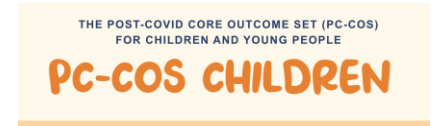


# Appendix 4

## PC-COS Children ‘How to measure’ Consensus workshop report

Meeting date and time: 31<sup>st</sup> July 2023

Location: Online (Zoom)



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## **1. Summary**

After conducting a two-round expert Delphi survey on outcome measures, an online consensus workshop took place on 31st July 2023. The purpose of this workshop was to deliberate on which outcome measures ought to be included or excluded from the core outcome set (COS). This report provides a summary of the discussions, voting results, and the finalised core outcome measurement instruments set for post-COVID-19 condition in children and young people.

## **2. Consensus workshop participants**

Forty-six individuals attended the consensus workshop. This included six non-voting members from the study team, nine observers, one facilitator, and 30 voting participants. All voting participants had completed both rounds of the online Delphi survey. Of these, 22 were health professionals or researchers, and **eight** were individuals with Long COVID or their carers.

Some participants could not remain present for the entire workshop due to intermittent internet connection and/or other commitments. The final tally of voting participants for each outcome is detailed in this report.

## Consensus workshop participants

	Total number (%) <sup>3</sup>	Voting participants (%)
<b>Healthcare professionals/Researchers</b>	<b>29 (100)</b>	<b>22 (100)</b>
<i>Delphi stakeholder group:</i>		
- Health professional (including those who also do research) <sup>1</sup>	16 (55)	11 (50)
- Researcher (without any clinical patient care duties) <sup>2</sup>	13 (45)	11 (50)
<b>Country of residence</b>		
Australia	2 (7)	1 (4.5)
Chile	2 (7)	1 (4.5)
Germany	1 (3.4)	1 (4.5)
Israel	1 (3.4)	1 (4.5)
Italy	1 (3.4)	1 (4.5)
Lithuania	1 (3.4)	0 (0)
Latvia	1 (3.4)	1 (4.5)
Malaysia	1 (3.4)	1 (4.5)
Netherlands	1 (3.4)	1 (4.5)
Poland	1 (3.4)	1 (4.5)
Romania	2 (7)	2 (9)
Switzerland	1 (3.4)	0 (0)
UK	9 (31)	7 (32)
USA	5 (17)	4 (18)
<b>Children and young people (≤18 years old) with Long COVID and their family and carers</b>		
<i>Delphi stakeholder Group:</i>		
- Family/caregivers of CYP with Long COVID	9 (100)	8 (100)
<b>Country of residence</b>		
Ireland	1 (11)	1 (13)
Netherlands	1 (11)	1 (13)
UK	6 (66.6)	5 (63)
USA	1 (11)	1 (13)
<sup>1</sup> Health professionals who care for people with Long COVID/post COVID-19 condition <sup>2</sup> Researchers who undertake research in Long COVID/post COVID-19 condition <sup>3</sup> One observer did not provide information on their stakeholder group and country of residence		

### 3. Voting and discussions

#### 3.1 Cardiovascular functioning, symptoms and conditions outcome measures discussion

Researchers emphasised the challenges associated with using questionnaires, particularly when children are involved. They noted that children often face difficulties comprehending questionnaires, suggesting that simpler tests like the sit to stand or NASA lean test might be more effective. The efficacy and importance of simple testing was a recurring theme. It has been re-emphasised that PC-COS Children project is aiming to deliver COMS that will be applicable worldwide regardless of settings and it has been agreed a priori that tests and/or tools requiring physician's/researcher's assistance and/or access to clinical/research facilities will be excluded.

The discussion also delved into concerns about the applicability of certain instruments. Some researchers felt that specific questionnaires could sometimes cover too few domains or include questions that might not be relevant or valid for disabled patients. For instance, while PedsQL was seen as encompassing fewer domains than POTS, the latter has not yet been validated and lacks the longstanding track record that PedsQL possesses.

