# Appendix 2

THE POST-COVID CORE OUTCOME SET (PC-COS)
FOR CHILDREN AND YOUNG PEOPLE
PC-COS CHILDREN

**PC-COS Children 'What to measure' Consensus meeting report**

**Meeting date and time: 28th April 2023**

**Location: Online (Zoom)**

## Contents

## 1 Summary

Following a two-round online Delphi survey an online consensus meeting was held on the 28th April 2023 to discuss outcomes where, according to the pre-agreed definition of consensus, consensus for inclusion in, or exclusion from, the core outcome set (COS) had not been reached. This report summarises these discussions and the resulting core outcome set.

## 2 Pre-Meeting for children and young people (≤18 years old) with Long COVID and their family and carers

Participants were invited to attend one of the pre-meeting sessions on the 26th April 2023 (10:00-10:30 AM or 5:00-5:30 PM, UK time). This session was aiming to provide information on core outcome sets and what to expect at the meeting and to offer an opportunity to meet the PC-COS Children team and to ask any outstanding questions.

## 3 Consensus meeting participants

Thirty-nine participants, including 9 non-voting members of the study team, four observers, one facilitator and 25 members of stakeholder groups, who had completed both rounds of the online Delphi survey, attended the online meeting. Twenty-three participants of the meeting were voting (12 health professionals/researchers, 11 children and young people (≤18 years old) with Long COVID and their family and carers). (Table 1)

Some participants were unable to attend for the entire meeting or dropped 'in' and 'out' as a result of internet connection. The final number of voting participants for each outcome is included in this report.

In the online Delphi survey, the results in Round 2 were presented for three stakeholder groups:

(a) Health professionals working with children and young people *(≤18 years old)* with Long COVID;
(b) Researchers studying Long COVID in children and young people *(≤18 years old)*;
(c) Children and young people (≤18 years old) with Long COVID and their family and carers.

All were invited to express their interest in attending the online consensus meeting on completion of Delphi survey. An additional online poll was distributed between potential meeting participants to vote for the most convenient date and time of the consensus meeting, which was scheduled for the slot preferred by most participants. Potentially interested participants were informed that the consensus meeting will be undertaken in English.

For feasibility purposes a decision was made prior to the meeting to have two voting groups only: (a) Children and young people (≤18 years old) with Long COVID and their family and carers; and (b) Health professionals/researchers. Similar approach has previously been implemented for the consensus meeting of the PC-COS adult project.

**Table 1. Consensus meeting participants**

| | N (%) | Voting (%) |
|---|---|---|
| **Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old)** | **14 (100)** | **12 (100)** |
| **Delphi stakeholder group** | | |
| Health professionals working with children and young people (≤18 years old) with Long COVID | 6 (43) | 6 (50) |
| Researchers studying Long COVID in children and young people (≤18 years old) | 8 (57) | 6 (50) |
| **Country of residence** | | |
| Malaysia | 1 (7) | 1 (8) |
| Germany | 1 (7) | 1 (8) |
| Lithuania | 1 (7) | 1 (8) |
| Italy | 2 (14) | 2 (17) |
| Norway | 1 (7) | 1 (8) |
| Romania | 1 (7) | 1 (8) |
| UK | 4 (29) | 3 (25) |
| USA | 3 (21) | 2 (17) |
| **Children and young people (≤18 years old) with Long COVID and their family and carers** | **11 (100)** | **11 (100)** |
| **Country of residence** | | |
| Ireland | 2 (18) | 2 (18) |
| UK | 8 (73) | 8 (73) |
| USA | 1 (9) | 1 (9) |

# 4 Outcomes

Twenty-five outcomes were rated in Round 2 of the online Delphi survey. The pre-agreed definition of consensus (Appendix 1) was applied to ratings submitted in Round 2 for each of the three stakeholder groups: (a) Children and young people (≤18 years old) with Long COVID; (b) Health professionals who have experience treating children and young people (≤18 years old) with Long COVID; (c) Researchers studying Long COVID in children and young people (≤18 years old).

As a result of the Delphi survey, four outcomes met a priori definition for "consensus in" to be included in the core outcome set and eight met the definition of "consensus out" and were excluded from the core outcome set. During the consensus meeting 13 outcomes were discussed: 11 outcomes with no consensus but at least one group voted "in" and two outcomes with no "in" or "out" votes.

At the consensus meeting the outcomes for discussion were presented along with the outcomes from the same domain, already included in the COS. Meeting participants were then invited to provide comments on outcomes and their value for the COS. After outcome discussion, participants were asked to anonymously rate each outcome using the 1-9 Likert scale (1 "not that important" – 9 "critically important"). Voting was organised by the study team using Zoom Video Communications Inc (Zoom) online polling mode. The discussion and rating of outcomes was facilitated by an experienced independent facilitator.

