Phenotyping Long COVID in Children in Primary Care: A Case-Based Study Using the Human Phenotype Ontology

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Abstract

Background: Pediatric Long COVID is an emerging but still under-recognized condition in general practice. Children affected by post-COVID symptoms often present with fatigue, cognitive disturbances, post-exertional intolerance, and significant functional decline, yet remain clinically invisible.

Objective: This study aims to characterize pediatric Long COVID through a case-based approach, using semantic standardization via the Human Phenotype Ontology (HPO).

Methods: Out of a cohort of 307 patients followed in general practice for Long COVID between 2021 and 2025, ten consecutive non vaccinated children aged 6 to 15 were selected as the youngest subgroup. Each case was assessed using a multimodal protocol combining standardized questionnaires (ComPaRe and COOP/WONCA), recorded clinical interviews, and HPO-based semantic symptom extraction. The approach emphasized lived experience, narrative analysis, and functional assessment.

Results: All ten children displayed a complex, multisystem symptomatology—most commonly fatigue and post-exertional intolerance (10/10), cognitive complaints (8/10), sleep disturbances, various types of pain, and signs of dysautonomia. Functional impairment was marked, with significant limitations across physical, cognitive, and social domains. HPO indexing enabled the transformation of narrative symptoms into reproducible phenotypic profiles, supporting both clinical decision-making and patient-family communication.

Conclusion: This study shows how general practice, using narrative and phenotypic tools like HPO, can legitimize subjective complaints and help uncover invisible conditions such as pediatric Long COVID.

Keywords: Post-Acute COVID-19 Syndrome; Child; Primary Health Care; Family Practice; Fatigue; Cognitive Dysfunction; Quality of Life; Phenotype; Narration; Human Phenotype Ontology; Medical Informatics Applications

Context

Since 2021, the Long COVID in children has been increasingly recognized in the scientific literature [1], although its existence remains occasionally contested and is still less well documented than in adults. In the recent consensus paper by Ewing et al. [2], the authors emphasize that the long-term impacts of COVID-19 infection on children should be considered a research priority.

Identifying the initial SARS-CoV-2 infection is often challenging in this population: exposure is predominantly intrafamilial, occurring during epidemic waves, and frequently lacks formal virological confirmation. The acute phase is often asymptomatic or associated with mild symptoms, making it difficult to precisely date the infectious episode.

The onset of post-viral symptoms is usually insidious, marked by a gradual deterioration in overall health. Children may present with persistent fatigue, diffuse pain, cognitive disturbances, or atypical somatic symptoms. These manifestations are sometimes minimized or mistakenly attributed solely to psychosocial factors [3].

In some cases, a constellation of symptoms emerges weeks or even months after the initial infection, leading to a significant decline in quality of life, learning abilities, and daily functioning. In every case, a biographical rupture becomes evident: a clear "before" and "after" COVID experience takes shape. The child, previously in good health, sees their everyday life profoundly altered.

The identification of these clinical presentations primarily relies on attentive listening, a longitudinal contextualization of the child's and family's narrative, and a functional assessment grounded in lived experience. As a privileged witness to the child's development within their environment, the family physician is often on the front line in detecting subtle warning signs: declining academic performance, loss of interest in leisure activities, social withdrawal, or parental concern over a child who is perceived as not quite the same as before.

> *"I sleep much more than I used to. Before, I only slept at night — now I sleep almost all the time. Even after playing or doing an activity, I often have to lie down. But sometimes I feel heavy... [..]... It's like my whole body is crushing me — I don't know how to explain it — like I've been flattened... Sometimes, when I go up the stairs, I'm really out of breath, like an old steam engine... [..]... I've had episodes where I passed out: I fall to the ground and I don't realize it — everything goes black, like a buzzing beehive. When I wake up, I realize I've fallen... [..]... I used to do well in school. Now I get tired quickly. My mom goes over lessons with me: sometimes I say silly things, like '1+1=3'. Then the next day, it's back to normal."*
>
> — M. Jamoulle, Consultation 2025 (11-year-old boy with Long COVID)

"Long COVID" refers to a constellation of persistent or recurrent symptoms appearing more than four weeks after an initial SARS-CoV-2 infection, with no other identifiable cause. In children, this condition may present as chronic fatigue, diffuse pain, cognitive impairments, post-exertional intolerance, signs of dysautonomia, or sleep disturbances, among other manifestations.