Another area of discussion revolved around the potential discrepancies in perceptions between children and their parents. This discrepancy became especially salient when considering scales that were designed primarily for adults and might not be entirely suitable for a paediatric audience. Despite this, some participants believed that these tools could still serve as screening instruments, even if they have not been validated for the target population.

<b>COS outcome</b>	<b>Outcome Measure</b>	<b>N (%) participants voting to INCLUDE in consensus meeting</b>	<b>Result</b>
<b>Cardiovascular functioning, symptoms and conditions</b>	PedsQL Cardiac Module	16/28 (57)	Not included in the COMS
	Symptom Burden Questionnaire for Long COVID (Circulation scale)	7/27 (25)	Not included in the COMS
	Malmo POTS score (MAPS)	18/27 (64)	Not included in the COMS

### 3.2 Gastrointestinal functioning, symptoms and conditions outcome measures

The simplicity of the SBQ was widely acknowledged and appreciated by the participants. However, debates surfaced around other tools, with some considering them overly extensive and superfluous. A crucial point raised was the current lack of validation for SBQ in the paediatric population, concerning its universal applicability.

A divergence in perspectives was evident between health professionals/researchers and carers concerning the persistence and variability of gastrointestinal symptoms. While some health professionals and researchers deemed the PedsQL too intricate and exhaustive, carers leaned towards appreciating its thoroughness, provided the questions remained pertinent. This sentiment underscored a broader theme, where carers often desired comprehensive tools that might be perceived as cumbersome by researchers. Carers also pointed out the limitation in the '7 days' timeframe stipulated in some questionnaires. They felt it insufficient to encapsulate the ebb and flow of symptoms, a sentiment not universally echoed by the health professionals/researchers.

Notably, some caretakers highlighted gaps in the existing tools. They pointed out certain areas where the questionnaires fell short, such as emphasising vomiting but neglecting nausea. A glaring omission, as noted by the carers, was the absence of queries about alterations in taste, as well as eating and drinking habits – aspects that are especially relevant in the context of post-COVID-19 conditions. This brought to light the necessity for tools to be both exhaustive and specific to capture the unique challenges faced by the CYP cohort. An interesting point was made regarding the environment in which these questionnaires are administered. Carers mentioned that children might feel more at ease and authentic in answering questions in familiar settings, contrasting the sometimes intimidating clinical environment.

In conclusion, while there was an agreement on the importance of capturing gastrointestinal symptoms comprehensively, the tools and methods to achieve this effectively remained a subject of debate. All participants converged on the idea that including questions about taste and swallowing would be crucial to provide a holistic understanding of the children's experiences.

<b>COS outcome</b>	<b>Outcome Measure</b>	<b>N (%) participants voting to INCLUDE in consensus meeting</b>	<b>Result</b>
<b>Gastrointestinal functioning, symptoms, conditions and</b>	PedsQL Gastrointestinal Symptoms Scales	23/26 (88)	Included in the COMS
	Questionnaire on Pediatric Gastrointestinal Symptoms (QPGS)	2/26 (8)	Not included in the COMS
	Symptom Burden Questionnaire for Long COVID (Stomach and Digestion Scale)	6/26 (23)	Not included in the COMS

### 3.3 Fatigue or exhaustion outcome measures

The group highlighted the value of questionnaires which integrate self-reports, with the consensus being that children are quite adept at articulating their fatigue symptoms. An essential aspect identified was the inclusion of cognitive components in these measures. Some participants raised concerns about the lack of such components in certain questionnaires, such as PROMIS. Another area of contention, similarly to earlier discussions, was the timeframe with the general feeling that a '7-day' window was not sufficiently representative of the nature of Long COVID fatigue.

The Chalder Fatigue Scale gained some praise for its straightforwardness, but there were reservations regarding its validation. One of the health professionals/researchers expressed a preference for tests validated in multiple languages, emphasising the importance of accessibility to a wider audience.

An underlying theme was the desire to encompass basic functioning in the measures. Carers voiced their wish for questions that reflect everyday tasks like dressing and showering. Unfortunately, they noted that none of the current questionnaires delve into these nuances.