## 4.1 Selection of outcomes for consensus meeting discussion

Outcomes that reached the definition of consensus after Round 2 of the Delphi survey were presented prior to the voting. (Appendix 2)

Eleven outcomes with at least one group voted "in" (but not fulfilling the criteria of the consensus 'in') were presented for discussion at the consensus meeting. Two outcomes with no "in" or "out" votes after Round 2 of the Delphi survey ("Healthcare resource utilisation", "Family/carer burden") were presented at the end of the voting process.

## 4.2 Outcomes discussed in the consensus meeting

### 4.2.1 Mortality outcomes

One outcome “survival” was prioritised for discussion in the mortality domain.

### Survival

During the meeting participants were mainly acknowledging the great importance of survival outcome, but as mortality rate among paediatric population with post-COVID-19 condition is known to be very low, the general agreement was that “survival” is not critical enough to be included in the core outcome set.

**Outcome of discussion and rating:**

| **Outcome: Survival** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers (n=11) | 4 (36) | 4 (36) | 3 (27) |
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old) (n=13) | 8 (66) | 3 (25) | 1 (8) |
| **Result** | **Outcome not included in COS** | | |

### 4.2.2 Physiological/clinical outcomes Mortality outcomes

The physiological/clinical domain included seven outcomes:

- Post-exertion symptoms
- Mental / Psychological functioning; symptoms; and conditions
- Respiratory functioning; symptoms; and conditions

- Pain
- Sleep-related functioning; symptoms; and conditions
- Gastrointestinal functioning; symptoms; and conditions
- Muscle and joint symptoms and conditions

### Post-exertion symptoms

All participants (11/11, 100%) representing the "children and young people (≤18 years old) with Long COVID and their family and carers" group were in favour of this outcome inclusion in the core outcome set, highlighting great importance of this feature for children and young people with post-COVID-19 condition. Parents of the child(-ren) with Long COVID believe that post-exertion symptoms are hard to recognise by general practitioners, so they are convinced that it is crucial to include this outcome in the core outcome set. It was also commented that this outcome is often named by the family members as the one substantially associated with reduction in quality of life. Health professionals/ researchers were providing similar feedback and during voting most of them suggested that this outcome is critical (5/12 voted "9", 5/12 voted "8"), with 17% (2/12) considering the outcome important, but not critical enough to be included in the COS.

| **Outcome: Post-exertion symptoms** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers (n=11) | 0 | 0 | 11 (100) |
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old) (n=12) | 0 | 2 (17) | 10 (84) |
| **Result** | **Outcome included in COS** | | |

## Mental/Physiological functioning symptoms; and conditions

Stakeholders from both groups, including health professionals, researchers and representatives from "Children and young people (≤18 years old) with Long COVID and their family and carers", have expressed their concerns about the challenges associated with distinguishing whether a child was already, prior to COVID infection, experiencing mental health issues or mental health issues are the consequence of Long COVID condition. This fact limits the possibility of including the mental/physiological functioning symptoms and conditions in the core outcome set. It was also highlighted by one of the participants from the "Children and young people (≤18 years old) with Long COVID and their family and carers" group, that a significant number of parents are troubled and hesitant to discuss mental problems of their child with healthcare providers, as they and their children are often not understood and the symptoms of their children are often attributed to mental health diseases. Overall, representatives of this stakeholder group was supportive of this view and although acknowledged importance of this outcome, they felt that it is not critical enough to be assessed in every study, particularly considering potential stigmatisation of children and young people.

| **Outcome:** **Mental/Physiological functioning symptoms; and conditions** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers<br>(n=10) | 3 (30) | 6 (60) | 1 (10) |
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old) (n=12) | 0 | 5 (42) | 7 (59) |
| **Result** | **Outcome not included in COS** | | |

### Respiratory functioning; symptoms; and conditions

Health professionals and researchers acknowledged the significance of respiratory symptoms and outcomes in children who have experienced COVID-19. They noted that while children generally experience milder symptoms of COVID-19 compared to adults, the aftermath can manifest in significant respiratory symptoms. On the other hand, carers provided a more intimate and personal account, reflecting the lingering challenges faced by their children. One carer recounted how their child, even two years post-infection, still struggles with breathlessness during routine activities such as dressing or climbing stairs. Another carer brought up the issue of chest tightness and the sensation of not getting enough air, which many children reportedly experience. They raised questions about how this symptom relates to Post-Exertional Malaise (PEM), a term often associated with other post-viral syndromes. From a medical perspective, a health professional clarified that PEM encompasses any physical or mental symptom resulting from exertion, not solely respiratory issues. However, the distinction between direct respiratory issues and symptoms that arise due to exertion remained a topic of concern for carers.

