NIHR/MRC Post-Infection Conditions Research Showcase

Current, new and future perspectives in ME/CFS and long COVID research

On 6 November, the National Institute for Health and Care Research (NIHR) and the Medical Research Council (MRC) co-hosted a research showcase to discuss and explore the ongoing research in the fields of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and long COVID at the Royal College of Physicians, London.

The event brought together research funders, commercial and academic researchers, clinicians, and patient representatives with lived experience of the conditions and was independently chaired by Dr Louise Wood, Chair of the Association of Medical Research Charities.

Recognising the importance of future research into ME/CFS and long Covid, the overall aims of the event included:

- Hearing from patients, charities, academia and industry to identify key gaps and important outstanding questions in ME/CFS and long COVID that require further exploration
- Providing an overview of the current state of research in ME/CFS and long COVID with a focus on future research opportunities and new avenues for investigation
- Facilitating collaboration and networking between researchers from diverse fields and disciplines, and generating discussion on how to build capacity and galvanise more research activity and collaboration in the field
- Spotlighting early career researchers in this field
- Highlighting the bespoke support available from NIHR and MRC for researchers in preparing applications

Format and Presentations

The morning session began with the personal experiences and journeys of two people with lived experience of these conditions - the first with ME and the second with long COVID. It was highlighted that research must be made inclusive to reach those who are worst-affected by illness, as they are most likely to be house-bound and unable to travel to participate in research. Speakers emphasised that lived experience should be regarded not only as a means to include patients and carers, but as a source of vital empirical evidence, such that patients should be involved from the first step of research planning to appropriately shape research questions and ensure relevance. This was followed by a series of presentations by senior researchers and a dedicated session for early career researchers to showcase the recent key research findings in this field of research.

Prof Danny Altmann from Imperial College London presented on immune mechanisms in long COVID and other post-viral sequelae. Despite common themes in research on the pathophysiology of post-viral sequelae with many biomarkers proposed, the lack of agreed biomarkers for diagnostics, public health, and study endpoints remain a major bottleneck.

Prof Amitava Banerjee from the University College London presented an overview of the STIMULATE-ICP programme of research involving patient experiences of long COVID clinics and the testing of drugs for the treatment of long COVID. He also highlighted the inequalities in receiving care and access to care amongst people living with long COVID.

Professor Manoj Sivan from the University of Leeds introduced the new Health Effects fRom Infection sequelae: Tailoring services and Advancing GuidancE (HERITAGE) study funded by NIHR. This new study aims to establish a national service framework (NSF) for long COVID and ME/CFS. The study also aims to establish the degree of diagnostic overlap between long COVID and ME/CFS as well as evaluating long-term clinical outcomes and considering the cost-effectiveness of different service models.

Prof Chris Ponting from the University of Edinburgh presented an overview and initial results from the DecodeME study, which identified eight genetic signals for ME/CFS involved in the nervous and immune systems.

Professor Dmitry Veprintsev from the University of Nottingham presented on the importance of identifying specific receptors (G-protein-coupled receptors) involved in ME/CFS, laying out an innovative methodology rooted in mapping patterns of drug-side effects against disease symptoms to identify potential disease pathways.

Charity and industry representatives also attended and spoke with passion to reinforce many of the key priorities in research - highlighting the urgent need to improve understanding of disease mechanisms, and to find evidence-based diagnostic tests and treatments for the growing numbers of patients with post-infectious conditions.

Finally, the funders NIHR and MRC presented a session to highlight the support that could be provided to researchers who are interested in building their careers in the field. The NIHR's Research Support Service and career development opportunities via the NIHR Academy were highlighted for career development funding and support for designing studies.

The afternoon session featured a series of roundtable discussions bringing together clinicians, researchers, charities, funders and patients to explore and discuss key issues. Insights from the afternoon session are summarised below.

The roundtable discussions centred around three questions:

1. What are the important outstanding research questions?
2. How can we encourage researchers to join the ME/CFS and long COVID field?
3. How can we enable new collaborations across specialties and disciplines to stimulate further vital research?

