

## Patient and public involvement within epidemiological studies of Long Covid in the United Kingdom

Routen, Ash ; O'Mahoney, Lauren L ; Aiyegbusi, Olalekan Lee; Alder , Yvonne ; Banerjee, Ami; Buckland, Lewis ; Brightling, Christopher E; Calvert, Melanie; Camaradou, Jenny ; Chaturvedi, Nishi ; Chong, Amy ; Dalrymple, Emma ; Eggo, Rosalind M.; Elliott, Paul; Evans, Rachael A ; Gibson, Andy; Haroon, Shamil; Herrett, Emily ; Houchen-Wolloff, : Linzy ; Hughes, Sarah

DOI:

[10.1038/s41591-023-02251-5](https://doi.org/10.1038/s41591-023-02251-5)

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*Document Version*

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*Citation for published version (Harvard):*

Routen, A, O'Mahoney, LL, Aiyegbusi, OL, Alder , Y, Banerjee, A, Buckland, L, Brightling, CE, Calvert, M, Camaradou, J, Chaturvedi, N, Chong, A, Dalrymple, E, Eggo, RM, Elliott, P, Evans, RA, Gibson, A, Haroon, S, Herrett, E, Houchen-Wolloff, L, Hughes, S, Jeyes, F, Matthews, K, McMullan, C, Morley, J, Shafran, R, Smith, N, Stanton, DE, Stephenson, T, Sterne, JAC, Turner, G, Ward, H & Khunti, K 2023, 'Patient and public involvement within epidemiological studies of Long Covid in the United Kingdom', *Nature Medicine*.  
<https://doi.org/10.1038/s41591-023-02251-5>

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1 **Patient and public involvement within epidemiological studies of Long Covid**  
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54 Several major epidemiological studies have been funded in the UK to better  
55 understand the epidemiology of persistent symptoms following SARS-CoV-2  
56 infection. Investigators from nine of these studies formed the National Long COVID  
57 Research Working Group in 2021 to share key findings and methodological  
58 developments, and explore ways of working across projects <sup>1</sup>.

59

60 Seven of these studies have substantively worked with diverse public and patient  
61 members and support groups, and have gone on to create patient involvement  
62 groups or panels specific to their research (Table 1). The large volume of patients  
63 living with Long Covid <sup>2</sup>, and the willingness of patients and support groups to  
64 engage with these studies, as well as the barriers of operating during periods of  
65 pandemic control measures have provided unique opportunities and challenges for  
66 patient and public involvement (PPI).

67

68 A particular example of the success of PPI is the Therapies for Long COVID in non-  
69 hospitalised individuals (TLC) study <sup>3</sup>, where patient partners identified the need to  
70 develop a new Symptom Burden Questionnaire™ for Long COVID (SBQ™-LC)<sup>4</sup>.

71 Patients with Long Covid were actively involved in the generation of item content for  
72 the SBQ™ and assisted with recruitment from Long Covid patient groups. The  
73 SBQ™-LC has since been licensed over 90 times across 50 countries. In addition to  
74 this important contribution, patient partners also actively co-produced a study to test

75 the feasibility and acceptability of delivering non-pharmacological, self-management  
76 interventions remotely in the community, shaping the study design and co-selecting  
77 intervention resources.

78 Advocacy and support groups have been invaluable to patients with Long Covid and  
79 a conduit for their involvement in research studies, through a diverse network of  
80 patients and carers with a wide range of lived experience. Members of these groups  
81 often assist with public engagement, which helps with the recruitment of study  
82 participants, as well as publicising events such as study webinars, the distribution of  
83 questionnaires, and dissemination of results. However, there is often a lack of  
84 diversity among patient contributors, who are often of similar age, sex, ethnicity,  
85 education level, and professional status. As a result, the CONVALESCENCE Long  
86 Covid study proactively recruited from under-served communities and included  
87 questions on equality and diversity in its PPI recruitment materials. Extensive training  
88 from the study PPI team was also provided so that patients felt qualified to contribute  
89 in areas such as quantitative data interpretation. When selecting patients, studies  
90 from the National Working Group have included a diverse PPI membership,  
91 delivering individualised training and discussions on preferences on involvement.

92

93 A particular area of learning regards the establishment of patient advisory groups  
94 (PAGs). Diversity of participants can be improved through recruitment from several  
95 PPI networks, avoiding recruitment from a single source. Clear pathways for inviting  
96 new members to join PAG's are needed to ensure that they are sustainable. It is  
97 important that PPI members receive regular updates and information on the project  
98 and are clearly informed of the purpose and importance of their involvement. PPI  
99 activities can be greatly strengthened, coordinated and made sustainable throughout

100 a project by a dedicated and trained PPI lead, which is a crucial role in long Covid  
101 research.