It was also noted that even after employing multiple examination methods, major findings are often absent. However, children still report feelings of chest tightness and breathlessness following minor physical activity or emotional stress. Consequently, parents find it challenging to differentiate between symptoms of respiratory function and post-exertional malaise, which can be attributed to various physical or mental issues. Given that most parents lack medical training, they struggle to discern between these two categories of symptoms. As a result, not all members from the group "Children and young people (≤18 years old) with Long COVID and their family and carers" are in favour of including respiratory functioning symptoms and conditions in the COS.

| **Outcome: Respiratory functioning; symptoms; and conditions** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers (n=11) | 1 (9) | 5 (45) | 5 (45) |
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young | 0 | 4 (34) | 8 (66) |

| | | | |
|---|---|---|---|
| people (≤18 years old) (n=12) | | | |
| **Result** | **Outcome not included in COS** | | |

## Pain

Carers predominantly voiced concerns about the chronic pains their children experienced following a COVID-19 infection. A recurring sentiment was that pain, particularly chronic pain, is a crucial outcome that often goes dismissed by some medical professionals. One carer highlighted the importance of recognising pain as an outcome, especially as it might be linked to other symptoms such as anxiety. Another shared a personal experience where their son suffered from a persistent headache for 18 months, and a consultant suggested the cause might be superficial – like having a 'top knot' – or even attention-seeking. Such experiences of having genuine pain symptoms dismissed were distressing for parents.

Carers also attested to the prevalence of pain in children with post-COVID-19 condition. They described it as widespread, manifesting in various forms such as migraines, muscle pain, abdominal pain, and musculoskeletal pain. Another carer noted that while pain is common in paediatric long COVID, it's a broad symptom that might not be unique to the condition. Thus, while it is essential to recognise, they expressed uncertainty about whether it should be prioritised as a critical outcome. However, the overall sentiment was that pain was both common and a significant concern for those with post-COVID-19 condition. That is why for most of the parents this outcome is critical. Health professionals and researchers were reiterating that several conditions could cause pain, and the outcome did not reach the threshold of 80% necessary for inclusion into COS.

| **Outcome: Pain** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers (n=10) | 0 | 2 (20) | 8 (80) |

|  |  |  |  |
|---|---|---|---|
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old) (n=12) | 2 (17) | 1 (8) | 9 (75) |
| **Result** | **Outcome not included in COS** |  |  |

### Sleep-related functioning; symptoms; and conditions

Almost all participants from the “children and young people (≤18 years old) with Long COVID and their family and carers” group believe that sleep-related functioning should be definitely included in the COS. Carers voiced significant concerns regarding their children's sleep disturbances post-COVID-19. One carer described their child's severe insomnia, noting the cyclical nature of the condition where increased fatigue exacerbated the insomnia. Another carer stressed the critical importance of assessing sleep due to its profound influence on various domains of a child's life. They pointed out that disturbances in sleep could impact cognitive function, pain, daily life functioning, and fatigue. As such, without a thorough assessment of sleep, it becomes challenging to understand or address other related domains effectively. This sentiment was echoed by another carer who reinforced the idea that sleep disturbances are a common symptom amongst children with the post-COVID-19 condition. A young participant raised an insightful question regarding the relationship between sleep and pain, pondering whether pain might be causing sleep disturbances or if a lack of sleep could intensify pain. This view has been reflected by the predominance (91%) of “children and young people (≤18 years old) with Long COVID and their family and carers” voting for inclusion into COS.

From a health professional and researcher's perspective, the importance of assessing sleep as an outcome was acknowledged. The professional pointed out that if sleep is chosen as a critical outcome, then the next step would be to determine the tools and methods to measure it effectively. Such an evaluation would not only consider the quantity of sleep but would also delve deeper to ascertain the reasons behind sleep disturbances, whether that be pain, breathing difficulties, or other factors.

However, although the outcome has been recognised as very important, it did not reach the necessary threshold as 75% of 'health professionals and researchers' voted this outcome as critical. Some concerns were raised suggesting that several factors may lead to sleep disturbance, making it difficult to measure this outcome.

| **Outcome: Sleep-related functioning, symptoms, and conditions** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers (n=11) | 0 | 1 (9) | 10 (91) |
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old) (n=12) | 1 (8) | 2 (16) | 9 (75) |
| **Result** | **Outcome not included in the COS** | | |

## Gastrointestinal functioning; symptoms; and conditions

Discussions were overall toned for "inclusion" of this outcome in the COS. One of the health professional-participants highlighted the recurrent observation of GI symptoms in their clinical practice, noting the often-elongated period it takes to establish a connection between these symptoms and a prior COVID-19 infection. One carer provided a personal perspective, sharing the struggles their daughter faced. Their child became intolerant to numerous foods following her bout with COVID-19, which, in turn, negatively affected her quality of life, energy levels, and appetite. This intolerance also necessitated the intake of multiple medications and supplements. Several other carers voiced concerns over GI dysfunctions being more prevalent in children than in adults. This was supported by statements highlighting the increase in children requiring feeding tubes or being diagnosed with conditions like coeliac disease. A sentiment that gained traction was that GI issues seem to be more widespread in children with long COVID than in their adult counterparts, even though adults are not entirely immune to these symptoms. Furthering this dialogue, another health professional concurred with the high incidence of GI symptoms they observed in their clinic. Another carer expressed that the vast majority of children encounter GI challenges at some stage in their long COVID trajectory, whether that manifests as nausea, new “food allergies”, persistent stomach aches, or digestion issues.

