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Quantifying all-cause healthcare resource utilization and costs of children with mild-to-moderate long COVID in France

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ABSTRACT

Background: Although children are known to be at risk of developing long COVID, its economic burden is poorly described. We aimed to assess the all-cause healthcare resource utilization (HCRU) and associated direct medical costs of children with mild-to-moderate long COVID in France.

Methods: This retrospective cohort study utilized The Health Improvement Network (THIN) primary care electronic health records to identify children aged <18 years with confirmed/probable COVID-19 diagnoses during March 2020 to December 2022 who developed long COVID, identified per the World Health Organization as suggestive symptoms present ≥ 3 months following SARS-CoV-2 infection. Patient characteristics, all-cause HCRU and direct healthcare costs from a national health insurance perspective were summarized. HCRU and costs were stratified into healthcare encounters, medical procedures, retail pharmacy usage, testing, caregiver sick leave, medical transport, and medical device usage.

Results: Of 27,537 children diagnosed with acute COVID-19, 3,888 (14.1%) developed long COVID; mean age was 8.9 years, 49.2% were female and, among those with comorbidity, 24.5% had a Charlson Comorbidity Index score ≥ 1 . During a mean post-diagnosis follow-up of 12.6 months, 93.6% of children had general practitioner consultations, 93.5% had pharmacy usage, and 61.0% had medical procedures. First-year costs were highest at €823 per patient per year; 4.3% of children required caregiver-related work absenteeism. Compared to children who did not develop long COVID, a long COVID diagnosis was associated with an incremental cost increase of €98 per patient per year.

Limitations: Our findings only represent a national payer perspective. The true societal burden of long COVID in children is likely underestimated since long COVID-related indirect costs are not fully captured and access to care varies.

Conclusion: Children living with long COVID managed in the community pose a non-neglectable burden on French health insurance, reinforcing the importance of managing long COVID with a multidisciplinary approach and optimizing resource allocation.

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Introduction

Children infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are often asymptomatic or have mild symptoms¹. Despite this, children can also develop long-term sequelae, so called “post coronavirus disease 2019 (COVID-19) condition (PCC)”

or “long COVID,” with reported prevalence rates ranging from 3.67% to 66.49%, depending on the study design, follow-up duration, population characteristics and other factors². Long COVID encompasses a wide range of symptoms and sequelae that develop, persist, or reappear after a previous infection with SARS-CoV-2.

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The most frequently reported symptoms among children include fatigue, dyspnea, headache, anosmia/ageusia, myalgia/arthritis, sleep disorders, decreased mental and cognitive status, rhinitis, cough, fever, loss of appetite, and mood symptoms^{2–4}.

There is no universally accepted definition of long COVID^{5,6}. The National Institute for Health and Care Excellence (NICE) in the United Kingdom (UK) has defined long COVID as “new or ongoing symptoms 4 weeks or more after the start of acute COVID-19,” with signs and symptoms of COVID-19 from 4 to 12 weeks and those continuing for >12 weeks with no alternative diagnostic explanation classified as ongoing symptomatic COVID-19 and post-COVID-19 syndrome, respectively. Using a Delphi consensus-based methodology, the World Health Organization (WHO) led the development of a clinical definition of long COVID, which was defined as a condition that occurs after a history of probable or confirmed SARS-CoV-2 infection; symptoms occur 3 months from the onset of acute illness, last for ≥ 2 months, and cannot be explained by an alternative diagnosis⁷. These symptoms may be new onset following the initial illness, and they generally have an impact on everyday functioning.

While data on the clinical presentation, risk factors and prevalence of long COVID in children is available, less is known regarding the associated economic burden^{2,4,8,9}. A study from Israel assessing the additive cost of healthcare utilization for long COVID has shown that among those aged 0–19 years, the mean net excess cost in cases was \$3.17 and \$54.45 per patient per month in outpatients and inpatients, respectively¹⁰. A study of commercially insured children in the United States with a COVID-19 diagnosis during April–August 2020 found that excess long COVID-associated costs were observed during one-, three-, and six-month periods following acute infection¹¹. Although these studies provide some insight into the longer-term economic burden associated with a SARS-CoV-2 infection, the findings used data from the early phase of the pandemic which may not generalize well to the post-pandemic period. Furthermore, to the best of our knowledge, no studies have evaluated the economic burden of mild-to-moderate COVID-19 patients with long COVID from primary care settings. The present study leveraged French national electronic health records (EHR) to assess the all-cause healthcare resource utilization (HCRU) and associated costs of children aged <18 years with mild-to-moderate long COVID in primary care settings in France from March 2020 through December 2022.

Methods

Study design and data source

This retrospective cohort study evaluated the all-cause HCRU and costs of children with long COVID following a confirmed and/or probable diagnosis of COVID-19 between March 2020 and December 2022 utilizing data from The Health Improvement Network (THIN[®]) general practitioner (GP) EHR database. THIN[®] is a large standardized European database containing anonymized EHR collected from about 2,000 GPs in retail practice^{12,13}. In 2020, the database included more than 14 million visits from >4.5 million active patients and the patient history of 40 million patients. The physician-collected patient data include demographic characteristics and medical information such as physical examination data, diagnoses, drug, procedure or test prescriptions, blood tests results, as well as medical or paramedical act reimbursement data. The THIN GP database is representative of the total National Institute of Statistics and Economic Studies (INSEE) population of France based on gender, age group and region^{13–16}. The study design is outlined in [Supplementary Figure 1](#).

