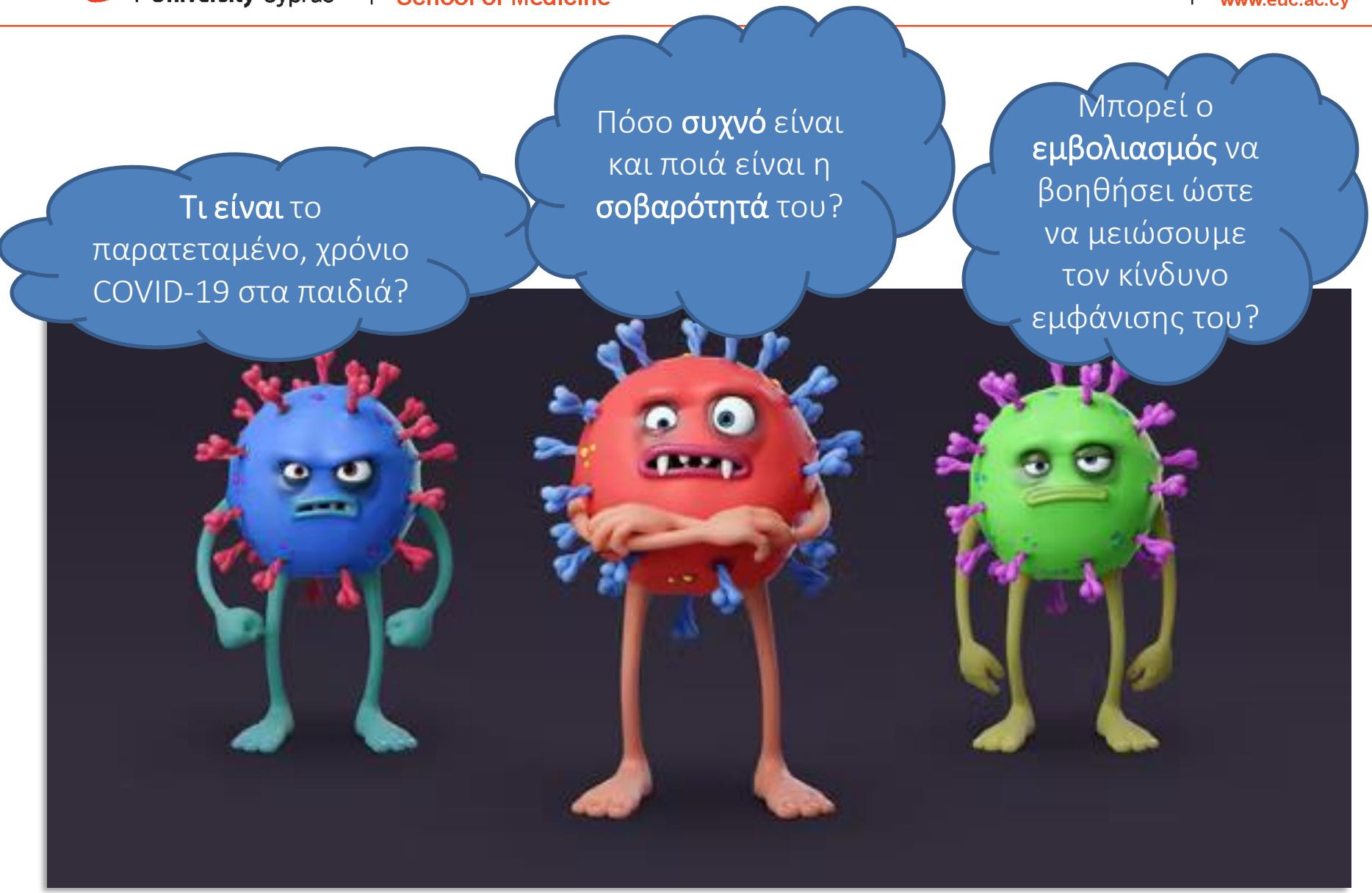
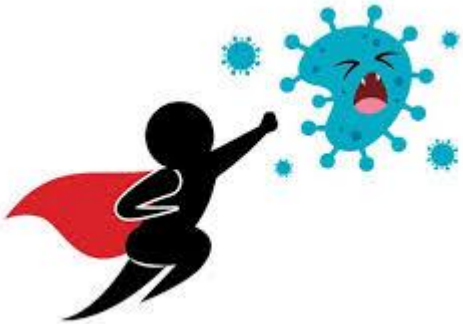
Post COVID-19 καταστάσεις στην παιδική ηλικία. Πόσο επηρεάζουν τα παιδιά μας?

Ζωή Δωροθέα Πανά, MD, MSc, PhD


Τι είναι το παρατεταμένο, χρόνιο COVID-19 στα παιδιά?
Πόσο συχνό είναι και ποιά είναι η σοβαρότητά του?
Μπορεί ο εμβολιασμός να βοηθήσει ώστε να μειώσουμε τον κίνδυνο εμφάνισης του?


Webinar:
Mitigating the Direct and Indirect Consequences of COVID-19 on the Health and Well-Being of Young People in the Americas
THURSDAY, MARCH 10TH, 2022
10:00 -11:30 hrs. EST
English; Español
PAHO
Pan American Health Organization
World Health Organization
Americas
PAHO 120th ANNIVERSARY



'It's terrifying': parents' struggle to get help for children with long Covid

Lack of research into area means children are being sent away from A&E and parents told they are overanxious

- Coronavirus – latest updates
- See all our coronavirus coverage

A growing numbers of parents say they are being regarded with suspicion by medical professionals over their child's unexplained symptoms. Photograph: Supplied

On Christmas Day, Gail Jackson's 16-year-old daughter said she was in so much pain she thought she would die. Liliana had been briefly admitted to hospital with Covid in September. Her symptoms never went away and, as time went on, new ones had emerged.

"For months she had a relentless, agonising headache, nausea, tinnitus, fatigue and insomnia, but the worst thing was the agonising nerve pain," said Jackson. "I couldn't even touch her without her screaming in pain."

On Christmas morning, Jackson drove to hospital with her daughter vomiting from pain in the passenger seat. When they got to the hospital, however, the A&E doctor said there was no such thing as long Covid in children. "He said she just needed to go home and get on with her life," Jackson said. "It was jaw-dropping."

LongCovidSOS

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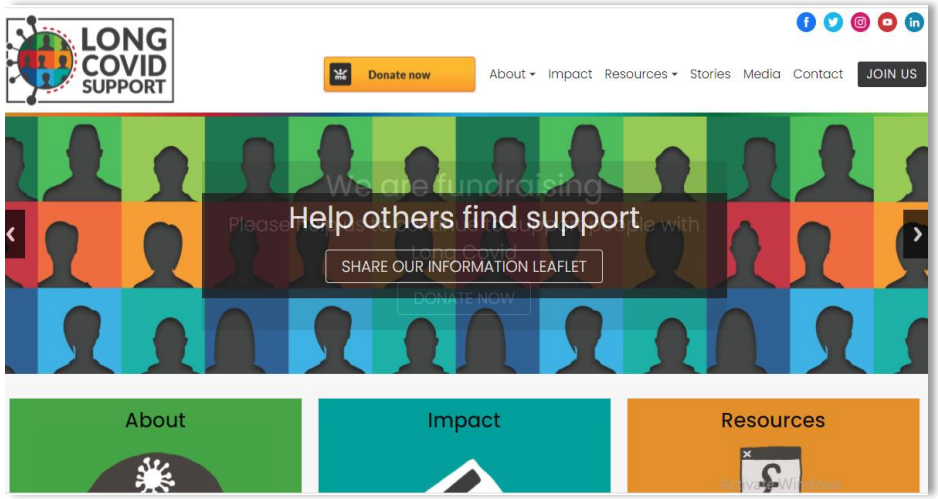
Prime Minister Boris Johnson, respond to our SOS.


Long Covid Kids
& Friends Supporting each other.
Home
About
Awareness
Support
Recovery
Blog
Our Purpose
We believe all children should be able to thrive and look forward to a positive future.
That is why we represent and support children and young people living with Long Covid and related illnesses and the parents and caregivers that look after them.
Contact Us