Health professionals chimed in on the significance of these symptoms, suggesting that chronic GI symptoms may be more specific to children than other broader health challenges. There was also a reference to emerging evidence supporting the notion of viral persistence in the GI tracts of children post-COVID.

All representatives of the “Children and young people (≤18 years old) with Long COVID and their family and carers” (12/12, 100%) considered this outcome critical, while 10/12, 84% health professionals and researchers voted for inclusion of the outcome in the COS.

| **Outcome:** **Gastrointestinal functioning; symptoms; and conditions** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers (n=11) | 0 | 0 | 11 (100) |
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old) (n=12) | 0 | 2 (16) | 10 (84) |
| **Result** | **Outcome included in COS** | | |

### Muscle and joint symptoms and conditions

From the carers' perspective, muscle and joint symptoms were prevalent, though some believed they weren't as common as headaches. The distinction between muscle/joint symptoms and fatigue was emphasised by a health professional who noted that some parents often conflate muscle/joint problems with fatigue and/or post-exertional malaise. There was a shared understanding among the carers that the pain experienced in the joints was distinct. This was not due to deconditioning, a term they were often confronted with to explain away the symptoms. It was not linked to PEM either. Instead, the pain was consistent, and it typically manifested in similar joints among many children. However, there was some debate about its prevalence and its significance as a primary outcome. A few carers provided personal experiences: one mentioned their daughter faced these symptoms daily, hampering her participation in activities and diminishing her overall quality of life. Another carer raised the possibility of exploring the connection between muscle pains, “hypermobility", and “connective tissue disorders”. For many, muscle pain and weakness seemed to be an everyday reality, affecting various body parts from the calves to the neck.

Healthcare professionals and researchers flagged it as a relatively frequently observed symptom in children with post-COVID condition. A distinction was made between various types of pain, from joint pain to muscle fatigue, and it was emphasised that not including pain as an outcome could be an oversight.

In summary, although the consensus meeting showcased a collective recognition of muscle and joint symptoms post-COVID in children and young people; neither “Children and young people (≤18 years old) with Long COVID and their family and carers” or “health professionals/researchers” voted the outcome as critical enough to be included in the COS.

| **Outcome: Muscle and joint symptoms and conditions** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers (n=11) | 0 | 3 (27) | 8 (72) |
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old) (n=12) | 3 (25) | 5 (42) | 4 (34) |
| **Result** | **Outcome not included in COS** | | |

### 4.2.3 Life impact outcomes

The life impact domain includes three outcomes:

- Work/occupational and study changes
- Satisfaction with life; or personal enjoyment
- Social role-functioning and relationships problems (voted "out" according to the Delphi 2nd round)

#### Work/occupational and study changes

Almost all participants from each stakeholder group (100% – family and children, 91% – healthcare and researchers) agreed that this outcome should definitely be included in the core outcome set. During the consensus meeting it was noted by one researcher that in most of the studies this aspect is deprived of attention and that could explain why the difference between Long COVID and non-COVID children was not detected, so the lack of this outcome in most of the studies contributes to the misunderstanding of Long COVID.

Long COVID causes a range of issues that affect not only children, but also those who care for them. The majority of these children are unable to attend school and have to have a reduced timetable and have online learning. This makes it difficult for them to grasp knowledge, perform well academically, and socially engage with their peers. During consensus meeting a special attention was paid to extracurricular activity: due to their chronic condition children could not participate in any of the sports and activities that they used to enjoy before they experienced COVID-19 infection, which is a major concern for carers. The inability of children to attend school has an impact on the entire family, as parents have to stay home and take "days off work" in order to take care of their child. Thus, this outcome concerns the children and their parents, so almost all of the voting participants suggested that this outcome is critical and should be included in the final COS.

| **Outcome: Work/occupational and study changes** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers (n=9) | 0 | 0 | 9 (100) |

| | | | |
|---|---|---|---|
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old) (n=12) | 0 | 1 (8) | 11 (91) |
| **Result** | **Outcome included in COS** | | |

### Satisfaction with life; or personal enjoyment

Parents of children with Long COVID believe that due to the Long COVID the satisfaction with life of children has been changed. Due to the inability to attend school, to do extracurricular activities and lack of social engagement children can not live their life like before and escape from reflections on their condition. From the carer perspective, there was a deep sense of the profound impact post-COVID conditions had on the affected children's lives. A parent shared the drastic transformation their daughter underwent post-infection: from being a sporty, academic individual to becoming housebound and dependent on a wheelchair for more extended mobility. Such drastic changes, they pointed out, severely affected the child's identity and consequently, her quality of life and her overall life satisfaction. Drawing a poignant contrast, the parent highlighted how their child, while alive, wasn't truly living and enjoying her life. A young person further emphasised this outcome's importance, highlighting the emotional and social toll. Missing school, losing the opportunity to socialise with friends, and not being able to partake in previously enjoyed activities was a source of significant distress. The participant voiced concerns about the potential cascading effect on mental and psychological well-being and asserted the outcome's inclusion.

