ABSTRACT

Objective The aim of this study was to derive a research definition for 'Long COVID (Post-COVID-19 condition)' in children and young people (CYP) to allow comparisons between research studies.

Design A three-phase online Delphi process was used, followed by a consensus meeting. Participants were presented with 49 statements in each phase and scored them from 1-9 based on how important they were for inclusion in the research definition of Long COVID in CYP. The consensus meeting was held to achieve representation across the stakeholder groups. Statements agreed at the consensus meeting were reviewed by participants in the Patient Public Involvement (PPI) Research Advisory Group.

Setting The study was conducted remotely using online surveys and a virtual consensus meeting.

Participants 120 people with relevant expertise were divided into three panels according to their area of expertise: Service Delivery, Research (or combination of research and service delivery) and Lived Experience. The PPI Research Advisory group consisted of CYP aged 11-17 years.

Main outcome measures Consensus was defined using existing guidelines. If consensus was achieved in two or more panels or was on the border between one and two panels, those statements were discussed and voted on at the consensus meeting.

Results Ten statements were taken forward for discussion in the consensus meeting and five statements met threshold to be included in the research definition of Long COVID among CYP. The research definition aligned to the clinical case definition of the World Health Organisation is proposed as follows: *Post-COVID-19 condition occurs in young people with a history of confirmed SARS CoV-2 infection, with at least one persisting physical symptom for a minimum duration of 12 weeks after initial testing that cannot be explained by an*

COVID-19 condition or 'Long COVID' with the former terminology being considered least controversial and preferred by the World Health Organisation[1]. Acute SARS-CoV-2 infection in children and young people is usually asymptomatic[1] or mild[2] compared to adults[3]. More children[2] recover without sequelae compared to adults[3]. Over 200 symptoms have been associated with long COVID[4,5] in adults but the commonest symptoms in both adults and children are similar, especially fatigue and headache. Estimates of the prevalence of Long COVID in children and young people (CYP) vary. A UK survey of self-reported Long COVID in 320,825 people reported a prevalence of 0·16% for 2-11 years, 0·65% for 12-16 years, and 1·22% for 17-24 years[6]. A large national study of Long COVID in children, the CLoCk study,[1] found that at 3 months post COVID testing, 66.5% of CYP with a positive test, and 53.3% of CYP with a negative test still had symptoms, at least one of which was physical, whilst 30.3% and 16.2%, respectively, had 3 or more symptoms.

It is currently unclear whether Long COVID represents one or many different conditions and it has consequently been difficult to derive a universally accepted definition for the condition[7-14]. Definitions vary in the number and type of symptoms included, as well as the duration of symptoms[2,9,15-17]. Research into the prevalence and impact of Long COVID has consequently been hampered, thereby delaying the implementation of policies and services that could help affected CYP.

The Delphi process is a well-established method for achieving consensus amongst groups of key stakeholders on questions relating to health sciences. It has been used to identify outcomes of importance for a range of conditions[18-23], define metrics for monitoring the quality of provision of care in the NHS[24], develop a UK-wide pathway for managing CYP

[1] The term Long COVID is used throughout the manuscript as this was the term used in Delphi consensus process. The term is considered synonymous with Post-COVID-19 condition.

online Delphi process followed by an online consensus meeting to derive a definition for Long COVID in CYP that could be used for research to allow comparisons between studies.

METHOD

As per COMET[31], a three-phase online Delphi process followed by a consensus meeting was conducted (Figure 1). The scope of this consensus process was to develop a definition of Long COVID in CYP that could be used for research purposes. This definition was not intended to be used for the purposes of clinical referral, investigation or treatment.

Participants

People with relevant expertise were identified through published materials, clinical organisations, support groups and professional bodies. A combination of direct invitations to participate and invitations via existing mailing lists were used. Those confirming their interest in participating were categorised into three panels according to their area of expertise: (1) Service Delivery, (2) Research (or a combination of research and service delivery) and (3) Lived Experience.