Study population

Children aged <18 years diagnosed with confirmed and/or probable COVID-19 during 1 March 2020–31 December 2022 were identified using International Classification of Diseases, Tenth Revision (ICD-10) diagnosis code U07.1. The first confirmed or probable diagnosis of COVID-19 was defined as the index date. The period beginning 3–12 months after the index date was evaluated for the presence of WHO-defined long COVID⁷. The symptoms (listed in [Table 1](#)) were new-onset or persisting following initial acute infection, could fluctuate or relapse over time, and were not explained by an alternative diagnosis. Symptoms explained by alternative diagnoses were identified by associated pathologies per categories. The follow-up period began 3 months after the acute SARS-CoV-2 infection and continued for up to 21 months (two-year period following the acute infection) or was censored at death, reinfection, the last recorded contact with a THIN[®] physician (loss to follow-up), or the end of the study period, whichever occurred first. In alignment with the WHO long COVID definition, reinfection was defined as a new COVID-19 diagnosis that occurred ≥ 3 months after the index date. Children who had a COVID-19 reinfection prior to their long COVID diagnosis were excluded from the study.

We also performed a sensitivity analysis using the definition of long COVID from the UK's NICE,

Table 1. List of world health organization-defined long COVID symptoms.

Domain	Symptom	ICD-10 codes
Breathing	Shortness of breath	R06.0, R06.3, R06.6, R06.8
Pain	Chest pain	R07.1, R07.2, R07.3, R07.4
Circulation	Palpitations	R00.2
Fatigue	Fatigue	R53
	Post exertional fatigue	R53
Cognitive health	Amnesia	F06.7, R41.1, R41.2, R41.3, R41.8
	Brain fog	R41.0, R42
Sleep	Excessive sleep	G47.1
	Insomnia	G47.0
Ear, nose and throat	Anosmia	R43.0, R43.1, R43.2, R43.8
	Cough	R05
	Dysgeusia	R43.1, R43.2, R43.8
	Hearing loss	H91.2, H91.9
	Hyperacusis	H93.2
Stomach and digestion	Abdominal pain	R10.3, R10.4, R19.0, R19.3
	Constipation	R19.4, R19.8, K59.0
	Diarrhea	R19.5, K58, K59.1, K52.9
	Gastric reflux	R12
	Gastritis	K29.6, K29.7, K29.9
Muscles and joints	Joint pain	M13.8, M25.5, R07.3
	Muscle cramping	R25.2
	Muscle pain	M79.1, M79.7
	Paresthesia	R20.1, R20.2, R20.8
Mental health	Anxiety and depression	F41.2, F41.3, F41.9
	Depression	F32.0, F32.1, F32.2, F32.3, F32.8, F32.9, F33.0, F33.1, F33.2, F33.3, F33.4, F33.8, F33.9, F41.2
Eyes	Diplopia	H53.2
Reproductive health	Menorrhagia	N92.6
	Menstrual changes	N91.0, N91.2, N91.3, N91.5, N92.0, N92.1, N92.2, N92.5, N92.6
	Premenstrual syndrome	N94.3
Other symptoms	Allergies	J30.2, J30.3, J30.4, J45.0, T78.2
	Dizziness	R42, R55, H81.1, H81.3
	Fever	R50.1, R50.9
	Headache	R51, G44.0, G44.1, G44.2, G44.8

beginning one month after the acute infection and continuing up to one year. Children with NICE-defined long COVID were also required to meet the inclusion and exclusion criteria as described above.

Covariates

Demographic characteristics were evaluated as of the index SARS-CoV-2 infection date. Charlson Comorbidity Index (CCI) scores were based on the last known CCI score recorded prior to the index SARS-CoV-2 infection, which was calculated based on patient information in the GPs' medical records¹⁷. Clinical characteristics were determined using the most recent data available prior to and including the index date. The incidence of long COVID was

summarized according to the SARS-CoV-2 variant predominant at the time of acute infection using France's COVID-19 epidemiological data^{18,19}.

All-cause HCRU and costs

The all-cause HCRU and the national health insurance costs of children with community-managed long COVID were evaluated among children with at least one healthcare reimbursement for any reason ≥ 3 months after the index date. HCRU and costs were assessed during both the total and first 12 months of the follow-up period, and reported as the number and percentage of children with the HCRU, mean cost per child, percentage of the total cost, follow-up duration, and cost per patient per year (PPPY). The mean cost

per child was calculated as the total cost during the study time period, divided by the total number of children included in the cost analysis. The percentage of the total corresponds to the portion of HCRU-related costs out of the total cost. PPPY costs were calculated using an aggregated approach by dividing the total cost for all patients by the total follow-up time in years. To determine the costs associated with the consumption of care, total HCRU and costs associated with healthcare received after a diagnosis of long COVID were stratified into seven areas of care: healthcare encounters, medical procedures, retail pharmacy usage, biological testing procedures, sick leave, medical transport, and medical device usage.