Key themes of the discussion

1. **Attracting new researchers into the field**
    - Funding opportunities specifically targeting ME/CFS and long COVID research, with requirements for the inclusion of new skills and disciplines into the field, were highlighted as a potential route to drive new activity.
    - Strong scientific leadership is needed to address the perceptions that the ME/CFS and long COVID pathway lacks professional viability for early career researchers.
    - Research culture change is needed to highlight opportunities for ME/CFS as a viable career trajectory and foster more collaboration across ME/CFS and long COVID researchers across a wider range of disciplines.
    - Raising public and academic awareness about the importance of these conditions might attract new research teams.
    - Development of training and mentorship programs for early-career researchers through the NIHR Academy and with the support of NIHR RSS would be valuable (see suggested next steps regarding NIHR RSS support).
    - Cross-disciplinary initiatives to make the field more accessible to researchers from diverse backgrounds should be promoted.

2. **Building a cross-disciplinary research community**
    - Researchers from fields such as immunology, neurology, psychology, and virology should be encouraged to work with the field to establish new research collaborations and initiatives. This will help to improve understanding of the complex biological, microbiological and immunological factors underpinning these diseases.

  - More collaboration is needed between the ME/CFS and long COVID research communities - some of the researchers were meeting and having cross-condition conversations for the very first time.
  - Increasing the representation of allied health professionals at future ME/CFS events was advised, alongside considering their role in research and the formal identification of 'better care' for ME/CFS.
  - There was an opportunity to reframe and rebadge research efforts, for example as "post-acute infection conditions," to combat stigma, attract broader support and build a cross-disciplinary research community.
  - Designing trials upfront with a multidisciplinary lens, including workstreams aligned to multiple disciplines, would be important. Funders have existing models for encouraging this (such as NIHR Team Science).

3. **Enhancing research collaborations**
   - The field requires a clear, interdisciplinary effort, bringing together clinicians, basic scientists, epidemiologists, methodologists, and allied health professionals. Partnerships with clinicians and patients are deemed essential for robust study design.
   - Establishment of a large, inclusive virtual research hub or network in the UK to unify and consolidate efforts, which could include holding annual events would be welcomed. The PRIME project recently funded through MRC was proposed as a potential basis for this network.
   - It was recognised that the community needs strong scientific, national leadership to drive collaboration, capacity building and cultural change.
   - Researchers could draw on existing funding routes like the MRC Partnership Grants, NIHR Incubator, and NIHR Team Science Awards.
   - The community were keen to explore with NIHR and MRC opportunities to maintain and evolve existing collaborations such as PHOSP and STIMULATE.

4. **Funding challenges and strategy**
   a. While the success rate for funding applications is comparable to other fields, the total number of proposals is lower. A perceived difficulty in securing funding for new fields lacking preliminary data was noted as a barrier to new proposals – routes to reassure and support the community on these points were needed. Delegates acknowledged funders' position that funding committees showed no evidence of bias but emphasised that concerns remained in the community regarding some peer reviewers' attitudes.
   b. Several attendees requested that MRC/NIHR provide targeted funding calls (for example, by identifying post-acute infection conditions as a theme within research infrastructure) and mandate collaboration in

funding applications to ensure equity and support building the growth and expertise of this research community.

c. A strategic approach from the community outlining the economic impact of ME/CFS and long COVID would illustrate the importance of this research for UK government, with the long-term ambition to ensure funding and awards secured are proportionate to the level of suffering of those living with the condition.
d. Sandpits bringing together clinicians and scientists to agree on priorities were suggested as a good mechanism/approach for future funding in the field.
e. Engaging with industry for diagnostics research was a key challenge tied to sector-wide barriers for diagnostic development – the importance and value of reliable diagnostic tools both for supporting patients and for enabling future research was clear.

