



Eligibility criteria used to investigate long COVID in children and adolescents: a systematic review

Criterios de elegibilidad utilizados para investigar COVID persistente en niños y adolescentes: una revisión sistemática

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Abstract

Introduction: Long COVID is a heterogeneous chronic condition, which can have a substantial impact on daily life of children and adolescents. However, considerable variability in case definitions across studies limits the comparability and interpretation of the available evidence.

Objective: To identify and synthesize the eligibility criteria used in studies involving children and adolescents with long COVID and assess their consistency with the World Health Organization (WHO) clinical case definition.

Methodology: A systematic methodological review of systematic reviews was conducted by searching electronic databases from inception to May 2025. Primary studies involving individuals aged 0–18 years were included. Overlap among reviews was quantified using the Corrected Covered Area (CCA).

Results: Fifteen systematic reviews, comprising 370 primary studies, were identified. After removing overlapping and ineligible records, 86 primary studies were analyzed (CCA = 11%). Only 3% fully adhered to the WHO definition, 10% were partially consistent, and 87% were inconsistent. Although 94% required confirmed or probable infection, only 20% required symptoms to persist for at least 2 months, and just 13% specified symptom persistence for at least 3 months after the onset of COVID-19.

Conclusion: Studies investigating pediatric long COVID use highly heterogeneous eligibility criteria and demonstrate poor adherence to the WHO definition. This variability may compromise case identification, comparability across studies, and the reliability of epidemiological estimates. Greater methodological standardization of eligibility criteria is needed to improve the quality and support evidence-based clinical practice, health policy, and healthcare planning for children and adolescents with long COVID.

Keywords

Long COVID-19; pediatrics; post-COVID-19; SARS-CoV2.

Resumen

Introducción: El COVID prolongado es una condición pediátrica heterogénea, pero la variabilidad en sus definiciones de caso limita la comparabilidad de la evidencia disponible.

Objetivo: Identificar los criterios de elegibilidad en estudios sobre COVID prolongado en niños y adolescentes, evaluando su concordancia con la definición clínica de la OMS.

Metodología: Revisión metodológica sistemática de revisiones sistemáticas (búsqueda hasta mayo de 2025) que incluyó estudios primarios (0-18 años). La superposición se cuantificó mediante el *Corrected Covered Area* (CCA).

Resultados: De 15 revisiones (370 estudios primarios), se analizaron 86 estudios únicos (CCA = 11%). Solo el 3% cumplió plenamente la definición de la OMS, el 10% mostró concordancia parcial y el 87% fue inconsistente. Aunque el 94% exigió infección por SARS-CoV-2 confirmada o probable, solo el 20% requirió síntomas persistentes de al menos 2 meses, y únicamente el 13% especificó una duración mínima de 3 meses desde el inicio de la enfermedad.

Conclusión: Los estudios pediátricos emplean criterios altamente heterogéneos y muestran baja adherencia a las directrices de la OMS. Esta variabilidad compromete la comparabilidad y la fiabilidad epidemiológica, lo que subraya la necesidad de estandarizar los criterios de elegibilidad para guiar las políticas de salud, la planificación clínica y la atención sanitaria en esta población.

Palabras clave

COVID-19 prolongado; pediatría; post-COVID-19; SARS-CoV-2.

Introduction

Long COVID, also denominated to as post-COVID-19 condition, has emerged as a significant public health concern following the SARS-CoV-2 pandemic (Greenhalgh et al., 2024). The condition has been described using multiple terms, including long-duration COVID, chronic COVID, post-COVID-19 syndrome, and post-acute sequelae of SARS-CoV-2 infection (Geng et al., 2024; Seo et al., 2024). The National Academies of Sciences, Engineering, and Medicine (NASEM) characterize long COVID “an infection-associated chronic condition that occurs after SARS-CoV-2 infection and is present for at least 3 months as a continuous, relapsing and remitting, or progressive disease state that affects one or more organ systems” (Ely et al., 2024). Similarly, the World Health Organization (WHO) has proposed a clinical case definition that emphasizes symptom persistence and functional impact but allows substantial flexibility in symptom presentation (World Health Organization, 2022). As a consequence, long COVID is associated with a very broad range of symptoms and signs affecting multiple organ systems, including respiratory, cardiovascular, gastrointestinal, neurological, and endocrine systems (Seo et al., 2024; Soriano et al., 2022; Naldabandian et al., 2021). While this inclusive approach facilitates clinical recognition, it also poses challenges for consistent case identification in epidemiological research (Hua et al., 2024; Høeg et al., 2024).