Healthcare encounters included all-cause GP and specialist encounters, with costs representing the health care tariffs (standard rates) in France²⁰; encounters with missing or unknown specialty were assigned a tariff of €26.5²¹. Healthcare encounter-related HCRU and costs were further stratified by physician specialty. Medical procedures included all outpatient paramedical procedures performed after a long COVID diagnosis; costs were determined using the French national health insurance system's Classification Commune Des Actes Medicaux (CCAM) procedure pricing system²². These medical procedures were further stratified using the CCAM classification system. Retail pharmacy usage included prescriptions and reimbursement medication purchases; treatment rates corresponded to the national pricing reference table basic rates in 2023. Retail pharmacy-related HCRU and costs were further stratified by medication type. The pricing of biological testing was set by the health insurance system. Sick leaves taken by caregivers were recorded in the THIN[®] database and included any leaves occurring after the child's diagnosis of long COVID. However, given that caregiver sick leave is not reimbursed by the national health insurance, the associated economic implications were not presented. Medical transport included all healthcare-related transportation (ambulance, taxi, Véhicule de Tourisme avec Chauffeur, etc.) and was assigned a uniform rate of €58.53 corresponding to the average rate observed for each type of transport^{23,24}. Medical devices included products or services registered on the list of products and services covered by the Health Insurance Fund.

Statistical analysis

Descriptive statistics were used to summarize baseline characteristics, HCRU and the associated costs. Counts and percentages were reported for categorical

variables. Continuous variables were summarized using means and standard deviations (SD) for normally distributed variables and medians and interquartile range (IQR) for variables with skewed distribution. Analyses of reimbursement data were performed on children with a recorded reimbursement history. The specialist-related healthcare encounters, medical procedure classifications, and retail pharmacy treatment types that accounted for up to the ten highest proportions of healthcare costs for the associated care areas were reported. In addition, a comparison of the direct healthcare costs of patients who developed long COVID with that of patients previously infected with SARS-CoV-2 who did not develop long COVID using multivariate regression models was performed, with adjustment for demographics, clinical characteristics, and health seeking behavior prior to the index date (GP interaction history two-year prior to the index date). All the analyses were performed using R Statistical Software (v4.3.2; R Core Team 2021).

Results

Among the 27,537 children diagnosed with COVID-19 between March 2020 and December 2022, 14.1% ($n = 3,888$) had WHO-defined long COVID (Figure 1).

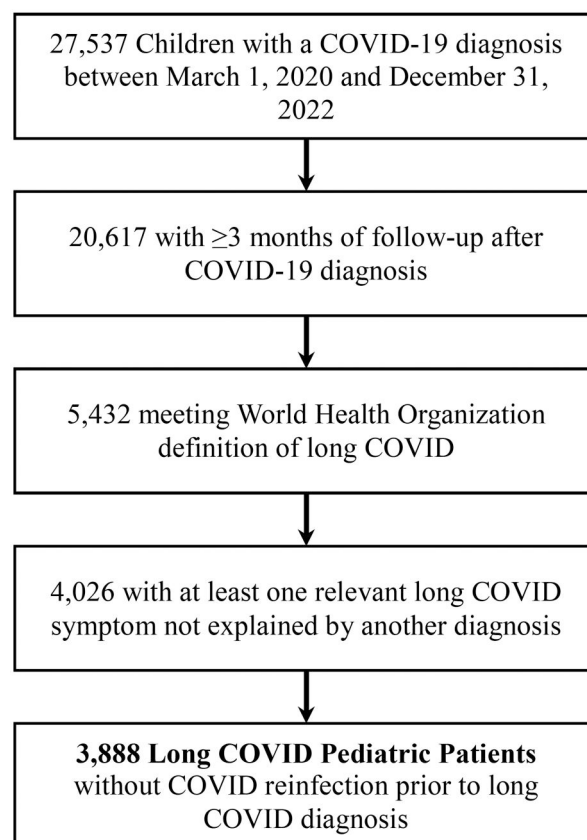


Figure 1. Study population flowchart.

These children had a mean (SD) age of 8.9 (5.2) years, 49.2% were female, and, among those with a calculable CCI score, 75.5% had no comorbidities (Table 2). During a mean follow-up of 13 months, 10% of the children were reinfecting with SARS-CoV-2 ($n = 389$). Evaluation of the incidence of long COVID according to the SARS-CoV-2 variant predominant at the time of acute infection revealed that the Omicron BA.1 variant led to the highest incidence of long COVID among all long COVID patients (20.7%), followed by the Omicron BA.2 (4.9%) and Omicron BA.5 (4.2%) variants (Figure 2). Evaluation of long COVID using the NICE definition resulted in a prevalence of 17.4% ($n = 4,779$). The distribution of patient demographics and clinical characteristics was similar to that observed with WHO-defined long COVID (Table 2).

Among children with WHO-defined long COVID, 80.0% had a reimbursement history and were included in the HCRU and cost analysis. During the first year following SARS-CoV-2 infection, mean per patient per year costs were €823 (Table 3). With mean costs of €860 per patient over the entire follow-up period, the total national health insurance cost of children with long COVID was €2.67 million. The majority of healthcare services were consumed during the first year after acute infection. Healthcare encounters accounted for the largest proportion of the healthcare costs of children with long COVID (31.9%), followed by retail pharmacy use (26.2%) and medical procedures (14.8%); 82.2% to 85.1% of these costs were incurred within the first year of follow-up. Nearly all patients had a healthcare encounter within the first 12 months. GP-related care accounted for 70.3% of the total cost of healthcare encounters and was received by approximately 94% of patients during both the overall and first year of initial infection (Table 4). While the next most frequent healthcare encounter was for nursing care, this specialty only accounted for 2.3% of the total healthcare encounter-related costs.