LONG COVID SUPPORT
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Help others find support
SHARE OUR INFORMATION LEAFLET
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Impact
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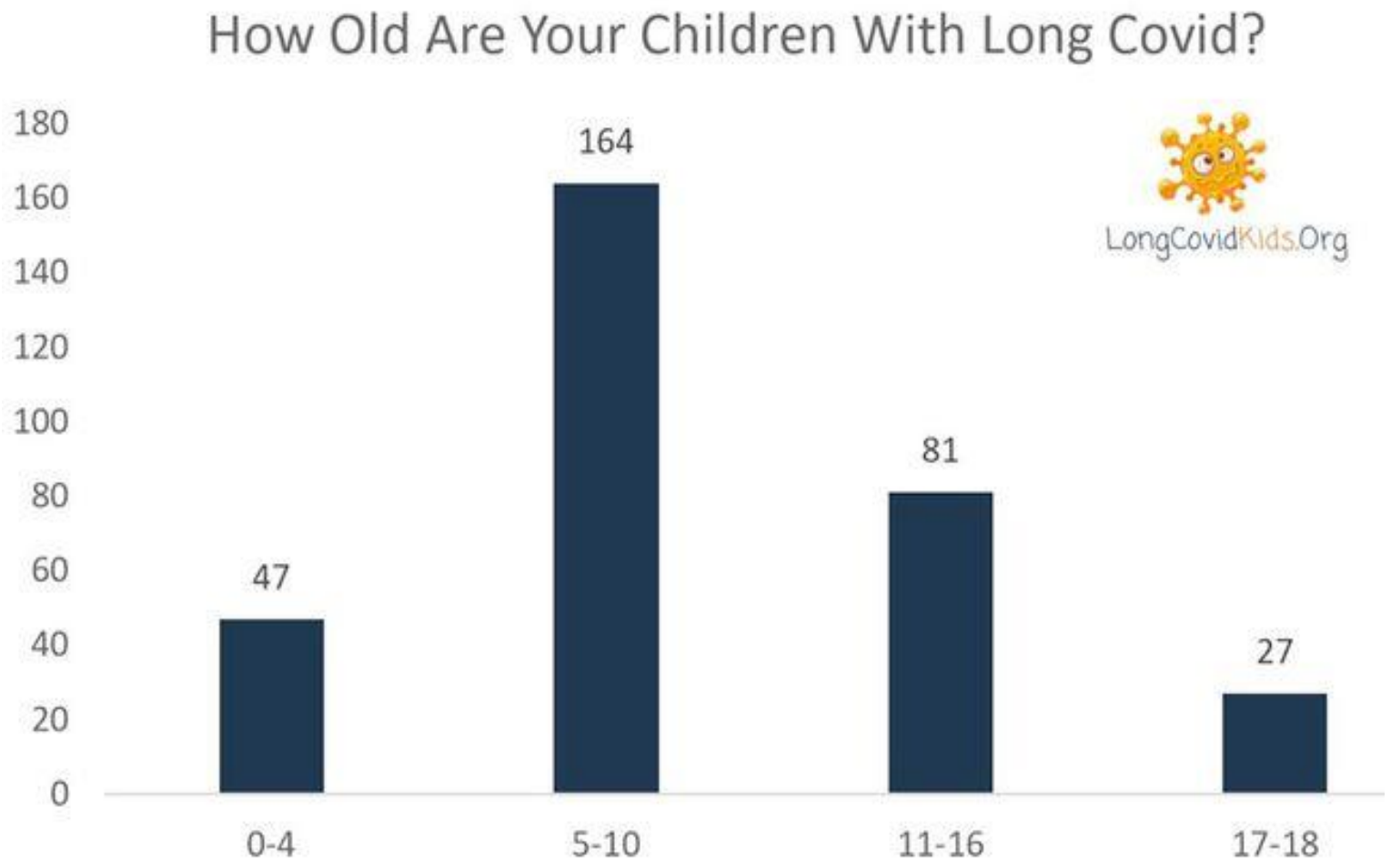
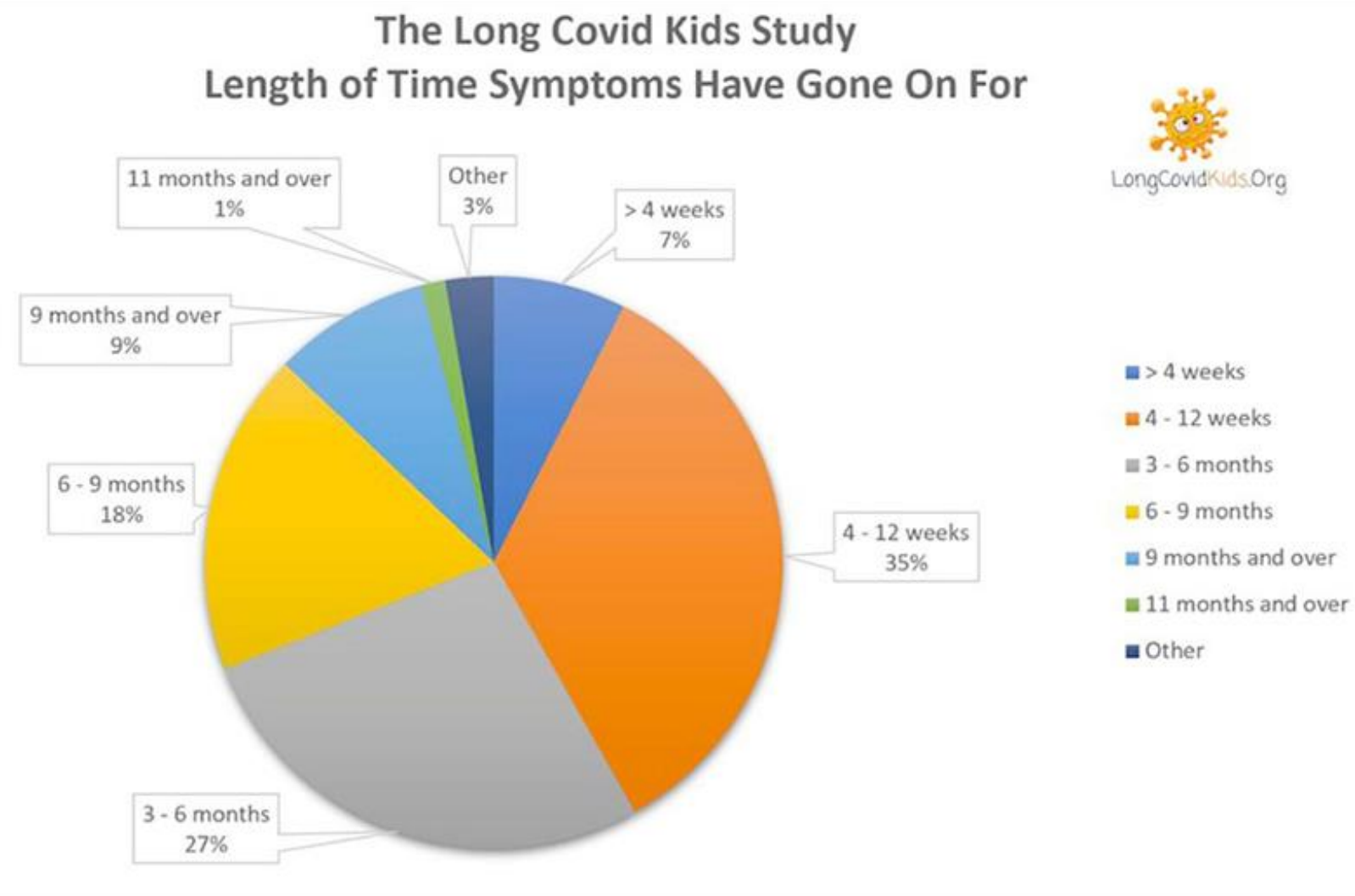

How Old Are Your Children With Long Covid?
180
160
140
120
100
80
60
40
20
0
47
164
81
27
0-4
5-10
11-16
17-18
LongCovidKids.Org


The Long Covid Kids Study
Length of Time Symptoms Have Gone On For
LongCovidKids.Org
11 months and over 1%
Other 3%
> 4 weeks 7%
9 months and over 9%
6 - 9 months 18%
4 - 12 weeks 35%
3 - 6 months 27%
> 4 weeks
4 - 12 weeks
3 - 6 months
6 - 9 months
9 months and over
11 months and over
Other

> *The hypothesis that is mostly talked about currently is inflammatory changes to small blood vessels that then will lead to organ dysfunction – Jakob Armann*

Oliveira told the BBC that in some cases children can sustain organ damage from the virus that causes Covid-19, Sars-CoV-2. It can invade the heart or the pancreas, causing conditions such as pericarditis or pancreatitis where that particular organ becomes inflamed – which can lead to breathing problems and other long-term complications, but this is relatively rare.

There are series of **theories for why long Covid occurs in adults**, ranging from the reactivation of a dormant virus, to lingering viral fragments within the body, to a viral-induced autoimmune reaction with so-called autoantibodies binding to cells in different tissues. The same may be true for children, but another idea being considered as a possible mechanism for long Covid in both children and adults is that the **virus induces damage to the circulatory system**.

"The hypothesis that is mostly talked about currently is inflammatory changes to small blood vessels that then will lead to organ dysfunction," says Jakob Armann, a paediatrician at Dresden University of Technology in Germany, who has been collecting blood samples from secondary school children to try to identify possible

The Children and young people with **Long COVID (CLoCk) study** is led by UCL and Public Health England

Up to one in seven (14%) children and young people who caught SARS-CoV-2 may have symptoms linked to the virus 15 weeks later

For the study, funded by the UK's National Institute for Health Research (NIHR) and UK Research and Innovation (UKRI), researchers surveyed:

