PRIME – building infrastructure for **P**atients, **R**esearchers and **I**ndustry for **ME**/CFS

PRIME Workshop 2: The Similarities and Distinctions between Long Covid & ME/CFS

Friday 24th April, 2026 2-5pm GMT

Online: To register see link:

https://us02web.zoom.us/webinar/register/WN_qs_AubvvQzGxXcxiezFBag#/registration

General abstract:

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and post-acute sequelae of SARS-CoV-2 infection (Long Covid) are complex, multisystem conditions with substantial symptom overlap and marked functional impairment. Epidemiological studies indicate that approximately two-thirds of individuals with ME/CFS report a preceding acute infection, most commonly viral, prior to symptom onset. Long Covid is defined by the persistence or emergence of symptoms for at least 12 weeks following acute SARS-CoV-2 infection, providing a clearly identified infectious trigger. Both conditions share core clinical features, including post-exertional malaise, disabling fatigue, cognitive dysfunction, sleep disturbance, autonomic symptoms, and pain, suggesting overlapping pathophysiological pathways.

Important distinctions between the two diseases remain. ME/CFS is a heterogeneous syndrome that can follow non-infectious triggers, whereas Long Covid is, by definition, post-viral. In addition, certain symptoms, such as anosmia and prominent respiratory complaints, are more prevalent in Long Covid, particularly early in the disease course.

This workshop will critically examine similarities and distinctions between ME/CFS and Long Covid across clinical, biological, and research frameworks, with the aim of leveraging insights from both fields to inform diagnosis, stratification, and therapeutic development.

Speakers:

- **Danny Altmann** – Professor of Immunology, Imperial College Faculty of Medicine
- **Andy Malinowski** – VP Disease Biology, PrecisionLife
- **Amy Proal** – CEO/Research Director, PolyBio Research Foundation
- **Manoj Sivan** – Professor & Honorary Consultant in Physical & Rehabilitation Medicine, Univ. Leeds
- **Nisreen Alwan** – Head of the Centre for Population Health Sciences and Professor of Public Health at the University of Southampton

Programme: **Talks 20mins + 10mins questions**

2-2.05pm
Welcome from the Chair (Prof. David Price)

2.05-2.35pm

Talk 1: Rosetta Stone - a new study funded by the ME Association to characterise shared pathways between ME/CFS and Long Covid
Danny Altmann – Professor of Immunology, Imperial College Faculty of Medicine.

2.35-3.05pm

Talk 2: Genetic Commonalities between ME/CFS and Long COVID: Insights from Combinatorial Analysis **Andy Malinowski** – VP Disease Biology, PrecisionLife.

3.05-3.35pm

Talk 3: Long COVID and ME/CFS: why persistent infections matter
Amy Proal – CEO/Research Director, PolyBio Research Foundation.

3.35-3.50pm - BREAK

Chair (Dr. Caroline Dalton)

3.50-4.20pm

Talk 4: The overlapping clinical syndromes of Long COVID and ME/CFS
Manoj Sivan – Professor & Honorary Consultant in Physical & Rehabilitation Medicine, Univ. Leeds.

4.20-4.50pm

Talk 5: What is the role of the 'case definition' in shaping the research and health inequalities landscapes of ME/CFS and Long Covid?
Nisreen Alwan – Head of the Centre for Population Health Sciences and Professor of Public Health at the University of Southampton.

4.50-5.00pm - Concluding Remarks

Abstracts of all of the talks can be found below.

Speaker Bios:

Danny Altmann is Professor of Immunology at Imperial College London, where he heads a lab at the Hammersmith Hospital Campus. He acted in a range of roles during the pandemic in advice to policymakers, including the House of Commons and House of Lords Science Committees, advice to the Cabinet Office, to Sir Keir Starmer and the Shadow Cabinet, the Welsh Assembly, the EU, The Scottish Parliament, WHO, NICE and the Department of Health. He has served for over 25 years as Editor across medical journals including Oxford Open Immunology, Immunology, and Vaccine. He is a trustee at Long Covid Support and co-author of the Penguin Long Covid Handbook. He previously headed up strategy on infection, immunity and population health at the Wellcome Trust. Professor Altmann's research interests focus on the immunology of infectious diseases including severe bacterial infections, SARS-CoV-2, Zika virus and Chikungunya virus, as well as a long record in autoimmunity research. His SARS-CoV-2 research is published in journals including the Lancet, Nature and Science. He is currently heading a research programme to look at pathogenesis of Long Covid.