However, “health professionals/researchers” displayed some reservations. One researcher pondered whether aspects like socialisation, school attendance, and sports, which directly influence life satisfaction, were adequately covered under another outcome ("life impact and functioning"). They questioned if the outcome of "satisfaction with life" might be seen as a mere consequence of these daily impacts, akin to how mental health was perceived in previous discussions. Drawing parallels, they alluded to concerns about how addressing "satisfaction with life" might mirror earlier challenges faced when discussing mental health. Another health professional interjected with a contrasting viewpoint, advocating for the inclusion of this outcome. While acknowledging concerns related to the mental health outcome, they argued that "satisfaction with life" offered a less contentious avenue to delve into the emotional well-being of the children, which could be more readily embraced by patients and their families.

In essence, the meeting accentuated the multifaceted implications of post-COVID-19 condition on children's lives, from their physical abilities to their emotional well-being. While there was a shared acknowledgment of the profound effects, the best approach to measure and address these impacts remained a point of discussion and did not reach the required threshold for inclusion in any of the stakeholder groups.

| **Satisfaction with life, or personal enjoyment** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers<br>(n=11) | 2 (18) | 2 (18) | 7 (63) |
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old) (n=12) | 3 (25) | 5 (42) | 4 (34) |
| **Result** | **Outcome not included in COS** | | |

### Social functioning and relationships problems

One carer suggested that aspects of social functioning were inherently intertwined with school outcomes. Given that children's primary social sphere is often centred around school, they found it challenging to distinguish between the two outcomes and questioned the need for redundancy. Echoing a similar sentiment, a health professional drew parallels between this outcome and school functioning. They pointed out that tangible aspects like school and sports attendance offer a more objective measurement framework, unlike the more abstract concept of general satisfaction. In their view, this general satisfaction was largely a by-product of the more tangible metrics like school attendance and the quality of relationships.

Another carer believed that the essence of "Social functioning and relationships problems" had already been encompassed in a previous core outcome. They raised an interesting perspective that while some individuals might become more insular post-COVID, it doesn't necessarily equate to unhappiness or dissatisfaction. Their stance was that if individuals feel contented with their life, then by extension, they are likely satisfied with their current level of social functioning.

There was a general agreement from the participants from both stakeholder groups that this outcome is similar to “Satisfaction with life; or personal enjoyment”. The participants gravitated towards the idea that the outcome of "Social functioning and relationships problems" might be too interwoven with other outcomes, particularly those related to school. The challenge lay in discerning its unique value amid other outcomes that seemingly encompass its core elements.

| **Social role-functioning and relationships problems** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers (n=11) | 1 (9) | 7 (63) | 3 (27) |
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old) (n=11) | 4 (36) | 5 (45) | 2 (18) |
| **Result** | **Outcome not included in COS** | | |

### 4.2.4 Resource use outcomes

This domain included two outcomes with no groups – no groups voted “in” or “out”:

- Healthcare resource utilisation
- Family/carer burden

## Healthcare resource utilisation

A young person with lived experience of long COVID shared their personal perspective, underscoring the significant role that healthcare plays in their daily life. From consistent doctor visits to taking medications, healthcare interactions have become an integral aspect of their existence. They emphasised the need to evaluate how healthcare resources are assisting children grappling with the condition. On the other hand, a health professional brought up the inherent challenges in measuring this outcome. They noted the extensive variability in healthcare experiences not only across different countries but even within individual countries. They highlighted that many factors, such as familial organisation and regional differences, contribute to this variability. Moreover, the treatment approach often differs based on the healthcare professional, making it a multifaceted issue. A carer, reflecting on their UK-based experience, expressed the intricate nature of healthcare resource utilisation. They shared that it took over 18 months for their child to receive an official diagnosis of long COVID. The carer attributed this delay not merely to capacity issues but also to the chronic nature of the condition. The advice they received was to avoid seeking appointments for chronic conditions that lacked treatments. This made the process cumbersome and highlighted the complexities involved. Another carer emphasised the importance of monitoring healthcare resource utilisation due to the inconsistent experiences of families. They argued that the treatment received and access to it widely differed, indicating a lack of a standardised care pathway. They strongly believed that geographic location or place of residence shouldn't dictate the quality or access to care, insisting on the need for a comprehensive understanding of standard healthcare and its effectiveness.