Recognizing the unique challenges of diagnosing post-COVID-19 condition in pediatric populations, the WHO published a separate clinical case definition for children and adolescents in 2023 (World Health Organization, 2023). According to the WHO, “Post COVID-19 condition in children and adolescents occurs in individuals with a history of confirmed or probable SARS-CoV-2 infection, when experiencing symptoms lasting at least 2 months which initially occurred within 3 months of acute COVID-19. Current evidence suggests that symptoms more frequently reported in children and adolescents with post-COVID-19 condition compared with controls are fatigue, altered smell (anosmia) and anxiety. Other symptoms have also been reported. Symptoms generally have an impact on everyday functioning such as changes in eating habits, physical activity, behaviour, academic performance, social functions (interactions with friends, peers, family) and developmental milestones. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. They may also fluctuate or relapse over time. Workup may reveal additional diagnoses, but this does not exclude the diagnosis of post COVID-19 condition” (World Health Organization, 2023).

Despite this effort toward standardization, reported prevalence estimates of post-COVID-19 conditions in children and adolescents remain highly variable, ranging from as low as 1.6% to as high as 70% across studies (Chiappini et al., 2023). In larger and more methodologically robust studies, prevalence estimates typically range between 4% and 62%, with most reports converging around 10%–20% within the first six months following infection (Zimmermann et al., 2021; Rao et al., 2024). Gross et al. (2025) recently reported that long COVID affects 10% to 20% of children with a history of COVID-19. The authors noted that with almost 6 million US children potentially affected, this prevalence exceeds that of asthma, the most common chronic health problem in children. Such wide variability suggests that methodological factors, rather than true differences in disease occurrence alone, substantially influence reported estimates (Zimmermann et al., 2021).

Compared with adult populations, where clearer patterns of risk factors, symptom clusters, and disease trajectories have been described (Vivaldi et al. 2023; Hu et al., 2025), the epidemiology of long COVID in children and adolescents remains poorly delineated (Ha, Kim and Ham, 2023). This uncertainty may be partly attributable to inconsistencies in study eligibility criteria, including variability in infection confirmation, symptom duration thresholds, symptom types required for inclusion, and exclusion of pre-existing conditions (Chiappini et al., 2023; Rao et al., 2024; Hahn et al., 2023). Inconsistent eligibility definitions can introduce selection bias, misclassification, and limited comparability across studies, thereby undermining the validity of pooled prevalence estimates and hindering meaningful synthesis of evidence (Benz et al., 2025; Zetterstrom & Waernbaum, 2022). Moreover, poorly specified or heterogeneous eligibility criteria may compromise the external validity of studies, thereby limiting the applicability of their findings to clinical practice, research, and health policy.

The long-term physical, social, educational, and psychological consequences of COVID-19 have the potential to significantly affect the transition of children and adolescents into adulthood (Coughtrey et al., 2025). Although many characteristics are shared across age groups, long COVID may present differently



depending on age. School-aged children are more likely to experience symptoms such as difficulty concentrating, sleep disturbances, back or neck pain, headache, abdominal pain, and vomiting. In contrast, adolescents are more likely to present with olfactory and/or gustatory dysfunction, pain-related symptoms, fatigue, memory impairment, and dizziness. In some children, symptoms may persist without resolution, whereas others may experience a fluctuating clinical course characterized by alternating periods of improvement and exacerbation. Furthermore, long COVID may affect any child, even those who experienced a mild or asymptomatic acute SARS-CoV-2 infection (Gross et al., 2025).

Regarding physical and functional outcomes, children and adolescents with post-COVID-19 condition may exhibit reduced exercise capacity, decreased inspiratory and peripheral muscle strength, lower levels of physical activity, and greater fatigue compared with healthy individuals. Given these impairments, an individualized, multidisciplinary approach that combines aerobic and resistance training, inspiratory muscle training, along with education and strategies for symptom management, should be considered part of routine care (Goicoechea-Calvo et al., 2025). Consequently, physical exercise is a key component of long COVID management, offering the potential for significant improvements in pulmonary function, physical activity, and emotional well-being (Du et al., 2025).