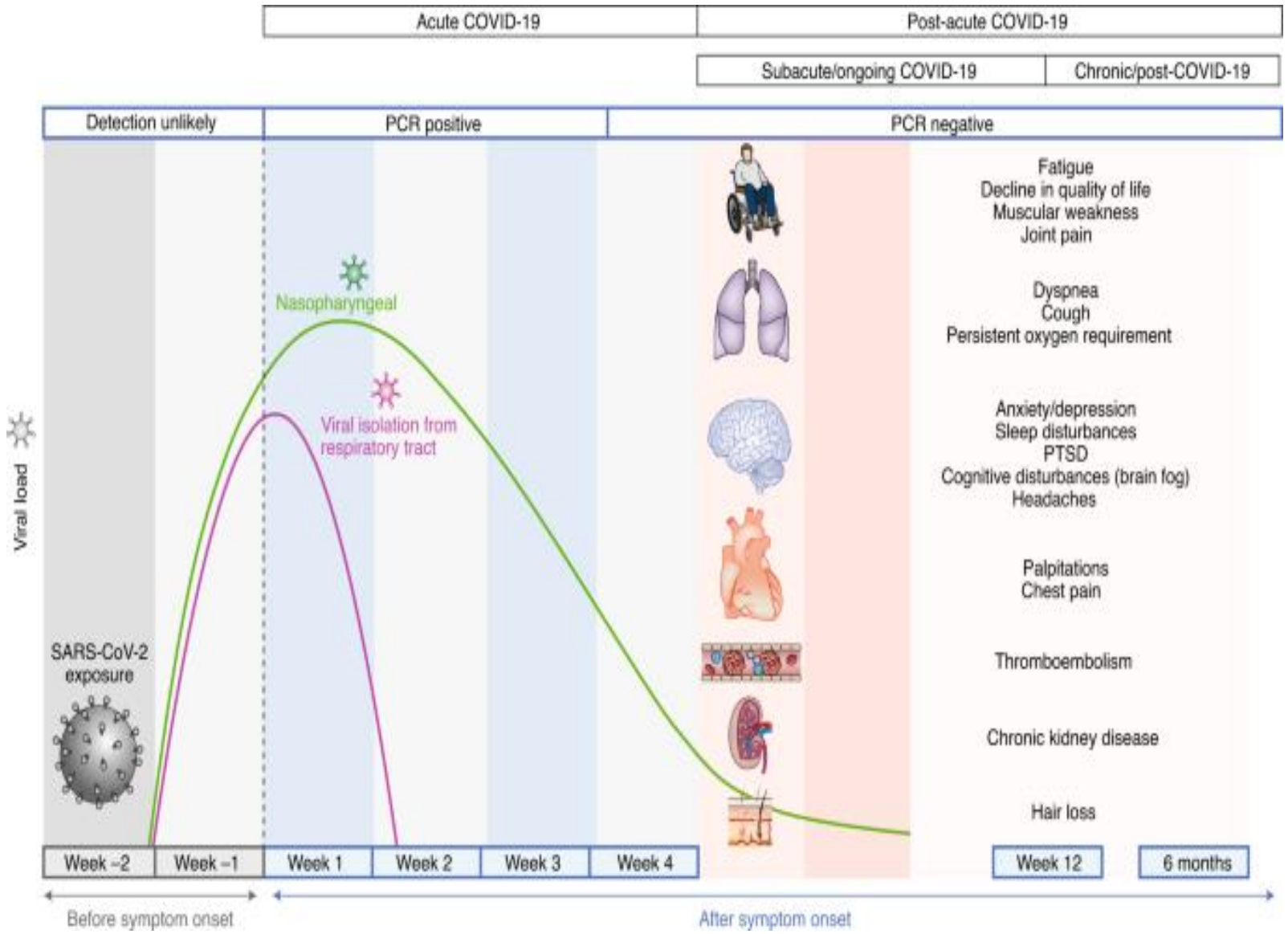
- 3,065 11- to 17-year-olds in England who had positive results in a PCR test between January and March
  a matched control group of 3,739 11- to 17-year-olds who tested negative over the same period.
- They found that, when surveyed at an average of 15 weeks after their test:
  14% more young people in the test positive group had three or more symptoms of ill health, including **unusual tiredness and headaches,** than those in the test negative group
- **7% (one in 14) more had five or more symptoms**

Definition of post COVID-19 conditions

Origin	Term	Definition
National Institute for Clinical Excellence (NICE)[5]	Long COVID (includes ongoing symptomatic COVID-19 and post-COVID-19 syndrome)	Long COVID is characterized as the persistence of COVID-19 signs and symptoms that continue to develop after acute COVID-19 and can include both ongoing symptomatic COVID-19 and post-COVID-19 syndrome. **Ongoing symptomatic COVID-19** Signs and symptoms which persist 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 alternate diagnosis.
Centers for Disease Control and Prevention (CDC)[6]	Post-COVID conditions	New, returning, or ongoing health problems that people experience 4 or more weeks after initial infection with SARS-CoV-2.
World Health Organization (WHO)[4]	Post COVID-19 condition	Post COVID-19 condition can be assumed in a patient who does not recover to baseline health after an initial infection or diagnosis of COVID-19.
Public Health Agency of Canada (PHAC)[7]	Post COVID-19 conditions	Symptoms persisting or recurring for weeks after acute COVID-19 illness. This can be further broken down into post COVID-19 conditions occurring 4-12 weeks (short term) and >12 weeks (long-term) after COVID-19 diagnosis

Science Briefs | www.covid19-sciencetable.ca/science-briefs September 14, 2021

Definition of post COVID-19 conditions



Nature Scientific Reports volume 11, Article number: 16144 (2021)

Systematic review: post COVID-19 conditions in adults

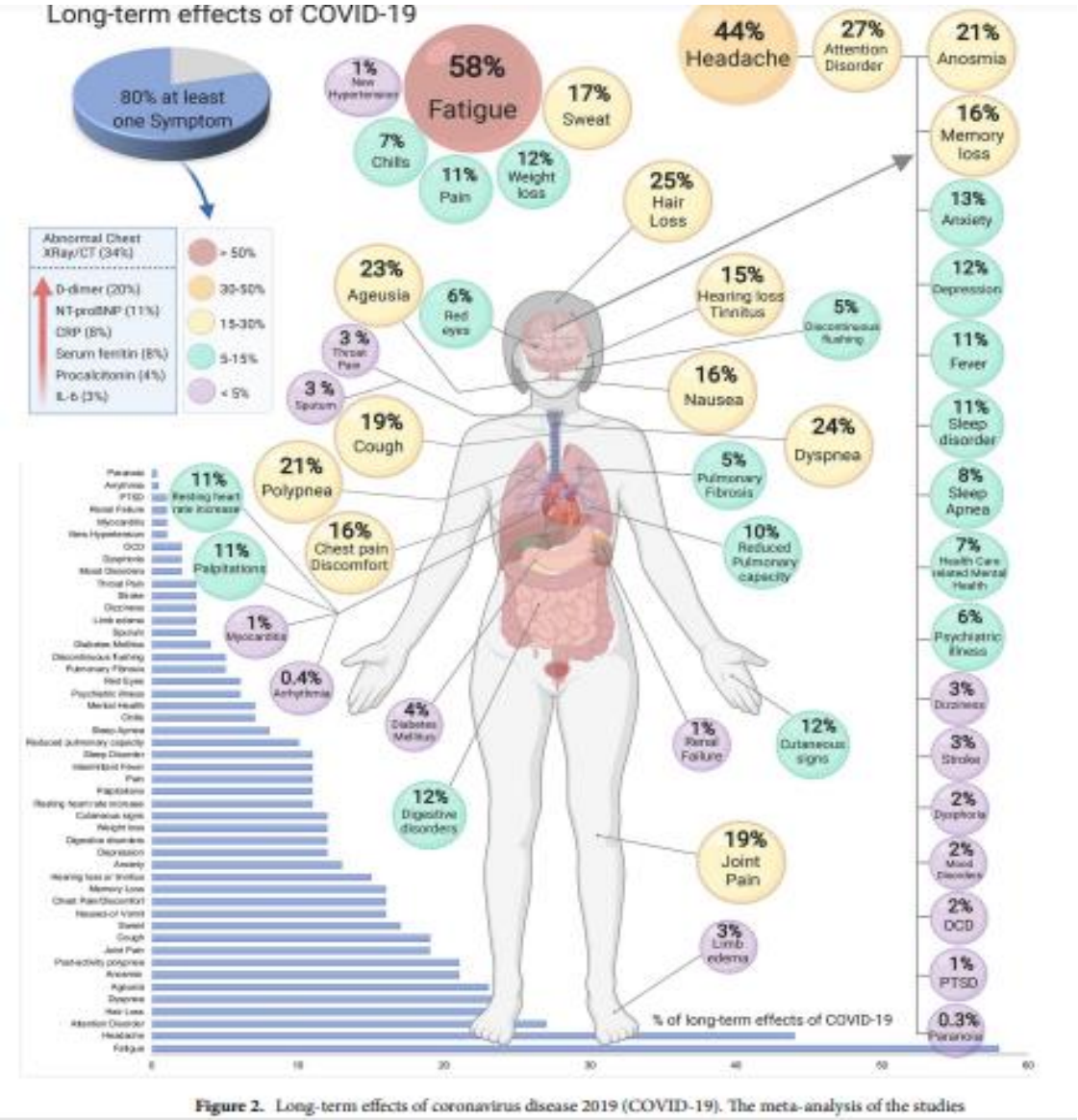


Figure 2. Long-term effects of coronavirus disease 2019 (COVID-19). The meta-analysis of the studies

Prevalence of 55 long-term effects
In 21 studies (47,910, age 17–87 years)
Period 4 to 110 days post-viral infection