Information sources

The survey consisted of 49 statements in eight categories, covering different areas of the definition of Long COVID in CYP (Table 2). These statements were developed on the basis of existing literature, including an unpublished systematic review (May 2021 – Lauren O'Mahoney, Leicester, personal communication), a NICE guideline on managing long effects of COVID-19[11], NHS advice on COVID-19[32], and empirical data from the CLoCk study[1].

scoring the statement 1-3 and <15% of participants scoring the statement 7-9. No statements were dropped or added between phases of the Delphi process.

Consensus meeting

Participants who completed all three phases of the Delphi process were invited to the consensus meeting in a purposive manner to achieve spread across the stakeholder groups. The meeting was held virtually (Zoom Video Communications, version 5.1.0), and was independently chaired by an expert in consensus methodology. Statements that had achieved 'consensus important' status in two or more panels at the end of the Delphi process were automatically discussed and voted upon for inclusion in the definition of Long COVID in CYP. Other statements could be promoted for discussion and scoring by the attendees as long as they had not met the threshold for 'consensus unimportant' status in two or more panels at the end of the Delphi process.

Those statements that 70% or more of the consensus meeting participants felt were important for inclusion in a research definition of Long COVID in CYP were incorporated into the definition.

Views of Children and Young People

In order to ensure the voices of CYP were heard, members of the PPI Research Advisory Group (RAG) for the CLoCk study were invited to attend a virtual meeting to review the statements upon which consensus importance was agreed at the main consensus meeting. The PPI RAG consists of 12 participants who have been recruited to reflect the age range of the

discussion at the consensus meeting by the study team. A total of 10 statements were therefore taken forward for discussion at the consensus meeting. Fifteen statements were defined as consensus unimportant in two or more panels and were therefore not eligible for inclusion in the definition. There was one or no panel consensus for the remaining 24 statements, none of which were promoted for discussion or voting at the consensus meeting by the study team or consensus meeting attendees (Table 2).

Consensus Meeting and the views of children and young people

Seventeen experts participated in the consensus meeting, four (23%) from the Service Delivery panel, eleven (65%) from the Researcher panel, and two (12%) from the Lived Experience panel. Following discussion and voting in the consensus meeting, five of the ten statements met the threshold for inclusion in the definition of Long COVID in CYP (Table 3). Detailed discussion was also held around excluding specific conditions, and there was agreement that it was important that the symptoms experienced by a child or young person needed to be attributable to Long COVID and not to another disease. However, it was also agreed that the definition should not require a particular test for a specific disease to be conducted for the purpose of ensuring that the symptoms were attributable to Long COVID.

Eight CYP from the PPI RAG attended a separate virtual session to discuss the Delphi consensus statements. There was broad agreement from the CYP with the statements that had been deemed consensus importance from the main consensus meeting (Table 3)

Included statements for the research definition of Long COVID in CYP

The included statements for a research definition of Long COVID in CYP were as follows:

To the best of our knowledge this is the first research definition for Long COVID among CYP. It is comparable to the clinical case definition in adults proposed by WHO (Box 1)[29]. The WHO additionally describes the typical symptoms in adults which are similar to those found in CLoCk [1]. It is reassuring that the domains (SARS-COV-2 confirmation test, burden of symptoms, persisting symptoms and duration) of this WHO definition overlap with our definition of Long COVID among CYP.

This study has both strengths and limitations. We would argue that that the provision of data from the CLoCk study to inform the process to supplement the literature review was innovative. Although the Delphi consensus process is designed to arrive at a definition in the absence of compelling data, the speed of research in the field meant that by the time the Delphi was in progress, such data were available but not in print and it therefore seemed appropriate to provide that information to participants. The Delphi methodology was robust and modelled on best-practice, with the consensus meeting led by an experienced and independent Chair. The views of CYP were considered; they voted on the inclusion of statements within the definition; and they were not dominated by adults in a face-to-face panel.

