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Post-COVID-19 syndrome in children: a scoping review

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ABSTRACT

Post-COVID-19 syndrome (PCS) and multisystem inflammatory syndrome in children (MIS-C) have emerged as significant pediatric health challenges, yet the true prevalence and long-term effects remain unclear. Children typically experience milder acute infections than adults, but a subset develop persistent physical, neurological, and psychological symptoms that impair quality of life. To synthesize current evidence on the long-term symptoms, risk factors, and outcomes of PCS and MIS-C in children and adolescents from 2021–2025. Following the PRISMA-ScR framework, 30 studies involving children aged 0–19 years were systematically reviewed across major databases. Thematic analysis identified clinical patterns, risk determinants, and mechanistic explanations. The construal level theory (CLT) was used to interpret behavioral and psychological adaptations influencing recovery. While most pediatric cases resolved fully, 15–30% of MIS-C survivors exhibited prolonged neuropsychological symptoms, fatigue, cognitive impairment, and mood disturbances lasting beyond 12 weeks. Risk factors included adolescent age, severe acute illness, and preexisting conditions. Major gaps include inconsistent definitions, limited longitudinal follow-up, and the absence of standardized rehabilitation or psychosocial care protocols. Post-COVID-19 sequelae in children warrant structured follow-up programs integrating neurocognitive assessment, mental health support, and standardized care pathways to reduce long-term disability and guide policy formulation. Post-COVID-19 syndrome, MIS-C, pediatrics, long COVID, scoping review.

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1. INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of coronavirus disease 2019 (COVID-19), a systemic illness with a wide variety of symptoms. Cough, sputum production, and dyspnea are typical pulmonary symptoms, but gastrointestinal issues, skin rashes, and cardiac arrhythmias are examples of extra-pulmonary symptoms [1], [2]. The World Health Organization (WHO) labeled the epidemic a global pandemic in March 2020 after it started in Wuhan, China, in December 2019. Over 480 million individuals were sick by March 2022, and 6.1 million deaths were predicted worldwide [1].

SARS-CoV-2 infection in pediatric populations can result in new or chronic symptoms after recovery, even though they make up less than 10% of COVID-19 cases, and the majority of them have milder

acute illness than adults. These include long-term COVID-19 and, less frequently, children's multisystem inflammatory syndrome (MIS-C/PIMS-TS) [1], [2]. Numerous symptoms have been reported, such as headaches, exhaustion, respiratory issues, chest pain, insomnia, mood disorders, anosmia, heart problems, and cognitive impairment (also known as "brain fog"). These aftereffects could have a major impact on social, psychological, and physical functioning, making it harder to participate in everyday activities and school [3], [4].

In 2023, the WHO established a clinical case definition tailored to children for post-COVID-19 conditions to standardize care and research. As to these criteria, the illness usually manifests within three months of beginning in children and adolescents who have a history of suspected or proven SARS-CoV-2 infection. The symptoms must remain for at least two months and cannot be attributed to any other diagnosis (WHO, 2023). The need for pediatric-focused research is emphasized by this definition, which also underlines significant disparities in presentation between children and adults [4], [5].

A significant percentage of children experience persistent symptoms months after infection, even though prevalence estimates vary greatly depending on methodology, according to recent large-scale studies like the UK CLoCK cohort and the US NIH RECOVER effort [4]–[6]. The identified risk factors include older age within childhood, pre-existing respiratory or allergic conditions, obesity, severe acute COVID-19, and hospitalization. Adolescents seem to be more affected than younger children [7]–[10]. Viral persistence, immunological dysregulation, and autoimmunity, dysautonomia, endothelial dysfunction, microvascular damage, and changes in mitochondrial or microbiome function are some of the mechanistic theories for post-COVID-19 syndrome in children [11]–[13]. These processes might change depending on the developmental stage, which could explain why pediatric populations have such diverse clinical characteristics. New variations, broad past infections, and rising vaccination rates have all contributed to the pandemic's ongoing evolution. Although caution is still required, the incidence of MIS-C has decreased in comparison to the early pandemic [14], [15]. Additionally, preliminary data indicate that the COVID-19 vaccine may lower children's risk of post-acute sequelae, although results are conflicting and need more research [16], [17].

Uncertainties remain about the occurrence, duration, risk factors, and long-term consequences of post-COVID-19 syndrome in children, despite the rapidly growing body of information between 2020 and 2025. To map the scope of existing research, pinpoint knowledge gaps, and elucidate symptom clusters, risk factors, and underlying mechanisms, a scoping review is necessary. This review specifically aims to answer the following question: What are the long-term symptoms, risk factors, and outcomes identified in papers published between 2020 and 2025 for children and adolescents with post-COVID-19 conditions, including MIS-C? To support better children and families affected by post-COVID-19 disorders, this study attempts to provide insights that will guide rehabilitation and educational planning, improve clinical management, and shape public health measures by combining the available data [4], [18].

2. THEORIES OR CONCEPTUAL FRAMEWORK

Construal level theory (CLT) serves as the conceptual foundation that directs this investigation. According to psychological distance, the perceived separation between oneself and an event in terms of time (temporal distance), space (spatial distance), social interactions (social distance), or likelihood (hypothetical distance), CLT describes how people view, assess, and react to events [19], [20]. In contrast to psychologically distant events, which are processed in more abstract, generalized ways, events experienced as closer in distance are interpreted concretely and in depth. One of the main characteristics of human cognition is the capacity to mentally move beyond the present to think about the past, the future, or hypothetical situations.

Through lockdowns, isolation, and protracted uncertainty, the COVID-19 pandemic exacerbated social and temporal gaps and caused hitherto unheard-of disruptions to health systems and daily life. Understanding how children and families viewed these disruptions and how those perceptions influenced coping and adaptation is made easier with the help of CLT [21], [22]. For instance, whereas parents, doctors, and educators may think more abstractly about the long-term effects, children may concentrate on the immediate and palpable symptoms.