There was a strong agreement between participants representing both stakeholder groups that although this outcome is important it is not critical enough to be included in the COS, particularly as it may vary across geographies, from one medical centre to another.

| **Outcome: Healthcare resource utilisation** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers | 1 (11) | 4 (44) | 4 (44) |

| | | | |
|---|---|---|---|
| (n=9) | | | |
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old) (n=12) | 2 (16) | 9 (75) | 1 (8) |
| **Result** | **Outcome not included in COS** | | |

### Family/carer burden

All representatives from the “Children and young people (≤18 years old) with Long COVID and their family and carers” group found this outcome critical and viewed the carer burden as underestimated. Many carers shared personal testimonies on the multifaceted challenges they face as they support their children with long COVID. One carer articulated that the effects are not just emotional and psychological but also economic, affecting a broad spectrum of households. They pointed out that parents of children with long COVID often grapple with the capacity to maintain their jobs, thus intensifying the overarching burden. They felt that this burden was considerably underestimated and merited some form of measurement to understand its true magnitude.

Echoing this sentiment, another carer mentioned that the ramifications had forced them to change jobs and curtail their working hours, impacting their home circumstances and finances. The implication was clear: having a child with long COVID invariably alters a family's dynamics, from its emotional fabric to its economic stability. While a health professional acknowledged the gravity of the situation, stating the need to assist these families, the narratives of carers were profound. One self-employed carer revealed a substantial cutback in their work hours to support their child with long COVID. Another carer expressed their inability to continue working at all, illustrating the drastic shift in their financial state since their children fell chronically ill with the condition.

As for voting, the health professionals and researchers agreed that the burden on families and caregivers is very important, but the outcome is not too critical to be included in the COS.

| **Outcome: Family/carer burden** | **% rating 1-3** | **% rating 4-6** | **%rating 7-9** |
|---|---|---|---|
| Children and young people (≤18 years old) with Long COVID and their family and carers (n=8) | 0 | 0 | 8 (100) |
| Health professionals working with children and young people (≤18 years old) with Long COVID/ Researchers studying Long COVID in children and young people (≤18 years old) (n=12) | 2 (17) | 6 (50) | 4 (34) |
| **Result** | **Outcome not included in COS** | | |

## 5 Discussion

Four outcomes were included in the core outcome set after the two round online Delphi survey and work/occupational and study changes, post-exertion symptoms, gastrointestinal functioning; symptoms; and conditions were added at the consensus meeting.

**Table 2. Outcomes included in the Core Outcome Set**

| **Domain** | **Outcome** | **Outcome description** |
|---|---|---|
| **Physiological/ Clinical Outcomes** | **Cardiovascular functioning; symptoms; and conditions** | New onset or worsening of problems affecting the heart (e.g. pounding or racing heart) and the blood vessels (e.g., veins or arteries) |
| | **Fatigue or Exhaustion** | New onset or worsening in severity or duration of feeling exhausted, having too little energy, or needing more rest |
| | **Neuro-cognitive system** | New onset or worsening of dizziness/lightheadedness, tics (involuntary movements |

| | | |
|---|---|---|
| | **functioning; symptoms, and conditions** | caused by spasm-like contractions of muscles, most commonly involving the face, mouth, eyes, head, neck or shoulders; vocal tics are sounds uttered unintentionally), fainting, headache, migraine, abnormal movements, tremors/shaking, seizures/fits, muscle twitching, tingling feelings, decreased sensation, inability to move part of the body, lack of coordination, speech difficulty; Problems with memory, communication, concentration, having "brain fog", understanding instructions, including interpretation of words; Abnormal child development (e.g. learning new skills, such as crawling/walking and talking, developmental regression) |
| | **Post-exertion symptoms** | New onset or worsening of different symptoms following physical or mental activities or emotions that could previously be tolerated (e.g. thinking, moving, socialising), which that can last for a prolonged duration (multiple days/weeks) |
| | **Gastrointestinal functioning; symptoms; and conditions** | New onset or worsening of problems with swallowing, stomach aches, nausea (feeling the need to vomit), vomiting, heartburn/reflux (stomach acid coming back up into the mouth and causing an unpleasant, sour taste), diarrhoea, constipation, gas, indigestion, lack of pleasure while eating (some children describe this as “food and eating is yuck”) |
| **Life Impact Outcomes** | **Physical functioning; symptoms; and conditions** | New onset or worsening problems with physical abilities, including muscle strength, arm/leg shaking or unsteadiness, walking, dressing, or eating |
| | **Work/occupational and study changes** | New onset or worsening problems with being able to resume usual level of work, study, attendance, less engagement/ participation in extracurricular activities |

## References

1. Tong A, Baumgart A, Evangelidis N, et al. Core Outcome Measures for Trials in People With Coronavirus Disease 2019: Respiratory Failure, Multiorgan Failure, Shortness of Breath, and Recovery. *Crit Care Med*. 2021;49(3):503-516. doi:10.1097/CCM.0000000000004817

## Appendix 1

**Pre-defined definition of consensus applied in the consensus meeting**

| **Consensus classification** | **Description** | **Definition** |
|---|---|---|
| Consensus in | Consensus that outcome should be included in the core outcome set | 80% or more of participants in each group rating the outcome 7-9 |
| Consensus out | Consensus that outcome should not be included in the core outcomes set | 50% or fewer in each group scoring 7-9 |
| No consensus | Uncertainty about importance of outcome | Anything else |