The study also had some limitations. In the final consensus meeting, only two individuals with lived experience were present. However, on no occasion did the participants with lived experience vote differently from the majority of the group. English language was selected and the study was performed primarily within the UK. Given that an aim is to derive a definition to allow international studies to be compared, representation from other countries, including non-English speaking and less developed countries, is desirable. Response rates were typical for studies of this type but there was attrition between rounds.

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Contributorship Statement

Terence Stephenson and Roz Shafran conceived the idea for the study, designed the study and drafted the manuscript

Benjamin Allin designed the study, contributed to and reviewed the manuscript

Manjula Nugawela conducted the statistical analyses for the manuscript and drafted the manuscript

Natalia Rojas supported the drafting of the manuscript and conducted the PPI meeting

Emma Dalrymple conducted the PPI meeting, contributed and reviewed the manuscript

Snehal M Pinto Pereira provided statistical input to the design, conducted the statistical analyses and reviewed the manuscript.

Manas Soni contributed to and reviewed the manuscript

Marian Knight Chaired the Consensus meeting, contributed to the design, contributed to and reviewed the manuscript

Emily Y Cheung supported the drafting of the manuscript and statistical analysis.

Isobel Heyman contributed to and reviewed the manuscript

All members of the CLoCk Consortium made contributions to the conception or design of the work.

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Table 2: Delphi Phase Three – Important and Less important statements for the definition of Post-COVID-19 condition

Statement Category	Statement	Important		Less Important	
		Three panel Consensus important	Two panel Consensus important	One or No panel Consensus important	Three or two panel Consensus unimportant
Testing	At least one positive COVID test		√		
	A positive PCR test for COVID			√	
	A positive lateral flow test for COVID				√
	An antibody test for COVID			√	
Type of initial symptoms	Before or at the time of their COVID test			√	
	During which time they had at least one recorded fever				√
	During which time they lost their sense of smell			√	
	During which time they lost their sense of taste				√
	During which time they had a persistent cough				√
	During which time they had headache				√
	During which time they had unusual tiredness			√	
	During which time they had a sore throat				√
Number of initial symptoms	1 symptom only at the time of testing				√
	2 or more symptoms at the time of testing			√	
	3 or more symptoms at the time of testing				√
	4 or more symptoms at the time of testing				√
	5 or more symptoms at the time of testing				√
Persisting physical symptoms	Persisting unusual tiredness			√	
	Persisting headaches			√	
	Persisting unusual shortness of breath			√	
	Persisting loss of smell or taste			√	

Burden of symptoms	The young person has symptoms that continue or develop after COVID-19 which impact their physical, mental or social-well-being.	√			
	The young person has symptoms that are interfering with some aspect of daily living (e.g., school, work, home, relationships)	√			
	The young person can judge the level of interference with their life themselves			√	
	The level of interference is assessed by a professional			√	
	The impact of the symptoms on functioning is at least moderate**		√		
Tests to exclude other disease	Persisting COVID antibodies				√
	A negative glandular fever (monospot, antibody or EBV PCR) test**		√		
	A normal full blood count			√	
	An abnormal full blood count				√
	A normal full blood count, CRP, ESR, urea and electrolytes, creatinine, calcium, liver function tests, random blood glucose**		√		
	A normal full blood count, CRP, ESR, urea and electrolytes, creatinine, calcium, liver function tests, random blood glucose, creatine kinase, thyroid function tests, coeliac disease screen, ferritin, vitamin D			√	

*Close to three panel consensus important
**Close to two panel consensus important
NOTE: Statements closer to three /two panel Consensus important were identified it the percentage of people in each panel rating 7-9 was closer to 70% and 1-3 was closer to <15%

A negative glandular fever (monospot, antibody or EBV PCR) test	0 (0%)	1 (13%)	Exclude
A normal full blood count, CRP, ESR, urea and electrolytes, creatinine, calcium, liver function tests, random blood glucose	0 (0%)	0 (0%)	Exclude
* One CYP was unable to vote due to technical problems			

Figure 1. Consensus process