When applied to children's post-COVID-19 condition, CLT explains the variation in perceptions and approaches to managing lingering symptoms. Long-lasting symptoms may be seen differently by adolescents who are developmentally more oriented toward abstract and future-focused thinking than by younger children, which could have an impact on coping mechanisms, resilience, and health-seeking activities [13], [23]. However, parents and medical professionals frequently interpret these results on a longer-term, more comprehensive scale, directing treatments and support systems. Additionally, CLT illuminates the psychological toll of prolonged COVID. A child's current experience and the anticipation of "full recovery" are psychologically separated by persistent symptoms, including exhaustion, mood swings,

and cognitive fog. This distance can influence family resilience and adaptation while also lowering motivation for education, social interaction, and rehabilitation [3], [4].

This study emphasizes how psychological distance shapes children's and families' perceptions of disease and recovery by placing post-COVID-19 syndrome within CLT. Along with more general social-cognitive viewpoints, CLT offers a framework for comprehending the behavioral and cognitive mechanisms that help kids and families deal with the long-term effects of COVID, as well as for interpreting the disease's clinical manifestations [24]. Matplotlib Chart in Figure 1. Conceptual diagram relating post-COVID-19 syndrome in children to CLT. It demonstrates how temporal, social, spatial, and hypothetical distance dimensions influence children's and families' perceptions of sickness. These perceptions, in turn, impact outcomes such as coping, resilience, school engagement, and family adaptation.

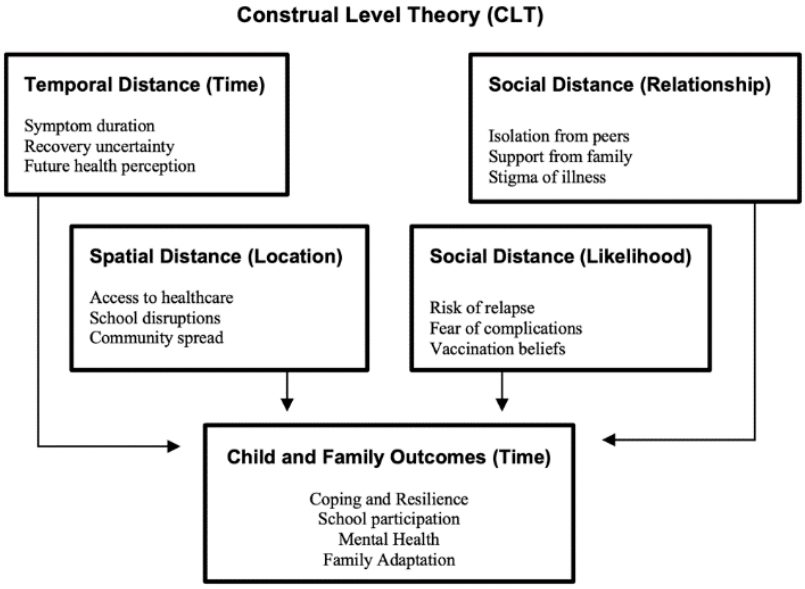

Figure 1. Matplotlib chart

3. METHOD

3.1. Study design

The review methodology adhered to Arksey and O'Malley [25], [26] scoping review approach and its later improvements [27]. Using aspects of the PRISMA 2020 statement for systematic reviews [28], it was further linked with the PRISMA extension for scoping reviews (PRISMA-ScR) [28] to guarantee transparency and repeatability. Using literature released between January 2021 and August 2025, this method enabled a systematic synthesis of the data about the long-term impacts of COVID-19 and multisystem inflammatory syndrome in children (MIS-C) in pediatric populations.

3.2. Data sources and search strategy

Six databases: Google Scholar, Thoreau, SAGE Journals, BioMed Central, Medline, and CINAHL were thoroughly searched. Only English-language publications published between January 2020 and December 2025 were included in the search. The Boolean operators merged and used outcome are: ("children" OR "adolescents" OR "youth") AND ("long-term effects" OR "post-COVID" OR "MIS-C"). Search strategies were tailored to the indexing requirements of each database. In addition, the reference lists of relevant reviews were screened to capture additional eligible studies.

3.3. Screening and selection process

There were 1,046 items found in the first search. Following deduplication, two reviewers independently checked abstracts and titles against the inclusion and exclusion criteria (Table 1). Due to their lack of focus on pediatric long-term COVID-19 outcomes, duplication, or irrelevance, articles that did not fit the criteria were eliminated. After that, full-text publications of possibly qualifying research were evaluated for ultimate inclusion. Reviewers' disagreements were settled through dialogue until an agreement was reached. The PRISMA-ScR flow diagram shows the study selection procedure (Figure 2).