The progression of these symptoms is often slow and insidious, gradually transforming the child's overall state of health. This deterioration is frequently misunderstood, even by those closest to the child. Profound changes in habitus—such as withdrawal, increased fatigability, attention difficulties, and social disengagement—often elude the conventional frameworks of parents and educators. This lack of understanding may mislead healthcare professionals, prompting them to favor inappropriate interpretations: rapid psychologization, moral judgments, or referrals to child psychiatry. Diagnoses such as childhood depression, avoidant personality, autism spectrum disorder, or functional neurological disorder may then be proposed without clear etiological basis. In the absence of an adequate nosological framework, these symptoms are sometimes perceived as behavioral issues, intentional opposition, or school refusal, thereby reinforcing stigma and the child's sense of injustice [3].

The child is thus confronted with a double burden: a genuine somatic suffering that is unrecognized, and a lack of acknowledgment of their condition, leading to emotional isolation, loss of self-confidence, and worsening of symptoms. This situation underscores the vital importance of empathic listening, a decentered clinical perspective, and a multifactorial approach centered on the child's lived experience and the needs of their family.

From a biological standpoint, several pathophysiological hypotheses have been proposed to explain the mechanisms of Long COVID. Studies have identified the presence of SARS-CoV-2 RNA in no fewer than 84 distinct anatomical sites and body fluids [4]. The suggested mechanisms include: viral persistence, with prolonged detection of viral fragments in certain tissues potentially maintaining local or systemic inflammation; immune dysregulation involving sustained activation of innate and adaptive immunity, T-cell response imbalance, and autoantibody production; endothelial and microvascular damage impairing organ perfusion and function; and neurovegetative disturbances consistent with dysautonomia, such as Postural Orthostatic Tachycardia Syndrome (POTS).

Moreover, the identification of antisense RNA from ORF1a—transcribed only during active viral replication—in a subset of patients within our cohort strengthens the hypothesis of residual viral activity or persistent infection [5]. These findings support the possibility of chronic or latent infection, particularly in children presenting with prolonged symptomatology.

The exact prevalence of pediatric Long COVID remains difficult to determine, due to variability in the diagnostic criteria employed [6]. Nonetheless, recent clinical studies confirm the existence of sustained and potentially disabling forms in a significant proportion of children and adolescents [7].

This study examines ten non vaccinated children with prolonged symptoms compatible with Long COVID, seen consecutively in primary care. They represent the youngest subgroup of a broader cohort of 307 patients (67% female), in which individuals under 20 account for approximately 6% [8]. By focusing on this pediatric subset, the analysis highlights the clinical and functional challenges faced by younger patients—an often overlooked population in Long COVID research. Through concrete clinical cases, this article presents a method for identifying, structuring, and interpreting pediatric symptoms using an integrated approach that combines narrative, semantic, and terminological tools within a patient-centered general practice framework.

Method

Narrative Medicine Approach

The identification of pediatric Long COVID cases within our general practice population is grounded in a longitudinal clinical approach. Initially, children and their parents—first from our own patient panel, later from across Belgium—completed a standardized online questionnaire based on the ComPaRe survey [9, 10], designed to detect persistent symptoms following SARS-CoV-2 infection. Functional status was assessed using the COOP/WONCA charts [11, 12], also made available online. The child's medical record, accessible via the Réseau Santé Wallon platform [13], was reviewed prior to the consultation, during which the child and their parents were seen in person.

A structured clinical interview was conducted during the consultation. Symptom reporting was recorded, with the consent of both the child and the parents. The interview, symptom-oriented, followed a systematic plan exploring all bodily systems as well as psychosocial repercussions. The main objective was to identify symptoms as experienced by the child, in order to capture their experiential knowledge. In the context of an emerging disease, the patient becomes an expert in their own lived experience.

Digital Clinical Practice

Standardizing this subjective knowledge is essential for understanding the pathological phenomenon. The patient's own words can be transformed into semantic markers, enabling the creation of a reproducible terminological biomarker [8]. The full set of available narrative materials—descriptive emails written by parents, relevant specialist reports, and structured clinical interviews—forms a rich source of data for identifying relevant symptoms.

Current digital tools enable immediate automated transcription of recorded speech. The transcribed texts are then analyzed using a Large Language Model (LLM), specifically ChatGPT-4o [14], via a dedicated prompt designed to extract, index, and classify symptoms according to the Human Phenotype Ontology (HPO) [15].

The HPO is a structured medical ontology comprising over 18,000 clinical phenotypes, each linked to a unique identifier (e.g., HP:0012378 for chronic fatigue). Originally developed as a diagnostic tool for rare diseases [16], it appears particularly well-suited to a condition as elusive as Long COVID. It allows for rigorous semantic standardization of reported symptoms [17].