Andy Malinowski, PhD is a Principal Disease Biologist at PrecisionLife where Andy develops drug discovery programs for genetics-derived targets linked to specific patient subgroups within chronic diseases. With a background in stem cells and epigenetics, Andy has held positions at Novo Nordisk, Helmhzentrum München, Imperial College London, and MRC London Institute of Medical Sciences, focusing on areas such as genomics, pharmacology, and cell signalling. Their work includes creating in vitro models, effect testing of small molecules/ligands, and studying cell-cell communication.

Amy Proal, PhD, is a leading microbiologist redefining how the medical and scientific communities understand chronic Lyme disease, post-treatment Lyme disease (PTLD), and other infection-associated chronic illnesses. Her work focuses on the molecular mechanisms by which persistent pathogens disrupt immune function, gene expression, metabolism, and neurological signalling, leading to long-term, debilitating symptoms. Dr. Proal is widely recognized for advancing the concept that many chronic illnesses traditionally labelled as "autoimmune" or "idiopathic" may instead be driven by ongoing, hidden infection and immune dysregulation.

Dr Manoj Sivan MD FRCP (Ed) is an academic physician in Physical and Rehabilitation Medicine (PRM) with the University of Leeds and Leeds Teaching Hospitals NHS Trust. Sivan is the Chief Investigator of NIHR health service research studies LOCOMOTION (for LC) and HERITAGE (for LC & ME/CFS). Sivan manages patients with LC and ME/CFS in Leeds Teaching Hospitals NHS Trust and Leeds Community Healthcare NHS Trust. He served as a WHO advisor and consultant for leading the response to LC in the Europe Region. He developed the C19-YRS (Yorkshire Rehabilitation Scale), a patient-reported outcome measure translated into >40 languages and recommended by NICE and NHS England. He developed the use of a 10-minute Lean Test in clinics for diagnosing autonomic dysfunction and orthostatic intolerance in both conditions.

Prof Nisreen Alwan is Head of the Centre for Population Health Sciences and Professor of Public Health at the University of Southampton. She is an Honorary Consultant in Public Health at University Hospital Southampton NHS Foundation Trust. She does research around how to prevent disease and optimise the wellbeing of young families leading to better long-term health and focusing on narrowing health inequalities. Prof Alwan has contributed to the public health response to the pandemic, particularly focusing on the recognition and the quantification of morbidity from COVID19, having initiated the call to Count 'Long COVID'. She is now doing research on Long Covid particularly focusing on inequalities in prevention, recognition and care. Prof Alwan qualified in Medicine and obtained the membership of the Royal College of Physicians (MRCP UK). She then pursued a career in Public Health Medicine by obtaining a Master of Public Health (MPH) from the University of Nottingham and then joining the Public Health

Specialist Training Programme in the Yorkshire and Humber Region. During that time, she secured a Wellcome Trust Research Training Fellowship based at the University of Leeds, obtaining an MSc in Statistical Epidemiology and a PhD in Nutritional Epidemiology as part of that. She is a Fellow of the UK Faculty of Public Health (FFPH).

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Abstracts of Talks:

Talk 1: Rosetta Stone - a new study funded by the ME Association to characterise shared pathways between ME/CFS and Long Covid
Danny Altmann – Professor of Immunology, Imperial College Faculty of Medicine.