Concluding the discussions, there seemed to be a collective nod towards the PedsQL Multidimensional Fatigue Scale. Participants appreciated its extensive coverage, the inclusion of self-reports, and its timeframe, which captures a month, thus allowing for the consideration of symptom fluctuation. The overall sentiment was that the PedsQL offered a comprehensive insight into the fatigue experienced by children and young people with post-COVID-19 conditions.

COS outcome	Outcome Measure	N (%) participants voting to INCLUDE in consensus meeting	Result
Fatigue or Exhaustion	Chalder fatigue questionnaire	3/26 (12)	Not included in the COMS
	PROMIS Paediatric Fatigue	3/26 (12)	Not included in the COMS
	PedsQL Multidimensional Fatigue Scale	26/26 (100)	Included in the COMS
	Symptom Burden Questionnaire for Long COVID (Fatigue scale)	3/26 (12)	Not included in the COMS

### 3.4 Post-exertion symptoms outcome measures

Researchers identified an overlap between post-exertion malaise (PEM) and fatigue, acknowledging the challenge in distinguishing the two due to the limited number of tools that specifically measure PEM. Health professionals expressed concerns about the wording in the CDC's set of questions, deeming it too intricate, which might lead to misinterpretations. Carers voiced their belief in the necessity to adapt and modernise specific questions in the DePaul questionnaire to better represent the current realities, such as the shift to remote learning brought about by the pandemic. They suggested revising the phrase 'attending school' to a broader term like 'Participating in any education.'

An interesting dynamic emerged wherein health professionals initially expressed a positive perspective on PEM items from DePaul Symptom Questionnaire as a measure. However, after hearing some carers articulate their reservations, their stance evolved, leading to a change in opinion.

A common thread of concern from the researchers was the belief that the available questions and their framing may not accurately encapsulate the unique manifestation of PEM in Long COVID and the exacerbation of symptoms that accompany it. In echoing this sentiment, carers resonated with the feeling that the existing instruments fall short of truly portraying their children's experiences and the impact of the condition.

<b>COS outcome</b>	<b>Outcome Measure</b>	<b>N (%) participants voting to INCLUDE in consensus meeting</b>	<b>Result</b>
<b>Post-exertion symptoms</b>	CDC symptom inventory for CFS	5/26 (19)	Not included in the COMS
	PEM items from DePaul Symptom Questionnaire	10/26 (38)	Not included in the COMS
	Symptom Burden Questionnaire for Long COVID (Fatigue scale)	6/26 (23)	Not included in the COMS

### 3.5 Neuro-cognitive symptoms functioning, symptoms and conditions outcome measures

All participants acknowledged the merits of the PROMIS questionnaire, commending its straightforward nature and practicability. Yet, concerns arose regarding its narrow scope and how suitably it can be applied across varied age groups. The PedsQL tool seemed to garner more favour, especially from the researchers, as they highlighted its adaptability, given that it's available in multiple languages and is tailored for a range of age demographics. Another facet of PedsQL that stood out, especially to carers, was its dual reporting approach – allowing both parents and children to share their experiences. This was seen as particularly vital, given doubts over children's capacity to accurately convey their cognitive symptoms.

However, a unanimous call from carers was to refine the questions to make them more child-centric. They felt that certain scales, like the 'mild to severe' gradation in SBQ, might be challenging for children to grasp and provide accurate feedback on. More critically, they identified a gap in the current assessment

tools: none seemed to encompass certain pivotal symptoms such as hindered learning capacities or speech difficulties, both of which are paramount in evaluating neuro-cognitive abilities.