This HPO-oriented semantic extraction enables homogeneous categorization of expressed complaints, facilitating comparisons between patients and contributing to the construction of a structured phenotypic database for Long COVID.

An Ethical Co-Construction

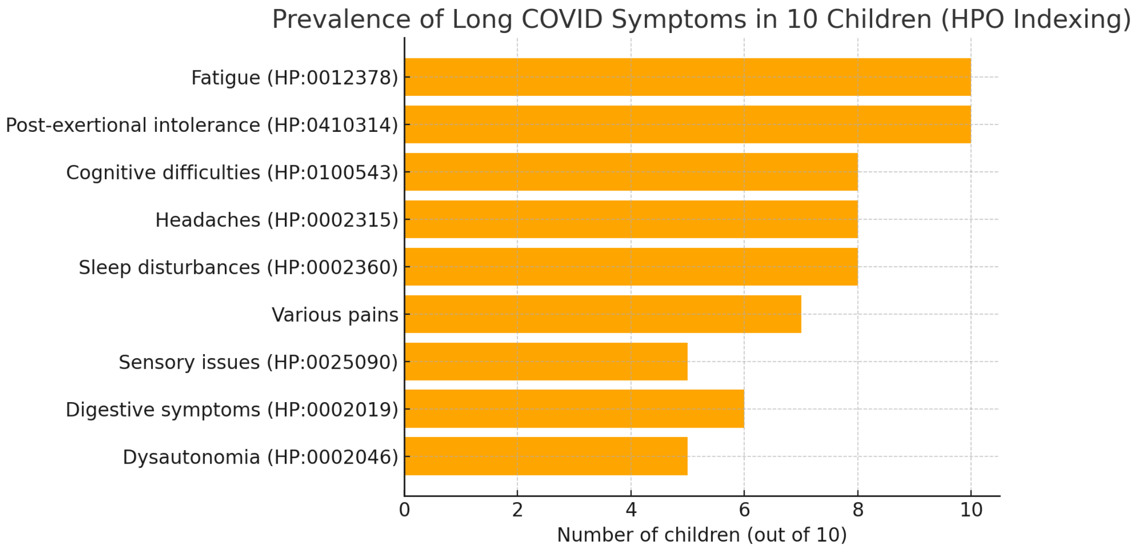
The smartphone-based recording (Google Pixel 6), with consent from the patient and their parents, and its subsequent automatic transcription, is not used solely for data extraction. Rather, it serves to co-construct, with the patient, a clear and shared representation of their lived experience. According to the opinion of the University Hospital-Faculty Ethics Committee of Liège, dated 27 January 2022, the descriptive and narrative study of Long COVID cases in general practice does not fall under the scope of the Law of 7 May 2004 on human experimentation. No negative ethical opinion was issued.

Results

The ten youngest children in our cohort, aged 6 to 15, represent approximately 3% of the total patient population. Among them, seven are female. This sub-sample shows a gender distribution similar to that observed in the overall cohort (n = 307 as of July 1, 2025), where women account for approximately 67% of cases.

Table 1 highlights the semantic recognition power of the system used, which is capable of extracting patient-reported symptoms from natural language in a matter of seconds. What was previously expressed as vague, fragmented, or disjointed discourse is suddenly transformed into an intelligible list of clinical terms—at the very moment of the consultation, and for both patient and physician.

Figure 1: Prevalence of Long COVID Symptoms in 10 Children Seen in General Practice in 2024–2025 (HPO Indexing)



This system can be used directly during the consultation, serving as a tool for both analysis and communication. Patients—or their parents—can be actively involved in reviewing the list of items identified by the system. This shared visualization often acts as a catalyst: it enables the patient and their family to see that the problem is not only acknowledged, but also clearly articulated before their eyes.

A Previously Unknown Syndrome

The physician must adopt a systematic hystory taking approach, due to the very nature of Long COVID—a multisystemic condition resulting from SARS-CoV-2 tissue invasion and the many disorders it can generate. Potentially, all bodily systems may be affected to varying degrees, which necessitates a rigorous and structured clinical exploration.

The recorded portion of the consultation is limited to capturing the symptoms experienced by the child, along with their functional and social repercussions. In the case illustrated in Table 1, the duration of the recorded interview was 19 minutes. It becomes evident that a consultation lasting less than an hour does not allow for an in-depth encounter with the child and their family, nor for truly qualitative listening.