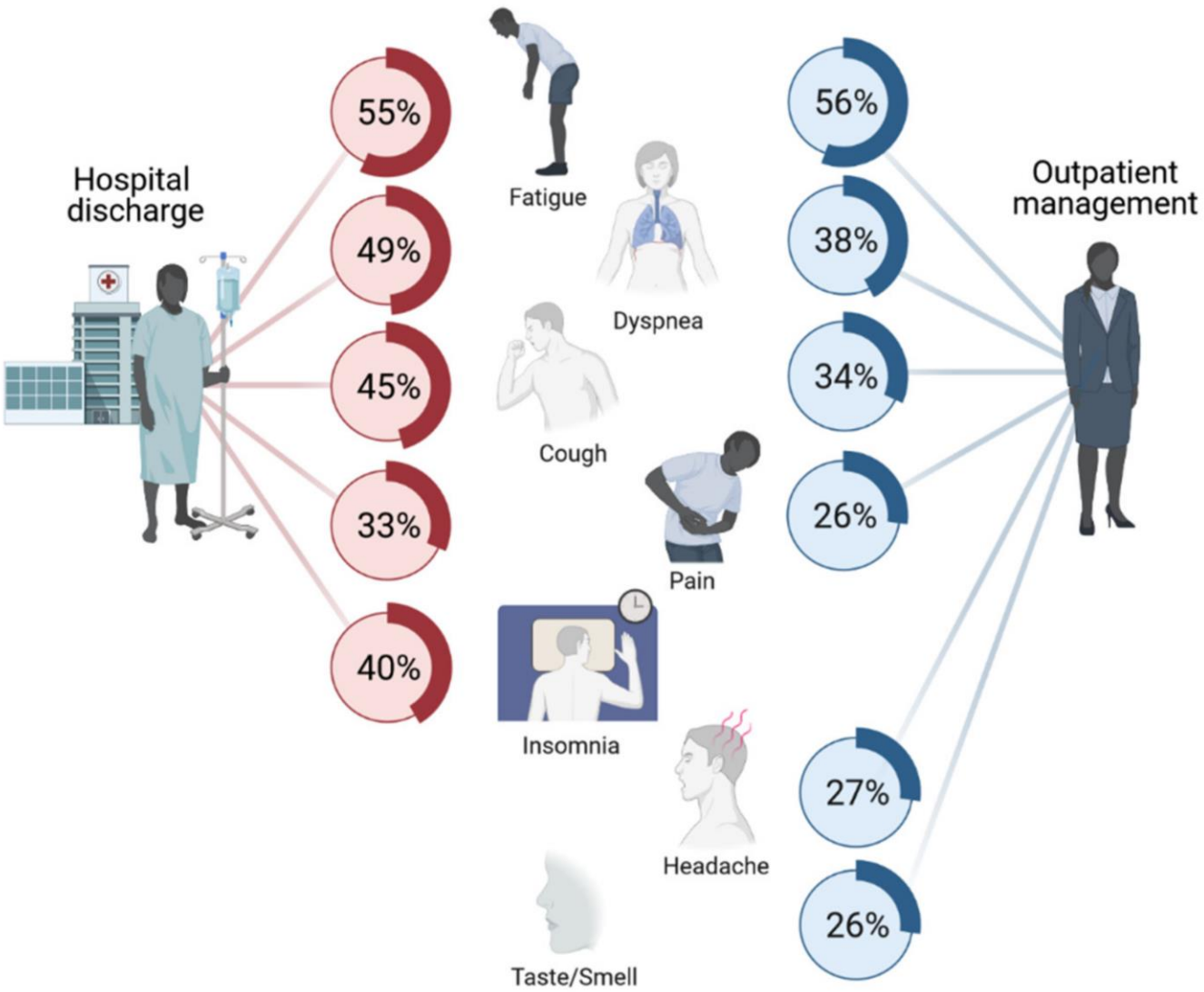
80% of the infected patients
with SARS-CoV-2 developed
one or more long-term symptoms

The five most common symptoms were

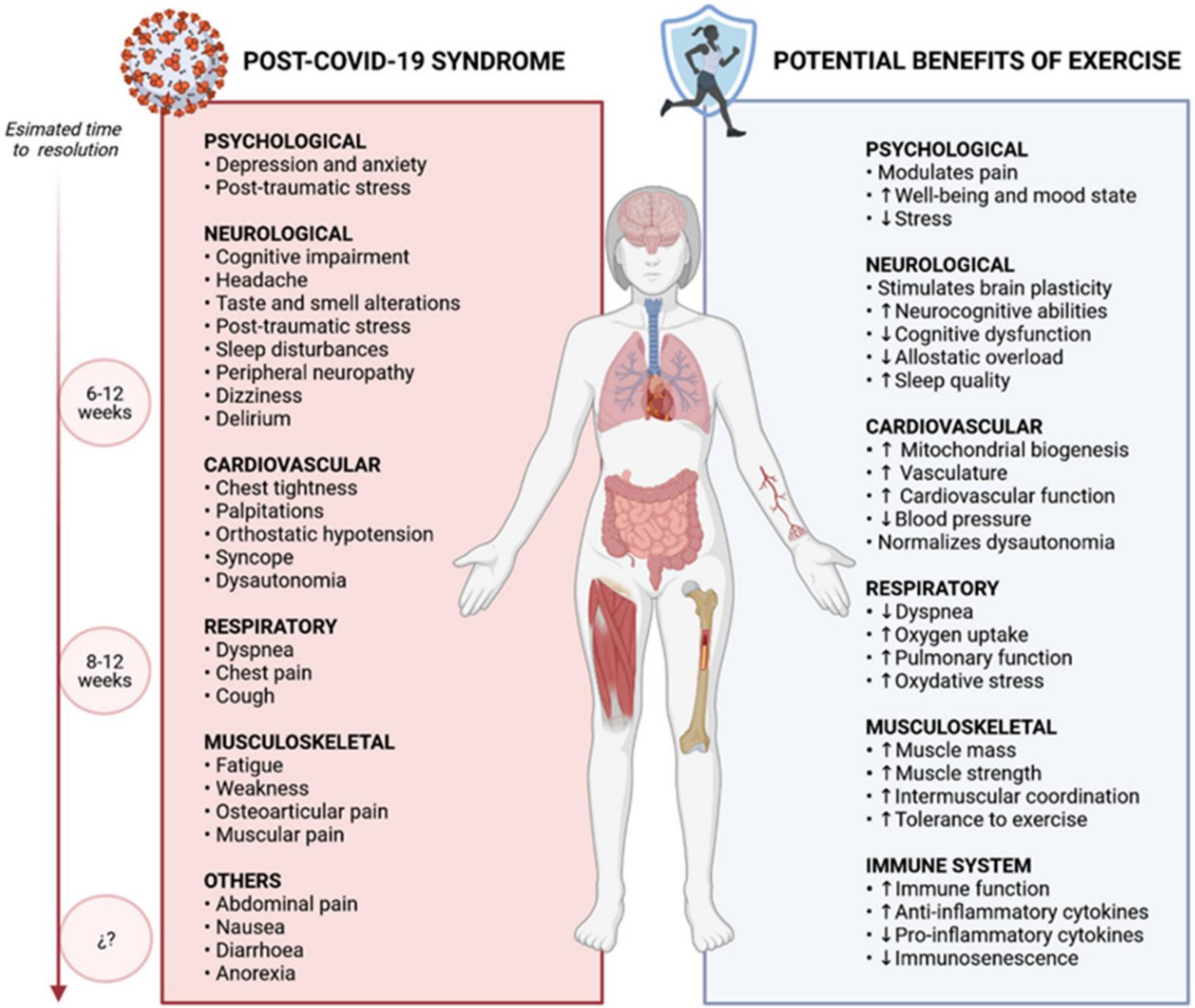
- ✓ fatigue (58%)
- ✓ headache (44%)
- ✓ attention disorder (27%)
- ✓ hair loss (25%)
- ✓ dyspnea (24%)

Nature Scientific Reports volume 11, Article number: 16144 (2021)

POST-COVID-19 SYNDROME MAIN SYMTOMS (4-12 WEEKS)



Int. J. Environ. Res. Public Health **2021**, *18*(10), 5329



Int. J. Environ. Res. Public Health **2021**, *18*(10), 5329

Post COVID-19 conditions in children/adolescents

- The prevalence of long COVID symptoms varied between ped studies: 4–66%
- Large variation in the reported frequency of persistent symptoms

- The most common reported symptoms were:
  - ✓ headache (3 to 80%)
  - ✓ fatigue (3 to 87%)
  - ✓ sleep disturbance (2 to 63%)
  - ✓ concentration difficulties (2 to 81%)
  - ✓ abdominal pain (1 to 76%)
  - ✓ myalgia or arthralgia (1 to 61%)
  - ✓ congested or runny nose (1 to 12%)
  - ✓ cough (1 to 30%)
  - ✓ chest tightness or pain (1 to 31%)
  - ✓ loss of appetite or weight (2 to 50%)
  - ✓ disturbed smell or anosmia (3 to 26%)
  - ✓ rash (2 to 52%)

Pediatr Infect Dis J 2021;40:e482–e487

Prevalence: Post COVID-19 in children/adolescents

- UK cohort pediatric study: 5-17 yrs old
- Positive SARS-CoV-2 test
- Period: September 1, 2021 to January 24, 2021

	Children with positive SARS-CoV-2 test (n=1734)					Children with negative SARS-CoV-2 test (matched cohort, n=1734)
	Younger group (aged 5–11 years, n=588)	Older group (aged 12–17 years, n=1146)	Symptom duration <10 days (n=1183)	Symptom duration ≥28 days (n=77)	Full cohort (n=1734)	
Females	301 (51·2%)	569 (49·7%)	565 (47·8%)	42 (54·5%)	870 (50·2%)	869 (50·1%)
Males	287 (48·8%)	577 (50·3%)	618 (52·2%)	35 (45·5%)	864 (49·8%)	865 (49·9%)
Age, years	9 (7–10)	15 (13–16)	13 (10–15)	14 (12–16)	13 (10–15)	13 (10–15)
Body-mass index (kg/m^2)	17·0 (15·1–19·7)	20·1 (17·8–22·3)	19·0 (16·5–21·8)	18·6 (16·3–21·8)	19·2 (16·6–21·8)	19·0 (16·5–21·5)
Asthma	69 (11·7%)	147 (12·8%)	134 (11·3%)	10 (13·0%)	216 (12·5%)	229 (13·2%)
Heart disease	1 (0·2%)	1 (0·1%)	2 (0·2%)	0	2 (0·1%)	0
Diabetes	2 (0·3%)	5 (0·4%)	4 (0·3%)	0	7 (0·4%)	6 (0·3%)
Renal disease	0	2 (0·2%)	0	1 (1·3%)	2 (0·1%)	4 (0·2%)
Presentation to hospital	16 (2·7%)	21 (1·8%)	20 (1·7%)	1 (1·3%)	37 (2·1%)	26 (1·5%)
Illness duration, days	5 (2–9)	7 (3–12)	4 (2–6)	46 (32–58)	6 (3–11)	3 (2–7)
Number of symptoms in the first week	3 (2–5)	4 (2–6)	3 (2–5)	6 (4–8)	3 (2–6)	2 (1–4)

Data are n (%) or median (IQR). The cohort of children with positive SARS-CoV-2 testing is presented here both as younger and older groups, and for usual (ie, short) versus extended illness duration. Data refers to children with symptom onset between Sept 1, 2020, and Jan 24, 2021. Common paediatric comorbidities such as neurological or neurodisability disorders (eg, cerebral palsy) were not assessed. Presentation to hospital included presenting to the emergency department or admission to hospital.