However, the effectiveness and generalizability of physical activity and rehabilitation interventions depend on the consistent identification of eligible patients across studies. Without standardized eligibility criteria, it becomes difficult to compare outcomes across trials or translate findings into evidence-based clinical guidelines, directly affecting the design of future studies evaluating physical activity and structured exercise programs as therapeutic strategies in pediatric long COVID. Given these concerns, a systematic examination of the eligibility criteria used in studies investigating long COVID in children and adolescents is warranted (Hua et al., 2024; Høeg et al., 2024), as a clearer understanding of how pediatric cases are defined and selected is essential for interpreting existing evidence, informing healthcare planning and targeted interventions—including physical activity and exercise-based strategies (McDowell et al., 2025)—and improving the design of future research. Therefore, this systematic review aimed to identify and synthesize the eligibility criteria used in studies involving children and adolescents with long COVID, assess their consistency with the WHO clinical case definition, and evaluate the extent of heterogeneity across studies, with the goal of informing greater standardization and enhancing comparability, reproducibility, and epidemiologic inference in this field.

Method

Study design

This study was a systematic methodological review conducted to examine the eligibility criteria used in primary studies investigating long Covid in children and adolescents. We used systematic reviews as a source to identify relevant primary studies, the unit of analysis for this review was individual primary studies. The review was conducted in accordance with Cochrane methodological guidance for systematic reviews (Cochrane, 2024) and is reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (Page et al., 2022). The study protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD 420251062554).

Eligibility criteria

Primary studies were eligible for inclusion if they investigated long COVID or post-COVID-19 condition in children and adolescents aged 0 to 18 years. This age range was selected in accordance with the WHO definitions of childhood (birth to 12 years) and adolescence (12 to 18 years) (World Health Organization, n.d.). No restrictions were applied regarding study design, setting, year of publication, or language.

Systematic reviews, as sources for identifying primary studies, were eligible when to explicitly address long Covid or post-COVID-19 condition in pediatric and adolescent populations. Narrative reviews, scoping reviews, editorials, commentaries, and opinion papers were excluded. Systematic reviews and primary studies that included mixed-age populations were retained only if pediatric-specific eligibility criteria or subgroup data were explicitly reported; otherwise, they were excluded from the main analysis but documented.



Search Strategy

A systematic literature search was conducted in MEDLINE (via PubMed), EMBASE (via Elsevier), the Cochrane Library, and Web of Science from database inception through May 2025. Search strategies were developed for each database using a combination of controlled vocabulary terms and free-text keywords related to post-COVID-19 condition and pediatric populations. Searches were restricted to the title and abstract fields. Reference lists of eligible systematic reviews were manually screened, and citation tracking was performed using Google Scholar to identify additional relevant systematic reviews.

The core search concepts included terms related to “post-acute COVID-19 syndrome,” “long-Covid,” “child,” “adolescent,” and “pediatrics.” The search strategies are available in Supplementary Material 1.

Study selection

Selection of systematic reviews was conducted independently by two reviewers using a two-stage process. First, duplicate records were removed. Titles and abstracts were screened for relevance, followed by full-text assessment of potentially eligible articles. Disagreements were resolved through discussion, with adjudication by a third reviewer when necessary. All records were managed and screened using Covidence systematic review software. For the selection of primary studies, all primary studies included in the eligible systematic reviews were retrieved. Full-text assessment of primary studies was conducted independently by two reviewers to confirm eligibility. Disagreements were resolved by consensus through discussion.

Data extraction

Data extraction was performed independently by two reviewers using standardized extraction forms, with discrepancies resolved by consensus. Data extraction occurred in two sequential stages:

Stage 1 – Identification of Primary Studies: From eligible systematic reviews, we extracted review objectives, inclusion criteria, and references to primary studies.

Stage 2 – Primary Studies: From each eligible primary study, data were extracted on study objectives, design, population characteristics, and, critically, the eligibility criteria verbatim used to define long COVID.