<b>COS outcome</b>	<b>Outcome Measure</b>	<b>N (%) participants voting to INCLUDE in consensus meeting</b>	<b>Result</b>
<b>Neuro-cognitive system functioning, symptoms, and conditions</b>	PROMIS Pediatric Cognitive Function - Short Form 7a	9/24 (36)	Not included in the COMS
	PedsQL Cognitive Functioning Scale	21/25 (84)	Included in the COMS
	Symptom Burden Questionnaire for Long COVID (Memory, Thinking & Communication scale, movement scale, muscles and joints, pain scales)	4/24 (16)	Not included in the COMS

### 3.6 Physical functioning, symptoms and conditions outcome measures

The EQ5DY, a measure designed to gauge health-related quality of life, was generally well-received by attendees. It was commended for its comprehensive reach, pragmatism, and succinctness. However, concerns were raised about its 'daily' time frame, given the inherent variability of Long COVID symptoms. Moreover, a notable omission from the EQ5DY was the aspect of sleep quality, which many believed was a crucial facet to assess.

On the other hand, questions derived from the PROMIS tool faced criticism, especially from carers. They took issue with its complexity and expressed doubts over its capability to procure precise answers. For instance, connections between perspiration and intense physical activities were deemed problematic. There was a prevailing sentiment among carers that the PROMIS framework might exclude those most severely affected by Long COVID, particularly those who grapple with routine daily tasks.

With regards to SBQ, several carers highlighted potential incompatibilities, particularly regarding its format and specific items such as housework, which might not be applicable to younger populations. Yet, the '7 days' time frame it employed found favour with the researcher contingent, as they believed it aptly captured the oscillating nature of Long COVID symptoms, in contrast to a 'daily' window.

In summary, while the EQ5DY was broadly appreciated for its holistic approach and almost unanimously voted for inclusion in COMS, the discussion underlined the necessity for more nuanced tools that capture the intricacies of Long COVID in young individuals, particularly given the shifting nature of its symptoms.



<b>COS outcome</b>	<b>Outcome Measure</b>	<b>N (%) participants voting to INCLUDE in consensus meeting</b>	<b>Result</b>
<b>Physical functioning, symptoms, and conditions</b>	EQ5DY instrument	24/25 (96)	Included in the COMS
	PROMIS Physical Activity	2/25 (8)	Not included in the COMS
	Symptom Burden Questionnaire for Long COVID (Impact on Daily Life Scale)	3/25 (12)	Not included in the COMS

### 3.7 Work/occupational and study changes outcome measures

There was a shared ambivalence towards the tools under discussion, specifically the WHO DAS 2. While some researchers acknowledged potential of this instrument, pointing out its comprehensive nature, they also raised concerns about its exhaustive list of questions, fearing it might not be fitting for those already contending with fatigue. Similarly, while some carers recognised its thorough approach and how it encapsulates the multifaceted roles children and young people assume, others expressed reservations. These carers seemed to be sceptical about the questionnaire's relevance, feeling that it did not genuinely reflect the unique challenges of Long COVID.

A recurrent theme was the need for a more expansive approach. Health professionals/researchers suggested that the domain might have to widen its parameters, as the repercussions on daily life transcended mere shifts in work or study patterns. Carers, on the other hand, were critical of the manner in which questions were framed for children. They advocated for more empathetic phrasing, with an emphasis on being mindful of the potential impacts on children's mental well-being.

Nevertheless, despite these varied perspectives and the evident need for refining this domain, there was a consensus on its significance. Both experts and carers concurred that understanding the ramifications on education and social growth was indispensable, and this necessitated the development of suitable investigative methodologies. Some suggestions were made with regards to potential addition of a simple question or two, which, although not been validated, could serve as a triage questions allowing for detection of problems requiring more in-depth investigation.

<b>COS outcome</b>	<b>Outcome Measure</b>	<b>N (%) participants voting to INCLUDE in consensus meeting</b>	<b>Result</b>
<b>Work/occupational and study changes</b>	Symptom Burden Questionnaire for Long COVID (Impact on Daily Life Scale)	5/22 (23)	Not included in the COMS
	WHO DAS 2 Children and Youth 36-Item Version	7/23 (30)	Not included in the COMS

## 4. Post voting discussion

One salient issue was the need for greater precision around the timeframes used in questions. Carers felt that the cyclical and fluctuating nature of Long COVID symptoms were not adequately represented in specific testing moments. Given that these symptoms can vary significantly, perhaps even daily, it was proposed that more frequent iterations of questionnaires, focused on shorter time frames such as the past week, might offer a more accurate reflection of the lived reality of Long COVID. There was also a clarion call to incorporate the perspectives of children more actively. Since questionnaires are often filled out on behalf of the children, it's crucial that their experiences and voices are not marginalised or overshadowed.