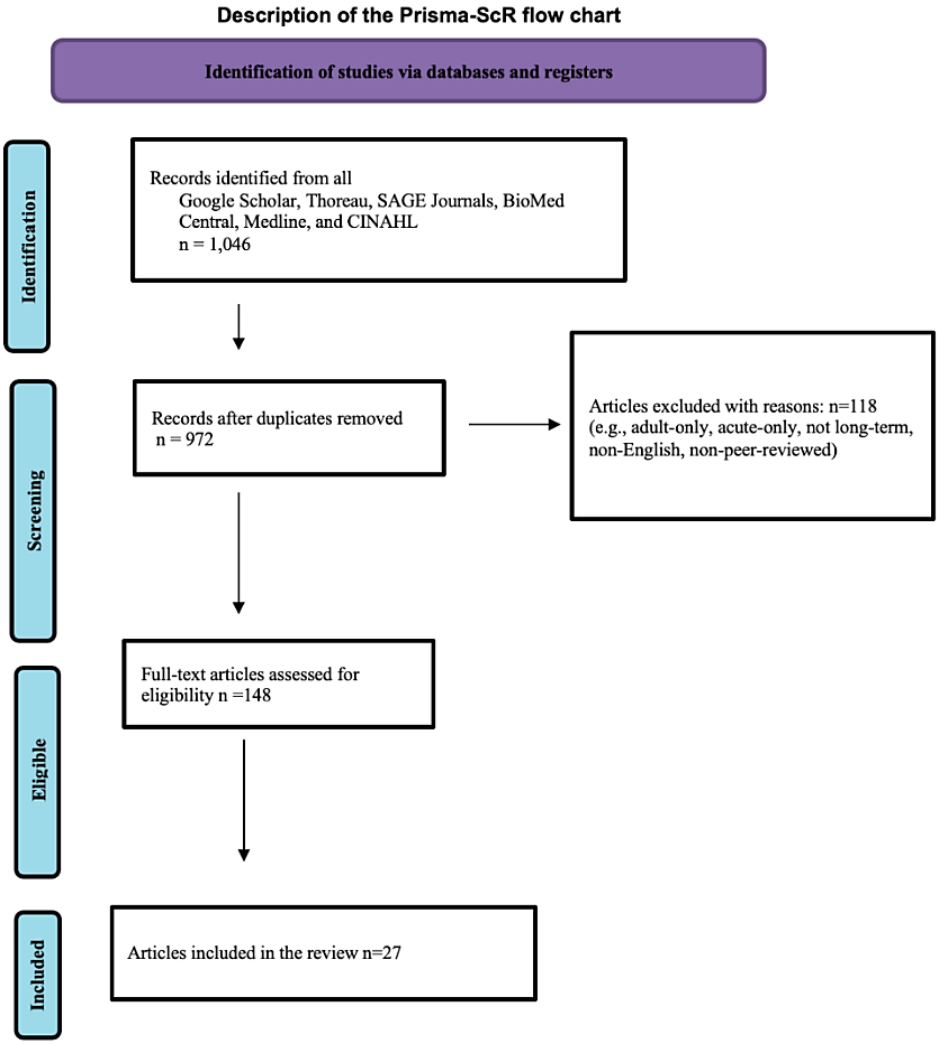

Figure 2. Prisma flow chart

Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Were published between January 2020 and December 2025, Represented original research, reports, or reviews, Focused on the long-term effects of COVID-19 or MIS-C in children, adolescents, or youth, and Were written in English.	Were published outside the specified date range, Did not focus on the long-term effects of COVID-19 or MIS-C, Did not involve children, adolescents, or youth, Were duplicates, or Were non-peer-reviewed sources.

3.4. Data extraction

Data were extracted using a standardized form with two reviewers independently working to extract data, with discrepancies resolved by consensus. The captured data are included in Table 2 [4], [29]-[55] (see Appendix): i) Author(s) and year of publication; ii) Study design and setting; iii) Population and sample size; iv) Key findings on long-term effects of COVID-19 or MIS-C; and v) Reported limitations. Long-term effects, risk factors, and outcomes.

3.5. Data synthesis

The results were compiled narratively and thematically in light of the inherent variability in study designs, participants, and outcomes throughout the literature. Data was extracted into five key, actionable topics to organize this process: research gaps, long-term symptoms, risk factors, outcomes, and study design/setting/population. A systematic comparison of the evidence between long COVID and MIS-C was made possible by this column-based theme approach, which also ensured that methodological constraints

were evaluated directly alongside significant findings to identify trends, differences, and important knowledge gaps.

3.6. Data analysis

To detect recurring themes, conclusions, and gaps, data from the included publications were taken out and examined. To identify recurrent trends in the long-term impacts of COVID-19 and MIS-C on kids and teenagers, a thematic analysis was carried out. The findings were combined to give a thorough summary that covered potential causes, long-term effects, and potential research topics. A systematic checklist that considered study design, sample size, methodology, and the reliability of conclusions was used to evaluate the quality of the included studies. Finally, key findings, techniques, and identified gaps were summarized in an organized manner.

4. RESULTS AND DISCUSSION

A summary of the main conclusions from a scoping assessment of the literature about the post-acute aftereffects of SARS-CoV-2 infection in children and adolescents is provided in this section. The main source of evidence is the accompanying table, which includes excerpts from 23 studies covering the years 2021–2025, including prospective cohorts, systematic reviews, and meta-analyses. The two main clinical entities that form the basis of the analysis are Multisystem Inflammatory Syndrome in Children (MIS-C) and long COVID after a typical SARS-CoV-2 infection. The table lists the main conclusions, long-term symptoms, and study design for each item. This makes it possible to directly compare the results, emphasizing the difference between the more severe cognitive and functional impairments observed in a subgroup of MIS-C survivors and the typically low symptom load documented in long COVID cohorts. The synthesis that follows employs these extracted data to uncover consistent patterns and important research gaps across the pediatric post-infection spectrum.

4.1. Synopsis of the main research results

An overview of MIS-C and pediatric post-acute COVID-19 sequelae. Two main methodological approaches form the basis of the data on pediatric post-infection sequelae: prospective, single-center follow-up cohorts that describe outcomes in high-risk groups, including MIS-C survivors, and large-scale cohort studies that provide population-level prevalence.

4.1.1. Cohort studies and general COVID-19 sequelae

Large-scale cohort studies intended to produce reliable, population-level estimates were the main source of information regarding the prevalence and overall burden of Long COVID after acute SARS-CoV-2 infection. Research using the Nationwide Danish cohorts [32], [33] falls under this type. This research compared infected children to sizable control groups using registry data, providing early, broadly applicable proof that the symptom load was low and decreased over time [32]. Multiple systematic reviews and meta-analyses of controlled trials later confirmed this finding, demonstrating minimal absolute risks across a variety of international populations but an increased risk of persistent symptoms compared to controls [31], [45]. To further understand healthcare consumption and uncover new hazards, researchers also used large multicenter electronic health record (EHR) or claims data [36], [51]. For example, they found that reinfection is linked to a higher risk of long COVID characteristics [51].

