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# Post-COVID-19 condition in children: a COS is urgently needed



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See **Position Paper** page 715

A rapidly increasing number of studies worldwide is investigating the frequency, characteristics, and risk factors of post-COVID-19 condition (also commonly known as long COVID) in adults<sup>1</sup> and in children and young people.<sup>2</sup> Some studies are also aiming to evaluate underlying mechanisms and treatment interventions in these populations. However, multiple methodological limitations have been highlighted, including a lack of standardisation of terminology and definitions<sup>3,4</sup> and the absence of an agreed set of research and clinical outcomes that should be routinely assessed.

The core outcome set (COS) concept was proposed and has been implemented across disciplines to ensure that the most important and relevant research outcomes are reported to facilitate data harmonisation and collaborative analysis.<sup>4</sup> A COS is an agreed-upon minimum set of outcomes that should be measured and reported in all studies in a specific field. Consensus on the outcomes is typically reached with involvement

of all relevant stakeholders, including people with lived experience and their families, researchers, and health-care professionals. A Position Paper<sup>5</sup> in *The Lancet Respiratory Medicine* outlines a long-awaited list of core outcomes that such stakeholder groups agreed are essential for assessment of adults with post-COVID-19 condition in research and clinical settings. Growing evidence also suggests an urgent need to develop a COS for post-COVID-19 condition in children and young people<sup>6</sup> to ensure that domains or outcomes that have specific importance to this group are not missed.

Research into post-COVID-19 condition in children and young people is lagging behind that in adults.<sup>1</sup> This gap might partly be due to studies early in the pandemic indicating that children and young people infected with SARS-CoV-2 were mainly asymptomatic or had mild symptoms. Later studies have shown that post-COVID-19 condition can affect both children and adults even after mild COVID-19.<sup>1</sup> The prevalence of post-COVID-19 condition in children and young people is unclear, with studies suggesting that between 4% and 66% of those who have had COVID-19 can be affected, depending on the outcome definition and methods used.<sup>7</sup>

In 2021, a group of experts set out some of the unmet needs in post-COVID-19 condition research and the potential impact on children and society.<sup>6</sup> Most of these unmet needs are still relevant a year later owing to a lack of inclusion of children and young people in studies of this condition. In December 2021, the International Paediatric Post-COVID Condition in Children Collaboration (IP4C), a large group of researchers, paediatricians, health-care workers, and children and young people with lived experience of post-COVID-19 condition and their family members, held a meeting to identify research priorities for paediatric post-COVID-19 condition. Priorities included the following: development of an international, living guideline on post-COVID-19 condition to facilitate equity of access to diagnostics and care and to reduce the risk of use of non-evidence-based treatments; facilitation of international collaborative research programmes and evidence exchange aimed at timely translation of new evidence into guidelines; and development of a COS and a universal clinical case definition.

Although recommendations by the Core Outcome Measures in Effectiveness Trials (COMET) Initiative

## Panel: Rationale and challenges for the development of a COS for children with post-COVID-19 condition

### Rationale

- Setting of minimal requirements for outcomes that should be assessed in research and clinical settings
- Transparency and agreement among key stakeholders on outcomes for use in intervention trials
- Harmonisation of data collection
- Improvement of data quality and potential for data synthesis for meta-analyses
- Increased opportunities for guideline development

### Challenges

- Maintenance of balance between rapid development and high methodological standards
- Involvement of children and young people in the consensus process
- Language barriers restricting participation from some geographical locations
- Potential bias in participation of relevant stakeholders (eg, dominance of patient group representatives and lack of involvement of people attending clinical services)
- Potential need for development of different sets of outcomes for different age groups
- Absence of age-appropriate measurement instruments for some outcomes
- Selection of too many outcomes, making a COS unfeasible

COS=core outcome set.

For more on the **COMET Initiative** see <https://www.comet-initiative.org/>

on the methodological process of COS development are similar for different age groups,<sup>8</sup> there are some challenges that are especially pertinent to children and young people (panel). People with lived experience are usually involved in the COS development process; however, recent research<sup>9</sup> has shown that only a tenth of core paediatric outcome sets developed for other conditions had direct input from children and young people. Most initiatives instead engaged parents or carers as proxies for children and young people. The methods that are best suited to involvement of this group and that lead to the most robust results are unclear. COS development exercises in international settings with language barriers and that involve children and young people from different age groups are especially challenging. Innovative methods using visual approaches might therefore be required. Outcomes of critical importance might vary among children and young people depending on their age. Developmental aspects might be of higher importance in early age groups, whereas social engagement and participation in education, sport, and other activities might be more important in older children and young people. An age-adjusted modular COS for children and young people might need to be considered; however, development of a single COS would facilitate harmonisation and enable comparisons of data from children and young people of different ages. If a single COS for children and young people is developed, the selection of measurement instruments should be age appropriate.

Another challenge is delivery of a high-quality COS under time pressure, which requires a balance between rapid development and methodological rigour. Previous COS initiatives across various specialties and conditions have shown that without appropriate COS development there is a risk of overlooking certain domains or outcomes of importance to patients. Furthermore, lack of appropriate COS development might also lead to measurement of heterogeneous domains or outcomes using many different instruments, thereby impairing comparability and effective synthesis of results.

Although the prevalence of post-COVID-19 condition in children and young people might be lower than in adult populations, the impact on physical and psychological health could be lifelong, not only creating increased demands on health services but

also having wider socioeconomic implications for the affected children and society—eg, by adversely affecting career opportunities and earnings, productivity, and economics, as well as social activities, relationships, and longevity. There is an urgent need to initiate projects that aim to develop a COS and associated measurement and data harmonisation tools for research on post-COVID-19 condition in children and young people—with involvement of these groups in the consensus process—to help to improve the long-term outcomes of COVID-19 across all age ranges.

DM is a co-chair of the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) Global Paediatric Long COVID working group. DB has participated in the Paediatric Adolescent and Adult COVID-19 Education (PAACE) peer-to-peer exchange programme on long COVID that was sponsored by Pfizer. All other authors declare no competing interests.

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