5. Focus areas for future research

- **Characterising biological mechanisms:** Noting the exciting research presented at the meeting, major outstanding questions remained in the understanding of biological mechanisms underpinning ME/CFS and long COVID, which is vital for identifying targets for future interventions.
- **Diagnostic biomarkers:** There is a critical need for research to identify new biomarkers, coupled with a need for consensus on appropriate sets of accurate, reliable, and accessible diagnostic biomarkers to move beyond 'diagnosis by exclusion' and help monitor disease progression.
- **Case Definitions:** Beyond improved accuracy of diagnosis, better case definitions are required to understand the different patient pathways and potential disease subtypes within the population, to support both patient care and research.
- **Aetiology:** Observational work investigating risk factors, genetic disposition, and finding commonalities and differences across conditions to improve understanding, is needed.
- **Collaborative working**: To maximise impact and reduce the burden on patients, collaborative research initiatives, such as consortia or multi-institutional studies, should be prioritised, especially when leveraging existing data, biobank samples, and patient cohorts.
- **Data sharing and AI**: In parallel, it is vital to encourage the sharing of interoperable data and outcomes to build a collective, robust evidence base. There is a need for a good, structured data model for longitudinal tracking. The potential of AI, machine learning, and data science is recognised, but may require additional high-quality datasets for maximum benefit.

  - **Interventions and treatment approaches:** There is a need for clinical trials focusing on both pharmacological and non-pharmacological interventions, including the repurposing of drugs as possible new treatments. The NIHR EME drug repurposing call was discussed as a potential source of hope, and researchers were encouraged to submit applications to this NIHR development award. This development award is focussed on the feasibility of a phase 2 platform clinical trial that tests multiple repurposed pharmaceutical interventions and/or non-pharmacological interventions and devices. Researchers noted signs of institutional collaboration and translational investment, but concerns were raised about initiating a platform trial without clear phenotyping which may pose methodological challenges, as stronger foundational evidence is needed to ensure progress in the field.

Other research recommendations from the showcase

- **Public and Patient Involvement and inclusive research practices:** Lived experience contributors, particularly those with ME/CFS and long COVID, play a vital role in shaping the research agenda. These individuals are best positioned to inform the research process and help define what constitutes recovery and quality of life for ME/CFS and long COVID patients. Their involvement in all stages of the research process is therefore essential for ensuring that the research is relevant and impactful. Future studies should ensure inclusivity of both patients and public involvement (PPI) representatives. It is crucial that researchers continue to prioritise the voices of patients and their families. Researchers should be supported and encouraged in engaging with community groups ensuring that those with lived experience have meaningful input into research agendas, particularly to ensure those worst-affected by illness are included – research funders should ensure these issues are prominent in guidance to applicants and in consideration of future applications.

- **Interdisciplinary and international collaboration:** To address the multifaceted nature of ME/CFS and long COVID, interdisciplinary research teams should be encouraged to share knowledge and expertise. Cross-disciplinary collaborations, both within the UK and internationally, will drive innovation in the field. Collaborative efforts should extend beyond national boundaries, involving international teams in the pursuit of finding answers.

Concluding remarks

The event highlighted the pressing need for increased focus and collaboration in ME/CFS and long COVID research. Moving forward, continued engagement with inter-disciplinary teams, establishing wider networks, accessing research funding, engaging industry, making better use of existing data, and the involvement of lived experience contributors will be essential for addressing the unanswered questions in these fields.

Next steps

The NIHR and MRC remain committed to advancing research into post-acute infection conditions, including ME/CFS and long COVID, to improve treatment and management of these conditions. Building on discussions from this research showcase, both funders will continue to work to stimulate further vital research in this area. As part of this, the NIHR is assessing applications to the application development award on repurposed pharmaceutical and non-pharmacological interventions, and both the NIHR and MRC encouraged continued engagement from the community following the showcase event. The NIHR Research Support Service also offered to host workshops for researchers to support capacity building in the field.

The NIHR and MRC have a shared goal to strengthen research capacity and collaboration in this field through national infrastructure. Both also remain committed to funding high-quality research through established mechanisms, including partnerships with research charities where appropriate, ensuring continued progress and long-term capacity in this critical field.