During the first year of follow-up, 57.4% of the children included in the cost analysis had a medical procedure (Table 5). Otorhinolaryngology-related procedures were received by 6.8% of children during the follow-up period, accounting for 5.0% of annual medical procedure costs.

Most patients (93.5%) had retail pharmacy use during both the overall and first year of follow-up. Medications for the respiratory system were the received by 2,163 (69.5%) of children and accounted for the largest proportion of costs (Table 6). Prescribed to a large proportion of children, systemic anti-infectives (66.1%), nervous system (82.3%), and digestive system/

Table 2. Patient demographic and clinical characteristics of children with long COVID.

	WHO definition ($n = 3,888$)	NICE definition ($n = 4,779$)
Age (years) at index date		
Mean (SD)	8.9 (5.2)	9.0 (5.2)
Median (IQR)	9 (10)	9 (10)
Sex, n (%)		
Female	1,914 (49.2%)	2,357 (49.3%)
Male	1,974 (50.8%)	2,422 (50.7%)
Charlson comorbidity index (CCI) ^a		
Mean (SD)	0.27 (0.53)	0.27 (0.53)
Median	0	0
CCI per class, n (%) ^a		
0	2,783 (75.5%)	3,394 (75.0%)
1–2	878 (23.8%)	1,098 (24.3%)
3–4	23 (0.6%)	29 (0.6%)
>4	3 (0.1%)	3 (0.1%)
Body mass index (BMI) ^b		
Mean (SD)	17.9 (3.9)	17.9 (3.9)
Median (IQR)	17 (4)	17 (4)
BMI class, n (%) ^b		
<18.5	1,907 (67.5%)	2,354 (68.0%)
18.5 to <25.0	752 (26.6%)	910 (26.3%)
25.0 to <30.0	121 (4.3%)	142 (4.1%)
≥30.0	46 (1.6%)	58 (1.7%)
Follow-up duration, months		
Mean (SD)	12.6 (6.1)	14.1 (6.5)
Median (IQR)	13 (9)	15 (10)

Abbreviations. IQR, interquartile range; NICE, National Institute for Health and Care Excellence; SD, standard deviation; WHO, World Health Organization.

^aCCI scores were assessed among children with reported comorbidities (WHO: $n = 3,687$, 94.8%; NICE: $n = 4,524$, 94.7%).

^bAlthough BMI is not an optimal measure of overweight and obesity in children without adjustment for sex and age, elevated BMI has been associated with an increased risk of long COVID among children and young adults. BMI was assessed among children with reported BMI values (WHO: $n = 2,826$, 72.7%; NICE: $n = 3,463$, 72.5%).

metabolism-related treatments (66.2%) represented 16.7%, 11.4%, and 7.8% of retail pharmacy costs, respectively. Although dermatological treatments, musculoskeletal treatments, medications for the sensory organs, and systemic hormones were received by 33.3% to 38.9% of children during the overall follow-up period, none of these medication types accounted for more than 2.8% of the total pharmacy costs.

In the sensitivity analyses, the relative proportions of HCRU and costs attributed to the studied areas of care for children with NICE-defined long COVID were similar to that of children with WHO-defined long COVID (Tables 3–6). However, 2.7% and 2.1% of children with NICE-defined long COVID received inpatient psychiatric care during the entire and first year of follow-up, respectively, which accounted for approximately 2% of total healthcare encounter costs (Table 4). Similarly, medical procedures related to pediatrics and inpatient cardiology each accounted for 2% of the procedure-related costs of children with NICE-defined long COVID, whereas neither of these medical procedures was present in children with WHO-defined long COVID (Table 5).

