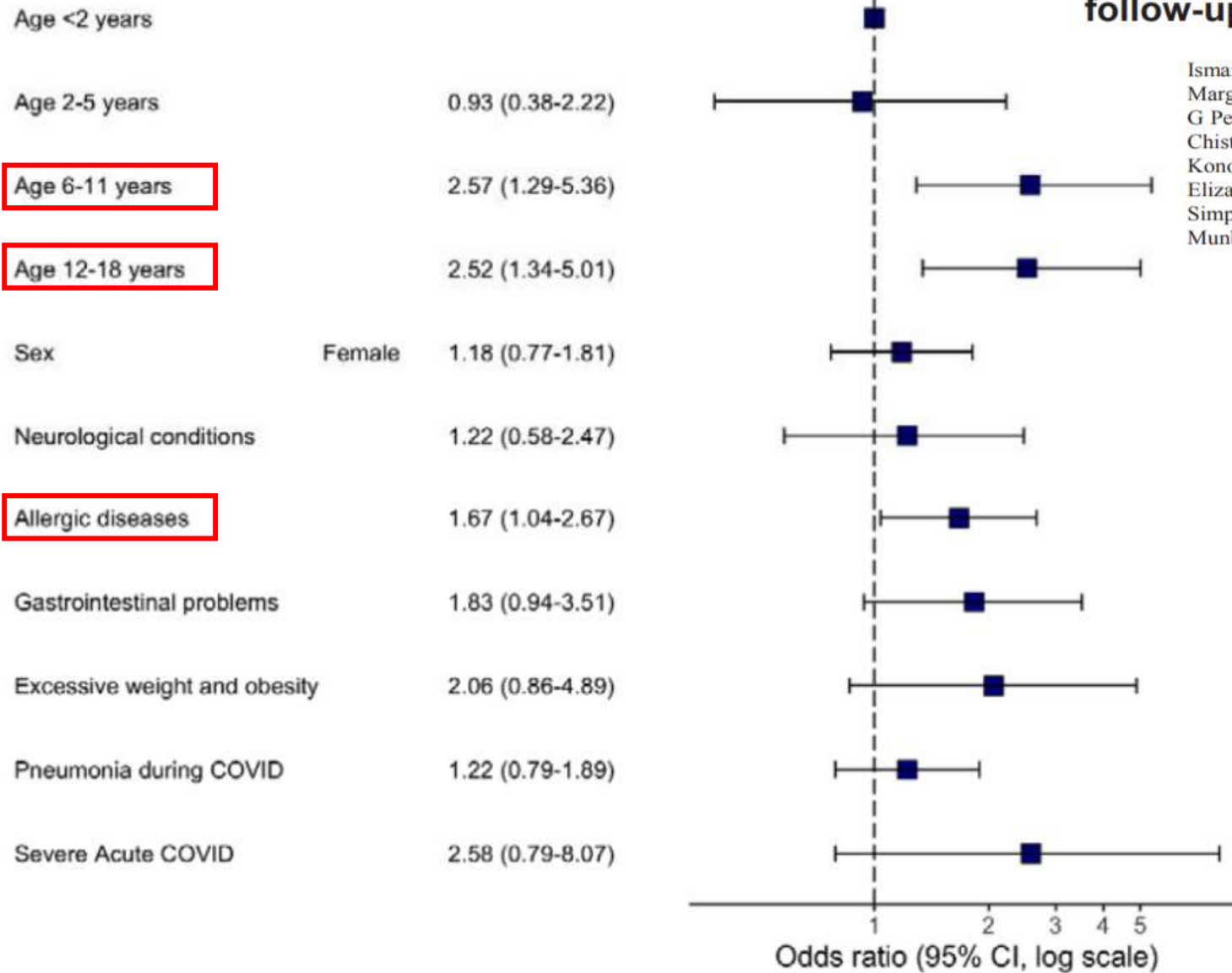
4.4% (95%CI 3.5-5.5) ha sintomi > 28 giorni da infezione

Fattori di rischio per Long COVID – popolazione pediatrica



Risk factors for long covid in previously hospitalised children using the ISARIC Global follow-up protocol: A prospective cohort study



Ismail M Osmanov, Ekaterina Spiridonova, Polina Bobkova, Aysylu Gamirova, Anastasia Shikhaleva, Margarita Andreeva, Oleg Blyuss, Yasmin El-Taravi, Audrey DunnGalvin, Pasquale Comberati, Diego G Peroni, Christian Apfelbacher, Jon Genuneit, Lyudmila Mazankova, Alexandra Miroshina, Evgeniya Chistyakova, Elmira Samitova, Svetlana Borzakova, Elena Bondarenko, Anatoliy A Korsunskiy, Irina Konova, Sarah Wulf Hanson, Gail Carson, Louise Sigfrid, Janet T Scott, Matthew Greenhawt, Elizabeth A Whittaker, Elena Garralda, Olivia Swann, Danilo Buonsenso, Dasha E Nicholls, Frances Simpson, Christina Jones, Malcolm G Semple, John O Warner, Theo Vos, Piero Olliaro, Daniel Munblit, Sechenov StopCOVID Research Team



Older age and allergic diseases were associated with higher risk of persistent symptoms at follow-up

Fattori di rischio per Long COVID – popolazione pediatrica

Prevalence of persistent symptoms in children during the COVID-19 pandemic: evidence from a household cohort study in England and Wales Preprint June 2021

Faith Miller, Vincent Nguyen, Annalan MD Navaratnam, Madhumita Shrotri, Jana Kovar, Andrew C Hayward, Ellen Fragaszy,  Robert W Aldridge,  Pia Hardelid

Adolescenza
Sesso femminile
Condizioni pre-esistenti o a lungo termine



**AUMENTO SIGNIFICATIVO DELLA
PROBABILITÀ DI SINTOMI PERSISTENTI**

Variable	Persistent symptom prevalence n/N (%)	aOR (95% CI)**
Age group		
<2	5/329 (1.5)	1.87 (0.66, 5.32)
2-11 years	25/2522 (1.0)	1
<u>12-17 years</u>	50/1827 (2.7)	2.67 (1.56, 4.57)
Sex		
Male	31/2091 (1.5)	1
<u>Female</u>	45/1898 (2.4)	1.79 (1.07, 2.99)
Missing	4/689 (0.6)	0.50 (0.16, 1.54)
Any long-term condition reported		
No	59/4202 (1.4)	1
<u>Yes</u>	21/476 (4.4)	2.95 (1.59, 5.45)
History of SARS-CoV-2 infection before symptom onset*		
No	72/4504 (1.6)	1
<u>Yes</u>	8/174 (4.6)	2.48 (1.00, 6.13)

The aim of the study was to describe and compare the clinical characteristics of adults and children affected by long COVID and to investigate the role of age and gender.

This study analyzed data from two independent prospective cohorts of adult and pediatric patients with prior confirmed SARS-CoV-2 infection followed in Parma, Italy.



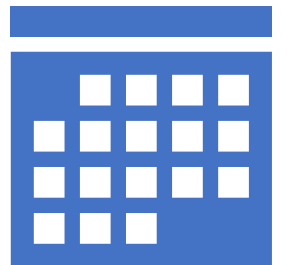
The adult cohort consisted of patients hospitalized due to COVID-19 and subsequently monitored after discharge.



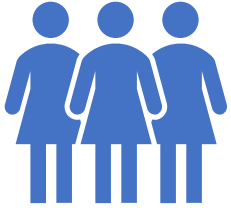
Pediatric patients were enrolled on the basis of molecular tests, regardless of the severity of the infection, and were represented mostly by outpatients

Clinical data collection was performed using adult- and child-specific versions of validated questionnaires (ISARIC).

The mean time points of the surveys for both cohorts were 2.5-3.3 months, 5.4-6.9 months, and 8.4-9.9 months in the two cohorts.



RESULTS



425 adults:

- mean age = 58.4 years (SD 13.7)
- females = 195 (43%)

925 children:

- mean age = 8.5 years (SD 3.8)
- females = 443 (47.9%)

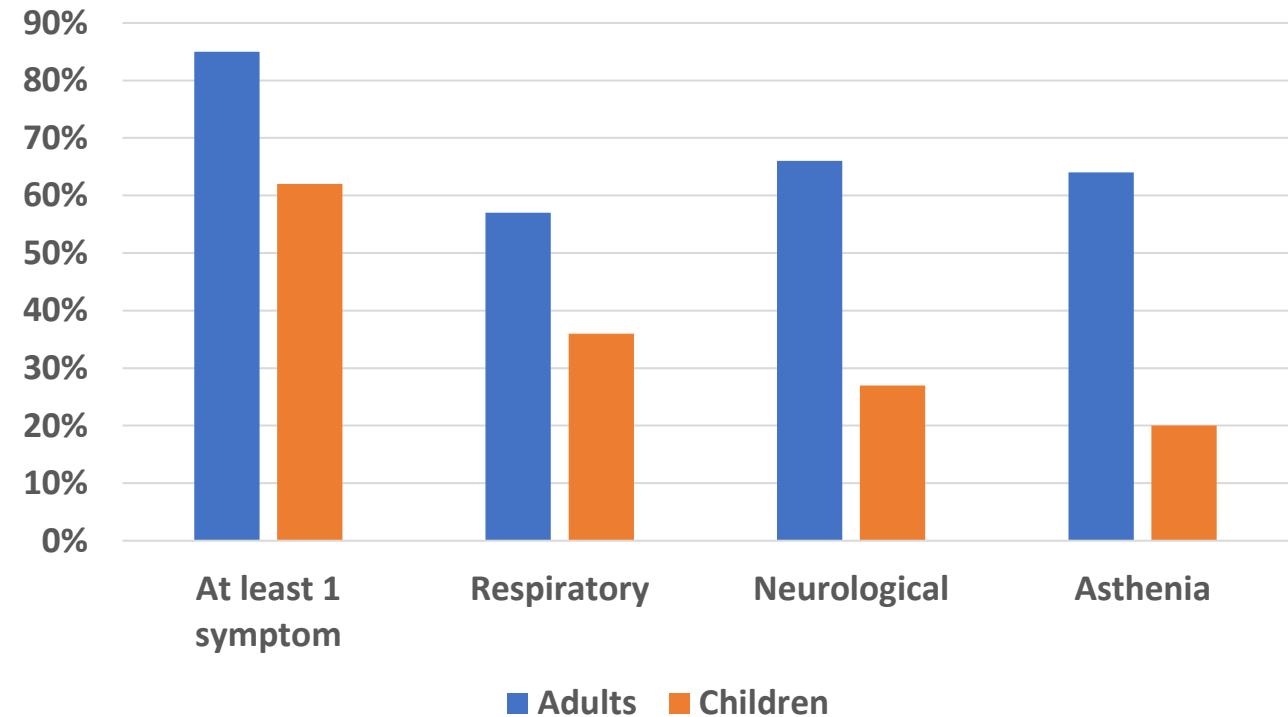


Overall, adults experienced at least one symptom more frequently than children (62% vs. 85%; $p < .001$).