Table 1: Child aged 11 years and 9 months, acute COVID in October 2021, currently out of school. Previously athletic and a *gamer*, he excelled at several strategy games. M. Jamoulle. Consultations, June 2025

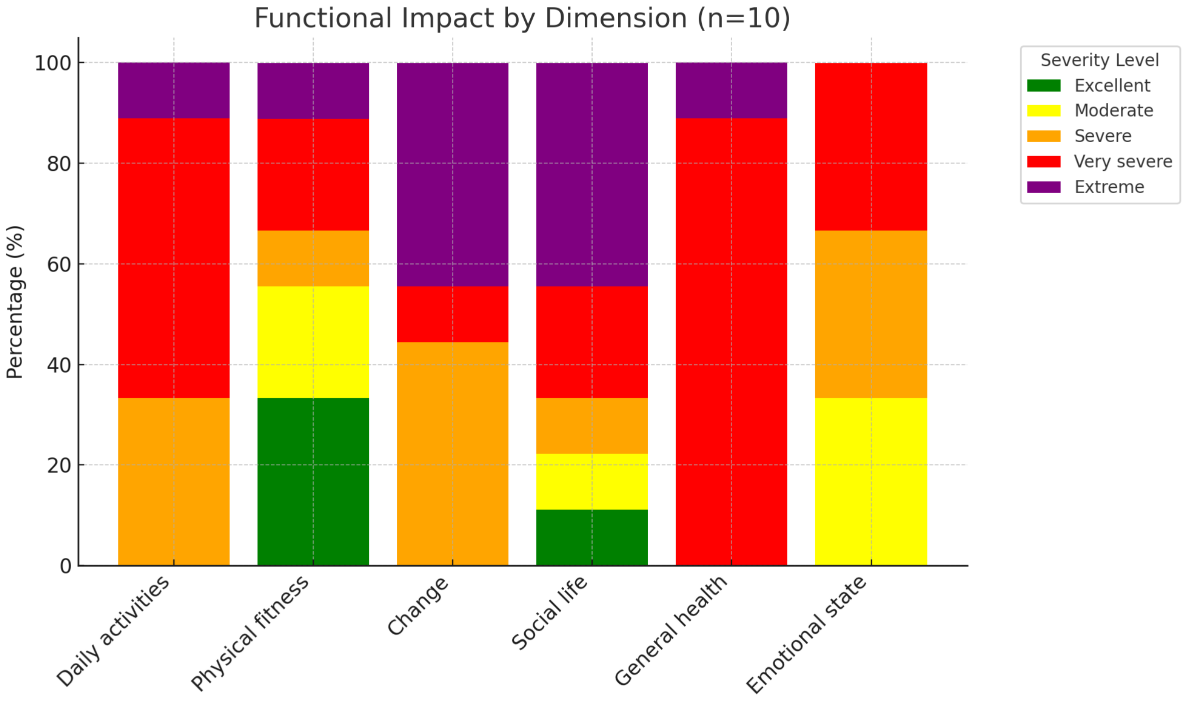
Symptom	**HPO Code**	**Child's Formulation**
Chest pain	HP:0100749	It really hurts in my sternum
Chest tightness	HP:0031355	It feels like someone is squeezing my chest
Violent heartbeats	HP:0001962	Like hammer blows
Palpitations	HP:0001962	My heart beats faster and faster
Cold sweats	HP:0025144	Cold sweats
Pallor	HP:0000970	He can look pale
Nocturnal palpitations	HP:0033775	We checked the pulse but there was no tachycardia
Concentration difficulties	HP:0002315	I can't concentrate
Executive dysfunction	HP:0033666	I can't find the right keys anymore
Cognitive fluctuation	HP:0033687	The next time he wakes up and says "oh yes, that's it"
Memory problems	HP:0002354	I have to ask Mom for the word
Word-finding difficulty	HP:0030784	You want to say "ball"... but you can't find the word
Visual dimming	HP:0002324	I see a beehive, all black
Syncope	HP:0001279	I realize I fainted
Paresthesia	HP:0003401	I feel pins and needles in my feet and back
Dizziness	HP:0002321	The room spins around me
Abnormal body weight sensation	HP:0033832	It's like my whole body is crushing me
Excessive daytime sleepiness	HP:0001259	I sleep all the time
Post-exertional fatigue	HP:0030973	I play a bit and then I need to go to sleep
Fatigability	HP:0002322	I'm too tired so I stop
Sleep-wake rhythm disturbance	HP:0002360	Now I sleep all the time
Mental fatigue after effort	HP:0033755	He's exhausted after 20 minutes
Exertional dyspnea	HP:0002877	I go upstairs and I'm out of breath
Effort intolerance	HP:0003546	I need to take breaks, I sit down on the bench
Post-exertional drowsiness	HP:0033747	After exertion, he falls asleep no matter what
Reduced endurance	HP:0033670	I used to play Fortnite for a long time, now I can't anymore

Moreover, the consultation requires careful preparation beforehand, including analysis of the child's electronic medical record, review of the results from the two standardized questionnaires, and examination of relevant medical documents. This further extends the time needed to ensure appropriate care.