4.1.2. High-risk cohorts: MIS-C and critical illness

The results of MIS-C, a high-severity hyperinflammatory condition, are the subject of a separate and essential body of research. To get comprehensive, long-term phenotyping in high-risk patients, these studies usually use prospective, single- or multicenter follow-up groups. For example, multicenter prospective cohorts using age-matched or disease controls followed hospitalized MIS-C patients for up to two years in the United States and Italy [50], [56]. This strategy was essential in determining that approximately 20% of patients had ongoing cognitive problems, despite relatively good physical recovery [56]. Additionally, targeted data on the most severely affected patients were obtained from studies conducted specifically on Pediatric Intensive Care Unit (PICU) survivors with COVID-19/MIS-C [43], [53]. The crucial context for understanding results is provided by this methodical approach, which progresses from population-level data to deep phenotyping in survivors of catastrophic illnesses. A more critical evaluation of the data is possible when one is aware of the populations and research methodologies that produced these results. Using this basic understanding of study settings, the following section describes the particular long-term symptoms, risk factors, and overall results found in these two primary clinical groups.

4.2. Synthesis of long-term symptoms, risk factors, and outcomes in pediatric post-infection studies

4.2.1. Long COVID: Transient functional symptoms and demographic risks

- Observed sequelae: Long-term symptoms, risk factors, and outcomes

While highlighting a positive overall prognosis, the literature on pediatric post-infection sequelae consistently highlights important symptomatic clusters and demographic/clinical variables that require ongoing care. The main clinical entity under study, severe hyperinflammation (MIS-C) vs general SARS-CoV-2 infection (long COVID), naturally separates the synthesis.

- Long COVID: Transient functional symptoms and demographic risks

The most common long-term symptoms for children after an acute SARS-CoV-2 infection (long COVID) are functional and frequently non-specific. According to studies, the most prevalent problems that last longer than 12 weeks are headache, fatigue, mood/sleep disorders, and cognitive symptoms [30], [32], [48]. Although they are observed, respiratory symptoms and loss of taste and smell are frequently less common than in adults [33], [52]. Adolescent age and female sex are the most commonly found risk factors for these chronic illnesses [4], [30], [54]. Hospitalization and increased acute symptom severity are also linked to this [31], [54]. Importantly, Omicron-era findings indicate that reinfection can increase the likelihood of long COVID characteristics [51].

There is broad agreement that most children recover and that symptoms go away in a matter of months, and overall results are favorable [32], [33], [55]. The results for the minority with symptoms highlight the necessity of interdisciplinary supportive care and steady progress over time [30], [38]. These results highlight a CLT difference: the persistent minority needs high-construal planning about schooling, future health, and social roles, whereas the majority face proximate, low-construal sickness problems.

4.2.2. MIS-C: neuropsychological and cardiac follow-up needs

The profile of long-term symptoms in children who went through the severe acute phase of MIS-C changes to emphasize systemic and cognitive aftereffects. Although early cardiac involvement is typical, persistent fatigue, decreased exercise tolerance, and serious concentration, mood, and sleep problems are the main symptoms in the later stages [29], [53], [56]. Additionally, the potential for a small minority to have lingering immunological dysregulation and the sporadic necessity for long-term cardiac surveillance [34], [42]. The intensity of the acute sickness is a major risk factor for long-lasting impairments following MIS-C. There is a clear correlation with worse chronic cognitive and functional outcomes and indicators such as intensive care unit admission, major cardiac involvement, elevated inflammatory markers, or the need for organ support at presentation [29], [43], [53], [56]. Although continuous monitoring is required, the long-term results with MIS-C are generally positive. Studies reveal that even if cardiac recovery is largely complete, a sizable minority (up to 20%) still need assistance with mental health, education, and rehabilitation because of ongoing cognitive or functional impairments [53], [56].

4.2.3. Pathophysiological mechanisms

Complex pathophysiological processes, including immunological dysregulation, chronic inflammation, and endothelial dysfunction, underlie persistent post-COVID-19 conditions (PCS) [15], [57]. A mechanistic connection between immune activation and neurological outcomes is supported by emerging mechanistic insights that indicate dysregulated cytokine profiles correspond with symptoms persistence [58], [59] and neuroinflammatory markers have been detected in adolescents with prolonged cognitive deficits [39]. These biochemical disturbances have a significant effect on psychological health and function; anxiety, melancholy, social disengagement, and decreased academic engagement are commonly documented, especially in teenagers. Additionally, certain immunological and proteomic biomarkers may be able to predict prolonged recovery trajectories, according to prognostic studies [60]. Psychosocial and environmental factors exacerbate this biological variation, since social determinants and a lack of support networks influence resilience and long-term adaptation. Construal level theory (CLT) integration offers a useful framework for interpretation: situational factors (low-level construal) drive short-term care adherence, whereas abstract thinking about identity, social roles, and future coping (high-level construal) is necessary for long-term adaptation to chronic symptoms. These results highlight the necessity of precision medicine strategies to lessen long-term impacts; yet, numerous methodological and information gaps in the present research must be filled first.

4.3. Synthesis of identified research gaps in pediatric post-infection studies

Several significant and recurring methodological flaws and information gaps in the literature on pediatric Long COVID and MIS-C outcomes are brought to light by the scoping review extracts. The need for more standardized and controlled research is the most common and overwhelming gap found [31], [45], [52], [55]. To enable meaningful comparison across locations and studies, researchers have repeatedly called for harmonizing definitions and assessment methodologies, as well as using well-controlled longitudinal cohorts [31], [40], [55]. Pooled prevalence estimates are less reliable due to factors such as research design

heterogeneity, conflicting symptom definitions, and the possibility of selection bias and residual confounding, particularly in clinic-based cohorts without non-COVID controls [4], [30], [31], [45].