Long Covid (LC) is a multi-system, multi-organ disease comprising persistent symptoms still present 12 weeks after the SARS-CoV-2 viral infection and often, continuing for years. It has triggered renewed focus on the wider question of post-viral sequelae, notably, similarities to ME/CFS - another poorly characterised, post-infectious disease. Current estimates are of a prevalence of around 2M in the UK with Long Covid and 1.25M with ME/CFS. Together, they comprise a considerable disease burden and challenge to healthcare and an estimated loss to the economy of >3% of the contributory workforce. There are several mechanistic similarities between LC and ME/CFS, arguing for added value from a bespoke study encompassing detailed, side-by-side, mechanistic comparisons. Interestingly, passed studies have sometimes highlighted identical mediators implicated in both diseases. Our objective in this new study is thus to look for mechanistic disease correlates at a cellular and molecular level, side-by-side in well-characterised existing cohorts with LC and ME/CFS compared to healthy controls. The aim is to inform disease mechanism, offer therapeutic candidates and supply serum markers to be used in diagnostic and prognostic pathways and in the stratification of clinical trials. We will compare four groups: those with ME/CFS, LC, COVID-19 with full recovery within 4wk and pre-COVID-19 healthy controls. Participants will donate blood, saliva and stool samples offering the opportunity to interrogate proteomic, autoantibody, gut microbiota, T cell function and metabolism, and herpesvirus reactivation to explore similarities and differences between groups. Analysis of these datasets will allow us to better understand: whether sensitive assessment of serum proteins (proteomics) offer disease correlates and clinically useful diagnostic biomarkers? Whether analysis of immune function including autoimmunity offers correlates of disease, clues as to mechanism

and points the way to new treatments? And, what is the role of immune responses to reactivated herpesviruses in these diseases? Finally, are any shared disruptions to the gut microbiota (gut bacterial communities) implicated in both conditions?

Talk 2: Genetic Commonalities between ME/CFS and Long COVID: Insights from Combinatorial Analysis
Andy Malinowski – VP Disease Biology, PrecisionLife.

PrecisionLife (PL) is a precision medicine company developing personalised diagnostic tools and treatment strategies for complex chronic diseases. Using combinatorial analysis, PL stratified ME/CFS and Long COVID patients into subgroups defined by specific genetic drivers, revealing shared genetic patterns between the two diseases—and reproducing them across multiple cohorts (UK Biobank, Sano GOLD, All of Us, and DecodeME) and ancestries. These findings indicate common biological pathways (and some differences), enabling novel diagnostic approaches and targeted drug repurposing to address subgroup-specific mechanisms, thereby accelerating therapeutic development for both diseases.

Talk 3: Long COVID and ME/CFS: why persistent infections matter
Amy Proal, PhD, CEO/Research Director, PolyBio Research Foundation

Long COVID is condition in which individuals develop chronic symptoms after infection with the SARS-CoV-2 virus. Similarly, ME/CFS cases often begin after an infection and/or patient symptoms can be exacerbated by infectious exposures over time (1). In Long COVID and ME/CFS cases, the specific infections that initiative or exacerbate symptoms are important to disease pathogenesis. That is because growing evidence supports research showing that, in at least a subset of patients with a Long COVID or ME/CFS diagnosis, the pathogens that initiate symptoms may persist in patient tissue as a "reservoir," where they can drive inflammation, mitochondrial dysfunction and other issues (2). For example, SARS-CoV-2 RNA and protein has been identified in Long COVID gut tissue months to years after initial infection, associated with inflammation. Similarly, ME/CFS cases have been linked to persistent enterovirus infection in tissues such as the gut and brain (3, 4), or to bacterial infections such as Babesia (5), that can drive symptoms such as fatigue, post-exertional malaise, and others required to meet ME/CFS diagnostic criteria. This talk will overview research on persistent infection in Long COVID and ME/CFS, and discuss why - if such infections matter in disease pathogeneses - improved testing to diagnose the infections, and stratification of patients into specific treatment groups based on infectious burden and history - are imperative.

References:
1. Proal A, Marshall T. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome in the Era of the Human Microbiome: Persistent Pathogens Drive Chronic Symptoms by Interfering With Host Metabolism, Gene Expression, and Immunity. Front Pediatr. 2018 Dec 4;6:373. doi:10.3389/fped.2018.00373. PMID:30564562
2. Proal AD, VanElzakker MB, Aleman S, Bach K, Boribong BP, Buggert M, et al. SARS-CoV-2 reservoir in post-acute sequelae of COVID-19 (PASC). Nat Immunol. 2023 Oct;24(10):1616-1627. doi:10.1038/s41590-023-01601-2
3. Chia JKS, Chia AY. Chronic fatigue syndrome is associated with chronic enterovirus infection of the stomach. J Clin Pathol. 2008 Jan;61(1):43-48. doi:10.1136/jcp.2007.050054. PMID:17872383