No significant differences between males and females but with a clear association with increasing age:

- 0-5 years: 59%;
- 6-11 years: 64%;
- 12-50 years: 71%;
- > 50 years: 85%, $p < 0.001$

LONG-COVID SYMPTOMS



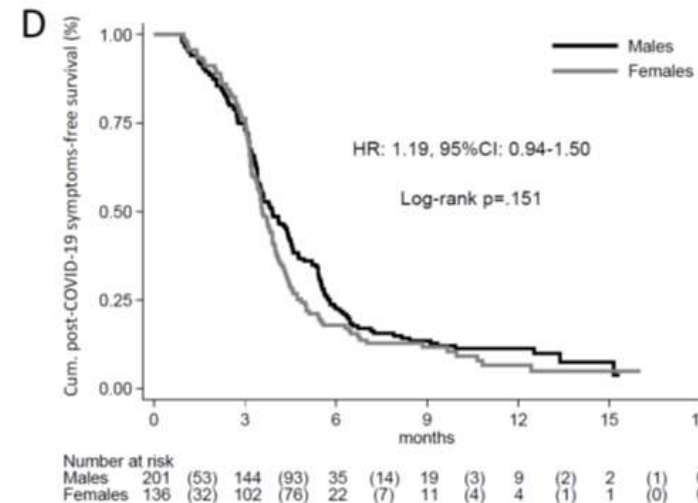
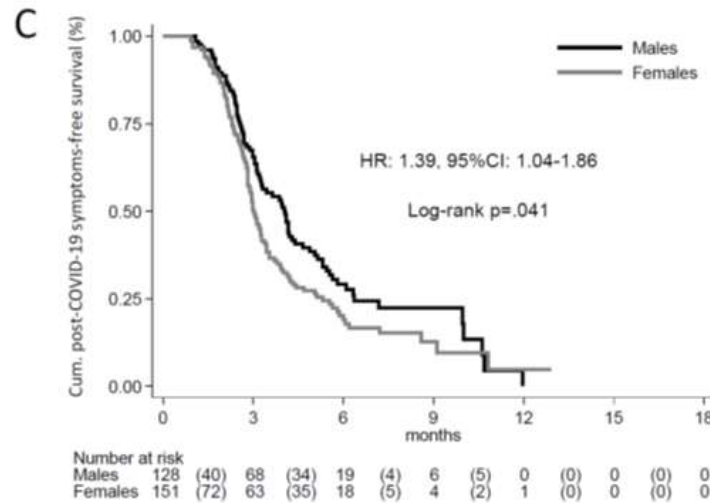
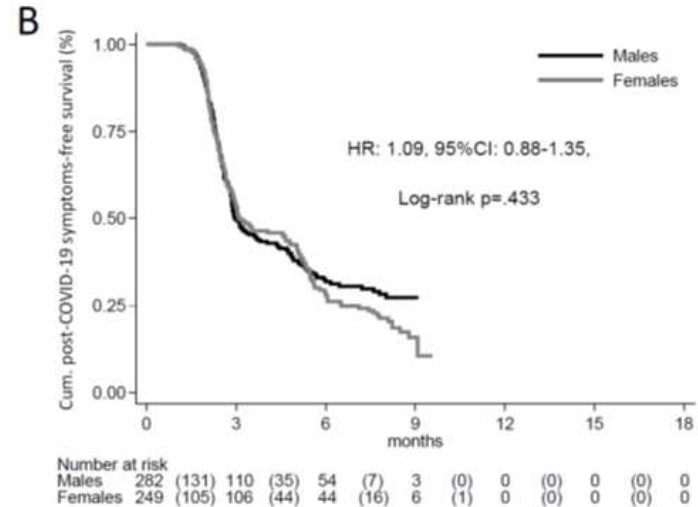
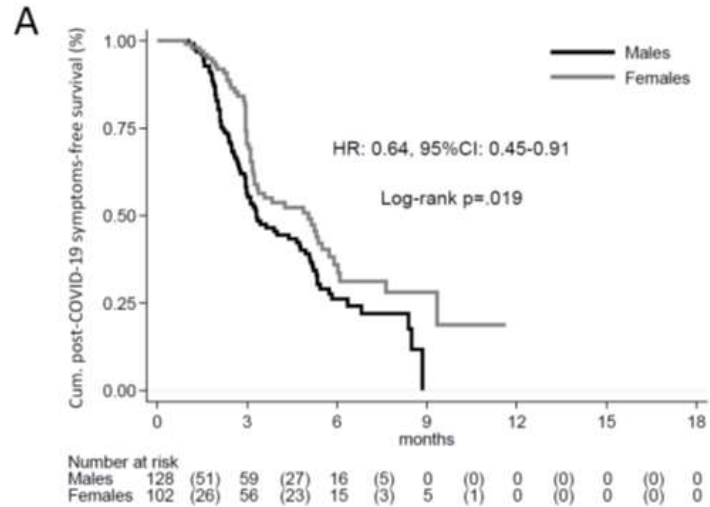
RESULTS

Analyzing the different age subgroups, female gender represents a significant protective factor for children aged < 5 years and a risk factor in patients aged 12-50 years.

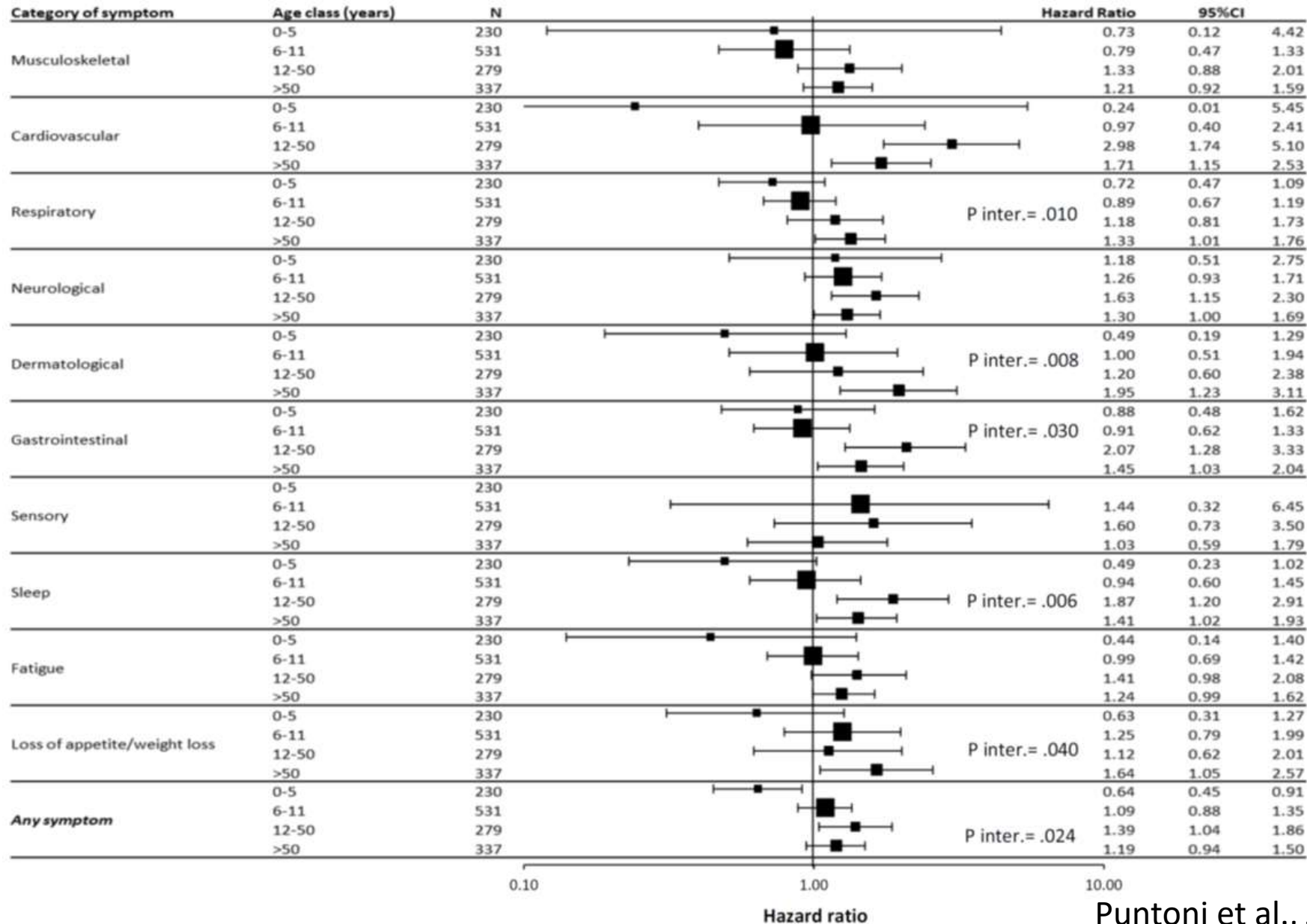
AGE GROUPS	RISK OF LONG-COVID RELATED TO FEMALE GENRE Hazard ratio (IC95%)	p
< 5 anni	0.64 (0.45-0.91)	0.012
6-11 anni	1.09 (0.88-1.35)	0.436
12-50 anni	1.39 (1.04-1.86)	0.025
> 50 anni	1.19 (0.94-1.50)	0.155

Increasing age represents a significant risk factor while the role of the female gender seems limited to patients aged 12-50 years, probably due to specific hormonal factors.

Kaplan-Meier estimates of cumulative reported frequency of post-COVID-19 symptoms, by sex, (A) in subjects aged 0-5y, (B) 6-11y, (C) 12-50y and (D) >50y



Forest plot of the risk estimate (hazard ratio, HR) of post-COVID-19 symptoms for females vs. males in each symptom category, stratified by age group



Prevalence of clinical manifestations of pediatric patients with long COVID

(Fainardi et al., Life 2022)

Cardiovascular	Neurological/Neuropsychiatric
Chest tightness or pain (1–31%)	Brain fog
Palpitations (4–18%)	Concentration difficulties (2–81%)
Dermatological	Sleep disturbance (2–63%)
Skin rashes (2–52%)	Dizziness (3–20%)
Gastrointestinal	Irritability and mood changes (5–24%)
Stomachache (5–70%)	Headache (3–80%)
Abdominal pain (1–76%)	Memory loss
Diarrhea (2–24%)	Smell disorder (12–70%)
Vomiting (2–24%)	Taste disorder (20–70%)
General	Nocturnal sweating
Fatigue (3–87%)	Respiratory
Persistent fever (2–40%)	Cough (1–30%)
Loss of appetite or weight (2–50%)	Dyspnea (40–50%)
Muscular	Upper Airway
Myalgia or arthralgia (1–61%)	Nasal congestion or rhinorrhea (1–12%)
	Sore throat (4–70%)

Preliminary evidence on long COVID in children

Danilo Buonsenso  Daniel Munblit, Cristina De Rose, Dario Sinatti, Antonia Ricchiuto, Angelo Carfi, Piero Valentini

	All
Persisting symptoms	N 129
Fatigue (compared to before COVID-19 diagnosis)	
Less	1 (0.8%)
A bit less	16 (12.4%)
Same	98 (75.9%)
A bit more	13 (10.1%)
More	1 (0.8%)
<u>Insomnia</u>	<u>24 (18.6%)</u>
Nasal congestion/ rhinorrhoea	16 (12.4%)
Persistent muscle pain	13 (10.1%)
<u>Headache</u>	<u>13 (10.1%)</u>
<u>Lack of concentration</u>	<u>13 (10.1%)</u>
Weight loss	10 (7.7%)
Joint pain or swelling	9 (6.9%)

Joint pain or swelling	9 (6.9%)
Skin rashes	9 (6.9%)
Chest tightness	8 (6.2%)
Constipation	8 (6.2%)
Persistent cough	7 (5.4%)
Altered smell	6 (4.6%)
Palpitations	5 (3.8%)
Chest pain	4 (3.1%)
Altered taste	4 (3.1%)
Hypersomnia	4 (3.1%)
Stomach/abdominal pain	3 (2.3%)
Diarrhoea	2 (1.5%)
Menstruation	2 (1.5%)
other: yes	3 (2.3%)
Any persisting symptoms	
None	54 (41.9%)
1-2	46 (35.6%)





Tra i sintomi più frequenti:

- **Insomnia;**
- Sintomi respiratori;
- **Difficoltà nella concentrazione;**
- **Stanchezza cronica;**
- Dolore muscolare e/o articolare.