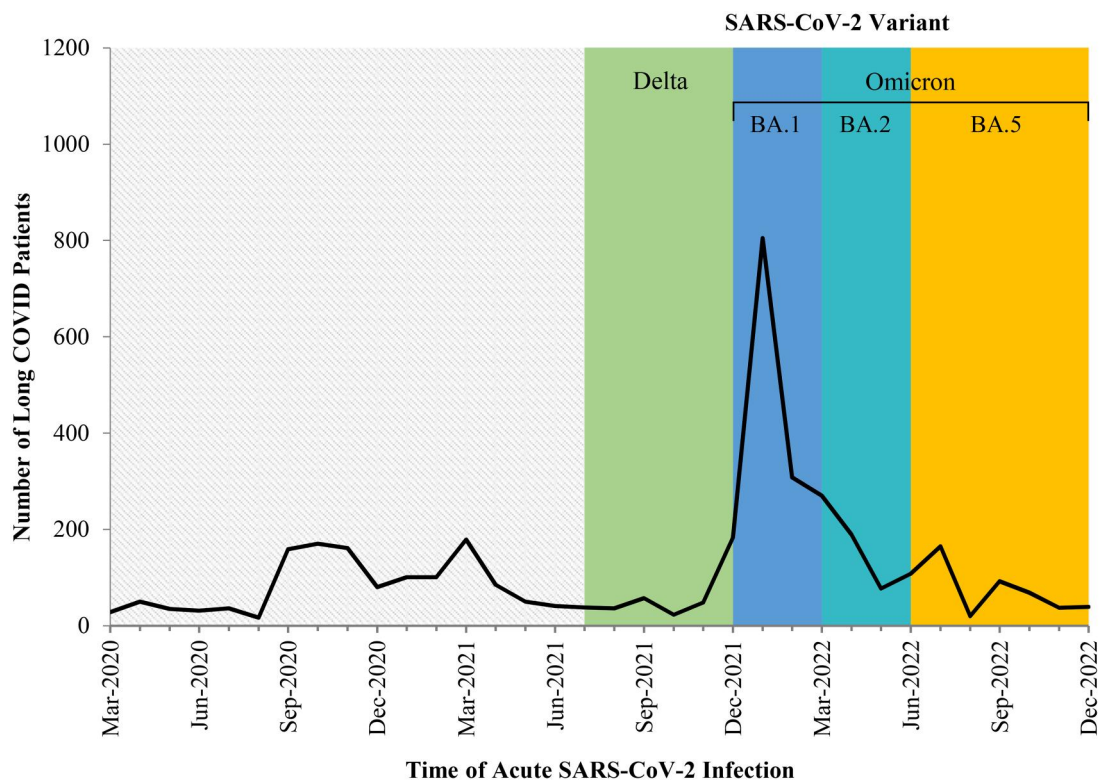


Figure 2. Incidence of long COVID by SARS-CoV-2 variant predominance in France. The number of children diagnosed with COVID-19 who developed long COVID was stratified by the predominant SARS-CoV-2 variant at the time of acute infection. SARS-CoV-2 variant predominance in France during the index SARS-CoV-2 infection identification period was determined using the Santé publique France's national COVID-19 epidemiological data. The SARS-CoV-2 variant that accounted for more than 50% of the test samples sequenced during the week was designated as the predominant variant for that week. The predominant SARS-CoV-2 variants were Delta from 28 June 2021 to 20 December 2021, Omicron BA.1 from 27 December 2021 to 21 February 2022, Omicron BA.2 from 28 February 2022 to 6 June 2022, and Omicron BA.5 from 13 June 2022 to 6 February 2023.

When children who developed long COVID were compared with those previously infected with SARS-CoV-2 who did not develop long COVID, a diagnosis of long COVID was associated with an incremental PPPY cost increase of €98.03. Specifically, we have observed PPPY cost increases for GP consultations (€36.42), medical procedures (€8.54) and retail pharmacy usage (€54.63) among children with long COVID.

Discussion

To the best of our knowledge, this is the first study assessing the economic burden of children with mild-to-moderate long COVID in primary care settings. In the present study of 27,573 children diagnosed with COVID-19, 14.1% and 17.4% had long COVID per the WHO and NICE definitions, respectively. Evaluation of the all-cause HCRU and costs of these children demonstrated that pediatric long COVID managed in the community imposes a non-neglectable clinical and economic burden to the French healthcare system, particularly in the first year following SARS-CoV-2

infection, which resulted in total healthcare costs of €2.2 million.

Nearly a third of the total costs of children with long COVID were due to healthcare encounters. While most children received care from a GP, only 15% visited a pediatrician during the follow-up period. This distribution of care corresponds to a report on the structure of pediatric health care in France prepared by the General Inspectorate for Social Affairs in 2020, which revealed a significant decline in the number of pediatric practices. More than 85% of community care consultations for children <16 years of age were provided by GPs, who also manage the majority of long COVID cases^{25,26}. Furthermore, the report proposed a new pediatric care model that recommended increased utilization of community care pediatric nurses, which may be reflected in the finding that healthcare encounters with nurses were the second most frequent type of care.

Retail pharmacy use, the second highest HCRU category, accounted for a quarter of the total healthcare costs. In our study, the most frequently prescribed medications were for the nervous system, respiratory

Table 3. Healthcare utilization and costs during the total follow-up period and first year of the follow-up period.

Area of care	WHO definition				NICE definition											
	Total follow-up (n = 3,110)		First year of follow-up ^a (n = 3,044)		Total follow-up (n = 3,899)		First year of follow-up ^a (n = 3,825)									
	N (%)	Mean cost, €	% of total cost	PPPY cost, €	N (%)	Mean cost, €	% of total cost	PPPY cost, €	N (%)	Mean cost, €	% of total cost	PPPY cost, €				
All areas of care (Total)	3,110 (100%)	860	100.0%	757	3,044 (100%)	704	100.0%	823	3,899 (100%)	952	100.0%	756	3,825 (100%)	733	100.0%	829
Healthcare encounters	3,041 (97.8%)	274	31.9%	241	2,994 (98.4%)	231	32.2%	265	3,811 (97.7%)	302	31.7%	240	3,740 (97.8%)	239	32.0%	266
Medical procedures	1,896 (61.0%)	127	14.8%	112	1,748 (57.4%)	105	14.6%	120	2,499 (64.1%)	143	15.0%	114	2,252 (58.9%)	112	15.0%	124
Pharmacy use	2,909 (93.5%)	225	26.2%	198	2,850 (93.6%)	188	26.2%	216	3,640 (93.4%)	245	25.8%	195	3,534 (92.4%)	190	25.5%	211
Biological testing procedures	1,526 (49.1%)	53	6.1%	46	1,439 (47.3%)	46	6.4%	52	2,050 (52.6%)	59	6.2%	47	1,877 (49.1%)	48	6.4%	53
Sick leave ^b	148 (4.8%)	NA	NA	NA	130 (4.3%)	NA	NA	NA	211 (5.4%)	NA	NA	NA	182 (4.8%)	NA	NA	NA
Medical transport	124 (4.0%)	14	1.6%	12	109 (3.6%)	12	1.6%	13	155 (4.0%)	18	1.9%	14	132 (3.5%)	13	1.8%	15
Medical device use	1,393 (44.8%)	61	7.1%	54	1,265 (41.6%)	48	6.6%	55	1,869 (47.9%)	64	6.7%	51	1,640 (42.9%)	48	6.5%	54

Abbreviations. NA, not applicable; NICE, National Institute for Health and Care Excellence; PPPY, per patient per year; WHO, World Health Organization.