Finally, the consultation must be conducted with empathy and sensitivity, as parents often arrive in a state of distress, overwhelmed by their child's suffering and the persistent feeling of not having been heard.

All children presented with a polysymptomatic profile, with symptoms emerging progressively in the weeks following an initial viral infection. The average clinical profile shown in Figure 1 reveals persistent fatigue and post-exertional intolerance across all ten children. Eight reported fluctuating cognitive symptoms, headaches, and sleep disturbances. Additional symptoms included various types of pain (myalgia, headache, chest pain), sensory disturbances (visual dimming, paresthesia), gastrointestinal manifestations, and signs suggestive of dysautonomia (palpitations, dizziness, post-exertional somnolence).

Figure 2: Results of functional status assessment in 10 children aged 6 to 15 years with Long COVID, as reported by themselves and/or their parents. The predominance of orange (severe), red (very severe), and blue (extreme) indicates a perceived state of significantly impaired health. At this age, the indicator would typically be green (excellent), with occasional yellow (moderate) if the children were in good health.



A Concerning Functional Status

The assessment of functional status using the COOP/WONCA Charts, shown in Figure 2, reveals an alarming situation. At this age, a healthy child would typically achieve a global score close to 6 out of 30. The results observed here indicate a significant impairment in daily functioning across several dimensions.

The table presents the percentage distribution of responses for each dimension assessed. Five severity categories were distinguished:

- **Excellent**: optimal functioning or absence of significant complaints (green)

- **Moderate**: mild to moderate functional limitations (yellow)
- **Severe**: notable impairment with moderate impact (orange)
- **Very severe**: major limitations affecting quality of life (red)
- **Extreme**: profound disruption of daily functioning (purple)

Each row of the table corresponds to a functional domain: general health status, physical fitness, emotional well-being, daily activities, social life, and change in health status. Each column indicates the percentage of children whose responses placed them in the defined severity category for the respective domain.

All children experienced temporary or long-term school withdrawal. Most no longer participate in physical or social activities. Families expressed emotional exhaustion linked to diagnostic uncertainty and prolonged medical wandering.

Table 2: Examples of child or parent-reported expressions related to fatigue and sleep in children aged 6 to 15, who had no such issues before COVID. M. Jamoulle, Consultations 2022–2025

I'm tired all the time.
I feel exhausted after any effort.
I have no energy left, not even for simple things.
She would get tired quickly and needed to rest often.
What happens after exertion? I'm totally drained.
I have to take breaks between movements.
I sleep, but I still wake up tired.
I used to do sports — now I can't even stay on my feet.
She spends all her time sleeping in class.
I can sleep for three days straight… or not at all for three days.
I could sleep from 7 p.m. to noon, and still wake up tired.
Before, I only slept at night — now I sleep all the time.
Even a small effort can cause overwhelming fatigue…
…forcing me to sleep no matter what.
You sleep a lot. How much? 19 hours a day.

Discussion

Within a cohort of over 300 patients with Long COVID followed in general practice, we selected the ten youngest children to shed light on the complexity of an emerging syndrome—pediatric Long COVID—and to help bring it out of the clinical and social invisibility in which it too often remains confined.

This study proposes an innovative approach to documenting the syndrome, combining structured narrative collection with phenotypic indexing based on the *Human Phenotype Ontology* (HPO). This hybrid methodological framework, at the intersection of narrative medicine and digital health, enables the linkage of the child's and family's lived experience with standardized, interoperable clinical descriptors.

In the pediatric context, where symptoms are often expressed indirectly or mediated through parental narratives, the narrative approach is a fundamental tool for grasping the illness in its contextual complexity. HPO indexing subsequently allows for a formalized structuring of these clinical elements, facilitating transversal analysis, the formation of homogeneous cohorts, and integration into clinical databases.