102

103 Researchers should continually revisit what different PPI members want to contribute  
104 and can contribute, based on skill set, interests, return to work and other  
105 commitments, and the restrictions that come with having a chronic condition with a  
106 relapsing and remitting nature where a main symptom is fatigue. Different studies, or  
107 different aspects of a study, may have different requirements of PPI members, or  
108 may benefit from PPI members with specific experiences, knowledge or skills.

109 Certain studies are more complicated, more cognitively challenging, or more  
110 demanding on PPI members' time than others. Studies can benefit from working with  
111 PPI members with significant knowledge and extensive experience of Long Covid, as  
112 well as PPI members who are able to attend and actively contribute to frequent  
113 meetings, in order to ensure effective PPI is ingrained throughout the study. This can  
114 include working on various aspects of the study such as study design, contributing to  
115 patient-facing materials, interpreting results, co-authoring papers and participating in  
116 public engagement events.

117

118 Researchers may not always be aware of how much PPI is needed to improve their  
119 research. Researchers should consider the experience, skills, and capabilities of  
120 each PPI member and what they want to contribute to, rather than this being  
121 decided, perhaps inappropriately, by the research team.

122

123 Patients with Long COVID often suffer from fatigue and can also experience some  
124 cognitive dysfunction, which may require adjustments as with any disability. PPI

meetings should be flexible (for example on timing and duration) and consider patient needs, with all materials and documents for review provided with sufficient advance notice. Other meeting adjustments should include the potential need for breaks and allowing cameras to be optional as PPI members may tire, be experiencing sensory or vision issues, or be concerned about appearing on camera.

The pandemic presented logistical challenges to working with patients on research due to strict public health measures such as social distancing. However, a rapid upskilling in the use of online communication technology has resulted in the studies from the Working Group having access to a wide range of patient contributors from across the UK. Although online PPI activities raise concerns around digital exclusion, studies such as CLoCk have found that online recruitment and virtual meetings helped achieve more representative geographical coverage and diversity from across the UK, both in terms of ethnicity and socioeconomic status.

The level of patient involvement we have experienced has undoubtedly strengthened the applicability and rigour of our findings, and increased public trust in the veracity of these studies. There remains a limited understanding on the causes of Long Covid and the development of effective treatments, and so placing patients at the heart of future research in this area continues to remain imperative <sup>5</sup>.

## **Acknowledgments**

Some of the studies described in this correspondence were jointly supported by the National Institute for Health Research and UK Research and Innovation (OpenPROMPT: Ref: COV-LT2-0073). The views expressed in this article are those

of the author(s) and not necessarily those of UKRI, the NIHR, or the Department of Health and Social Care.

### **Competing Interests**

MC receives funding from NIHR Birmingham Biomedical Research Centre, the NIHR Surgical Reconstruction and Microbiology Research Centre and NIHR ARC West Midlands at the University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, Health Data Research UK, Innovate UK (part of UK Research and Innovation), Macmillan Cancer Support, UCB and GSK Pharma; personal fees from Astellas, Aparito Ltd, CIS Oncology, Takeda, Merck, Daiichi Sankyo, Glaukos, GSK and the Patient-Centered Outcomes Research Institute (PCORI) outside the submitted work. OLA receives funding from the NIHR Birmingham Biomedical Research Centre (BRC), NIHR ARC West Midlands, NIHR Birmingham-Oxford Blood and Transplant Research Unit (BTRU) in Precision Transplant and Cellular Therapeutics, The Health Foundation, Innovate UK (part of UK Research and Innovation), Janssen Pharmaceuticals, Gilead Sciences Ltd, GSK, and Sarcoma UK; declares personal fees from Gilead Sciences Ltd, GSK and Merck outside the submitted work. AB has received research grants from Astra Zeneca, National Institute for Health and Care Research (including as CI of the STIMULATE-ICP study: COV-LT2-0043, European Union, British Medical Association; and is a Trustee of Long Covid SOS. CM receives funding from NIHR Surgical Reconstruction and Microbiology Research Centre (SRMRC), the NIHR Oxford-Birmingham Blood and Transplant Research Unit (BTRU) in Precision Therapeutics UKRI, and declares personal fees from Aparito Ltd outside the submitted work. SEH receives funding from the NIHR Oxford-Birmingham Blood and Transplant Research



Unit (BTRU) in Precision Therapeutics, UK Research and Innovation (UKRI), UK  
SPINE and declares personal fees from Cochlear Ltd, Astra Zeneca, CIS Oncology,  
and Aparito Ltd. NC has received funding from AstraZeneca to serve on Data Safety  
and Monitoring Committees for clinical trials. KK is a trustee of the South Asian  
Health Foundation, chair of the Ethnicity Subgroup of the Scientific Advisory Group  
for Emergencies (SAGE), and member of SAGE. PE, ED, SH, RS and TS receive  
funding from NIHR and UKRI. TS is Chair of the Health Research Authority and  
therefore recused himself from the CLoCk Research Ethics Application. RAE  
receives funding from NIHR, UKRI/MRC, BMJ and Wolfson Foundation.