^aThe patient count for the first year of follow-up is lower than that of the total follow-up due to patients with no reimbursed healthcare services during the first year after the acute diagnosis; their earliest reimbursed care occurred after the first year of follow-up.

^bGiven that caregiver sick leave is not reimbursed by the French national health insurance, the associated cost estimates were not presented.

Table 4. Healthcare encounters and costs during the total follow-up period and first year of the follow-up period.

Physician specialty	WHO definition				NICE definition											
	Total follow-up (n = 3,110)		First year of follow-up (n = 3,044)		Total follow-up (n = 3,899)		First year of follow-up (n = 3,825)									
	N (%)	Mean cost, €	% of total cost	PPPY cost, €	N (%)	Mean cost, €	% of total cost	PPPY cost, €	N (%)	Mean cost, €	% of total cost	PPPY cost, €				
Any healthcare encounter	3,041 (100.0%)	274	100.0%	241	2,994 (100.0%)	231	100.0%	265	3,811 (97.7%)	302	100.0%	240	3,740 (97.8%)	239	100.0%	266
General medicine	2,911 (93.6%)	192	70.3%	169	2,861 (94.0%)	163	70.5%	187	3,656 (93.8%)	211	70.0%	168	3,575 (93.5%)	169	70.4%	187
Other not applicable or <100 patients	674 (21.7%)	23	8.4%	20	598 (19.6%)	19	8.3%	22	702 (18.0%)	16	5.4%	13	590 (15.4%)	13	5.4%	14
Pediatrics	456 (14.7%)	13	4.7%	11	421 (13.8%)	11	4.8%	13	612 (15.7%)	14	4.7%	11	548 (14.3%)	12	4.8%	13
Dental surgery	847 (27.2%)	8	3.0%	7	721 (23.7%)	7	2.9%	8	1,129 (29.0%)	9	3.0%	7	920 (24.1%)	7	2.8%	7
Speech therapist	328 (10.5%)	6	2.1%	5	294 (9.7%)	5	2.1%	5	439 (11.3%)	7	2.3%	5	385 (10.1%)	5	2.2%	6
Nurse	1,020 (32.8%)	6	2.3%	5	931 (30.6%)	6	2.4%	6	1,383 (35.5%)	7	2.3%	5	1,212 (31.7%)	6	2.3%	6
Inpatient psychiatry	0 (0.0%)	-	0.0%	-	0 (0.0%)	-	0.0%	-	107 (2.7%)	7	2.2%	5	82 (2.1%)	5	2.1%	6
Otorhinolaryngology (E.N.T.)	257 (8.3%)	5	1.7%	4	225 (7.4%)	4	1.8%	5	344 (8.8%)	5	1.7%	4	280 (7.3%)	4	1.7%	5
Physiotherapist	366 (11.8%)	4	1.5%	4	336 (11.0%)	3	1.5%	4	490 (12.6%)	5	1.5%	4	438 (11.5%)	4	1.6%	4
Ophthalmology	340 (10.9%)	4	1.3%	3	287 (9.4%)	3	1.3%	3	477 (12.2%)	4	1.4%	3	385 (10.1%)	3	1.4%	4

Abbreviations. NICE, National Institute for Health and Care Excellence; PPPY, per patient per year; WHO, World Health Organization.

Table 5. Medical procedures and costs during the total follow-up period and first year of the follow-up period.

CCAM classification ^a	WHO definition				NICE definition										
	Total follow-up (n = 3,110)		First year of follow-up (n = 3,044)		Total follow-up (n = 3,899)		First year of follow-up (n = 3,825)								
	N (%)	Mean cost, €	% of total cost	PPPY cost, €	N (%)	Mean cost, €	% of total cost	PPPY cost, €	N (%)	Mean cost, €	% of total cost	PPPY cost, €			
Any procedure	1,896 (61.0%)	127	100.0%	112	1,748 (57.4%)	105	100.0%	120	2,499 (64.1%)	143	100.0%	114	2,252 (58.9%)	112	100.0%
Other not applicable or <100 patients	1,444 (46.4%)	68	53.1%	59	1,313 (43.1%)	56	53.9%	65	1,836 (47.1%)	70	48.8%	55	1,599 (41.8%)	55	49.5%
Dental surgery	833 (26.8%)	33	25.7%	29	699 (23.0%)	26	24.8%	30	1,129 (29.0%)	38	26.2%	30	913 (23.9%)	29	25.7%
Ophthalmology	714 (23.0%)	16	12.9%	14	602 (19.8%)	13	12.7%	15	975 (25.0%)	18	12.7%	14	783 (20.5%)	14	12.4%
Otorhinolaryngology (E.N.T.)	212 (6.8%)	6	5.0%	6	176 (5.8%)	5	5.0%	6	285 (7.3%)	7	5.0%	6	229 (6.0%)	6	5.0%
General medicine	177 (5.7%)	4	3.3%	4	160 (5.3%)	4	3.6%	4	246 (6.3%)	5	3.4%	4	205 (5.4%)	4	3.3%
Pediatrics	0 (0.0%)	-	0.0%	-	0 (0.0%)	-	0.0%	-	141 (3.6%)	3	2.2%	3	116 (3.0%)	2	2.2%
Inpatient cardiology	0 (0.0%)	-	0.0%	-	0 (0.0%)	-	0.0%	-	107 (2.7%)	2	1.7%	2	96 (2.5%)	2	1.9%

Abbreviations. CCAM, Classification Commune des Actes Médicaux; NICE, National Institute for Health and Care Excellence; PPPY, per patient per year; WHO, World Health Organization.