Table: **Characteristics of school-aged children who tested positive for SARS-CoV-2, and the control cohort of children (matched 1:1 for age, gender, and week of testing) who tested negative for SARS-CoV-2**

Lancet Child Adolesc Health 2021; 5: 708–18

Prevalence: Post COVID-19 in children/adolescents

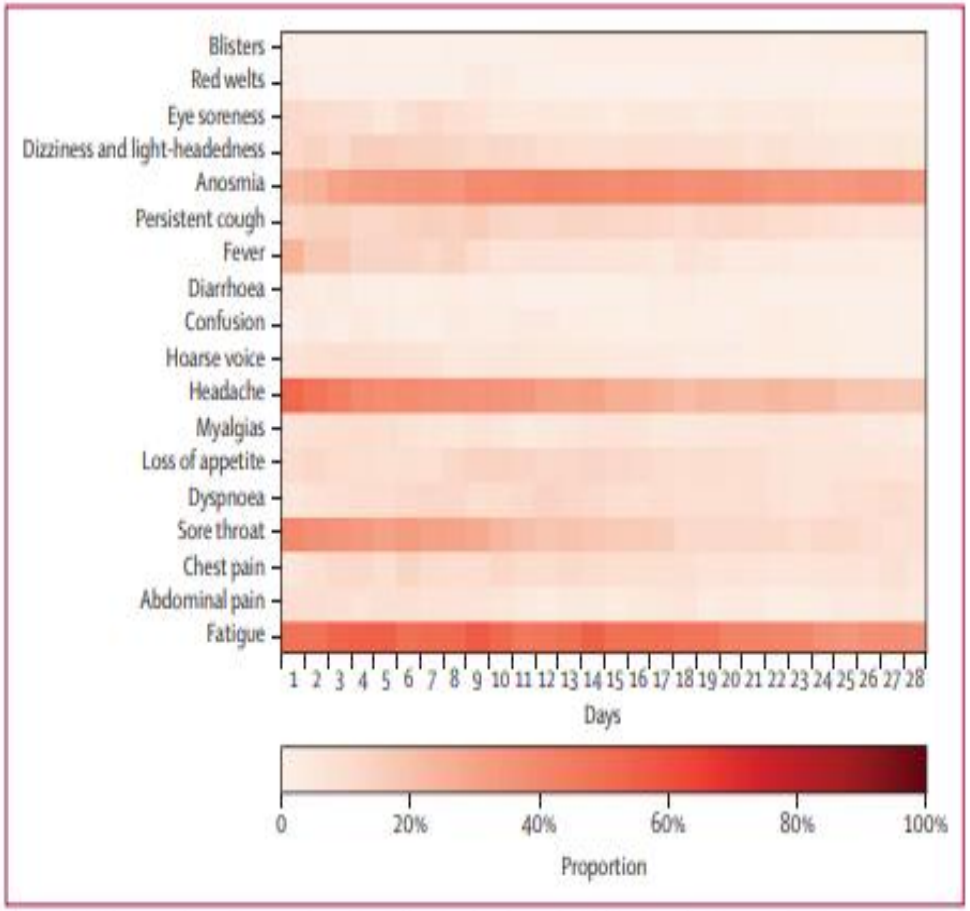


Figure 4: **Heat maps showing symptom duration in school-aged children (age 5–17 years) testing positive for SARS-CoV-2 in whom at least one symptom persisted for at least 28 days**

n=77. Colour bar provides a percentage comparison. Data refers to children with symptom onset between Sept 1, 2020, and Jan 24, 2021.

- 4.4% experienced prolonged symptoms (28 days after infection)
- 1.8% experienced symptoms (56 days after Infection)

- The most common prolonged symptoms:
  - ✓ Fatigue
  - ✓ Headache
  - ✓ loss of smell
  - ✓ sore throat

Lancet Child Adolesc Health 2021; 5: 708–18

Prevalence: Post COVID-19 in children/adolescents

Open access Protocol

BMJ Open

Long COVID and the mental and physical health of children and young people: national matched cohort study protocol (the CLoCk study)

Terence Stephenson [1], Roz Shafran,[1] Bianca De Stavola,[1] Natalia Rojas [1], Felicity Aiano,[2] Zahin Amin-Chowdhury [2], Kelsey McOwat,[2] Ruth Simmons,[2] Maria Zavala,[2] CLoCk Consortium,[1] Shamez N Ladhani,[2] CLoCk Consortium members

- Age: 11-17 yrs old (database of test results held by Public Health England)
- Period: January to March 2021
- Questionnaires: 220 000 (17 000 responses)
- Sample size: 3065 tested positive for SARS-CoV-2 and a matched cohort of 3739
- Timing of questionnaire: **three months** after their test
- Results: 66.5% of people who had tested positive and 53.3% of those who had tested negative had one or more symptoms. About 30% of those who had tested positive for covid-19 had three or more symptoms, compared with 16% of those who tested negative.
- 14% of people who test positive for covid have persistent symptoms
- The most common symptoms reported were headaches and tiredness

Stephenson T, et al. BMJ Open 2021;11:e052838. doi:10.1136/bmjopen-2021-052838

Prevalence: Post COVID-19 in children/adolescents

- Pediatric cohort study
- Unicenter: Children's Clinical University Hospital in Latvia
- Population: pediatric COVID-19 patients vs children with other non-SARS-CoV-2-community-acquired infections

- Period: July 1, 2020, and April 30, 2021

- Results: 236 pediatric COVID-19 patients vs 142 comparison group
- Most pediatric COVID-19 survivors (70%, N=152) reported at least one persistent symptom but more than half of the patients (53%, N=117) noted two or more long-lasting symptoms.

Front. Pediatr. 9:2021: 752385. doi: 10.3389/fped.2021.752385

Prevalence: Post COVID-19 in children/adolescents

- 105 (44.5%) COVID patients had persistent symptoms after the 12-week cut-off point, with irritability (27.6%, N=29), mood changes (26.7%, N=28), and fatigue (19.2%, N=20) being the most commonly reported ones.
- Differences in symptom spectrum among the various age groups were seen
- Logistic regression analysis showed that long-term persistent symptoms as fever, fatigue, rhinorrhea, loss of taste and/or smell, headaches, cognitive sequelae, and nocturnal sweating were significantly associated with the COVID-19 experience when compared with the controls.

Front. Pediatr. 9:2021: 752385. doi: 10.3389/fped.2021.752385

Prevalence: Post COVID-19 in children/adolescents

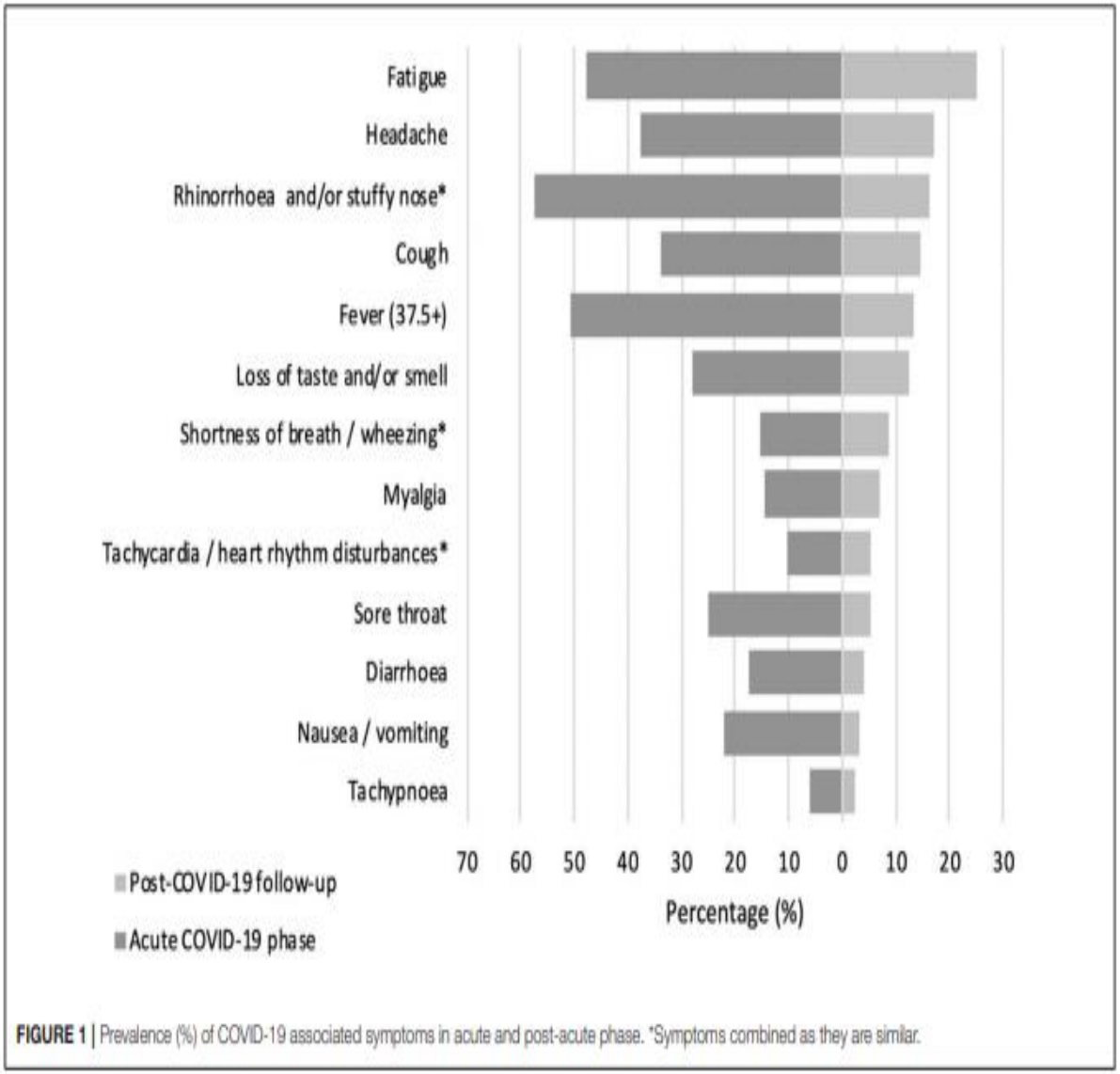


FIGURE 1 | Prevalence (%) of COVID-19 associated symptoms in acute and post-acute phase. *Symptoms combined as they are similar.