Questi **sintomi**, descritti sia nei bambini con COVID-19 acuta sintomatica che asintomatica, sono stati **particolarmente frequenti nei pz valutati > 60 giorni dopo la diagnosi iniziale.**

LONG COVID PEDIATRICO e SFERA NEUROPSICHIATRICA – EVIDENZE ATTUALI

ACTA PÆDIATRICA
NURTURING THE CHILD

REGULAR ARTICLE |  Open Access |   

Case report and systematic review suggest that children may experience similar long-term effects to adults after clinical COVID-19

Jonas F. Ludvigsson 

Materiali e Metodi – Case report inerente una piccola coorte: 5 bambini e ragazzi svedesi, dai 9 ai 15 anni (4 ragazze, età mediana 12 anni).

Sintomi riportati dai genitori e sperimentati per più di 2 mesi dopo la diagnosi clinica di COVID-19, per un periodo variabile dai 6 agli 8 mesi.



SINTOMI più comuni:

- Stanchezza cronica;
- Dispnea;
- Palpitazioni/dolore toracico;
- Cefalea;
- Difficoltà nella concentrazione;
- Debolezza muscolare;
- Vertigini.

SINTOMI meno comuni:

- Dolore addominale;
- Perdite di memoria;
- Depressione;
- Rash cutanei;
- Dolori muscolari;
- Disordini del sonno;
- Diarrea, vomiti;
- Febbre remittente.

4 bambini su 5: nessuna comorbidità.

Una sola bambina: asma, allergie, ASD, con ricovero a circa 3 mesi dalla diagnosi di COVID-19 per mio-pericardite.

CONCLUSIONI: scarsità del campione, ma risultati in linea con studi più numerosi condotti sull'adulto.

Case report and systematic review suggest that children may experience similar long-term effects to adults after clinical COVID-19

Jonas F. Ludvigsson ✉

Sintomi riportati dai genitori e che i soggetti coinvolti nello studio hanno sperimentato più di 2 mesi dopo la diagnosi clinica di COVID-19, per un periodo variabile dai 6 agli 8 mesi.16

Sintomi a 2 mesi dall'infezione

- Fatigue
- Dispnea
- Dolore toracico
- Palpitazioni

A 6-8 mesi dall'infezione:

- **Tutti** lamentano **fatigue**
- **Nessuno** è tornato alle attività **scolastiche full time**

Materiali e Metodi: Case report inerente una piccola coorte: 5 bambini e ragazzi svedesi, dai 9 ai 15 anni (4 ragazze, età mediana 12 anni).

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Sex, age	Female, 13 years	Female, 12 years	Male, 11 years	Female, 9 years	Female, 15 years
Earlier comorbidities	-	Asthma, allergies and mild autism spectrum disorder (normal schooling)	-	-	-
Symptoms	6.5 months	7.0 months	6.0 months	8.0 months	8.0 months
Other contacts at COVID-19 onset	Other family members sick	Father fell sick 10 days before child	Mother and patient's friend fell sick at the same time	Mothers and two siblings were also ill	Child and several travel companions sick during holiday abroad
Initial COVID-19	Fever, abdominal pain, upper respiratory symptoms, extreme fatigue. Body felt very heavy. Deep cough. Lost taste and smell after 2 weeks	High fever with abdominal pain and headache. Lost taste and smell. Dyspnoea. Extreme fatigue. Dizziness	Headache and sore throat. Tired. Thirsty for first 2 weeks. Abdominal pain, diarrhoea, nausea and anorexia. Lost taste and smell	Fever, diarrhoea, headache, abdominal pain, nausea and dyspnoea for several weeks	High fever, headache, sore throat, dyspnoea and chest pain. Very tired
Long COVID- (after 2 months)	Stayed in bed for 3 months (mid-April to August), except to visit shower and toilet. Developed skin rash after two months and severe pain in her arms and hyperaesthesia after 4 months	Sick for 11 weeks. Depressed, angry. Lots of abdominal pain. Repetitive behaviour. Worsening autism spectrum disorder. Increased tics. Developed peri-myocarditis. Admitted to hospital for 3 days due to this cardiac complication. Recent exercise ECG normal	Fluctuating symptoms. Distorted smell and taste. Anorexia and nausea. Abdominal pain, especially in evenings. Constipated. Fatigued. Usually stayed in bed until noon. Sub febrile (37.8 C). Could not walk > 100 metres. Swollen lymph nodes. Chest pain. Skin rash. Hyperaesthesia, but numbness in some fingers. Joint pain and back pain. Dizziness. High pulse, even with limited physical exertion	Symptoms escalated 4-5 months after disease onset, with chest pain, sensory impairment. Fever, nausea and abdominal pain. Extreme fatigue. No strength to speak. Dyspnoea. Could not climb stairs. Felt legs and other body had 'died'	Slept for 16-18 h per day. Dyspnoea, chest pain, dizziness. Cognitive impairment

Post-acute COVID-19 outcomes in children with mild and asymptomatic disease

Daniela Say • Nigel Crawford • Sarah McNab • Danielle Wurzel • Andrew Steer • Shidan Tosif ✉

Materiali e Metodi: studio cross-sectional osservazionale di 171 bambini in follow-up per pregressa infezione da SARS-CoV2
(Royal Children's Hospital RCH, Melbourne, Australia)

Long-COVID

8% (12/171) dei pz lamenta sintomi a distanza

Più frequente:
Tosse (50%)

	Children (n=12)
Sex	--
Male	7 (58%)
Female	5 (42%)
Age, years	--
Mean	3.7 (3-5)
Median	2 (1-7)
Age group, years	--
0-2	8 (67%)
6-12 years	4 (33%)
13-18 years	0
Comorbidities	3 (25%)
Congenital cardiac disease	1 (8%)
Chronic respiratory condition	2 (17%)
Symptom duration, days	--
Mean	14.6 (12-8)
Median	11.5 (3.5-25.5)

Acute disease severity	--
Asymptomatic	0
Mild disease	11 (92%)
Moderate disease	0
Severe disease	1 (8%)
Admitted to hospital*	6 (50%)
For observation	2 (17%)
For fluid rehydration	1 (8%)
Received intensive care unit care*	3 (25%)
Post-acute COVID-19 symptoms	--
Post-viral cough	6 (50%)
Fatigue	3 (25%)
Both cough and fatigue	1 (8%)
Inflammatory conditions	2 (17%)

Data are n (%), mean (SD), or median (IQR). *All hospital admissions were for acute COVID-19 illness except for two children who were admitted to the intensive care unit due to post-acute inflammatory conditions.

Pediatric long-COVID: An overlooked phenomenon?

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Eveline J. Langereis MD¹ | Michiel A. G. E. Bannier MD⁷ |
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Sintomi più comuni di long-COVID

Fatigue	77	87%
Dyspnea	49	55%
Concentration difficulties	40	45%
Headaches	34	38%
Thoracic pain complaints	31	35%
Stomach ache	29	33%
Myalgia	25	28%
Diarrhea	21	24%
Memory loss	12	13%
Cardiac palpitations	16	18%
Skin irritation/lesions	6	7%
Dizziness	3	3%
Brain fog	2	2%
Weight loss	2	2%
Loss of appetite	2	2%
Persistent fever	2	2%
Other ^a	8	9%
Total admitted to the hospital because of long-COVID ^b	16	18%

Materiali e Metodi: studio cross-sectional osservazionale nazionale basato su un'indagine online compilata dai PLS (Paesi Bassi)

Questionario:

1. Prevalenza di long-COVID
2. Manifestazioni cliniche
3. Severità di malattia ed impatto sulle attività quotidiane
4. Coinvolgimento di team multidisciplinare

→ 89 bambini (età media 13 anni) con long-COVID

Qualità di vita

Limitations in daily functioning

No limitations	7	8%
Mild limitations in daily functioning ^c	43	48%
Severe limitations in daily functioning ^d	32	36%

^cFor example, can go to school but excessively tired.

^dFor example, less or no school possible.

Conclusione: 89 bambini con sintomi di long-COVID:

- **Fatigue e dispnea** soprattutto
- **Limitazione** delle attività di vita quotidiana

Sequelae of COVID-19 in Hospitalized Children: A 4-Months Follow-Up

Denina, Marco MD^{*}; Pruccoli, Giulia MD^{*}; Scolfaro, Carlo MD^{*}; Mignone, Federica MD^{*}; Zoppo, Marisa MD^{*}; Giraud, Isaac MD[†]; Silvestro, Erika MD^{*}; Bertolotti, Luigi DVM[‡]; Rosati, Sergio DVM[‡]; Ramenghi, Ugo MD, PhD^{*}; Garazzino, Silvia MD, PhD^{*}

Esami ematochimici

	Hospital Admission	Ambulatory Follow-up
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Laboratory tests (references values—alteration)

White blood cells—(reference values according to the age)—decreased	2/22	0/25
Lymphocytes—(reference values according to the age)—decreased	4/22	0/25
Platelets—(150,000–450,000/mm ³)—decreased	6/22	0/25
C-reactive protein—(<5 mg/L)—increased	3/22	0/25
D-dimer—(<500 ng/mL)—increased	11/16	1/25
Erythrocyte sedimentation rate—(3–13 mm/h)—increased	8/11	2/25
Fibrinogen—(200–400 mg/dL)—increased	5/16	1/25
Ferritin—(12–60 (ng/mL)—increased	7/14	3/25
Alanine aminotransferase—(8–40 UI/L)—increased	3/21	0/25
Creatinine—(reference values according to the age)—increased	2/21	1/25

Materiali e Metodi: studio osservazionale di 25 **bambini** con pregressa ospedalizzazione per COVID-19 (Ospedale Pediatrico Regina Margherita, Torino, Italia)

Follow-up: 130 giorni (4 mesi)

- Telefonico
- **Clinico**
- **Laboratoristico**
- Strumentale (**Ecografia polmonare**)