Methodological quality assessment

The methodological quality of included systematic reviews was assessed using AMSTAR 2.0, a validated tool comprising 16 items addressing critical and non-critical domains of systematic review quality (Shea et al., 2007). Each domain was rated as “Yes,” “No,” or “Partial Yes” according to predefined criteria. Overall confidence in the results of each review was classified as high (no or one non-critical weakness), moderate (more than one non-critical weakness), low (one critical weakness), or critically low (more than one critical weakness) based on the presence of critical and non-critical weaknesses, following established guidance (Shea et al., 2017). Quality assessments were conducted independently by two reviewers.

Data analysis

Overlap of primary studies across systematic reviews was quantified using the corrected covered area (CCA) method (Pieper et al., 2014). Overlap was classified as low (0–5%), moderate (6–10%), high (11–15%), or very high (>15%) (Pieper et al., 2014).

Eligibility criteria reported in primary studies were evaluated against the 2023 WHO case definition for post-COVID-19 condition in children and adolescents, which requires: (i) a history of confirmed or probable SARS-CoV-2 infection; (ii) symptom persistence for at least two months; and (iii) symptom onset at least three months after acute infection (World Health Organization, 2023). Primary studies were classified as consistent if all WHO criteria were applied, partially consistent if at least two criteria were applied, and inconsistent if one or none of the criteria was applied.

Eligibility criteria were categorized independently by two reviewers using conventional content analysis (Hsieh and Shannon, 2005). Conceptually similar criteria were grouped into broader thematic categories through iterative comparison and discussion until consensus was reached. The resulting categories were summarized using descriptive statistics, including frequencies and proportions. Inclusion



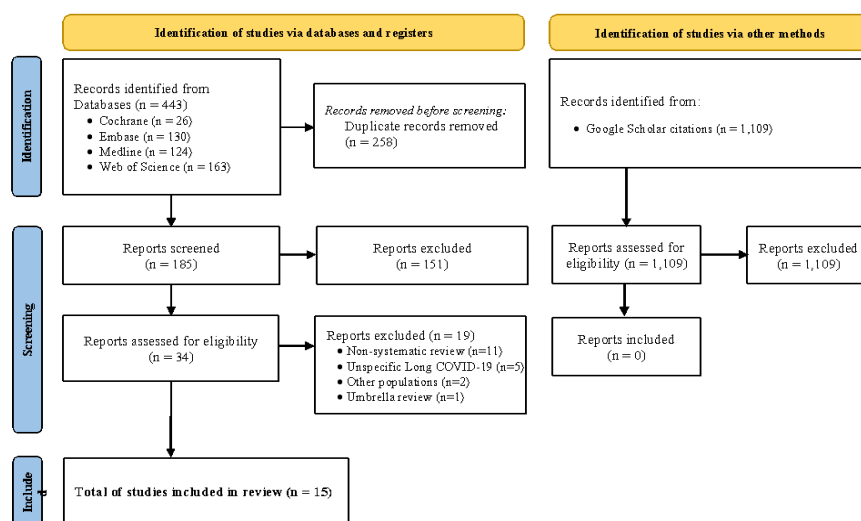
and exclusion criteria were analyzed separately. Additionally, the number of eligibility domains applied within each primary study was recorded to characterize the complexity and restrictiveness of case definitions across studies.

Results

Review selection

The literature search identified 443 records. After title and abstract screening, 34 full-text articles were assessed for eligibility. Following full-text evaluation, 15 systematic reviews met the inclusion criteria and were included in the present study (Figure 1). A list of excluded reviews and reasons for exclusion are available in Supplementary Material 2.

Figure 1. Flow diagram for selection of systematic reviews.



Source: authors

Methodological quality of studies

Of the 15 included systematic reviews, 10 were rated as having critically low methodological quality (Ahmadi et al., 2024; Behnood et al., 2022; Behnood et al., 2023; Silva et al., 2024; Mat Hassan et al., 2023; Jiang et al., 2023; Lopez-Leon et al., 2022; Pellegrino et al., 2022; Putri et al., 2025; Martino et al., 2023), four were classified as low quality (Hirt et al., 2023; Rahmati et al., 2023; Rayner et al., 2024; Zheng et al., 2023), and one was rated as high methodological quality (Franco et al., 2022). Detailed AMSTAR 2.0 assessments and domain-level ratings are available in Supplementary Material 3.