The gaps cluster into three primary areas:

- Methodological rigor and bias: Several studies, especially the early ones, are criticized for their lack of specified early childhood measures [39], reliance on claims-data coding accuracy [36], attrition and survivorship bias [43], [51], and parent-reported outcomes [32]. A common theme is the requirement for uniform follow-up procedures to reliably record results over time [40], [45].
- Long-term and mechanical understanding: It is acknowledged that both Long COVID and MIS-C lack a thorough grasp of the long-term mechanical foundations [42] and the entire range of neuropsychological aftereffects [44]. Despite their generally favourable results, studies on MIS-C outcomes point out limitations because of their small sample sizes and the requirement for longer-term, more thorough follow-up than the short- to mid-term [29], [47].
- Equity and contextual factors: The necessity of causative analyses to comprehend the identified socioeconomic and racial/ethnic differences in MIS-C incidence and outcomes is one gap that has been brought to light [61].

In conclusion, to go beyond descriptive findings and clarify the pathophysiology and long-term care requirements of impacted children, future studies must give priority to well-controlled, harmonized, and longitudinal study designs [52].

4.4. Summary and implications

The collective evidence from this research indicates that children who recover from COVID-19 or MIS-C may have long-lasting, multi-systemic, and functionally important side effects that impact their mental and physical well-being. Multifactorial risk factors include biological, clinical, social, and demographic aspects. The intricacy of PCS is shown by mechanistic studies, which show that long-term consequences are driven by neuroimmune and hyperinflammatory pathways [39], [59]. New findings of neurological involvement, biomarkers of extended recovery, and psychosocial effects are highlighted by emerging research, which makes monitoring, intervention, and policy planning more urgent [4], [39], [41], [46], [59].

Construal level theory (CLT) integration offers a framework for comprehending how kids and teenagers react to the long-term consequences of MIS-C and COVID-19. Short-term behaviors like following recovery guidelines or using healthcare services are influenced by situational and environmental factors. Long-term patterns of socialization, health-related decision-making, and coping with chronic illnesses are influenced by more abstract elements, including attitudes, beliefs, and social norms. Clinicians and policymakers can better anticipate present and future needs by using CLT to customize therapies that target social, emotional, and cognitive well-being in addition to physical healing.

Building on these revelations, some useful suggestions are revealed: Psychosocial and educational support, including counselling, school reintegration programs, and community-based initiatives to mitigate functional and emotional impacts; targeted interventions for high-risk children informed by clinical, social, and biomarker-based risk stratification to reduce the likelihood of prolonged or recurrent symptoms; and ongoing research to clarify mechanistic pathways, optimize therapeutic strategies, and refine evidence-based guidelines for long-term pediatric care. Prolonged monitoring of pediatric post-COVID patients using attention to multisystem and neurocognitive assessments to capture subtle but clinically significant outcomes. For children recovering from COVID-19 and MIS-C, this integrated approach guarantees that interventions are thorough, supported by evidence, and sensitive to their immediate as well as changing needs.

The wider socioeconomic and educational effects of PCS and MIS-C should also be considered in public health policy. Long-term emotional, cognitive, and developmental deficits can be avoided with early detection and intervention, especially in susceptible groups. Standardized procedures for evaluation and follow-up should be available to healthcare professionals, and families should be given instructions on how to identify and treat chronic problems. Ultimately, to successfully address the long-term effects of COVID-19 in children, a coordinated, multidisciplinary effort involving pediatricians, psychologists, educators, and legislators is necessary. All things considered, this data emphasizes how critical it is to address the long-term effects of COVID-19 and MIS-C in children, making sure that interventions are comprehensive, interdisciplinary, and grounded in new findings. Proactively addressing these issues would lessen the societal burden of post-COVID problems in juvenile populations while also improving individual results.

5. IMPLICATIONS FOR CLINICAL PRACTICE

We have outlined recommendations for clinical practice and policy based on the results of the systematic study. We recommend putting early identification, interdisciplinary treatment, and focused

therapies into practice. To close knowledge gaps and enhance long-term results for kids with PCS, it's also critical to keep investigating. Using the results of long-term follow-up research, policy planning must shift from managing the acute pandemic phase to addressing the chronic, multi-systemic needs of children with Long COVID and post-MIS-C disorders.

5.1. Prioritizing neuropsychological and functional support

Although acute cardiac risk received most of the policy attention at first, long-term data suggest that neurocognitive and mental health care should be given priority.

- Targeted screening and support are two ways to accomplish this. Comprehensive rehabilitation programs that incorporate physical, cognitive, and psychosocial care throughout the duration of illness must be funded by policy [37], [43]. This is important since studies with two-year follow-up have revealed that up to 20% of MIS-C survivors have ongoing cognitive problems, such as mood disorders and attention abnormalities [56]. Reduced quality of life and functional deficiencies frequently persist; therefore, school systems need resources and educational modifications to offset functional and academic disadvantages [34], [48].
- Standardized follow-up protocols: It remains essential to implement early primary care treatments, such as systematic screening and prompt identification of high-risk cases [52]. The current literature's measurement gaps and heterogeneity [52] require health systems to adopt standardized, harmonized follow-up strategies [40]. These procedures need to document subtle, delayed results across various domains, extending beyond basic vital signs to include comprehensive functional and neuropsychological assessments.

5.2. Refining clinical risk stratification and monitoring

Resources should be distributed by policies according to the particulars of the sequelae and the risk factors that have been recognized. This can be accomplished through:

- Risk-informed interventions: Although it necessitates rigorous cost-benefit analysis, medication management can aid in reducing hospital overcrowding [43]. Recognized risk factors must be used to customize policy: High acute disease severity (ICU hospitalization, cardiac involvement), female sex, and adolescent age are widely recognized as important risk factors for enduring symptoms [54], [56]. Additionally, the discovery that reinfection is linked to an increased incidence of long COVID characteristics [51] emphasizes the necessity of ongoing preventative measures.
- Long-term cardiovascular surveillance: One significant worry is cardiovascular problems. To lower inflammation and avoid medium- to long-term consequences, early intervention is required [47]. As MIS-C is more understood, cardiac surveillance and long-term follow-up are advised, possibly into adulthood [29]. These conclusions are supported by recent research that demonstrates mild cardiovascular abnormalities that remain in children for up to 18 months after infection [34], [42].