## Appendix 2

## Delphi process and Consensus meeting results

| Domain | Outcome | Outcome description | % Children and young people/Family and carers of children and young people (≤18 years old) with Long COVID voting 7-9 in R2 of online Delphi | % HCPs voting 7-9 in R2 of online Delphi | Researchers voting 7-9 in R2 of online Delphi | % Children and young people/ Family and carers of children and young people (≤18 years old) with Long COVID voting 7-9 in consensus meeting | % HCPs/ Researchers voting 7-9 in consensus meeting | Result |
|---|---|---|---|---|---|---|---|---|
| **Physiological/ clinical outcomes** | **Fatigue or Exhaustion** | New onset or worsening of feeling exhausted, having too little energy, or needing more rest, including fatigue not relieved by rest | 97·9 | 93·8 | 92 | N/A | N/A | Included in the COS following Delphi survey |
| | **Neuro-cognitive system functioning, symptoms, and conditions** | New onset or worsening of dizziness/lightheadedness, tics (involuntary movements caused by spasm-like contractions of muscles, most commonly involving the face, mouth, eyes, head, neck or shoulders; vocal tics are sounds uttered unintentionally), fainting, headache, migraine, abnormal movements, tremors/shaking, seizures/fits, muscle twitching, tingling | 94·7 | 93·8 | 96 | N/A | N/A | Included in the COS following Delphi survey |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | feelings, decreased sensation, inability to move part of the body, lack of coordination, speech difficulty; Problems with memory, communication, concentration, having "brain fog", understanding instructions, including interpretation of words; Abnormal child development (e.g. learning new skills, such as crawling/walking and talking, developmental regression) | | | | | | |
| | **Cardiovascular functioning, symptoms, and conditions** | New onset or worsening of problems affecting the heart (e.g. irregular heartbeat, palpitations, pounding or racing heartbeat, resting heartbeat changes, pericarditis/myocarditis (heart inflammation)); problems with the blood vessels (i.e., veins or arteries), changes in blood pressure | 88·3 | 84·4 | 88 | N/A | N/A | Included in the COS following Delphi survey |
| **Life impact outcomes** | **Physical functioning, symptoms, and conditions** | New onset or worsening problems with daily physical abilities (activities), including arm/leg shaking or unsteadiness, mobility, walking, | 97·9 | 90·6 | 92 | N/A | N/A | Included in the COS following Delphi survey |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | dressing, playing or eating, growth | | | | | | |
| **Physiological/ clinical outcomes** | **Post-exertion symptoms** | New onset or worsening of different symptoms following physical or mental activities or emotions that could previously be tolerated (e.g. thinking, moving, socialising), which that can last for a prolonged duration (multiple days/weeks) | 99 | 87·5 | 68 | 100 | 84 | Included in the COS following discussion at the consensus meeting |
| | **Gastrointestinal functioning; symptoms; and conditions** | New onset or worsening of problems with swallowing, stomach aches, nausea (feeling the need to vomit), vomiting, heartburn/reflux (stomach acid coming back up into the mouth and causing an unpleasant, sour taste), diarrhoea, constipation, gas, indigestion, lack of pleasure while eating (some children describe this as “food and eating is yuck”) | 84·2 | 81·3 | 44 | 100 | 84 | Included in the COS following discussion at the consensus meeting |
| **Life impact outcomes** | **Work/occupational and study changes** | New onset or worsening problems with being able to resume usual level of work, study, attendance, less engagement/ participation in extracurricular activities | 87·8 | 87·1 | 76 | 100 | 91 | Included in the COS following discussion at the consensus meeting |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Physiological/ clinical outcomes** | **Endocrine and metabolic functioning, symptoms, and conditions** | New onset or worsening of problems related to the glands (type of body organ) that make hormones, hormonal balance (e.g. diabetes, thyroid problems, adrenal gland or steroid problems, changes in body weight, bone mineral problems), menstrual cycle, early onset of puberty | 76·3 | 37·5 | 28 | N/A | N/A | Excluded following Delphi survey |
| | **Hearing-related functioning, symptoms, and conditions** | New onset or worsening of problems with hearing (e.g., hearing loss, ringing or buzzing in the ears, increased sensitivity to sounds) | 26·7 | 12·5 | 16 | N/A | N/A | Excluded following Delphi survey |
| | **Taste- and/or smell-related functioning, symptoms, and conditions** | New onset or worsening problems with altered or reduced/loss of taste or smell (e.g., familiar things smell or taste bad or different, tasting or smelling things that are not there) | 24·7 | 37·5 | 40 | N/A | N/A | Excluded following Delphi survey |
| | **Kidney and urinary-related functioning, symptoms, and conditions** | New onset or worsening problems with kidney function or need for dialysis or problems with urination (i.e., wee/pee) including infections, burning or stinging, higher frequency or urgency (i.e. feeling of needing), | 40·9 | 21·9 | 16·7 | N/A | N/A | Excluded following Delphi survey |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | incontinence (inability to control urination/“wetting yourself”) | | | | | | |