^aCCAM classification is a French clinical procedure coding system.

Table 6. Retail pharmacy utilization and costs during the total follow-up period and first year of the follow-up period.

Treatment type	WHO definition				NICE definition										
	Total follow-up (n = 3,110)		First year of follow-up (n = 3,044)		Total follow-up (n = 3,899)		First year of follow-up (n = 3,825)								
	N (%)	Mean cost, €	% of total cost	PPPY cost, €	N (%)	Mean cost, €	% of total cost	PPPY cost, €	N (%)	Mean cost, €	% of total cost	PPPY cost, €			
Any medication	2,909 (93.5%)	225	100.0%	198	2,850 (93.6%)	188	100.0%	216	3,640 (93.4%)	245	100.0%	195	3,534 (92.4%)	190	100.0%
Other not applicable or <100 patients	26 (0.8%)	66	29.1%	58	25 (0.8%)	48	25.7%	55	34 (0.9%)	57	23.4%	46	33 (0.9%)	36	18.8%
Respiratory system	2,163 (69.5%)	43	18.9%	37	2,071 (68.0%)	39	20.7%	45	2,767 (71.0%)	54	22.0%	43	2,584 (67.6%)	45	23.8%
Systemic anti-infectives	2,055 (66.1%)	38	16.7%	33	1,922 (63.1%)	32	17.2%	37	2,613 (67.0%)	43	17.4%	34	2,392 (62.5%)	35	18.6%
Nervous system	2,561 (82.3%)	26	11.4%	23	2,458 (80.7%)	21	11.3%	24	3,237 (83.0%)	28	11.5%	22	3,073 (80.3%)	22	11.6%
Digestive system and metabolism	2,059 (66.2%)	17	7.8%	15	1,937 (63.6%)	15	7.8%	17	2,618 (67.1%)	19	7.8%	15	2,412 (63.1%)	16	8.2%
Cardiovascular system	217 (7.0%)	6	2.7%	5	211 (6.9%)	5	2.9%	6	287 (7.4%)	7	2.7%	5	276 (7.2%)	6	3.2%
Systemic hormones ^a	1,110 (35.7%)	6	2.8%	6	1,000 (32.9%)	6	3.1%	7	1,438 (36.9%)	11	4.4%	8	1,272 (33.3%)	9	4.5%
Blood and blood-forming organs	392 (12.6%)	6	2.5%	5	351 (11.5%)	5	2.8%	6	505 (13.0%)	7	2.7%	5	445 (11.6%)	6	3.2%
Sensory organs	1,051 (33.8%)	6	2.8%	6	933 (30.7%)	6	3.1%	7	1,358 (34.8%)	6	2.5%	5	1,158 (30.3%)	5	2.7%
Dermatology	1,210 (38.9%)	4	1.8%	4	1,060 (34.8%)	3	1.7%	4	1,586 (47.8%)	5	2.2%	4	1,337 (37.8%)	4	1.9%

Abbreviations. NICE, National Institute for Health and Care Excellence; PPPY, per patient per year; WHO, World Health Organization.

^aExcludes sex hormones and insulins.

system, digestive system and metabolism, systemic anti-infectives, and dermatological agents, which is supported by the prevalence and clinical presentation of long COVID in children²⁷. According to a systematic review of 22 studies, the most frequently reported symptoms were fatigue (2–87%), headache (3.5–80%), arthro-myalgias (5.4–66%), chest tightness or pain (1.4–51%), and dyspnea (2–57.1%)³. A study of the prevalence of pediatric outpatient prescriptions in France between 2010 and 2019 reported that a substantial proportion of nervous system-related drug use was due to a single drug, paracetamol; its use for the treatment of common long COVID symptoms such as fever and joint/muscle pain may account for a portion of its usage in our study as well²⁸. However, other long COVID symptoms such as anxiety and depression, which may have begun during the acute phase of infection, are also treated with medications within the same therapeutic class^{29,30}.

Over 60% of children with long COVID had medical procedures accounting for 15% of the total healthcare costs. While the distribution of the procedure classes was similar between WHO-defined and NICE-defined long COVID episodes, pediatric and inpatient cardiology-related procedures were present with the application of NICE criteria. The difference in the timing of NICE- and WHO-defined long COVID (4 vs 12 weeks following an acute infection) is likely responsible for the absence of these procedures in the main analysis. It has been acknowledged that there are increased long-term cardiovascular risks in children and adolescents following acute COVID-19 infection^{31,32} and most of the cardiovascular cases require emergency care or urgent care within 24–48 hours or days to a few weeks, respectively^{33,34}. However, it is worth noting that, since all-cause HCRU was reported, some of the procedures received may not be directly related to long COVID.