Ecografia polmonare

	Hospital Admission	Ambulatory Follow-up
Pathologic lung ultrasound	13/24	5/25
Pulmonary consolidation	5	2
Interstitial B-lines pattern	13	5

Conclusion: **risoluzione** clinica, ecografica e laboratoristica completa entro 4 mesi dall'infezione

Test di funzionalità polmonare nel long-COVID

LANCET

ARTICLES | VOLUME 397, ISSUE 10270, P220-232, JANUARY 16, 2021

6-month consequences of COVID-19 in patients discharged from hospital: a cohort study

Chaolin Huang, MD * · Lixue Huang, MD * · Yeming Wang, MD * · Xia Li, MD * · Lili Ren, PhD * · Xiaoying Gu, PhD * · et al. [Show all authors](#) · [Show footnotes](#)

Materiali e Metodi: studio di coorte prospettico su 1733 pz **adulti** ricoverati per infezione da SARS-CoV2 (Jin Yin-tan Hospital, Wuhan, China)

Follow-up: medio 186 giorni dall'infezione SARS-CoV2+

Conclusioni

- **22-56%** dei partecipanti ha un **difetto** di pulmonary diffusion (DLCO) a **6 mesi** dall'infezione
- Persistenza di **anomalie polmonari interstiziali** all'imaging: opacità ground glass (GGO) e irregular lines



Correlazione con **severità** di malattia **all'esordio**

Scale di gravità alla diagnosi

	Seven-category scale			OR or β (95% CI)	
	Scale 3: not requiring supplemental oxygen	Scale 4: requiring supplemental oxygen	Scale 5-6: requiring HFNC, NIV, or IMV	Scale 4 vs 3	Scale 5-6 vs 3
Lung function					
Number of patients	89	172	88		
FEV ₁ <80%, % of predicted	7 (8%)	4 (2%)	11 (13%)	OR 0.14 (0.03 to 0.68)*	OR 0.50 (0.09 to 2.93)
FVC <80%, % of predicted	3 (3%)	1 (1%)	10 (11%)	OR 0.11 (0.01 to 1.59)	OR 2.09 (0.19 to 23.02)
FEV ₁ /FVC <70%	7 (8%)	13 (8%)	2 (2%)	OR 0.91 (0.29 to 2.80)	OR 0.26 (0.03 to 1.93)
TLC <80%, % of predicted	9/83 (11%)	17/165 (10%)	30/86 (35%)	OR 0.89 (0.33 to 2.42)	OR 3.00 (0.93 to 9.67)
FRC <80%, % of predicted	5/83 (6%)	6/165 (4%)	16/84 (19%)	OR 0.61 (0.17 to 2.16)	OR 3.93 (0.97 to 15.82)
RV <80%, % of predicted	16/83 (19%)	28/164 (17%)	43/86 (50%)	OR 0.76 (0.33 to 1.75)	OR 2.75 (1.03 to 7.37)*
DLCO <80%, % of predicted†	18/83 (22%)	48/165 (29%)	48/86 (56%)	OR 1.61 (0.80 to 3.25)	OR 4.60 (1.85 to 11.48)*
Chest CT					
Number of patients	95	163	95		
At least one abnormal CT pattern	49 (52%)	87/161 (54%)	50/92 (54%)	OR 0.93 (0.53 to 1.64)	OR 0.81 (0.38 to 1.72)
GGO	39 (41%)	78/161 (48%)	41/92 (45%)	OR 1.19 (0.68 to 2.09)	OR 0.93 (0.44 to 1.98)
Irregular lines	10 (11%)	24/161 (15%)	22/92 (24%)	OR 1.46 (0.60 to 3.52)	OR 1.89 (0.64 to 5.61)
Consolidation	0	4/161 (2%)	0	NA	NA
Interlobular septal thickening	1 (1%)	2/161 (1%)	0	NA	NA
Subpleural line	6 (6%)	5/161 (3%)	4/92 (4%)	NA	NA
Reticular pattern	0	1/161 (1%)	1/92 (1%)	NA	NA
Volume of lung lesions, cm ³	1.6 (0.6 to 5.6)	3.3 (0.8 to 12.4)	29.1 (4.6 to 77.3)	β 7.45 (-12.40 to 27.28)	β 34.37 (7.74 to 61.00)*
Volume of consolidation, cm ³	0.2 (0.1 to 0.4)	0.3 (0.1 to 1.0)	1.6 (0.2 to 4.4)	β 0.19 (-1.97 to 2.35)	β 3.05 (0.14 to 5.95)*
Volume of GGO, cm ³	1.4 (0.6 to 4.7)	2.9 (0.7 to 10.0)	26.3 (4.3 to 73.3)	β 7.26 (-10.70 to 25.25)	β 31.32 (7.16 to 55.48)*
Volume ratio of lung lesion to total lung, %	0.0 (0.0 to 0.1)	0.1 (0.0 to 0.3)	0.7 (0.1 to 2.2)	β -0.06 (-1.36 to 1.24)	β 1.44 (-0.30 to 3.18)
Volume ratio of consolidation to total lung, %	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)	NA	NA
Volume ratio of GGO to total lung, %	0.0 (0.0 to 0.1)	0.1 (0.0 to 0.2)	0.6 (0.1 to 1.9)	β -0.07 (-1.20 to 1.07)	β 1.23 (-0.29 to 2.76)
CT score	3.0 (2.0 to 5.0)	4.0 (3.0 to 5.0)	5.0 (4.0 to 6.0)	β 0.33 (-0.19 to 0.84)	β 1.25 (0.56 to 1.95)‡

Data are absolute values, n (%), n/N (%), or median (IQR), unless otherwise specified. OR=odds ratio. HFNC=high-flow nasal cannula for oxygen therapy. NIV=non-invasive ventilation. IMV=invasive mechanical ventilation. FEV₁=forced expiratory volume in one second. FVC=forced vital capacity. TLC=total lung capacity. FRC=functional residual capacity. RV=residual volume. DLCO=diffusion capacity for carbon monoxide. GGO=ground glass opacity. NA=not applicable. *p<0.05. †Carbon monoxide diffusion capacity was not corrected for haemoglobin. ‡p<0.001.

Table 3: Lung function and chest CT at follow-up according to severity scale

Test di funzionalità polmonare nel long-COVID



Eur Respir J. 2020 Jun; 55(6): 2001217.

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PMCID: PMC7236826

PMID: [32381497](https://pubmed.ncbi.nlm.nih.gov/32381497/)

Abnormal pulmonary function in COVID-19 patients at time of hospital discharge

Xiaoneng Mo,^{1,4} Wenhua Jian,^{2,4} Zhuquan Su,^{2,4} Mu Chen,¹ Hui Peng,² Ping Peng,² Chunliang Lei,³ Ruchong Chen,^{2,5} Nanshan Zhong,^{2,5} and Shiyue Li^{2,5}

Materiali e Metodi: studio di coorte su 110 pz adulti ricoverati per infezione da SARS-CoV2, sottoposti a test di funzionalità polmonare al momento della dimissione (Guangzhou Eighth People's Hospital, Guangzhou, China.)

Conclusioni

- Difetto di diffusione polmonare (DLCO) in tutti i gradi di malattia, maggiore nei casi di polmonite severa
- Valori spirometrici non significativamente ridotti nei partecipanti e confrontando la severità di malattia



Necessario follow-up post-dimissione

TABLE 1 Demographics and pulmonary function characteristics of discharged patients with COVID-19

	Total	Mild illness	Pneumonia	Severe pneumonia	p-value
Patients	110	24	67	19	
S_{po₂} on discharge %	98.7±1.0	98.6±1.2	98.7±1.0	98.5±1.0	0.73
Spirometry					
FVC % pred	93.59±12.25	94.06±10.48	94.12±12.31	91.12±14.30	0.632
FVC <80% pred	10 (9.09)	3 (12.50)	5 (7.46)	2 (10.53)	0.644
FEV ₁ % pred	92.70±11.57	94.26±11.00	92.59±11.87	91.12±11.58	0.676
FEV ₁ <80% pred	15 (13.64)	4 (16.67)	9 (13.43)	2 (10.53)	0.857
FEV ₁ /FVC %	80.70±5.81	81.84±5.48	80.39±6.12	80.19±5.15	0.509
FEV ₁ /FVC <70%	5 (4.55)	0 (0)	5 (7.46)	0 (0)	0.349
MMEF % pred	97.40±26.23	99.77±28.17	96.59±26.51	96.14±23.82	0.879
MMEF <65% pred [¶]	7 (6.42)	1 (4.17)	6 (9.09)	0 (0)	0.551
FEF _{50%} % pred	94.74±26.11	97.47±25.48	94.09±26.80	93.53±25.56	0.845
FEF _{50%} <65% pred [¶]	12 (11.01)	2 (8.33)	8 (12.12)	2 (10.53)	1
FEF _{75%} % pred	96.10±32.56	102.23±40.20	95.02±30.89	92.08±27.92	0.549
FEF _{75%} <65% pred [¶]	12 (11.01)	3 (12.50)	4 (6.06)	5 (26.32) [#]	0.035
Diffusion capacity					
D _{LCO} % pred	78.18±14.29	84.70±13.88	79.76±11.99	64.79±14.35 ^{*,##}	<0.001
D _{LCO} <80% pred	51 (47.22)	7 (30.43)	28 (42.42)	16 (84.21) ^{*,##}	0.001
D _{LCO} /V _A % pred	92.09±16.68	99.35±18.25	92.30±15.70	82.58±13.91 ^{*,##}	0.004
D _{LCO} /V _A <80% pred	29 (26.85)	3 (13.04)	18 (27.27)	8 (42.11)	0.09
Lung volume					
TLC % pred	86.32±11.32	87.13±10.43	88.11±10.72	79.16±12.13 ^{*,##}	0.008
TLC <80% pred	27 (25.00)	4 (17.39)	14 (21.21)	9 (47.37) ^{*,#}	0.049
RV % pred	86.83±19.37	87.17±16.88	89.79±19.21	76.16±19.96 ^{##}	0.024
RV <65% pred	10 (9.26)	2 (8.70)	3 (4.55)	5 (26.32) [#]	0.021
RV/TLC % pred	96.99±16.72	98.00±14.93	98.53±17.55	90.42±14.86	0.168

Data are presented as n, mean±SD or n (%), unless otherwise stated. Comparisons between continuous variables were performed with one-way ANOVA. Chi-squared test and Fisher's exact test were applied to categorical variables as appropriate. BMI: body mass index; S_{po₂}: oxygen saturation measured by pulse oximetry; FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 s; MMEF: maximal mid-expiratory flow; FEF_{50%}: forced expiratory flow at 50% of FVC; FEF_{75%}: forced expiratory flow at 75% of FVC; D_{LCO}: diffusing capacity of the lung for carbon monoxide; D_{LCO}/V_A: D_{LCO} corrected for alveolar volume; TLC: total lung capacity; RV: residual volume. *: p<0.05 versus mild illness; **: p<0.01 versus mild illness; #: p<0.05 versus pneumonia; ##: p<0.01 versus pneumonia; ¶: at least two of these <65% pred defined patients with small airway function anomalies.