| | **Skin, hair, dental and/or nail-related functioning, symptoms, and conditions** | New onset or worsening problems with ulcers, skin rash and/or peeling, itch, red spots or lumps on toes (COVID toes), hair thinning/loss, changes in nails and teeth | 23·4 | 9·4 | 8 | N/A | N/A | Excluded following Delphi survey |
| | **Vision-related functioning, symptoms, and conditions*** | New onset or worsening of problems with vision (e.g., problems seeing or blurred vision, increased sensitivity to light, colour misperception, loss of vision), dry eyes or feeling of a grit/sand in eyes | 48·4 | 12·5 | 12 | N/A | N/A | Excluded following Delphi survey |
| | **Fever/body temperature changes** | New onset or worsening of problems related to the body temperature without a known cause (e.g. fever that comes and goes, prolonged low-grade fever, chills or shivers, feeling too cold or too hot) | 53·7 | 12·5 | 8 | N/A | N/A | Excluded following Delphi survey |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Life impact outcomes** | **Stigma** | New onset or worsening problems with fear or experiences of being discriminated against, bullied, excluded from activities, ignored, including by employer/school/nursery/university, medical professionals, social groups, family/friends/neighbours, or others | 51·5 | 32·3 | 16 | N/A | N/A | Excluded following Delphi survey |
| **Mortality outcomes** | **Survival** | How long does someone live | 75·5 | 59·4 | 88 | 27 | 8 | Excluded following discussion at the consensus meeting |
| **Physiological/ clinical outcomes** | **Sleep-related functioning; symptoms; and conditions** | New onset or worsening of problems with falling or staying asleep, need for sleep medications/aids, excessive sleeping, or lack of refreshing sleep/poor sleep quality, increased nightmares and/or sleepwalking | 86·5 | 84·4 | 72 | 91 | 75 | Excluded following discussion at the consensus meeting |
| | **Muscle and joint symptoms and conditions** | New onset or worsening of joint or muscle problems, such as muscle weakness or joint stiffness or swelling/inflammation | 80·2 | 71·9 | 56 | 72 | 34 | Excluded following discussion at the consensus meeting |
| | **Mental / Psychological functioning** | New onset or worsening problems with emotions and mood, including | 78·9 | 96·9 | 92 | 10 | 59 | Excluded following discussion at the consensus |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | anxiety/worrying, panic attacks, separation anxiety, fear, aggression, irritability, anger, excessive crying, easily getting upset, feeling of guilt, depression, suicidal thoughts, or post-traumatic stress symptoms (having flashbacks to a stressful event), obsessions (intrusive unwanted thoughts) and compulsions (repetative actions or behaviours linked to obsessions) | | | | | | meeting |
| | **Respiratory functioning** | New onset or worsening problems with lungs or breathing (e.g., shortness of breath/shortness of air/not getting enough air, chest tightness or coughing/wheezing, problems with breathing through the nose including blocked and runny nose), sinusitis (infection of the sinuses (air-filled spaces in the bones of your face around the nose)) | 71 | 81·3 | 88 | 45 | 66 | Excluded following discussion at the consensus meeting |
| | **Pain** | New onset or worsening discomfort in the body that can include sharp or burning pain, dull ache, or stinging or | 88·7 | 87·5 | 68 | 80 | 75 | Excluded following discussion at the consensus meeting |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | throbbing, including pain that comes and goes, or is persistent, or chronic (ongoing) pain; increased sensitivity to pain (feeling pain even upon minor stimuli which have not caused pain before), inability to control pain with usual painkillers | | | | | | |
| **Life impact outcomes** | **Satisfaction with life; or personal enjoyment** | New onset or worsening of problems with satisfaction with life or personal enjoyment, loss of being the person who you were before COVID-19, feeling “left out”/“missing out”, feeling that “the world is moving, while you are stuck” | 89·7 | 75 | 73·1 | 63 | 34 | Excluded following discussion at the consensus meeting |
| | **Social role-functioning and relationships problems** | New onset or worsening problems with connecting with others, including family members and friends, maintaining and creating new friendships and personal/romantic relationship, social activities | 67 | 87·1 | 64 | 27 | 18 | Excluded following discussion at the consensus meeting |
| **Resource Use Outcomes** | **Family/carer burden** | Increasing/developing a burden on caregiver/family or friends/classmates/colleagues/teachers; impact of sickness on other people in your life, including relationships between the carers | 78·1 | 71·9 | 76 | 100 | 34 | Excluded following discussion at the consensus meeting |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **Healthcare resource utilisation** | Seeing more healthcare professionals (e.g., doctor, physiotherapist, psychologist), taking new medications, returning to the hospital or emergency care, including complementary/alternative medicine (e.g., acupuncturists, naturopaths), medical devices/technology | 77·6 | 62·5 | 73·1 | 44 | 8 | Excluded following discussions at the consensus meeting |