- fatigue (25.2%)
- irritability (24.3%)
- mood changes (23.3%)
- headaches (16.9%)
- rhinorrhea (16.1%)
- coughing (14.4%)
- anosmia/dysgeusia (12.3%)

Front. Pediatr. 9:2021: 752385. doi: 10.3389/fped.2021.752385

Prevalence: Post COVID-19 in children/adolescents

- Morbidity outcomes: 11 950 children/ adolescents with COVID-19
- Timing: 3 months after COVID-19 diagnosis

- The paediatric COVID-19 cohort higher incidence rates of symptoms:
  - ✓ Physical health domains (IRR overall: 1.31 (95% CI:1.24-1.38); IRR confirmed COVID-19: **254.58**; IRR control group: **194.45**) and
  - ✓ Mental health domains (IRR overall: 1.39 (95% CI:1.28-1.52); IRR confirmed COVID-19: 102.17; IRR control group: 73.24)
  - ✓ The outcomes with the highest IRR were malaise/fatigue/exhaustion, cough, and throat/chest pain.
- Similar IRRs were found in the age groups 0–11 years and 12–17 years

MedRxiv. 2021:2021.10.21.21265133. Available at: http://medrxiv.org/content/early/2021/10/22/2021.10.21.21265133

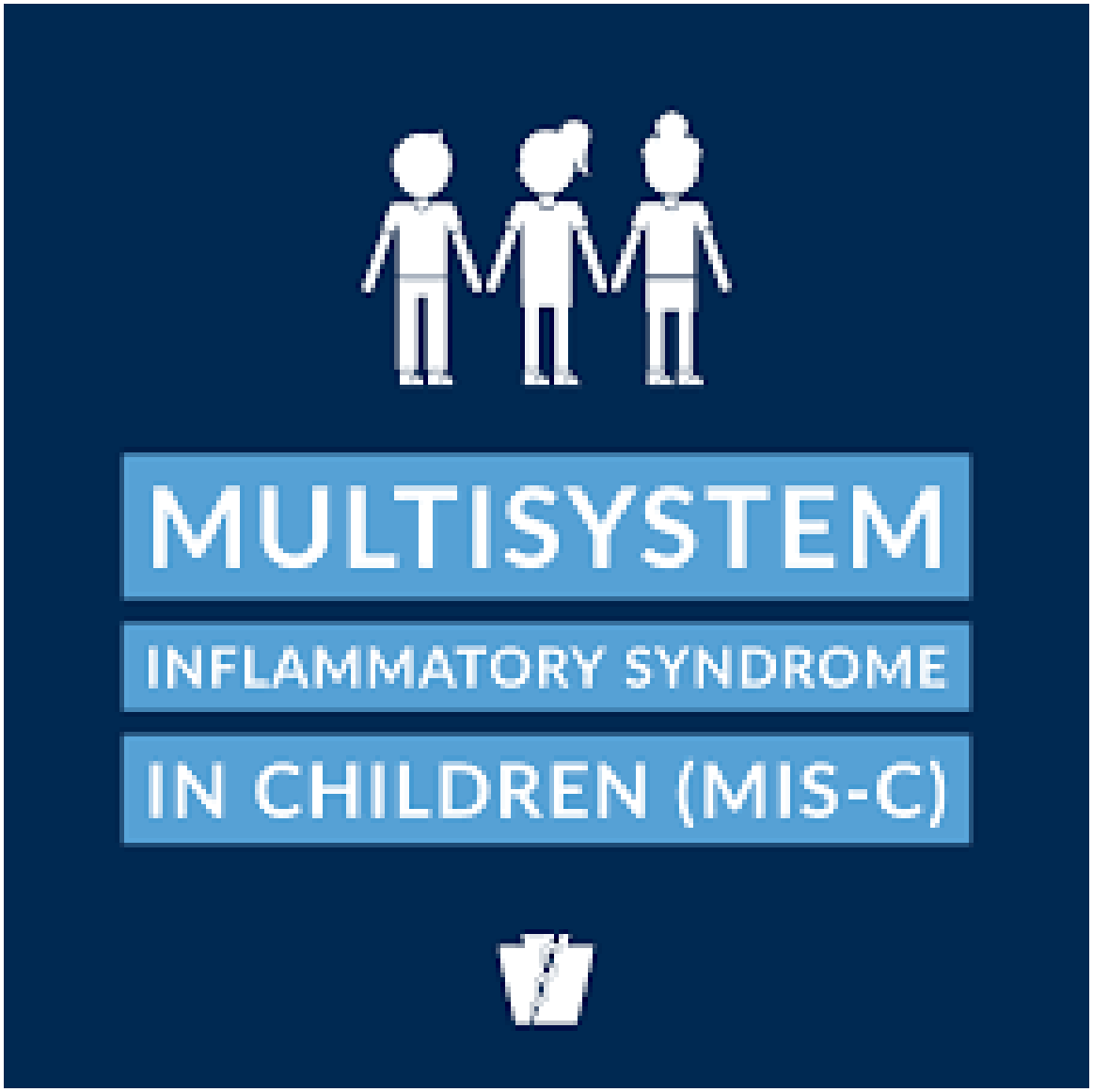
Prevalence: Post COVID-19 in children/adolescents

Table 2: 10 post COVID-19 outcomes in children/adolescents with highest IRRs and incidence of at least 1/100 person-years in the COVID-19 cohort

Rank	Name	IRR	95%-CI	IR COVID-19	IR Control
1	Malaise/fatigue/exhaustion	2.28**	[1.71-3.06]	12.58	5.51
2	Cough	1.74**	[1.48-2.04]	36.56	21.06
3	Throat/chest pain	1.72**	[1.39-2.12]	20.01	11.66
4	Adjustment disorder	1.71**	[1.42-2.06]	26.37	15.40
5	Somatization disorder	1.62**	[1.30-2.02]	17.90	11.06
6	Headache	1.58**	[1.35-1.84]	36.67	23.24
7	Fever	1.56**	[1.30-1.87]	27.84	17.84
8	Anxiety disorder	1.54**	[1.23-1.92]	16.70	10.87
9	Abdominal pain	1.45**	[1.27-1.64]	53.94	37.31
10	Depression	1.45**	[1.12-1.87]	12.05	8.32

Note: Significance levels: *=5%, **=1%

MedRxiv. 2021:2021.10.21.21265133. Available at: http://medrxiv.org/content/early/2021/10/22/2021.10.21.21265133


MULTISYSTEM
INFLAMMATORY SYNDROME
IN CHILDREN (MIS-C)

Multi inflammatory syndrome MS-C

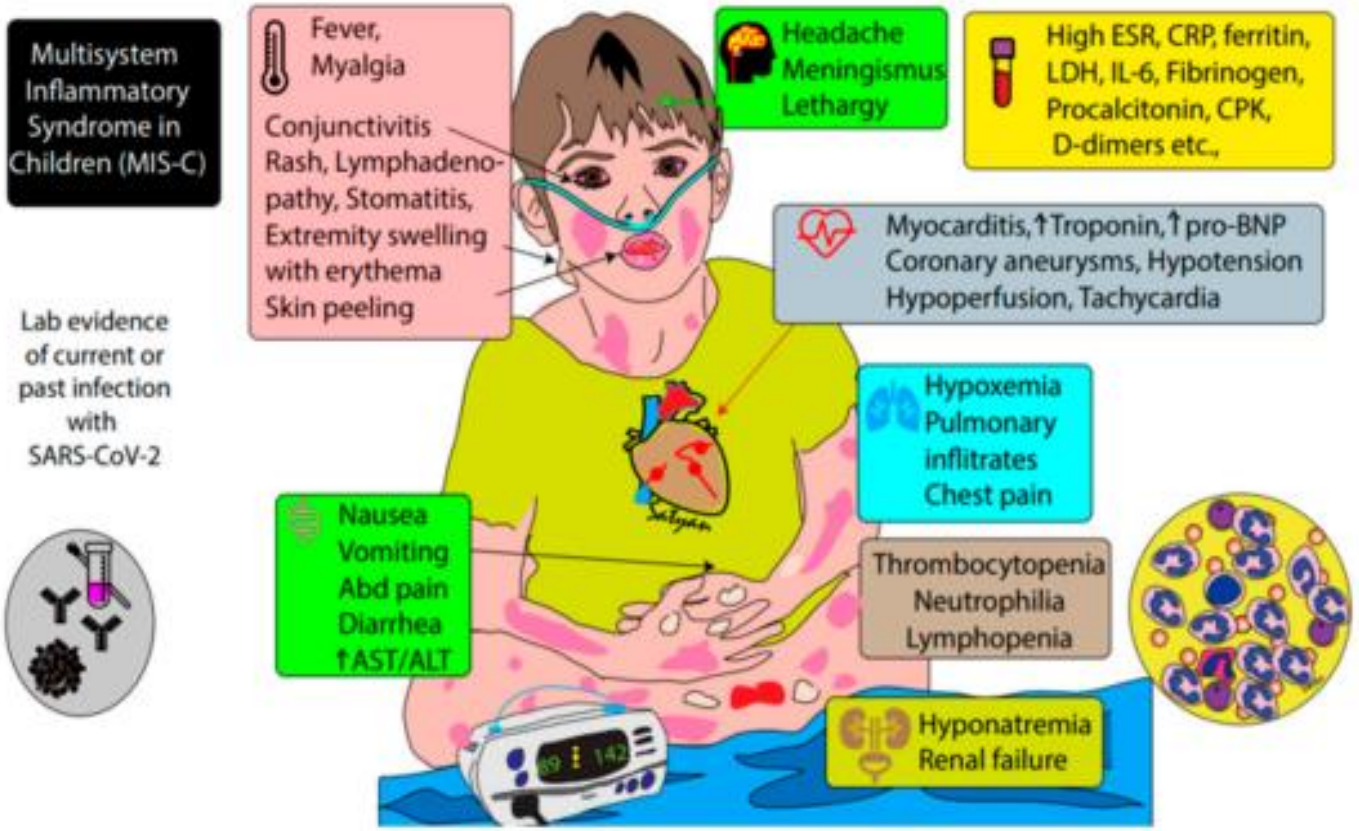


Figure 1. Infographic showing CDC criteria for the diagnosis of MIS-C. A combination of fever, evidence of inflammation, involvement of at least two organ systems, and prior evidence of SARS-CoV-2 infection are required to establish the diagnosis.