Characteristics of included reviews

The primary focus of the included reviews varied. Most addressed the incidence and prevalence of persistent symptoms following post-COVID-19 condition in children and adolescents (Behnood et al., 2022; Behnood et al., 2023; Silva et al., 2024; Lopez-Leon et al., 2022; Pellegrino et al., 2022; Putri et al., 2025; Martino et al., 2023; Zheng et al., 2023), as well as the presence, pattern, and duration of symptoms (Behnood et al., 2022; Behnood et al., 2023; Silva et al., 2024; Lopez-Leon et al., 2022; Pellegrino et al., 2022; Martino et al., 2023). Other reviews focused on long-term clinical characteristics (Jiang et al., 2023), cardiovascular complications (Ahmadi et al., 2024), risk of new-onset type 1 diabetes (Rahmati et al., 2023), risk factors for long Covid (Rayner et al., 2024; Zheng et al., 2023), post-acute sequelae of SARS-CoV-2 infection (Hirt et al., 2023), mental health outcomes (Mat Hassan et al., 2023), and broader issues related to well-being and recovery (Franco et al., 2022). Collectively, the 15 reviews included a total of 370 primary studies. Characteristics of the reviews included are available in Supplementary Material 4.



Primary studies identified through reviews

Across the 15 systematic reviews, an overlap rate of 11% was identified using the corrected covered area (CCA) method, indicating a high degree of overlap among primary studies.

After removal of overlapping records, 148 unique primary studies remained. During data extraction, 60 studies were excluded because they did not specifically address pediatric populations or long-Covid. Of the remaining studies, 86 primary studies were included in the final analysis of eligibility criteria (Supplementary Material 5). Two additional studies could not be analyzed due to unavailable eligibility information, despite repeated attempts to contact the authors (Heching et al., 2022; Messiah et al., 2022). Reasons for exclusion of primary study included inclusion of adult populations, exclusion of children or adolescents, focus on other conditions, or ineligible study designs (e.g., conference abstracts, letters). Excluded studies and reasons are available in Supplementary Material 6.

Consistency with WHO case definition

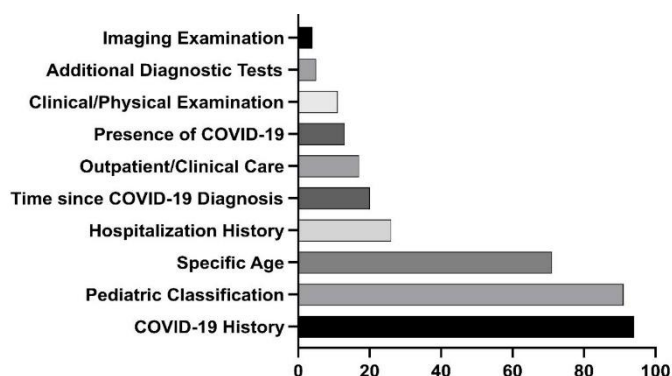
When eligibility criteria from the 86 included primary studies were compared with the 2023 WHO case definition for post-COVID-19 condition in children and adolescents, only 3% of studies were classified as consistent, 10% as partially consistent, and 87% as inconsistent with the WHO criteria. Specifically, a history of confirmed or probable SARS-CoV-2 infection was reported in 94% of studies ($n = 80$). In contrast, symptom duration of at least two months was required in only 20% of studies ($n = 16$), and symptom persistence for at least three months after acute infection was reported in 13% of studies ($n = 10$).

Categories of eligibility criteria

Across the 86 included primary studies, 10 categories of inclusion criteria and 16 categories of exclusion criteria were identified.

The most frequently reported inclusion criteria were the history of COVID-19 diagnosis (94%), classification as a pediatric population (91%), and age specification (71%). Less frequently reported criteria included history of hospitalization (26%), time since COVID-19 diagnosis (20%), history of outpatient or clinical care (17%), presence of long Covid without further specification (13%), clinical or physical examinations (11%), additional diagnostic tests (5%), and imaging examinations (4%) (Figure 2). The distribution of inclusion criteria is available in Supplementary Material 7.

Figure 2. Inclusion criteria categories reported in primary studies (data in percentage).