**References**

1. Routen, A., *et al. Nature Medicine* **28**, 11-15 (2022).
2. O'Mahoney, L.L., *et al. eClinicalMedicine* **55**(2023).
3. Haroon, S., *et al. BMJ Open* **12**, e060413 (2022).
4. Hughes, S.E., *et al. BMJ* **377**, e070230 (2022).
5. Shaffer, L. *Proceedings of the National Academy of Sciences* **119**, e2213524119 (2022).
6. Houchen-Wolloff, L., *et al. Thorax* **77**, 717 (2022).

<b>Study</b>	<b>Number of patient advisors</b>	<b>Profile of participants</b>	<b>Regularity and location of meetings</b>	<b>Main outcomes</b>
CLoCK	13	All aged 11-17 years; 67% white; all deprivation deciles included	Online quarterly meetings	<ul style="list-style-type: none"> <li>• Delphi definition of Long Covid</li> <li>• Dissemination of findings</li> <li>• Changes to survey questions</li> <li>• Input into qualitative design</li> <li>• Input into data presentation</li> <li>• Long Covid artwork</li> <li>• Changes to newsletters</li> <li>• Awards for involvement</li> </ul>
CONVALESCENCE	12	Diverse social and ethnic backgrounds	5 training workshops and 7 tailored workshops; 2 PAG members attend quarterly executive meeting	<ul style="list-style-type: none"> <li>• Changes to questionnaires and other instrument design</li> <li>• Refinement of ethics</li> <li>• Communications</li> <li>• Materials development for internal and external use</li> <li>• Changes to researchers' interpretations of qualitative work</li> </ul>
TLC	15	Diverse in terms of age, ethnicity and employment status	Ongoing online opportunities throughout lifetime of project.	<ul style="list-style-type: none"> <li>• Identifying need for new Symptom Burden Questionnaire™ and need to survey patients about self-management strategies</li> </ul>

				<ul style="list-style-type: none"> <li>• Changes to recruitment strategy</li> <li>• Improved participant facing study materials</li> <li>• Coproduction of feasibility study</li> <li>• Co-selected pacing resources</li> <li>• Co-design of study processes and app testing</li> <li>• Supported community engagement and recruitment</li> <li>• Identified key messages for research outputs</li> <li>• Dissemination of research outputs</li> </ul>
REACT-Long COVID	13 (plus 161 members of REACT: COVID-19 Community Network)	9 women and 4 men. Diverse group that includes people with lived experience of Long Covid and participants in the original REACT studies.	Quarterly online meetings. Each advisor is allocated to one of four work streams for close working with researchers; community network send updates and involvement opportunities	<ul style="list-style-type: none"> <li>• Changes to questionnaire design</li> <li>• Improved participant-facing study materials</li> <li>• Interpretation of pilot qualitative findings</li> <li>• Involvement in publications and dissemination</li> <li>• Worked with researchers to establish an online research involvement hub on VOICE- Global</li> </ul>

PHOSP-COVID	50 advisors and 11 charities	Diverse group in terms of age, ethnicity, socioeconomic status, including patients and carers with lived experience of acute COVID-19 and Long COVID, including hospitalised and non-hospitalised	PPI embedded throughout all stages of project, with regular meetings depending on project needs, conducted via email, phone or teleconference	<ul style="list-style-type: none"> <li>• Input into study design and conduct</li> <li>• Joint Research Question Priority Setting <sup>6</sup></li> <li>• Improved participant facing study materials</li> <li>• Reviewed and tested new study processes</li> <li>• Public webinars and newsletters for dissemination</li> </ul>
STIMULATE-ICP	11	PPI advisory group represents social, ethnic and geographic diversity	PPI attendance at monthly consortium meetings and separate monthly PPI online team meetings	<ul style="list-style-type: none"> <li>• Involvement in research publications</li> <li>• Educational videos</li> <li>• PPI blog on study website</li> <li>• Media and social media engagement</li> <li>• Policy and other articles in non-scientific publications</li> <li>• PPI-led eBook about experience of Long Covid</li> </ul>
OpenPROMPT	3	PPI advisory group is comprised of 3 individuals, and OpenSAFELY Digital Critical Friends (DCF) Group, feeds into the group on specific issues	Online webinar at study start; PPI attendance at online OpenPROMPT meetings every 6 months, with additional email feedback on research plans;	<ul style="list-style-type: none"> <li>• Adaptations to study protocols</li> <li>• Improved public facing study materials</li> <li>• Co-designed public explainer materials for OpenSAFELY</li> </ul>

		related to the data collection platform	OpenSAFELY DCF online meeting every 3 months; Ad hoc PPI online focus groups on specific topics.	
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