Children 2020, 7, 69; doi:10.3390/children7070069

MS-C syndrome: Pathology

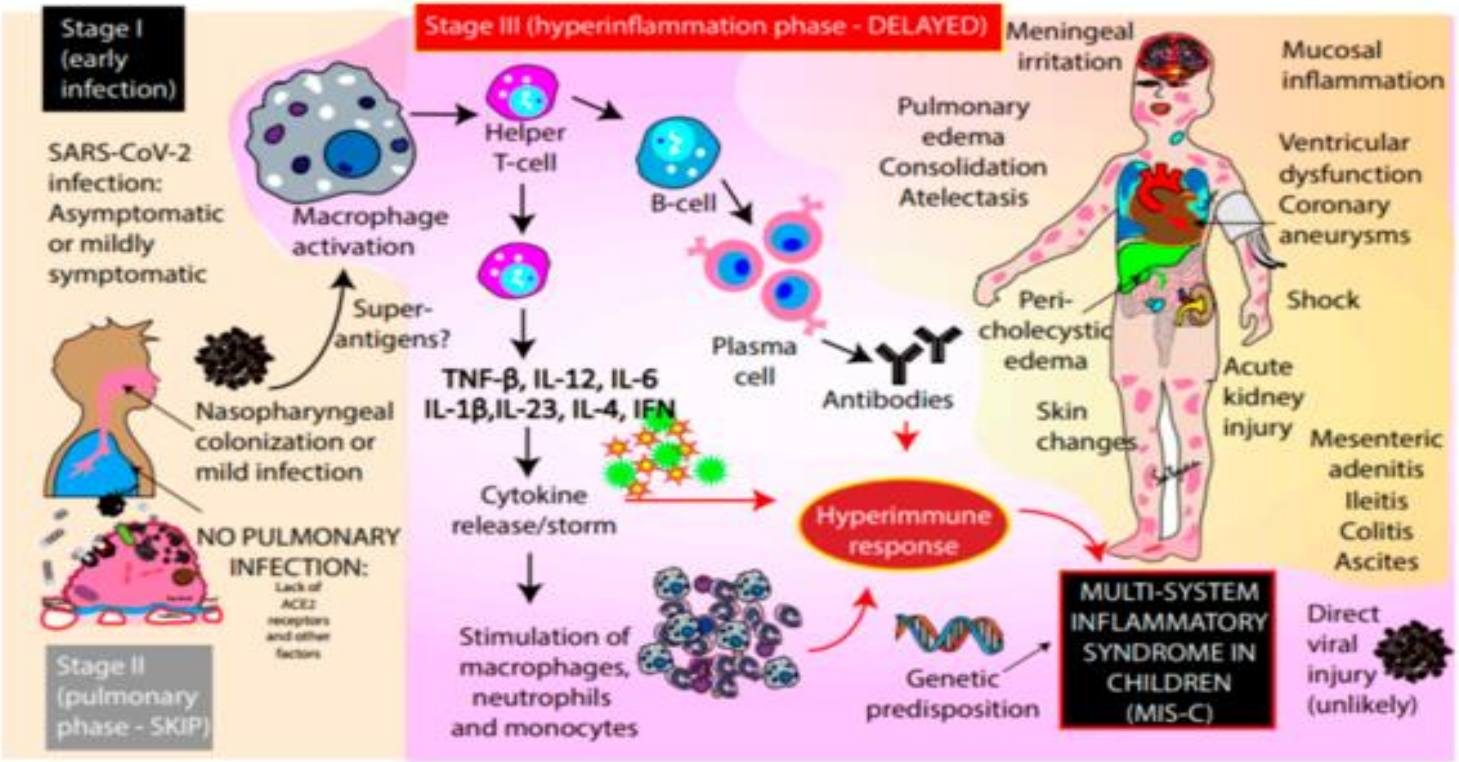


Figure 2. Pathogenesis of MIS-C. Early infection (phase I) with SARS-CoV-2 is likely to be asymptomatic or mildly symptomatic in children. The pulmonary phase (phase II) is severe in adults but is mild or absent in many children. The early infection appears to trigger macrophage activation followed by the stimulation of T-helper cells. This in turn leads to cytokine release, the stimulation of macrophages, neutrophils, and monocytes, along with B-cell and plasma cell activation with the production of antibodies leading to a hyperimmune response (stage III). This immune dysregulation is associated with the inflammatory syndrome in affected children. Direct infection with SARS-CoV-2 is less likely to play a role in MIS-C. ACE2—angiotensin converting enzyme 2 receptors; TNF-β—tumor necrosis factor β; IL—interleukins.

Children 2020, 7, 69; doi:10.3390/children7070069

Multi inflammatory syndrome MIS-C- Epidemiology

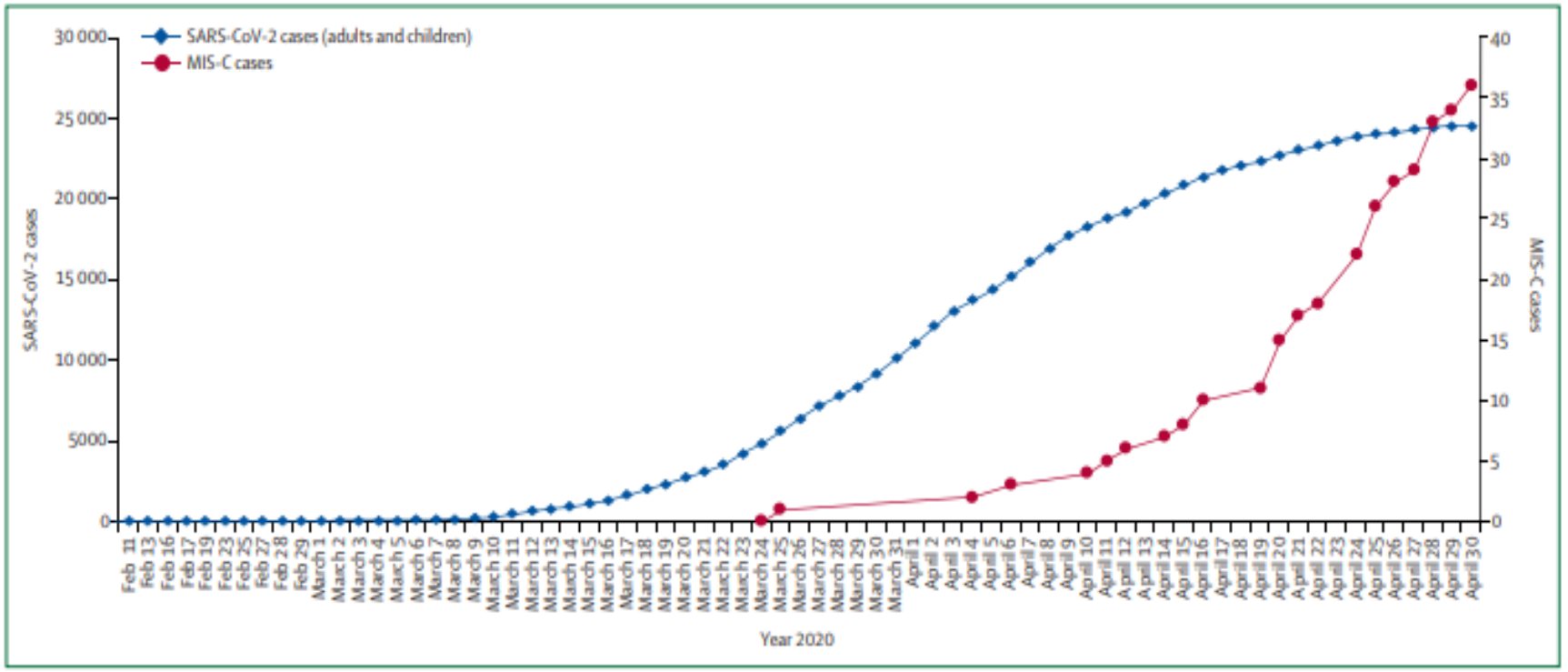


Figure 1: **Time course of MIS-C in PCR-positive COVID-19 cases**
Only incudes PCR-positive cases in London, UK. Data taken from Public Health England.[8] Figure courtesy of Alasdair Bamford and Myrsini Kaforou. MIS-C=multisystem inflammatory syndrome in children. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