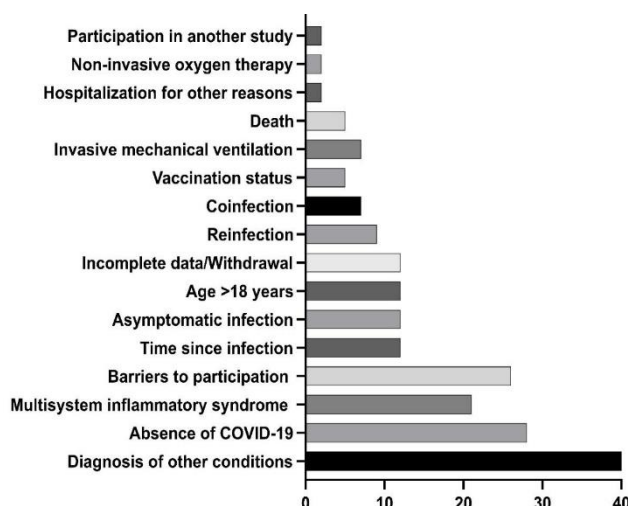


Source: authors

Exclusion criteria were reported in 42 of the 86 studies. The most common exclusion categories were diagnosis of other conditions (33%), absence of confirmed COVID-19 diagnosis (28%), diagnosis of multisystem inflammatory syndrome in children (MIS-C) (21%), and barriers to participation (19%) (Figure 3). Other exclusion criteria included time since infection, asymptomatic infection, age >18 years, incomplete data or withdrawal, reinfection, coinfection, vaccination status, need for invasive mechanical ventilation, death, hospitalization for other reasons, use of non-invasive oxygen therapy, and participation in another study (Figure 3). Frequencies and distributions are available in Supplementary Material 8.



Figure 3. Exclusion criteria categories reported in primary studies (data in percentage).



Source: authors

Breadth of eligibility criteria across studies

No primary study incorporated all 10 identified inclusion criteria categories. One study reported 9 of 10 categories (Ashkenazi-Hoffnung et al., 2021), two studies reported 7 categories (Leftin Dobkin et al., 2021; Palacios et al., 2022), two reported 6 categories (Buonsenso et al., 2022; Di Gennaro et al., 2022), and six reported 5 categories (Buonsenso et al., 2022; Gonzalez-Aumatell et al., 2022; Horikoshi et al., 2023; Knoke et al., 2022; Morand et al., 2022; Tian et al., 2022). Twenty-one studies included 4 of the 10 categories (Adler et al., 2022; Ahn et al., 2023; Asadi-Pooya et al., 2021; Asadi-Pooya et al., 2022; Bloise et al., 2022; Bossley et al., 2022; Bottino et al., 2021; Buonsenso et al., 2021; Cocciolillo et al., 2022; Erol et al., 2022; Matteudi T et al., 2021; Morand et al., 2021; Morello et al., 2023; Roge et al., 2021; Rusetsky et al., 2021; Samuel et al., 2020; Say et al., 2021; Seery et al., 2023; Tarantino et al., 2022; Vizzari et al., 2022; Werner et al., 2022). The remaining studies included three or fewer inclusion-criteria categories (Supplementary Material 7).

Regarding exclusion criteria, only 42 studies reported at least one. No study incorporated all 16 identified exclusion-criteria categories. The maximum reported was four categories, identified in two studies (Maddux et al., 2022; Roge et al., 2021). Ten studies included three categories (Buonsenso et al., 2022; Buonsenso et al., 2021; Bottino et al., 2021; Di Gennaro et al., 2022; Dumont et al., 2022; Fink et al., 2021; Morello et al., 2023; Powell et al., 2022; Smane et al., 2021; Stephenson et al., 2022), nine studies included two categories (Balderas et al., 2023; Baptista de Lima et al., 2023; Buonsenso et al., 2021; Castro et al., 2021; La Regina et al., 2022; Matteudi et al., 2021; Pinto Pereira et al., 2023; Rao et al., 2022; Seery et al., 2023), and 21 studies reported only a single exclusion criterion (Gonzalez-Aumatell et al., 2022; Knoke et al., 2022; Morand et al., 2022; Akçay et al., 2022; Bergia et al., 2021; Bergia et al., 2022; Blankenburg et al., 2022; Brackel et al., 2021; Clavenna et al., 2022; Cocciolillo et al., 2022; Demirbuğa et al., 2023; Guido et al., 2022; Miller et al., 2022; Nugawela et al., 2022; Pinto Pereira et al., 2023; Radtke et al., 2021; Rusetsky et al., 2021; Samuel et al., 2020; Sterky et al., 2021; Tarantino et al., 2022; Werner et al., 2022).