Evidence of lung perfusion defects and ongoing inflammation in an adolescent with post-acute sequelae of SARS-CoV-2 infection

Danilo Buonsenso*, Daniela Di Giuda*, Louise Sigfrid, Daniele Antonio Pizzuto, Gabriele Di Sante, Cristina De Rose, Ilaria Lazzareschi, Michela Sali, Fabiana Baldi, Daniela Pia Rosaria Chieffo, Daniel Munblit†, Piero Valentini†

Case-report: ragazza, 14 anni
(Roma, Italia)

Mild-COVID19 (fase acuta)

Febbricola (37,3°C)
Rinite
Anosmia
Ageusia

Dopo 30 giorni

Cefalea
Dolore toracico
Fatigue
Tachicardia

Dopo 7 mesi

RICOVERO

per persistenza di sintomi

1. **6-min walktest** → tachicardia nel 1° min (FC > 155bpm) + facile affaticabilità

2 **CPET** → lieve ipertensione polmonare

3. **EE** → ↑ IL-6, IL-1, TNF-α, B-cells
↓ regulatory T-cells

STATO INFIAMMATORIO

4. **Sierologia** → ↑ IgG e IgA per SARS-CoV2

Evidence of lung perfusion defects and ongoing inflammation in an adolescent with post-acute sequelae of SARS-CoV-2 infection

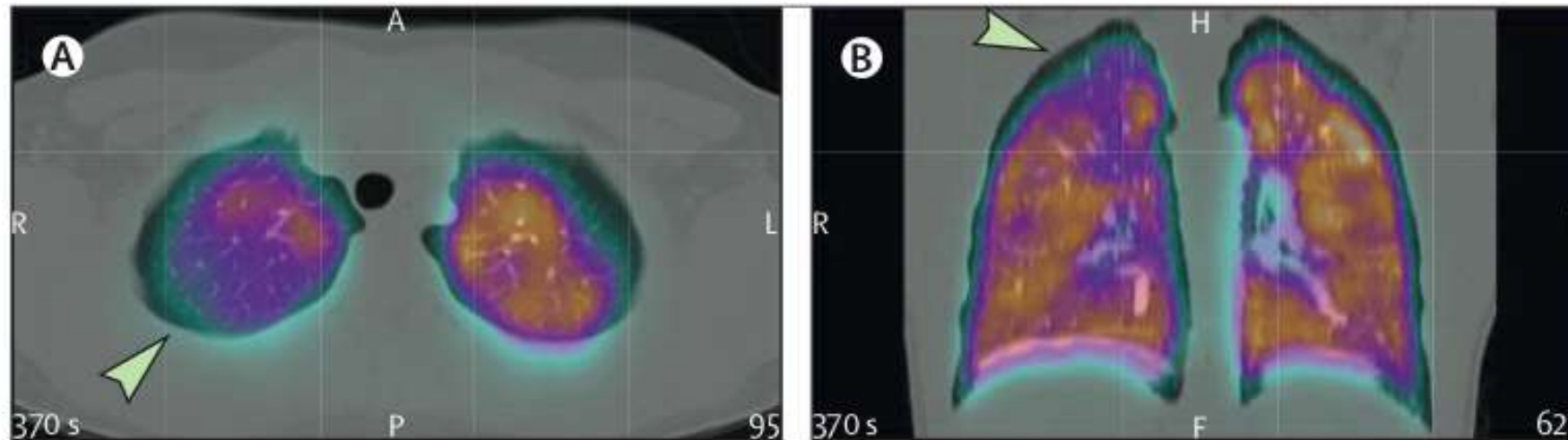
Danilo Buonsenso*, Daniela Di Giuda*, Louise Sigfrid, Daniele Antonio Pizzuto, Gabriele Di Sante, Cristina De Rose, Ilaria Lazzareschi, Michela Sali, Fabiana Baldi, Daniela Pia Rosaria Chieffo, Daniel Munblit†, Piero Valentini†

V/Q SPECT (Single photon emission computed tomography)



DIFETTI DI PERFUSIONE significativi al segmento apicale del lobo destro

NB: non corrispondenza con alterazioni di parenchima alla TC eseguita in contemporanea



Evidence of lung perfusion defects and ongoing inflammation in an adolescent with post-acute sequelae of SARS-CoV-2 infection

Danilo Buonsenso, Daniela Di Giuda*, Louise Sigfrid, Daniele Antonio Pizzuto, Gabriele Di Sante, Cristina De Rose, Ilaria Lazzareschi, Michela Sali, Fabiana Baldi, Daniela Pia Rosaria Chieffo, Daniel Munblit†, Piero Valentini†*

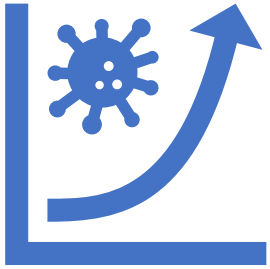
Diagnosi: "pulmonary circulation dysfunction with possible peripheral microvascular and endothelial damage».

Terapia: methylprednisolone 2 g/kg once daily for 2 weeks, then tapered over the next 4 weeks + low molecular weight heparin with a plan of changing to oral anticoagulants and continuation of therapy for 6–9 months in total.

LONG-COVID-Ped (L.O.V.e. cohort)



Prospective multicenter study conducted in 12 centers across 9 regions in Italy. A nation-wide cohort of children with a previous SARS-CoV-2 infection.



Children aged under 17 years with a SARS-CoV-2 infection during the previous 3 months were enrolled from February 2022 to November 2022

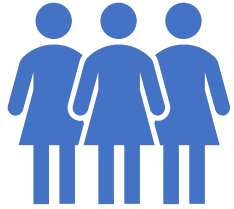
Previously validated ad hoc questionnaires (ISARIC) were used to investigate neurological symptoms and quality of life among enrolled patients.



Evaluations of symptoms were conducted at median time-points of 2.4 (range 2.0-2.9), 5.4 (range 5.0-5.9) and 8.4 (range 8.0-8.8) months after the infection. The first survey was conducted during a medical examination.

Follow-up is still ongoing and include further evaluations at 12, 18, and 24 months

RESULTS



1059 patients enrolled to date.

Preliminary results are available for 925 children:

- mean age = 8.5 years (SD 3.8)
- females = 443 (47.9%)

Overall, 252 (27.2%) patients reported neurological symptoms during the first 3 months after acute infection.

Children reporting neurological long-COVID were older, more often female, and presented at least one comorbidity and neurological symptoms during the acute phase

Neurological symptoms:

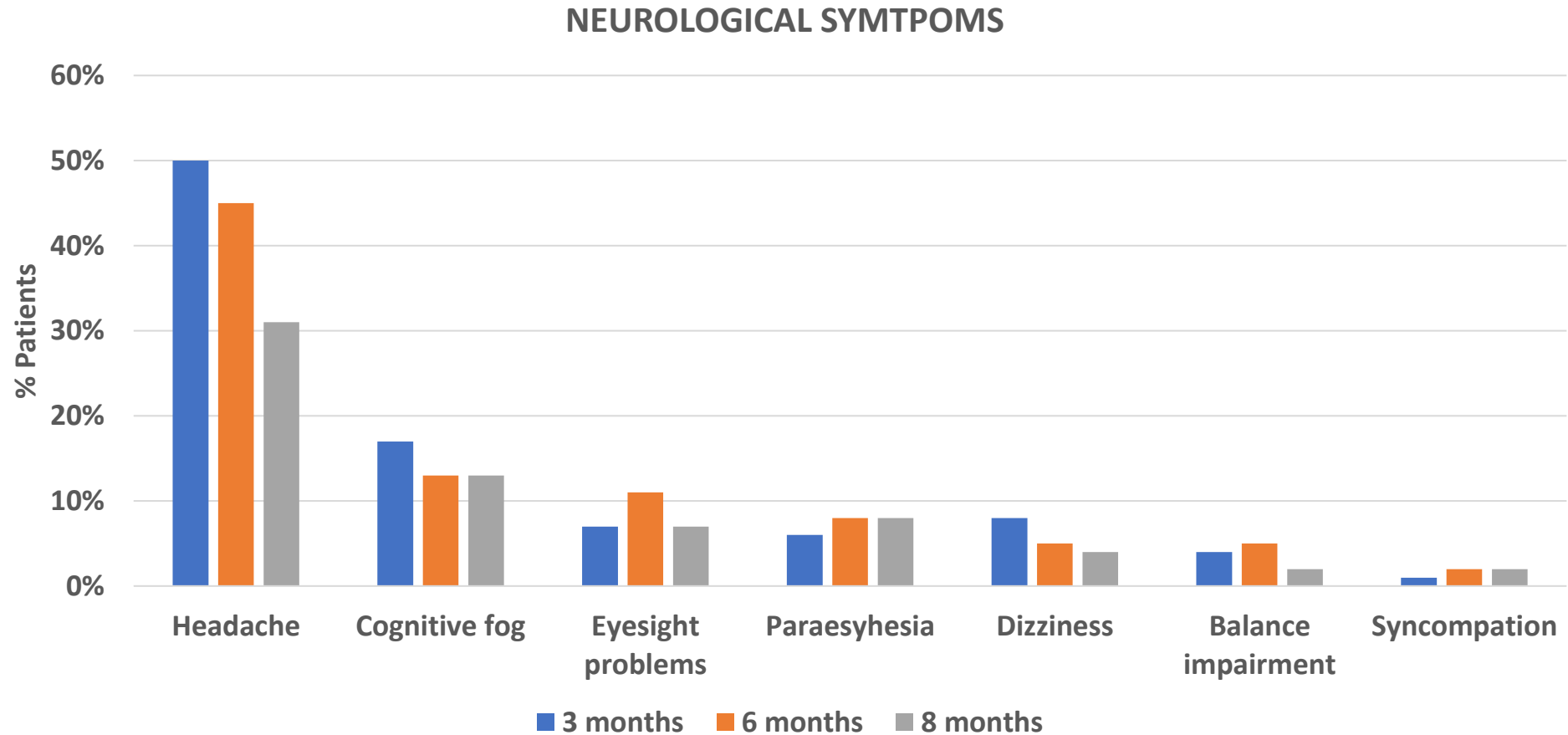
- Headache
- Brain fog or concentration problems
- Balance impairments
- Syncope
- Dizziness
- Eyesight problems
- Paraesthesia

	Patients with neurological long COVID (N=252)	Patients without neurological long COVID(N=673)	p
DEMOGRAPHICS			
Age; mean (SD); years	9.7 (3.3)	7.4 (4.3)	<0.001
Sex; n (%) female	145 (57.5)	298 (44.3)	<0.001
COMORBIDITIES; n (%)			
Neurological	14 (5.6)	13 (1.9)	0.021
Gastrointestinal	15 (6.0)	15 (2.2)	0.022
Allergy	49 (19.4)	73 (10.9)	0.003
At least 1	111 (44.1)	235 (34.9)	0.012
ACUTE PHASE; n (%)			
Headache	143 (56.8)	219 (32.5)	<0.001
Cognitive fog	9 (3.6)	2 (0.3)	<0.001

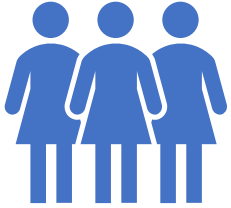
RESULTS

Headache and concentration deficits were the most commonly reported neurological symptoms in all time-points.