Lancet Infect Dis 2020;20: e276–88

MS-C syndrome: Incidence

Countries*	Estimated incidence based on recent ECDC report
USA	3 cases per 10.000 individuals younger than 21 years of age infected with SARS-CoV-2
Germany	2-5 cases per 10.000 SARS-CoV-2-infected children
France	44.6 cases per million children
Norway	1 case per 1.000 SARS-CoV-2-infected children
Denmark	1 case in 4.100 in children younger than 12 years 1 case in 3.700 in children older than 12 years

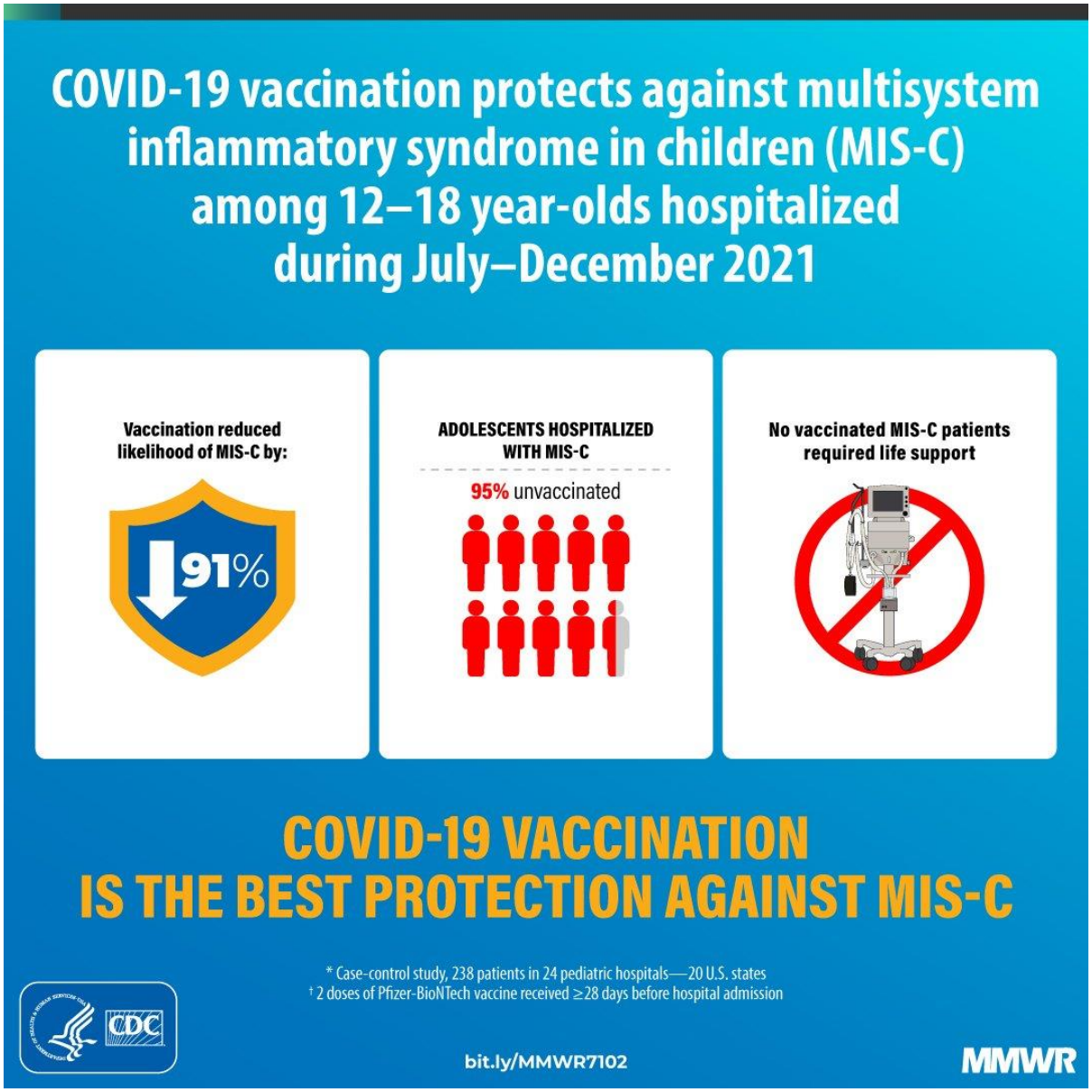
*As children often present with mild symptoms of COVID-19 and are less frequently tested than adults, the true proportion of cases that develop PIMS-TS/MIS-C remains unknown.

https://www.ecdc.europa.eu/en/publications-data/interim-public-health-considerations-covid-19-vaccination-children-aged-5-11

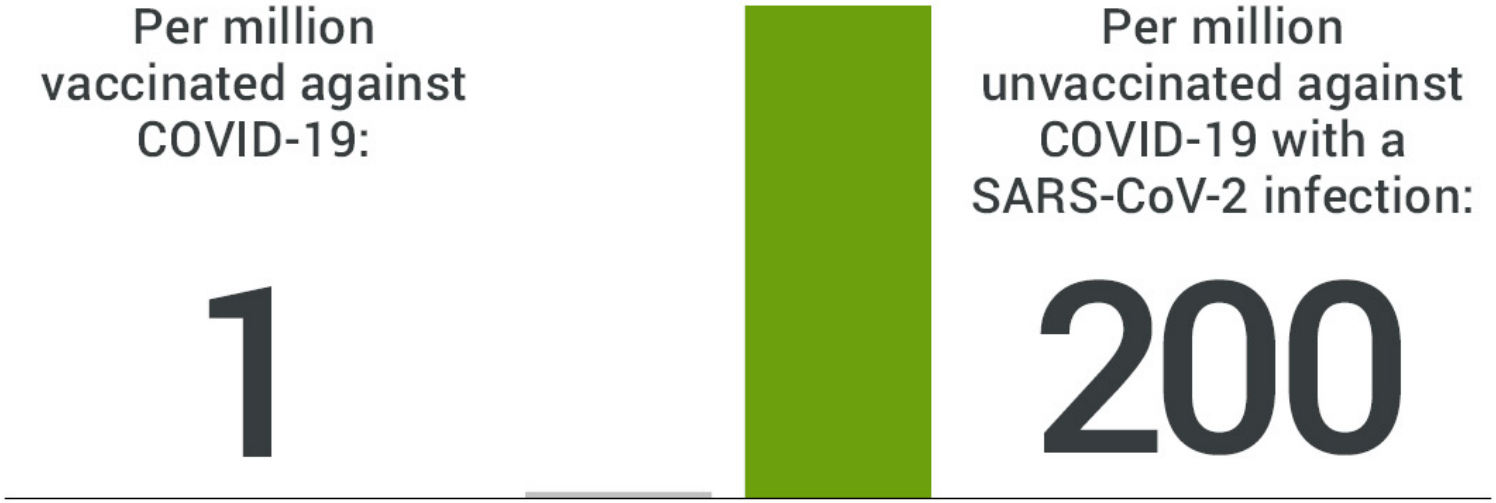
MS-C syndrome: Severity

Countries	Based on recent ECDC report
ICU admission/ Hospital stay	60% of children with PIMS-TS/MIS-C need to be admitted to an intensive care unit (ICU) Average length ICU stay around 5 days Average total hospital stay around 10 days
Persistent symptomatology	36% of children had persistent symptoms eight weeks after diagnosis
Symptoms	most commonly reported symptoms were fever (99.4%), gastrointestinal symptoms (85.6%) and cardiocirculatory manifestations (79.3%)
Risk factors	The most common risk factor for the condition was being overweight, which was present in 25% of the cases Data analysis from the Norwegian national COVID-19 registry showed an increased risk of PIMS-TS/MIS-C in children with chronic comorbidities
Mortality rate	approximately 1% in an observational cohort study of young people admitted to the hospital with COVID-19 in the UK

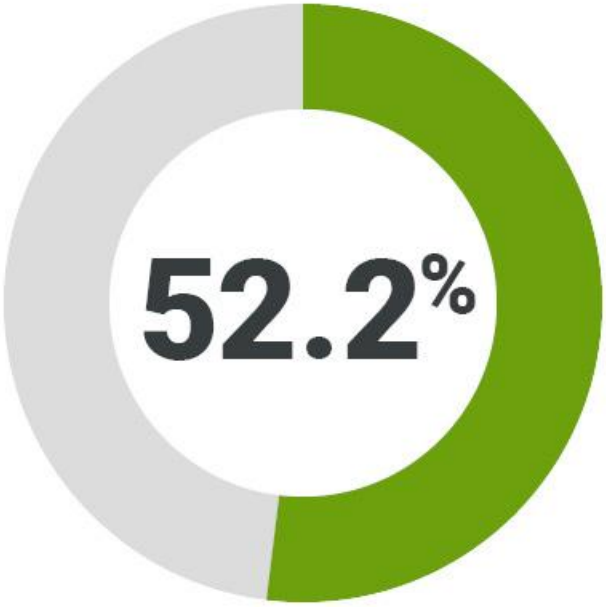
https://www.ecdc.europa.eu/en/publications-data/interim-public-health-considerations-covid-19-vaccination-children-aged-5-11


COVID-19 vaccination protects against multisystem inflammatory syndrome in children (MIS-C) among 12–18 year-olds hospitalized during July–December 2021
Vaccination reduced likelihood of MIS-C by:
91%
ADOLESCENTS HOSPITALIZED WITH MIS-C
95% unvaccinated
No vaccinated MIS-C patients required life support
COVID-19 VACCINATION IS THE BEST PROTECTION AGAINST MIS-C
* Case-control study, 238 patients in 24 pediatric hospitals—20 U.S. states
† 2 doses of Pfizer-BioNTech vaccine received ≥28 days before hospital admission
CDC
bit.ly/MMWR7102
MMWR

Estimated U.S. rate of multisystem inflammatory syndrome in children:



Among 46 pediatric patients with MIS-C:



experienced neurological symptoms

Ευχαριστώ για την προσοχή σας