Discussion

In a recent review, Rothensteiner et al. (2024) reported that the prevalence of long Covid appeared to differ across different pediatric age groups, with teenagers being more commonly affected than younger children. More recently, Reeder et al. (2026), using data from the Researching COVID to Enhance Recovery (RECOVER) pediatric observational cohort study, reported that long COVID in children and adolescents was associated with poorer functional outcomes, including declining academic performance, reduced attention, fewer peer interactions, and an increased need for educational services. In this context, the present systematic methodological review identified low adherence to the WHO clinical definition



among studies investigating long Covid in children and adolescents. Only two primary studies (Ahn et al., 2023; Ashkenazi-Hoffnung et al., 2021) fully applied all three WHO-defined criteria, whereas nearly 90% incorporated only one criterion or none. These findings demonstrated substantial inconsistency in the operationalization of long COVID in children and adolescents across studies and highlight the lack of standardized approaches to clinical case identification in this population. They further underscore the need for more standardized definitions, outcome measures, and adequate follow-up duration to inform recommendations for improving reporting approaches in future pandemic-related epidemiological research. Such improvements would, in turn, accelerate the reliable translation of findings into evidence-based clinical practices and public health policies (Appel et al., 2026).

Analysis of eligibility criteria revealed substantial heterogeneity in the selection of children and adolescents with long Covid. Some criteria appeared redundant or unnecessary when considered alongside the WHO clinical definition, whereas others reflected attempts to improve case identification through additional diagnostic procedures. Collectively, the use of incomplete WHO criteria together with heterogeneous supplementary criteria suggests imprecision in diagnostic reliability and limited comparability across studies. Importantly, this methodological variability is likely to introduce misclassification bias by including children and adolescents who do not meet accepted diagnostic criteria or excluding those who do, thereby affecting the validity of prevalence estimates. Inconsistent eligibility criteria may also lead to selection bias, as differences in participant inclusion can result in study populations with distinct ethnicity and clinical characteristics despite being described as having pediatric long Covid. Consequently, methodological heterogeneity compromises the comparability of observational studies, as apparently similar populations may be classified differently depending on the eligibility criteria adopted. Differences in prevalence estimates may therefore reflect methodological inconsistencies rather than true epidemiological variation, limiting comparisons across countries and healthcare systems and reducing the certainty of evidence synthesis (Appel et al., 2026).

The divergence between the WHO clinical case definition and the eligibility criteria used in primary studies does not invalidate the existing evidence but highlights the methodological challenges involved in investigating a heterogeneous and evolving condition in pediatric populations. Although the WHO definition represents an important global reference, its broad clinical applicability provides limited methodological guidance for epidemiological research. Our review demonstrated that criteria related to previous SARS-CoV-2 infection and age were widely adopted, whereas temporal aspects, particularly symptom duration and the interval between acute infection and symptom onset, were frequently overlooked. The inconsistent application of these temporal criteria may increase the risk of misclassification by including individuals with transient post-infectious symptoms who do not meet the criteria for persistent post-COVID-19 condition. Furthermore, differences in how study populations are defined may influence prevalence estimates, hinder comparisons across studies, and limit the interpretation of the true epidemiological burden of the condition in children and adolescents.

These findings are consistent with previous literature, including the review conducted by Zimmermann et al. (2021), which highlighted substantial limitations in how pediatric long Covid populations have been defined. Prior studies frequently relied on self-reported or parent-reported symptoms collected via questionnaires, often without standardized clinical evaluation or objective corroboration. While such approaches may be necessary in large-scale or population-based studies, they further amplify heterogeneity when eligibility criteria are poorly specified, particularly in younger children who may have difficulty reporting subjective symptoms. Despite this variability, several eligibility components emerged as potentially relevant across studies, including prior confirmation of SARS-CoV-2 infection, consideration of the temporal relationship between infection and symptom onset, and attention to age-related and developmental differences.