A slow reduction of the prevalence of neurological long-COVID was observed during follow-up.



RESULTS



1059 patients enrolled to date.

Preliminary results are available for 925 children:

- mean age = 8.5 years (SD 3.8)
- females = 443 (47.9%)

Gastro-intestinal symptoms were reported in 178 (19.2%) of children after 3 months from the infection. A slow decrease of GI symptoms was observed during follow-up.

No significant differences were found between children with and without GI-LC in terms of age, vaccination rates and hospitalization ($p > 0.05$).

A previous GI comorbidity and overweight/obesity were reported more frequently in children with GI-LC (7.9 % vs 2.1 %, $p < 0.001$, and 2.3% vs 0.5%, $p = 0.05$).

In children with GI-LC compared to those without, a higher prevalence of abdominal pain (21.4% vs 8.6%, $p < 0.001$) and diarrhea (19.1% vs 9%, $p < 0.001$) during the acute phase of COVID-19 was reported.

	3 months	5 months	8 months
N° children	925	559	328
Diarrhea, n (%)	43 (4.6)	27 (4.8)	18 (5.5)
Abdominal pain, n (%)	55 (5.9)	40 (7.1)	17 (5.2)
Vomiting, n (%)	29 (3.1)	13 (2.3)	9 (2.7)
Constipation, n (%)	20 (2.2)	18 (3.2)	9 (2.7)

FISIOPATOLOGIA RESPIRATORIA INFANTILE –CLINICA PEDIATRICA, AOU PARMA

VALUTAZIONE DELLA FUNZIONALITA' RESPIRATORIA NEI BAMBINI CON PREGRESSA INFEZIONE DA COVID19

M Motta, R Grandinetti, M Tornesello, K Skenderaj, C Quiligotti, V Fainardi, G Pisi e S Esposito'

Materiali e Metodi: 20 bambini afferenti al Centro FPR infantile di Parma con infezione da SARS-CoV2 nei 6 mesi precedenti

Età media: 11.1±3.6 anni

Sesso: 14 M, 6 F

16 in follow-up per **asma** bronchiale

SIMRI 2021

SPIROMETRIA	
FEV ₁ (percentile)	2.37 ± 0.91 L (100.5 ± 11.5 %)
FEV ₁ /FVC	89.2 ± 7.0
FEV ₂₅₋₇₅ (percentile)	2.85 ± 1.35 L (104.9 ± 30.8 %)
IOS (impulse oscillometry system)	
R5Hz (percentile)	0.68 ± 0.28 kPa/L/s (111.2 ± 27.3 %)
R20Hz (percentile)	0.51 ± 0.19 kPa/L/s (112.4 ± 27.6 %)
R5-20Hz	0.14 ± 0.14 kPa/L/s
MBW (multiple breath wash-out)	
LCI _{2.5%} (percentile)	6.8 ± 0.4 (104 ± 7.6 %)
Scond	132.9 ± 43.7 %
Sacin	127.6 ± 81.3 %