This pheno-narrative approach pursues a dual objective: to acknowledge the uniqueness of individual trajectories while rendering them analyzable through digital tools. It opens promising avenues for participatory research, the development of contextualized clinical instruments, and the training of a more reflective, humanistic, and patient-centered medical practice grounded in the patient's story.

> *"I want to go to school, but my body won't let me. I wake up already tired. When I try to run a little, everything hurts and I have to go to sleep."* (boy, 12 years old)

> *"I used to dance three times a week. Now, just getting up and washing my hair takes me all morning."* (girl, 13 years old)

> *"He's changed. He doesn't play with his friends anymore, he stays in his room, he doesn't want to go out. He tells us his stomach hurts, his head hurts, and that he hears strange noises in his head."* (mother of a 10-year-old boy)

The longitudinal follow-up implemented in this study allows for the identification of clinical patterns compatible with pediatric Long COVID, even in the absence of classical objective signs. The general practitioner plays a central role in this process—as a privileged observer of the child's trajectory, a care coordinator, and a key source of support for families.

Each child also completed the age-appropriate COOP/WONCA functional self-assessment charts, which provided insights into the impact of Long COVID on quality of life across multiple domains.

The combination of diverse sources of information—initial questionnaire, clinical interview, assisted analysis, and COOP Charts—offers a holistic and nuanced representation of how Long COVID affects the lives of children. This approach bridges the patient's subjectivity, clinical expertise, and digital decision-support tools.

One of the main strengths of this approach lies in its ability to surface clinical elements that, when considered in isolation, might seem minor or anecdotal. If only one child reports persistent fatigue, the complaint might be overlooked; but when several children describe similar symptoms, these acquire clinical legitimacy and emerge as relevant signals. Table 2 illustrates this dynamic by presenting fourteen excerpts from interviews that, when analyzed collectively, reveal recurring and clinically meaningful themes.

This methodological triangulation—combining narrative, semantic structuring, functional assessment, and assisted analysis—enables a more comprehensive understanding of the pediatric Long COVID experience. It reconciles the individual and the collective, the human and the digital, the subjective and the measurable, in an approach attuned to the clinical complexity encountered in primary care.

To our knowledge, no published study to date has employed a comparable methodology to explore pediatric Long COVID through a combination of narrative and phenotypic frameworks. Nonetheless, our approach draws inspiration from the work of Deer et al.[18], who, as early as 2021, used the *Human Phenotype Ontology* to analyze the content of 45 scientific publications on Long COVID, highlighting the prevalence of neuropsychiatric involvement in this condition.

The integration of Multimodal Large Language Models (MLLMs) into clinical workflows would significantly enhance the accuracy of HPO identification by physicians, offering promising potential to standardize phenotype descriptions in medical research. However, as highlighted by Zhong et al. [19], the notable hallucination rate observed in these models underscores the need for improved precision in HPO term identification, which will be further explored in subsequent phases of this work.

This study represents a single-clinician case observation, with the inherent limitations of such a design: subjectivity in data collection, narrative heterogeneity, and potential interpretive bias. These biases are partly mitigated by the structured nature of the data and the grounding in longitudinal field-based clinical practice.

To further deepen our understanding of this condition in children, several complementary resources can be leveraged. The website Long Covid Kids [20], supported by the UK National Health Service (NHS), provides valuable information, testimonials, and educational materials. In Belgium, the organization Long Covid Belgium recently released an online documentary [21], available in both French and English, specifically dedicated to pediatric Long COVID and highlighting family narratives and the associated clinical challenges.

Conclusion

Ultimately, this approach aims to reaffirm the central role of primary care in identifying, validating, and supporting pediatric forms of Long COVID, through an alliance between clinical practice, language, and technology. Originally developed to characterize rare diseases, the Human Phenotype Ontology (HPO) also proves valuable in shedding light on so-called “invisible” illnesses such as Long COVID. By enabling structured, interoperable symptom documentation, HPO helps reveal subtle and heterogeneous clinical pictures, particularly in children whose suffering often escapes traditional diagnostic frameworks. This opens new pathways for recognition, care, and research.

Conflict of Interest Statement

The author declares no conflicts of interest. No funding was received for this work.

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Availability of Data

Due to the sensitive nature of the clinical data involved, the primary dataset—formatted according to the OMOP Common Data Model and containing pseudonymized symptom profiles—cannot be made publicly available. However, access can be granted to qualified researchers upon reasonable request, provided that they obtain approval from a recognized ethics committee and agree to comply with all applicable data protection regulations.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT in order to proofread the manuscript. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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