5.3. Addressing social and mechanistic gaps

- Equity in care

Demographic and socioeconomic variables have a major impact on outcomes and vulnerability [46]. To address inequities, policy must support targeted family-level and psychosocial interventions as well as causal studies [48], [61]. In a similar vein, family-level and psychosocial therapies may improve recovery, with parental support acting as a buffer [37].

- Funding mechanistic research

Studies on cytokine-mediated and neuroimmune mechanisms must be given top priority when policymakers make judgments about long-term treatment trials [42], [56]. To find the best treatments that can stop coronary artery aneurysms and reverse inflammatory processes in MIS-C, clinical trials are necessary [44].

Finally, vaccination confidence is still a crucial part of preventative tactics [55]. To lessen long-lasting post-COVID problems, recent longitudinal studies [4], [37] also advocate combining immunization campaigns with educational and psychosocial interventions.

6. CONCLUSION

A thorough approach for finding, vetting, and evaluating pertinent research on the long-term impacts of COVID-19 and MIS-C in kids and teenagers is offered by this systematic literature review. This study highlights long-lasting clinical, neurological, and psychological consequences, as well as demographic and socioeconomic factors impacting outcomes, by combining findings from early and contemporary research, including those conducted in 2024–2025. The study shows a structurally divided body of evidence, with intense prospective cohorts describing severe neuropsychological abnormalities in a minority of MIS-C survivors and strong national cohorts demonstrating a low absolute risk for long COVID.

Additionally, the study highlighted the importance of conducting mechanistic research on hyperinflammatory and neuroimmune pathways and revealed significant methodological inadequacies. A useful interpretive perspective is offered by incorporating CLT, which contends that therapies should address both the high-level, abstract difficulties of long-term social and functional adaptation as well as the low-level, urgent physical demands. The methodical approach guarantees thorough coverage of the most recent research, providing insightful information for clinical practice and influencing public health policy, addressing the need for equitable, multidisciplinary pediatric treatment and standardized follow-up methods.

The concepts recommended in the updated future research section fall into three main areas, focused on resolving methodological limitations and advancing causal understanding; i) Standardized clinical and laboratory measures: The focus here is on developing and strictly applying harmonized metrics across different studies, especially for capturing subjective outcomes like fatigue and cognitive impairments, to ensure data is comparable internationally; ii) Multicenter, prospective longitudinal designs: moving away from small, retrospective or clinic-based studies to large-scale prospective cohorts with longer follow- up periods (beyond mid-term) to accurately track the true, long-term trajectory of symptoms; ii) Targeted follow-up and monitoring: research should adopt precise protocols for monitoring specific, high- risk outcomes, including subtle cardiovascular changes and the academic/functional impact of neuropsychological issues observed in MIS-C survivors; iv) Immunologic and cytokine pathway investigations: deep research into cellular and cytokine responses is critical to elucidate the hyperinflammatory and neuroimmune pathways driving persistent symptoms and neurological complications; v) Targeted therapeutic trials: conducting clinical trials to identify optimal treatments capable of reversing hyperinflammatory processes in MIS-C and addressing the underlying mechanisms of long COVID. This research is also key to informing the creation of effective SARS-CoV-2 vaccines for children; vi) Family-level mechanisms and interventions: focusing on the family unit to formally evaluate parental support and household strategies as protective factors that enhance recovery outcomes; vii) Causal analysis of disparities: moving beyond simply reporting socioeconomic and demographic disparities to conducting causal analyses to understand the root causes of disproportionately severe long-term effects in disadvantaged children; and viii) Theoretical integration: utilizing frameworks like CLT to guide intervention design, ensuring treatments address both immediate physical needs (low construal) and long-term adaptation to chronic symptoms (high construal).

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AUTHOR CONTRIBUTIONS STATEMENT

This journal uses the Contributor Roles Taxonomy (CRediT) to recognize individual author contributions, reduce authorship disputes, and facilitate collaboration.

Name of Author	C	M	So	Va	Fo	I	R	D	O	E	Vi	Su	P	Fu
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C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
Va : **Va**lidation
Fo : **Fo**rmal analysis
I : **I**nvestigation
R : **R**esources
D : **D**ata Curation
O : Writing - **O**riginal Draft
E : Writing - Review & **E**diting
Vi : **Vi**sualization
Su : **Su**pervision
P : **P**roject administration
Fu : **Fu**nding acquisition

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The authors state no conflict of interest.

DATA AVAILABILITY

The data that support the findings of this study are openly available in most open-access repositories.