4. O'Neal AJ, Hanson MR. The enterovirus theory of disease etiology in myalgic encephalomyelitis/chronic fatigue syndrome: a critical review. Front Med (Lausanne). 2021 Jun 18;8:688486. doi:10.3389/fmed.2021.688486. PMID:34222292

5. Breitschwerdt EB, Maggi RG, Bush JC, Kingston E. Babesia and Bartonella species DNA in blood and enrichment blood cultures from people with chronic fatigue and concurrent neurological symptoms. Pathogens. 2025 Dec 19;15(1):2. doi: 10.3390/pathogens15010002. PMID: 41598986

Talk 4: The overlapping clinical syndromes of Long COVID and ME/CFS
Manoj Sivan – Professor & Honorary Consultant in Physical & Rehabilitation Medicine, Univ Leeds.

Several studies have explored the overlap between Long COVID (LC) and ME/CFS. A study of 465 non-hospitalized LC patients assessed them at a mean of 70 weeks after infection and found 58% of LC patients met ME International Consensus diagnostic criteria for CFS/ME.[1] The most common overlapping symptoms were fatigue in 78 %, myalgias in 59 % and cognitive disturbances in 58 % of participants. Another study assessing LC patients at a median of 255 days after initial SARS-CoV-2 infection found 31 % of LC patients met CFS/ME criteria (the Canadian Consensus Criteria CCC).[2] A study of 106 LC patients at a mean of 20 months after initial SARS-CoV-2 infection, showed 55 patients (52%) met the CCC criteria for CFS/ME.[3] The clinical improvement trajectories were better in the non-ME/CFS group compared to ME/CFS group. These studies involved only LC patients, highlighting the need to do further longer-term studies involving separate cohorts for both conditions and estimating the true overlap between the conditions.

The Health Effects of Infection sequelae: Tailoring services and Advancing GuidancE (HERITAGE) NIHR study (2026-2028) is a multisite mixed-methods study studying various aspects of health services related to these conditions. One of the HERITAGE project aims is to study the overlap between conditions and trajectories in both LC and ME/CFS. We will collect outcome data using the condition-specific PROMS [Yorkshire Rehabilitation Scale for LC and DePaul Symptom Questionnaire DSQ-SF and FUNCAP for ME/CFS] 3-monthly from all participants using the DPROM digital platform we developed in the NIHR LOCOMOTION study.[4] We will collect data related to NICE diagnostic criteria for LC and ME/CFS and also collect prospective data from long-term ME/CFS patients, enabling the collection of comparable data from both conditions. We will estimate the overlap between symptoms and estimate the prevalence of participants meeting the criteria for both conditions.

References

1.   Jason LA, Dorri JA. ME/CFS and Post-Exertional Malaise among Patients with Long COVID. *Neurology International*. 2023; 15: 1-11.
2.   Reuken PA, Besteher B, Finke K, et al. Longterm course of neuropsychological symptoms and ME/CFS after SARS-CoV-2-infection: a prospective registry study. *Eur Arch Psychiatry Clin Neurosci*. 2024; 274(8): 1903-10.
3.   Legler F, Meyer-Arndt L, Modl L, et al. Long-term symptom severity and clinical biomarkers in post-COVID-19/chronic fatigue syndrome: results from a prospective observational cohort. *EClinicalMedicine*. 2023; 63: 102146.
4.   Sivan M, Lawrence R, O'Brien P. A Digital Patient Reported Outcome Measures platform for Long Covid (DPROM-LC): user-centred development and technical description. *JMIR Preprints*. 2023; 48632.

Talk 5: What is the role of the 'case definition' in shaping the research and health inequalities landscapes of ME/CFS and Long Covid?
Nisreen Alwan – Head of the Centre for Population Health Sciences and Professor of Public Health at the University of Southampton.

In this talk, I will delve into the similarities and differences of how we define LC and ME/CFS in research and how the different methods of classifying, analysing and reporting the data play a role in shaping what we term as the evidence-based policy and practice dictating the clinical care, support and public health approach to these conditions, including addressing the health inequalities associated with them. A flavour of some of what I would talk about is communicated in this piece: The Stigma of self-report in health research: Time to reconsider what counts as "Objective" | PLOS Global Public Health