Some carers expressed feeling somewhat sidelined during usual discussions around Long COVID, perceiving a differential treatment compared to health professionals and researchers. They commended the PC-COS Children project for transparency and democratic approach, but highlighted the need in a better dialogue between all relevant stakeholders. This sentiment underscores the broader challenge of balancing diverse stakeholder viewpoints in the future processes.

In essence, the post-voting dialogue underscored the need for a more nuanced approach to capturing the complexities of long COVID in children and young people, while also emphasising the importance of inclusivity in discussions and decisions.

**Table 1**

**Pre-defined definition of consensus applied in the consensus workshop \***

<b>Consensus classification</b>	<b>Description</b>	<b>Definition</b>
Consensus in	Consensus that instrument should be included in the proposed measure set	70% or more of participants voting 'yes'
No consensus	Uncertainty about importance of outcome	Anything else

**Table 2****Consensus workshop voting results**

<b>COS outcome</b>	<b>Outcome Measure</b>	<b>N (%) participants voting to INCLUDE in consensus meeting</b>	<b>Result</b>
<b>Cardiovascular functioning, symptoms and conditions</b>	PedsQL Cardiac Module	16/28 (57)	Not included in the COMS
	Symptom Burden Questionnaire for Long COVID (Circulation scale)	7/27 (25)	Not included in the COMS
	Malmo POTS score (MAPS)	18/27 (64)	Not included in the COMS
<b>Gastrointestinal functioning, symptoms, and conditions</b>	PedsQL Gastrointestinal Symptoms Scales	23/26 (88)	Included in the COMS
	Questionnaire on Pediatric Gastrointestinal Symptoms (QPGS)	2/26 (8)	Not included in the COMS
	Symptom Burden Questionnaire for Long COVID (Stomach and Digestion Scale)	6/26 (23)	Not included in the COMS
<b>Fatigue or Exhaustion</b>	Chalder fatigue questionnaire	3/26 (12)	Not included in the COMS
	PROMIS Paediatric Fatigue	3/26 (12)	Not included in the COMS
	PedsQL Multidimensional Fatigue Scale	26/26 (100)	Included in the COMS
	Symptom Burden Questionnaire for Long COVID (Fatigue scale)	3/26 (12)	Not included in the COMS
<b>Post-exertion symptoms</b>	CDC symptom inventory for CFS	5/26 (19)	Not included in the COMS

	PEM items from DePaul Symptom Questionnaire	10/26 (38)	Not included in the COMS
	Symptom Burden Questionnaire for Long COVID (Fatigue scale)	6/26 (23)	Not included in the COMS
<b>Neuro-cognitive system functioning, symptoms, and conditions</b>	PROMIS Pediatric Cognitive Function - Short Form 7a	9/24 (36)	Not included in the COMS
	PedsQL Cognitive Functioning Scale	21/25 (84)	Included in the COMS
	Symptom Burden Questionnaire for Long COVID (Memory, Thinking & Communication scale, movement scale, muscles and joints, pain scales)	4/24 (16)	Not included in the COMS
<b>Physical functioning, symptoms, and conditions</b>	EQ5DY instrument	24/25 (96)	Included in the COMS
	PROMIS Physical Activity	2/25 (8)	Not included in the COMS
	Symptom Burden Questionnaire for Long COVID (Impact on Daily Life Scale)	3/25 (12)	Not included in the COMS
<b>Work/occupational and study changes</b>	Symptom Burden Questionnaire for Long COVID (Impact on Daily Life Scale)	5/22 (23)	Not included in the COMS
	WHO DAS 2 Children and Youth 36-Item Version	7/23 (30)	Not included in the COMS