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APPENDIX

Table 2. Data extracted from the review corpus

S/ No	Author(s)	Study design/ setting/population	Key findings	Research gaps	Long-term symptoms	Risk factors	Outcomes
1	Short-, mid-, and long-term complications after MIS-C over 24 months [29]	Prospective cohort; 24-month follow-up after MIS-C Population: MIS-C children over 2 years	Short-, mid-, and long-term complications mapped; most recover, subset with cardiac/neuropsychic residuals	Single centre; modest sample size	Fatigue, exercise intolerance, and attention/ mood issues in some	Acute severity indicators (ICU, cardiac involvement)	Generally favourable with ongoing monitoring needs
2	Long COVID in children: Observations from a designated clinic [30]	Clinic-based observational cohort; designated long COVID clinic. Population: Children with suspected long COVID	Common symptoms beyond 12 weeks include fatigue, headache, cognitive and sleep problems	Referral/selection bias; no controls	Fatigue, headache, cognitive impairment, and sleep disturbance	Older age: females sex reported more symptoms	Gradual improvement; need for multidisciplinary clinics
3	Persistent symptoms in children/young people: Systematic review and meta-analysis [31]	Systematic review & meta-analysis of controlled studies Population: Children/YP with prior COVID vs controls	Elevated risk of some persistent symptoms vs controls, but absolute risks are low	Heterogeneity; residual confounding	Fatigue, mood/sleep, cognitive complaints	Older age; hospitalization	Emphasizes the need for well-controlled longitudinal studies
4	Long COVID symptoms in SARS-CoV-2–positive children (Denmark) [32]	Nationwide Danish cohort Population: SARS-CoV-2–positive children vs controls	Symptom burden is modest and declines with time; differences vs controls are small but present	Parent-reported outcomes; misclassification possible	Fatigue, mood/sleep, concentration	Adolescents > younger children	Most return to baseline within months
5	Long-COVID symptoms and duration in Danish children [33]	Nationwide Danish cohort Population: SARS-CoV-2-positive children; registry-based	Long-COVID symptoms and duration are generally low; most resolve within months	Symptom capture via registries; control matching nuances	Fatigue, mood/sleep, and anosmia are rare in children	Adolescents slightly higher risk than younger children	High recovery rates; short duration for most
6	Long-term health outcome and quality of life in children with MIS-C [34]	Prospective cohort; multicenter Italy Population: Children with prior MIS-C	QoL improved over time; minority with persistent symptoms and reduced QoL vs norms	Parent-reported measures; no non-COVID controls in some analyses	Fatigue, mood/sleep disturbances; occasional cardiac monitoring needs	Severe initial MIS-C associated with persistent issues	Gradual recovery with residual impacts in a subset
7	Post-COVID-19 condition at 6 and 12 months after infection in paediatric Eds [35]	Prospective cohort; ED-based follow-up at 6 & 12 months Population: Pediatric ED patients with SARS-CoV-2	Post-COVID-19 condition prevalence and predictors at 6/12 months	ED sample; attrition	Fatigue, headache, mood/sleep; functional impacts	Adolescence; severe acute symptoms	Most improve by 12 months; subset remains symptomatic
8	Long/post-COVID in children and adolescents (German claims-data cohort). Monatsschrift Kinderheilkunde, 172, 11491161[36].	Claims-data cohort (Germany) Population: Children/adolescents with coded post/long-COVID	Incidence and healthcare utilization patterns identified	Coding accuracy; limited symptom granularity	Recorded fatigue, respiratory, and neurocognitive	Age/adolescence; comorbidity patterns	Healthcare use elevated vs comparators
9	Long COVID in pediatric age: Observational multicenter study [37]	Observational multicenter study (Italy) Population: Pediatric long COVID clinic attendees	Common symptoms: fatigue, headache, sleep and concentration issues; impact on daily functioning	Referral bias; lack of controls	Fatigue, headache, sleep disturbance, cognitive issues	Adolescents and females reported more symptoms in some centres	Most improve with time; tailored rehabilitation is needed

Table 2. Data extract from the review corpus (continued)

S/ No	Author(s)	Study design/ setting/population	Key findings	Research gaps	Long-term symptoms	Risk factors	Outcomes
10	Long COVID in children [38]	Clinical review/perspective Population: Pediatric primary care context	Summarizes presentation and management considerations for pediatric long COVID	Calls for standardized definitions and longitudinal data	Fatigue, headache, sleep, and mood changes	Unclear; need better phenotyping	Variable: emphasizes supportive care and follow-up
11	Characterizing prolonged symptoms in early childhood after SARS-CoV-2 [39]	Prospective cohort in early childhood Population: Young children with post-acute sequelae	Characterizes prolonged symptom patterns in early childhood	Early childhood-specific measures are limited	Sleep, feeding/behavioural issues, respiratory	Possibly older toddlers vs infants; needs confirmation	Symptom trajectories map to targeted follow-up
12	Long COVID in children and adolescents: Prevalence, manifestations, risk factors [40]	Review Population: Children/adolescents	Summarizes prevalence, manifestations, and risk factors across East Asian and global studies	Heterogeneous definitions; need standardized tools	Fatigue, respiratory, neurocognitive, mood/sleep	Adolescents, female sex, severity	Calls for harmonized follow-up protocols
13	Long-COVID in children and their parents: A prospective cohort [41]	Prospective cohort; single pediatric hospital in Tokyo; 1/3/6-month follow-up Population: 108 children with COVID-19; 78 infected parents	Long-COVID prevalence in children declined 45%â†'38%â†'23% at 1/3/6 months; parents ~41% at 6 months; sleep disturbance and cough reduced QOL	Single centre; no control group; limited variant data; self-reported symptoms; underpowered vaccine analyses	Fatigue, cough, sleep disturbance; rare GI, headache, sensory loss at 6 months	Age â† associated with ME/CFS-type symptoms; no clear effect of sex, acute severity, vaccination	Most improved by 6 months; ~23% children still symptomatic; QOL impact from sleep issues/cough
14	Long-term outcomes and immune profiling in children with MIS-C [42]	Prospective cohort with immune profiling Population: Children with MIS-C; ~12-month follow-up	Most recover; 10â€- 15% show persistent cardiac/immune dysregulation	Small sample; single country; limited long-term mechanistic insight	Fatigue, reduced exercise tolerance; occasional arrhythmia	Severe acute MIS-C with delayed cytokine normalization	Generally favourable; subset requires cardiology/immune follow-up
15	Two-year functional and neuropsychic outcomes after pediatric COVID/MIS-C critical illness [43]	Prospective cohort; critical illness survivors (COVID/MIS-C) Population: PICU survivors with COVID-19/MIS-C	Two-year functional and neuropsychic outcomes show residual deficits in the subset	Centre variability; survivorship bias	Cognitive, fatigue, and mental health issues	Severity of illness; organ support	Rehabilitation needs persist for some
16	Multisystem inflammatory syndrome in children: Review [44]	Narrative review of MIS-C Population: Children with MIS-C (review)	Summarizes pathophysiology, management, and outcomes; most recover with timely treatment	Mechanisms and long-term neuropsychic outcomes	Cardiac follow-up needs: fatigue	Severe inflammation; delayed treatment	Generally favourable with appropriate care
17	Long-COVID in children and adolescents: Systematic review & meta-analysis [45]	Systematic review & meta-analysis Population: Children/adolescents with long-COVID across studies	Pooled prevalence estimates for common symptoms; heterogeneity is high	Study quality variability; definitions/ timeframes inconsistent	Fatigue, mood changes, sleep disturbance, headache, respiratory symptoms	Older age and hospitalization are associated in some analyses	Need for standardized follow-up cohorts
18	Disparities in MIS-C and longer-term outcomes [46]	Editorial/Commentary with data context Population: Contextualizes disparities in MIS-C	Highlights racial/ethnic and socioeconomic disparities in MIS-C incidence and outcomes	Observational disparities data need causal analyses	Not primary data	Social determinants: access to care	Policy and equity implications emphasized