As previously mentioned, data on the cost of community-managed long COVID among children and adolescents remain sparse. A study of commercially insured children in the United States without COVID-19 who were exact matched 4:1 to children with a COVID-19 diagnosis and assigned the same “diagnosis” date assessed healthcare expenditures one-, three-, and six-months post-infection, with cost analyses beginning 31 days post-COVID-19 diagnosis, and reported mean costs of \$434, \$1,252, and \$2,398, respectively¹¹, which is higher than our estimates at one year following an acute infection. However, it is extremely difficult to compare cost estimates across countries due to differences between healthcare

systems and reimbursement methods per care settings. Future studies in France are needed to further validate our findings and better understand the cost trajectory over time in long COVID patients.

When our study compared children with COVID-19 who did not develop long COVID to those that did, a diagnosis of long COVID was associated with an incremental cost increase. While this finding is supported by prior studies, pediatric data are sparse^{10,11,35}. For example, a U.S. study reported a 1.75-fold increase in direct medical costs two to seven months after infection for commercially insured children with a diagnosis of COVID-19 during April–August 2020 when compared to children without COVID-19¹¹. A matched cohort study using primary and secondary care EHRs in the UK has shown that individuals with long COVID had 44% higher costs than individuals without long COVID, with PPPY costs of approximately £2500 for those with long COVID versus £1500 for those without long COVID³⁶. However, since this study was conducted among the adult population, this finding may not be comparable to that of children. Therefore, it is important to continue monitoring long COVID burden as the SARS-CoV-2 virus evolves.

Limitations

Study findings should be interpreted in the context of several limitations. Patient identification relied on adapting definitions established by health authorities to the database; there may be discrepancies between medical assessment and algorithm coding. In addition, since the THIN database is generated from EHRs, there is the possibility of measurement or documentation errors which could compromise result validity and accuracy. However, quality controls are employed throughout the data collection process to minimize such errors. In addition, although BMI is not an optimal measure of overweight and obesity in children due to a need for further adjustment by sex and age, it has been included in this study as a descriptive variable based on a retrospective study that reported an increased risk of long COVID with elevated BMI^{37,38}.

In France, a primary care physician/GP coordinates care, centralizing patient information. While most primary and specialist care for children is reimbursed by the national health insurance, reimbursement is typically limited to 70% of official tariffs, and only 30% for non-referred consultations outside the coordinated care pathway. The remaining costs—whether out-of-pocket, covered by supplementary private insurance (mutuelle), or for over-the-counter medications—are

not captured in the GPs' EHRs nor in our database. As a result, both the healthcare utilization and associated costs of children with long COVID may be underestimated in EHR-based analyses.

The study was also limited by the inability to include children with undiagnosed asymptomatic/mild COVID-19 in the study. While asymptomatic/mild infections have a lower risk of developing long COVID and generally have less severe long COVID symptoms, asymptomatic children account for 43% to 68% of pediatric COVID-19 cases^{9,39}. In addition, the economic implications due to caregiver-associated work absenteeism were not presented in the current study as they are not reimbursed by the national health insurance. However, a qualitative study from UK demonstrated that long COVID affects the school experiences of children and young people⁴⁰. Additional studies to quantify the societal burden and indirect costs of long COVID are needed. Since the perspective of our cost analysis is the national payer in France, the true cost of medical consultations is likely underestimated given that the extra charges commonly seen with GP and specialist consultations may not be well captured and access to care varies depending on the patient's geographic location in France⁴¹. Consequently, our study likely provides a conservative estimate of the economic burden of children with long COVID.

Last but not least, like many other prior studies^{42–45}, we were only able to present the lump-sum medical costs of children with long COVID. We acknowledge that for children with underlying conditions prior to SARS-CoV-2 infection, who are at an increased risk of developing long COVID, it is challenging to differentiate long COVID-specific care from routine care for existing chronic conditions. The differentiation of such long COVID-specific care would largely depend on whether GPs are able to clearly code those consultations and prescriptions that are attributable to long COVID. Future studies are needed to better understand the specific clinical pathway of long-COVID patients to better quantify the burden.

Conclusion

Pediatric patients with long COVID have considerable HCRU, direct medical costs, and potential indirect costs, imposing an additional burden to the French healthcare system. A multidisciplinary approach is needed to address the unique challenges of long COVID each child faces.

Transparency

Declaration of funding

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Declaration of financial/other relationships

JY, PAS, AB, JLN, HRV, SF, MLB and HBR are Pfizer employees and may hold Pfizer stock. The remaining authors have no declarations. Peer reviewers on this manuscript have received an honorarium from JME for their review work but have no other relevant financial relationships to disclose.

Author contributions

The study design was developed by JY, CT and EA. CT and EA collected and analyzed the data. JY, CT, EA, PAS, AB, JLN, HRV, SF, MLB, HBR, CR, PC and OR participated in the interpretation of data and critical review of the manuscript for important intellectual content. All authors had full access to all the data in the study and decided to submit the paper for publication.

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Data availability

Access to anonymized patient data from THIN is subject to a data-sharing agreement containing detailed terms and conditions of use following protocol approval from THIN. All data relevant to the study are included in the article or uploaded as [supplementary information](#). Further queries can be directed to the corresponding author at Jingyan.yang@pfizer.com.

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