Limitations and Recommendations

Additional clinical assessments, imaging, or complementary investigations were variably employed, primarily intended to exclude alternative diagnoses rather than to define long Covid. Furthermore, as mentioned above, the inconsistent reporting and application of exclusion criteria may have introduced selection bias and reduced the external validity. Overall, this review highlights a clear gap in methodological guidance for defining eligibility criteria in pediatric long COVID research. Although the WHO clinical case definition provides an essential conceptual framework, greater methodological standardization



is needed to improve diagnostic consistency while maintaining appropriate clinical inclusivity. Standardized eligibility criteria would enhance reproducibility, comparability across studies, and the quality and interpretability of epidemiological evidence. Therefore, recommendations for future long COVID research in children and adolescents should go beyond clinical definitions and provide methodological guidance on participant selection, symptom duration, minimum follow-up periods, confirmation of SARS-CoV-2 infection, and standardized outcome assessment. Such recommendations would facilitate multicenter collaborations, improve evidence synthesis, and provide more accurate insights into the long-term effects of Covid-19 in pediatric population. Future research should also incorporate standardized assessment of physical function and exercise capacity, enabling the development and evaluation of individualized rehabilitation strategies for this population.

Implications

The rapid emergence and global spread of COVID-19 presented unprecedented challenges for researchers, highlighting a lack of methodology preparedness for collecting epidemiological data (Appel et al., 2026). In this sense, our findings highlight the need for better screening and standardized definitions to inform health policy and healthcare planning for affected children and adolescents. A more consistent approach to case identification may facilitate earlier recognition of long COVID, support evidence-based clinical decision-making, and improve long-term management through tailored interventions, including physical activity and rehabilitation programs. Given the growing recognition of the long-term health burden of pediatric long COVID, governments, healthcare systems, and funding bodies should prioritize this condition as a major medical and research focus, expand access to multidisciplinary care, and ensure that children and adolescents are adequately represented in future research and healthcare planning (Buonsenso, 2026).

In this context, rehabilitation programs and guidance regarding physical activity may represent relevant components of care. Evidence from adults with long Covid demonstrated that exercise-based rehabilitation is established as an effective strategy for improving physical fitness outcomes. A recent meta-analysis that included 51 randomized controlled trials showed that exercise training should be prioritized for improving cardiopulmonary function and exercise capacity in long Covid, supported by high-certainty evidence (Tan et al., 2025). Corroborating these findings, another meta-analysis demonstrated that inspiratory muscle training improved cardiorespiratory outcomes, while multicomponent physical training improved muscle strength, physical functioning, and fatigue (Correia et al., 2025).

In pediatric populations, however, evidence remains scarce. In a recent narrative review, Caliman-Sturdza et al. (2026) synthesized available evidence on post-COVID-19 condition in children and adolescents, emphasizing individualized management provided by a multidisciplinary team, with a focus on symptom relief and functional rehabilitation. Therapeutic strategies aim to alleviate symptoms and promote functional recovery through multimodal rehabilitation programs, which typically include graded exercise and cognitive behavioral therapy and have shown promising results in improving fatigue, mental health, and overall quality of life. A recent prospective, single-center randomized clinical trial evaluated individualized online exercise therapy in 14 patients aged 9–17 years with long COVID. After the intervention, the exercise program appears safe, feasible, and potentially beneficial in the multidisciplinary care of pediatric long COVID, particularly regarding physical function and school participation (Goretzki et al., 2026). Although these findings are promising, the small sample size, exploratory single-center design, the absence of cognitive assessments, and the lack of a non-intervention control group limit their generalizability, reinforcing the need for larger, multicenter trials before physical activity recommendations can be incorporated into standardized pediatric guidelines.

Conclusions

This systematic methodological review identified substantial heterogeneity and limited adherence to the WHO case definition among studies investigating long COVID in children and adolescents. Most primary studies diverged from WHO criteria, particularly regarding temporal requirements, limiting comparability across studies and increasing the potential for misclassification and selection bias. These methodological inconsistencies hinder a clear understanding of the epidemiology of pediatric long COVID and underscore the need for standardized eligibility criteria to improve the validity, reproducibility, and



interpretability of future research, thereby supporting evidence-based clinical decision-making, health policy development, and the delivery of care for children and adolescents with long COVID.

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