Table 2. Data extract from the review corpus (continued)

S/ No	Author(s)	Study design/ setting/population	Key findings	Research gaps	Long-term symptoms	Risk factors	Outcomes
19	Clinical characteristics and outcomes in MIS-C [47]	Retrospective multicenter cohort Population: Children with MIS-C	Clinical characteristics and outcomes; identified predictors of severe course	Retrospective design; regional scope	Limited long-term data; short- to mid-term outcomes	Inflammatory markers; organ involvement at presentation	Overall good recovery; subset with persistent issues
20	Quality of life and mental health in children with long COVID [48]	Cross-sectional/ observational Population: Children with long COVID	Quality of life & mental health burdens documented	Cross-sectional design; selection bias	Fatigue, concentration problems, mood/sleep	Older age; female sex; comorbidities	QOL reductions across domains
21	Data Resource Profile: The CLoCk study [49]	Data Resource Profile of the CloCk study Population: Design and cohort features of UK CloCk	Describes sampling, measures, and linkage for adolescent long COVID research	Not outcome-focused; resource description	N/A (resource profile)	N/A	N/A
22	Medium-term health and QoL after MIS-C vs JIA comparators [50]	Comparative cohort: MIS-C vs juvenile idiopathic arthritis (JIA) Population: Children with prior MIS-C and JIA comparators	Medium-term QoL and health outcomes are worse in MIS-C vs JIA in certain domains	Sample size; center effects	Fatigue, reduced physical functioning	Initial MIS-C severity	Residual deficits vs disease controls; targeted rehab
23	Long COVID associated with SARS-CoV-2 reinfection among children and adolescents in the Omicron era [51]	Retrospective multi-center HER cohort; Omicron era Population: Children/adolescents with documented SARS-CoV-2 infections in US health systems	Reinfection is associated with a higher risk of long-COVID features vs primary infection	HER coding/ underreporting; residual confounding; limited phenotyping	Fatigue, respiratory, and neurologic complaints are more frequent after reinfection	Reinfection; adolescent age > younger children	Reinfections extend risk window; prevention/vaccination emphasized
24	Neurological and psychological sequelae after MIS-C [37].	Prospective cohort Population: Children post-MIS-C	Neurologic and psychological sequelae measurable at follow-up vs controls	Sample attrition; measurement heterogeneity	Attention, mood, sleep issues	Acute severity indicators	Improvement over time, residual deficits in a subset
25	Neurologic and psychological outcomes 2 years after MIS-C hospitalization [40].	Multicenter prospective follow-up; 2 years post-MIS-C hospitalization Population: US cohort: MIS-C patients with age-matched controls	Physical recovery generally good; ~20% showed persistent neuropsychological issues (attention/mood) at 2 years	Limited controls; potential recall and selection bias	Cognitive/attention difficulties, anxiety/depression, sleep problems	Greater acute MIS-C severity linked to worse neuropsychic outcomes	Need for ongoing mental health and educational supports; most physical metrics normalized
26	Long COVID in children and adolescents: A critical review [52].	Critical review Population: Children/adolescents (review of evidence)	Synthesizes prevalence, symptom clusters, and methodological limitations	Calls for controlled cohorts, harmonized measures	Fatigue, cognitive/attention, sleep, and respiratory	Severity; psychosocial context; pre-existing conditions	Evidence evolving; need longitudinal registries
27	Long COVID in children and adolescents [4].	Observational study (CLoCk study overview) Population: Children and adolescents in the UK	Long COVID symptoms present but at lower prevalence than early reports; importance of controls	Symptom self-report; varying follow-up intervals	Fatigue, headache, mood/sleep	Older age; female sex in some analyses	Most improve with time; a minority persists
28	Six-month outcomes in individuals <21 y with MIS-C [53].	Prospective cohort; 6-month outcomes Population: Individuals <21 years with MIS-C	The majority with cardiac normalization; a subset with lingering symptoms and functional impacts at 6 months	Abstract-level access; potential loss to follow-up bias	Fatigue, exercise intolerance; occasional neurocognitive/psych complaints	Greater acute severity; ICU support requirements	Mostly favourable cardiac recovery: targeted follow-up indicated

Table 2. Data extract from the review corpus (continued)

S/ No	Author(s)	Study design/ setting/population	Key findings	Research gaps	Long-term symptoms	Risk factors	Outcomes
29	Prevalence & risk factors for pediatric long COVID: Meta-analysis [54].	Meta-analysis Population: Pediatric long COVID studies	Estimated prevalence and risk factors; heterogeneity is high	Publication bias; inconsistent definitions	Fatigue, mood, sleep, and respiratory	Adolescence, hospitalization, and female sex in some analyses	Need standardized criteria and follow-up
30	How common is long COVID in children and adolescents? [55]	Narrative review Population: Children/adolescents globally (synthesis)	Long COVID exists but appears less common in children than adults; higher in hospitalized groups	Heterogeneity, small cohorts; recall bias in early studies	Fatigue, sleep disturbance, headache	Severe acute disease; older pediatric age in some cohorts	Most recover within months; a minority with persistent issues

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