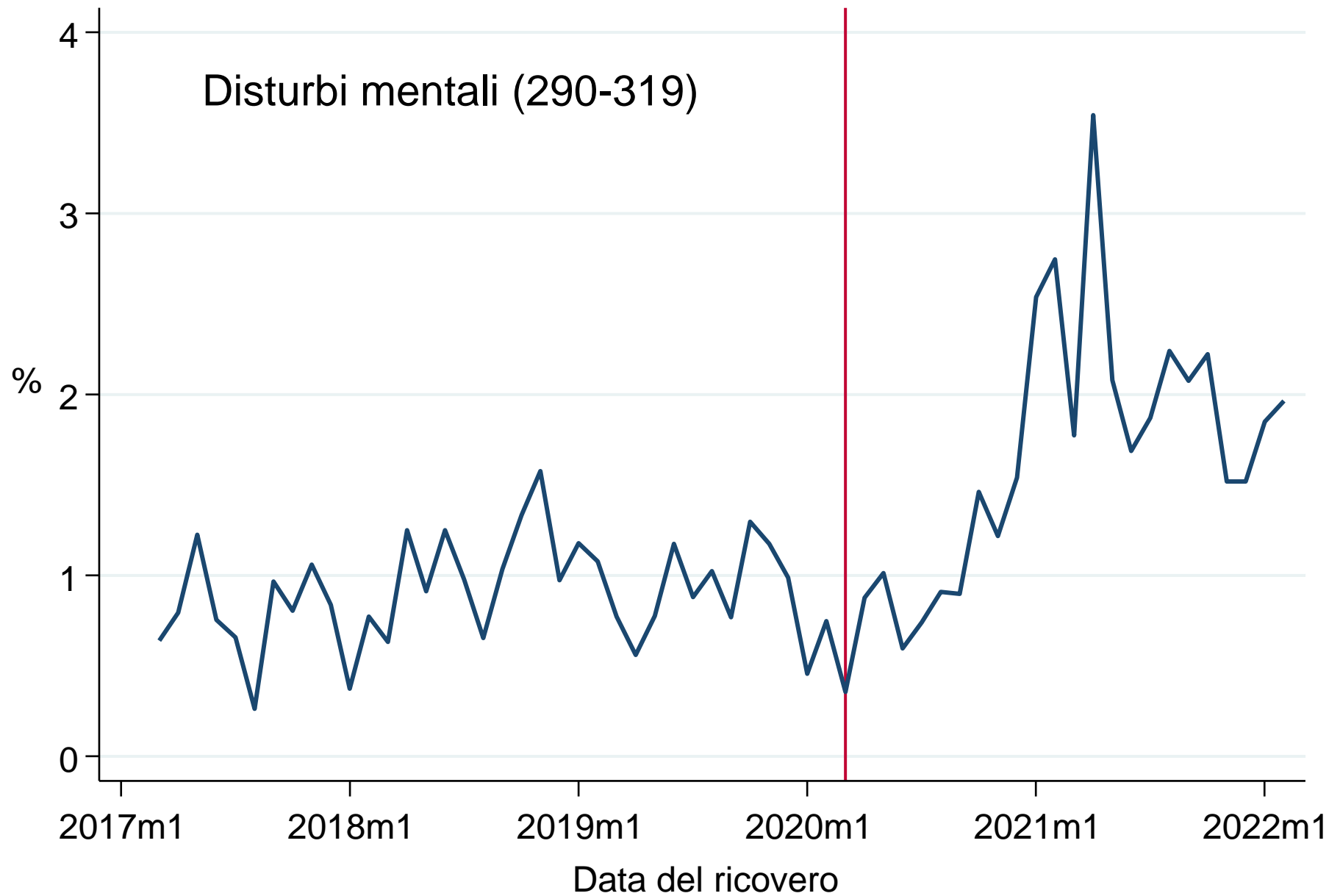
→ Nei limiti di **norma**

→ **Resistenze** centrali e periferiche **liev.** ↑ rispetto al predetto

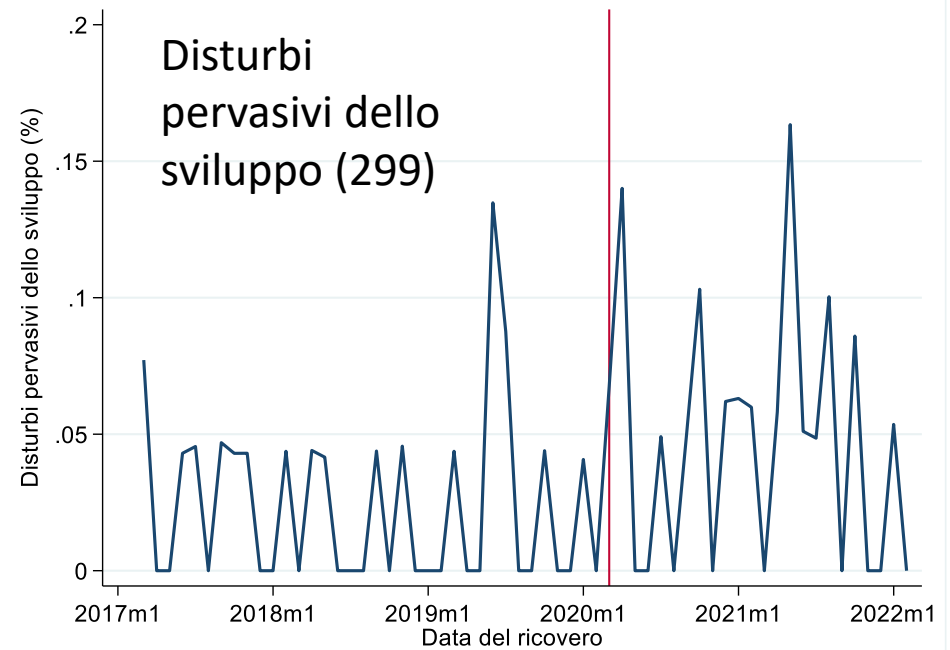
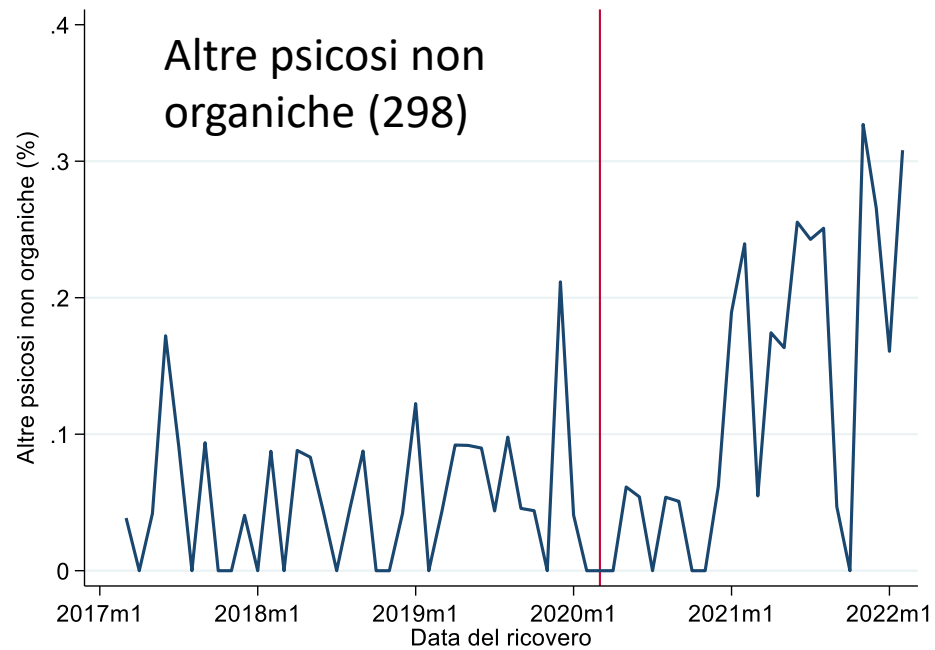
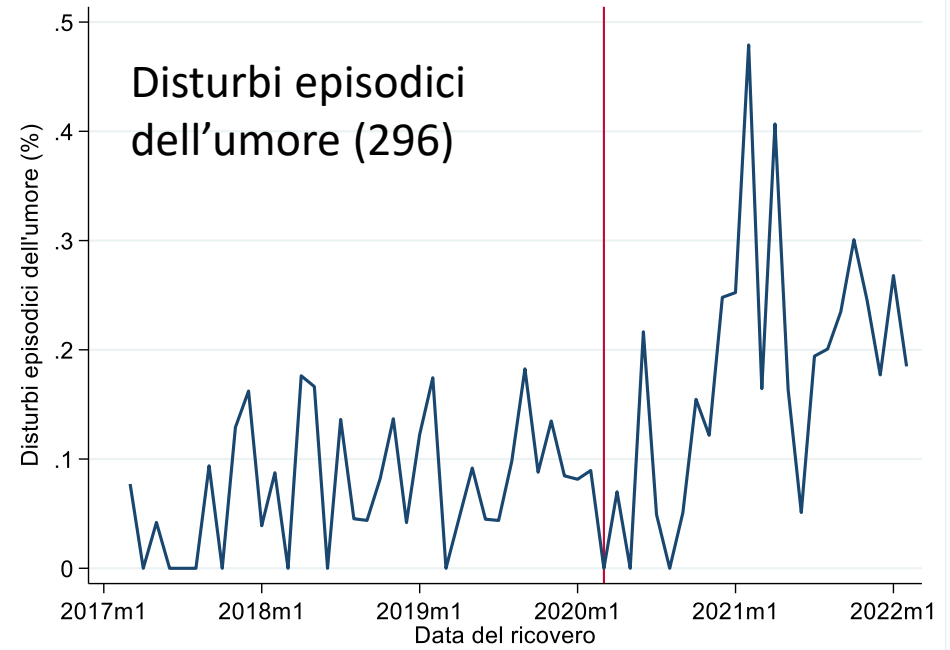
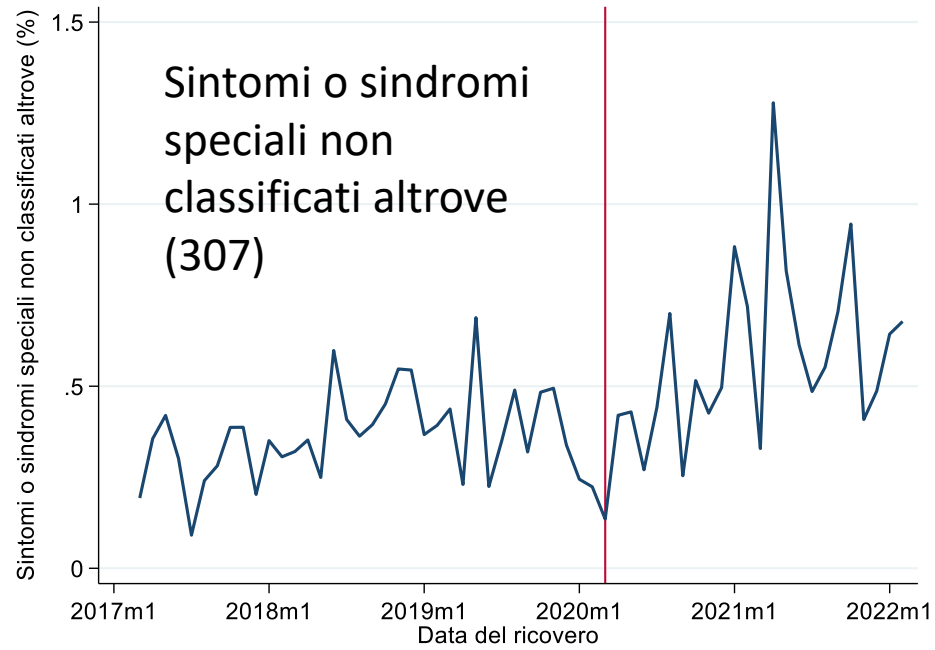
→ LCI nella **norma**, senza differenze nella disomogeneità ventilatoria tra vie respiratorie di conduzione e periferiche

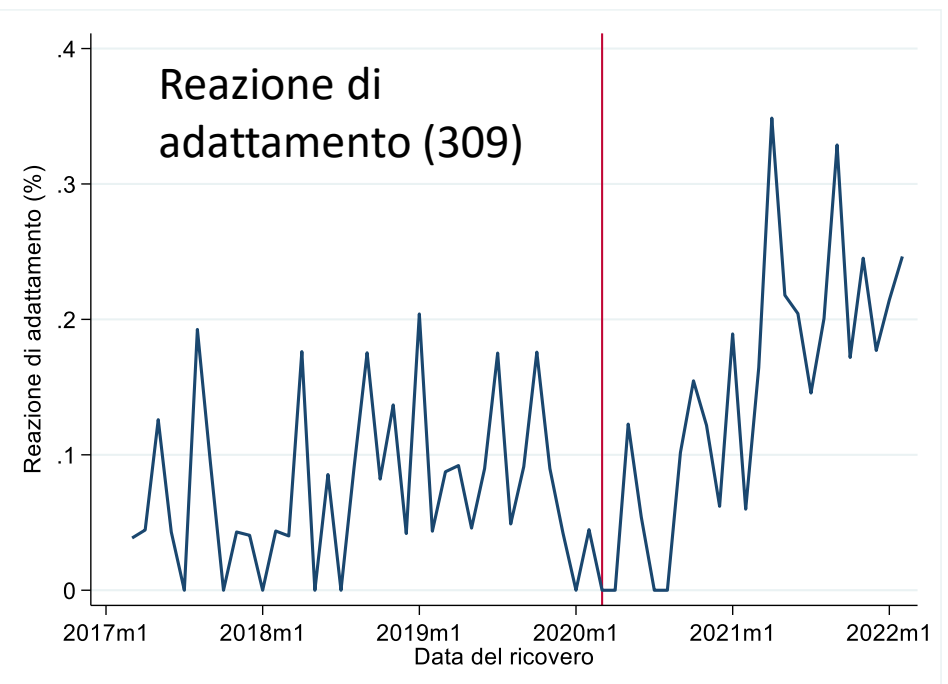
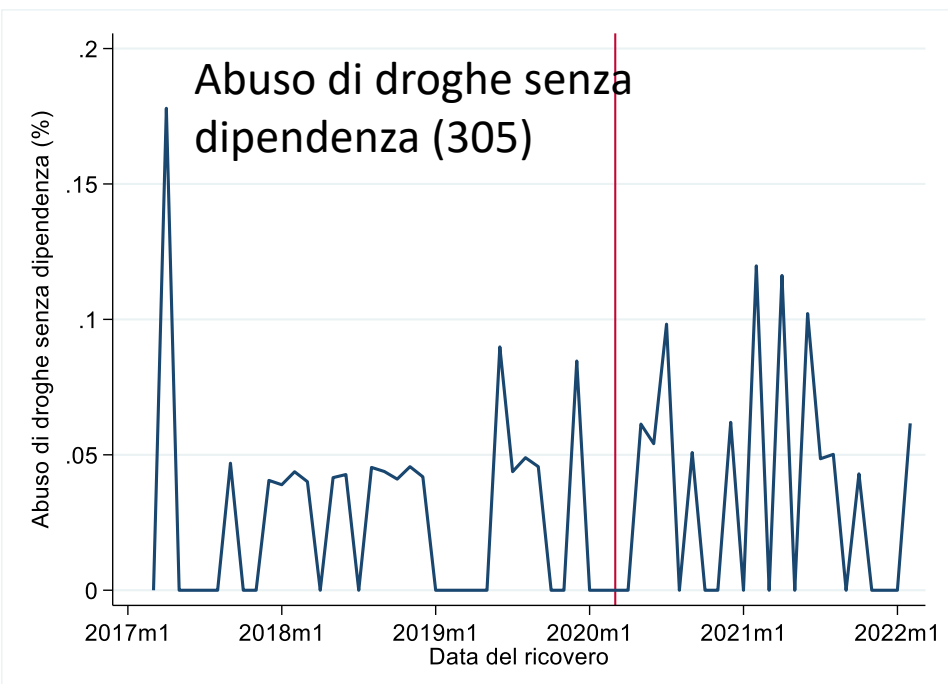
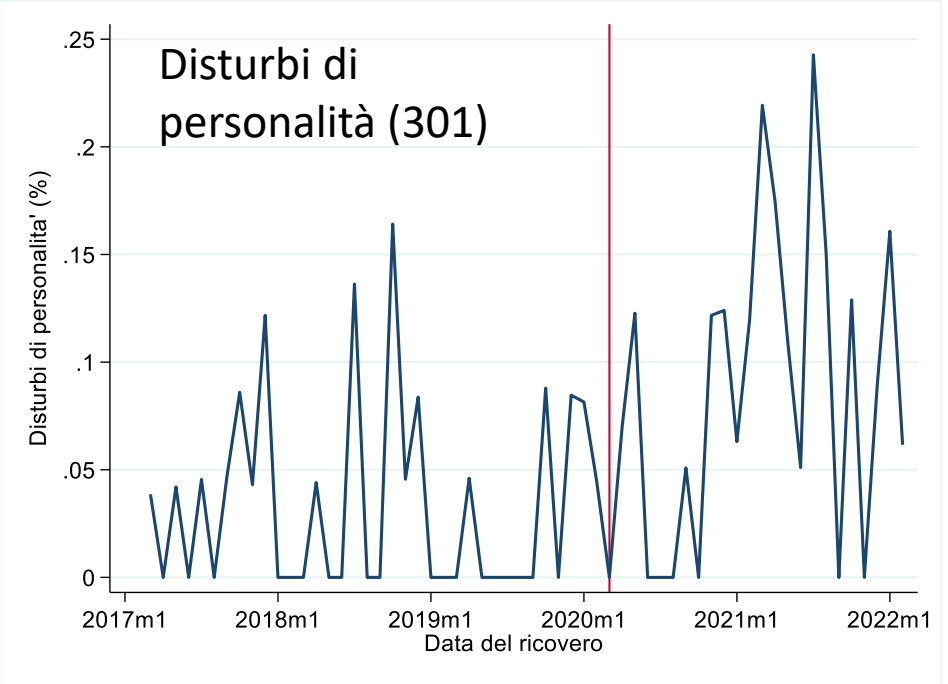
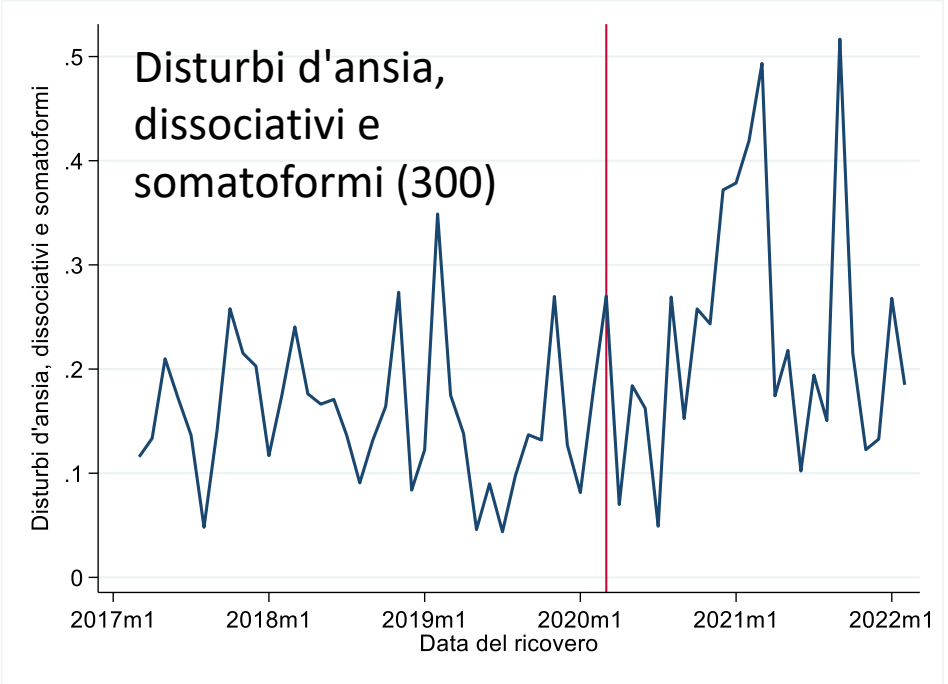
Hospital admissions in Pediatric Units in Emilia-Romagna Region

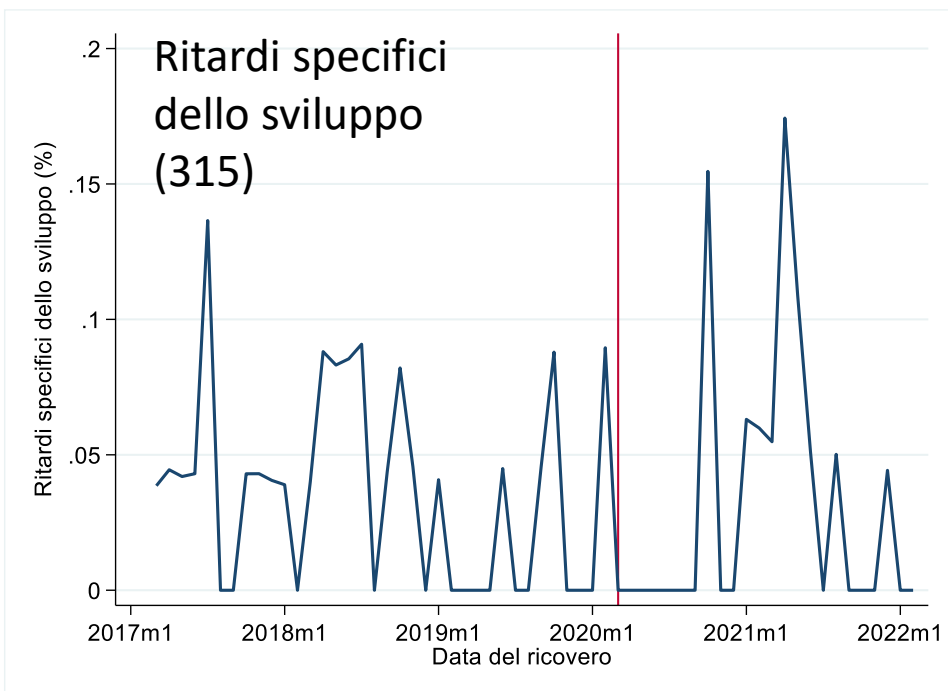
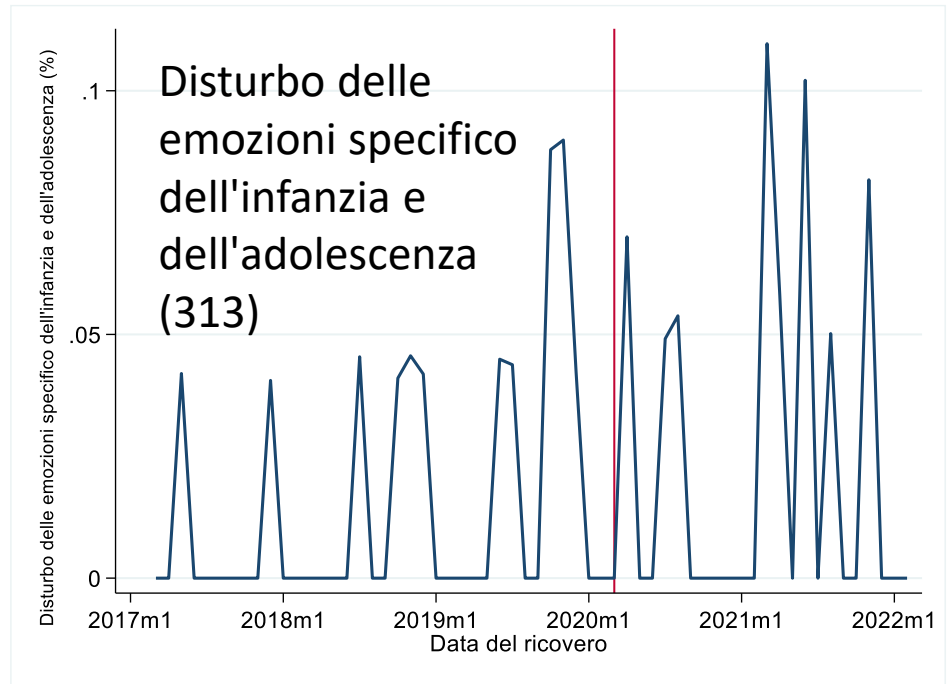
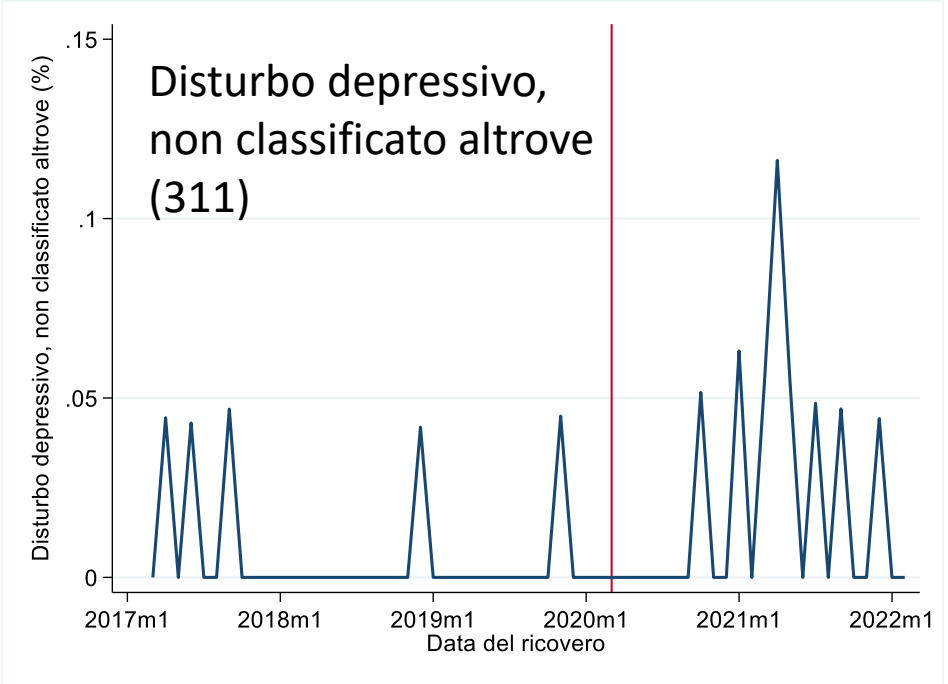
	Pre-COVID (Mar 1, 2017- Feb 28, 2020) (n=56,449)	Post-COVID (Mar 1, 2020- Feb 28, 2022) (n=27,919)	Whole period (Mar 1, 2017- Feb 28, 2022) (N=84,368)
<i>Sex, n(%) males</i>	32,262 (57.2)	15,798 (56.6)	48,060 (57.0)
<i>Age class, y n(%)</i>			
0-1	21,285 (37.7)	10,740 (38.5)	32,025 (38.0)
2-5	14,135 (25.0)	5,717 (20.5)	19,852 (23.5)
6-11	9,500 (16.8)	4,634 (16.6)	14,134 (16.8)
12-17	11,529 (20.4)	6,828 (24.5)	18,357 (21.8)



Esposito S, unpublished data







Viewpoint

ONLINE FIRST

FREE

March 16, 2023

Addressing the Long-term Effects of the COVID-19 Pandemic on Children and Families

A Report From the National Academies of Sciences, Engineering, and Medicine

Tumaini R. Coker, MD, MBA¹; Tina L. Cheng, MD, MPH²; Marci Ybarra, MSW, PhD³

» [Author Affiliations](#) | [Article Information](#)

JAMA. Published online March 16, 2023. doi:10.1001/jama.2023.4371

RAGAZZI, VACCINATEVI CONTRO COVID PER VOI!

L'appello dei pediatri agli adolescenti

Il Manifesto dei pediatri dell'Emilia-Romagna in 15 punti: vaccino efficace e sicuro, unica arma contro il virus

A fronte dei dati relativi alle coperture vaccinali contro Covid nei ragazzi di età compresa tra i 12 e 17 anni, sicuramente non ottimali in quanto inferiori al 50% in tutta Italia, e di notizie e passaparola basati su paure irrazionali, nel nostro ruolo di pediatri che lavorano in Ospedale e sul territorio intendiamo fare un appello univoco e convinto a favore della vaccinazione degli adolescenti, rivolgendoci in primis a loro e augurandoci che i genitori comprendano l'importanza di vaccinare subito i propri figli.

VACCINO COVID, L'APPELLO DEI PEDIATRI DELL'EMILIA-ROMAGNA AI GENITORI DEI BAMBINI TRA 5 E 11 ANNI

**“Genitori, vaccinate i vostri bambini contro COVID:
non è troppo presto”**

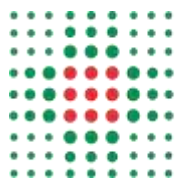
*Il manifesto dei pediatri SIP, SIN, ACP, FIMP e SIMPeF dell'Emilia-Romagna in 24 punti:
vaccino efficace e sicuro, uno straordinario regalo per la salvaguardia della salute dei più piccoli.*

TAKE HOME MESSAGES

- **Pediatric long COVID is a clinical problem that involve a relevant proportion of children**
- **Prognosis of these cases is generally good as in most of them symptoms disappear spontaneously**
- **The few children with significant medical problems should be early identified after the acute phase of the infection and adequately managed to assure complete resolution**
- **Most of persistent or emerging symptoms of long duration regard mental health**
- **A relevant psychological support for all the children during and after COVID-19 pandemic must be organized by health authorities and government that have to treat this as a public health issue**



Mi vaccino perché
so cosa c'è dentro,
ma soprattutto so
cosa c'è là fuori



SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA