Key Messages Summary: ME Genetics Breakthrough

Paper (preprint): Identification of Novel Reproducible Combinatorial Genetic Risk Factors for Myalgic Encephalomyelitis in the DecodeME Patient Cohort and Commonalities with Long COVID.

Find the full preprint paper here: https://precisionlife.com/locome-preprint

Important Dates

Embargo lifted: 7AM GMT, 4 December 2025

Summary

Groundbreaking myalgic encephalomyelitis (ME, also known as ME/CFS) genetics study identifies over 250 core genes associated with the disease in three independent patient cohorts, reveals shared biology with long COVID, and highlights many new drug repurposing candidates.

New analysis by PrecisionLife of UK Biobank and DecodeME data reveals more than 250 genes associated with ME risk involving at least four major disease mechanisms. These findings deepen our understanding of the complex biological processes involved in this serious condition.

They also show clear areas of overlap with long COVID biology, with 76 genes linked to both conditions. The study provides a more detailed framework for exploring ME's underlying mechanisms and points to several potential avenues for repurposing existing medicines in more targeted, stratified ways, which may in the future make clinical trials faster and more likely to succeed.

These results offer a foundational step toward building a biological map of ME - one that we hope researchers will continue to develop.

Key Findings

The study's findings provide a substantially deeper level of insight into the genetic risk factors and biology of ME that will have significant importance for the delivery of clinical care to patients.

1. **This is the most detailed genetic map of ME to date, reinforcing that it has a clear biological and genetic basis and is a serious chronic disease affecting multiple systems in the body**
    - 259 core genes found to be strongly associated with ME in multiple datasets, including 255 novel genes not previously linked to the disease.
    - 7,555 unique SNPs were found to be associated with ME across three independent patient cohorts.
    - ME is highly polygenic and heterogeneous, pointing to four potentially key mechanisms implicated in the disease etiology – neurological dysregulation, inflammation, cellular stress response and calcium signaling – which are well-understood targets for drug development.
    - The findings support that tests to identify the mechanisms relevant to an individual patient will be helpful in better targeting clinical trials and identifying potential treatments.
2. **Drug repurposing opportunity is substantial**
    - The analysis identifies dozens of genes that might potentially be targeted by pre-existing drugs that could be repurposed for ME
    - Identifying drugs via genetic techniques is a fast and cost-effective way of testing whether existing medicines might be beneficial to ME and/or long COVID patients.
3. **Strong genetic overlap between ME and long COVID**
    - 76 of 180 long COVID genes previously identified by PrecisionLife are also significantly associated with ME in DecodeME.

- The study indicates a partial genetic overlap, suggesting some shared biological mechanisms, while also confirming that the two conditions remain distinct. This is consistent with the lived experience of a subset of people with long Covid whose symptoms resemble those of ME.

4. **Mechanism-based biomarkers may enable precision medicine approaches for ME**
    - In the future, stratification of patients by their specific disease mechanism will be critical to developing accurate diagnostic tests and predicting which patients will benefit from which therapies.
    - The study's findings and other related results support the development of mechanism-based tests using simple genotyping arrays to stratify patients by disease mechanism, potentially enabling targeted recruitment and treatment selection for repurposed and novel therapies.

Quotes

Dr Steve Gardner, CEO of PrecisionLife:
"These results reinforce that ME has a clear biological and genetic basis and is a complex multisystemic disease. ME is highly polygenic and heterogeneous, so no single drug will help everyone. Stratifying patients by the mechanisms that are driving their disease will be essential for predicting who will benefit from which therapies and for developing accurate diagnostic tests. We're beginning to have this level of insight, and we hope that in the future the genetic biomarkers we've identified for existing and new drug repurposing candidates could help make trials with collaborators worldwide more successful."

Sonya Chowdhury, CEO of Action for ME:
"These findings offer further hope to people with ME around the world. For decades, people affected by ME have lacked recognition, access to proper diagnosis and effective treatments. PrecisionLife's results represent a major step forward in understanding the biology of the disease and provide real opportunities for targeted therapies to move into clinical testing. We are proud that DecodeME has helped pave the way for this progress, and we will continue to champion research that delivers meaningful benefits for the community."

Prof Chris Ponting, Chair of Medical Bioinformatics at the Institute of Genetics and Cancer, University of Edinburgh, and investigator on the DecodeME study:
"DecodeME was designed to reveal the complex genetics of ME by providing a dataset of the scale and quality required for robust discovery. PrecisionLife has shown how making such datasets available can quickly generate new insights into ME disease biology. This is an exciting outcome of making consented DecodeME data available to research partners and we look forward to enabling further future collaborations."

Helen Baxter, Patient Advocate and PPI Representative:
"These results greatly enhance our understanding of the biology of ME and present opportunities for drug repurposing which affords hope to the millions of people living with ME and long COVID around the world."

Background

- ME and long COVID affect an estimated 400 million people globally, contributing to more than $1 trillion annually in healthcare costs and lost economic productivity[1].
- A subset of people with Long Covid - around half, according to emerging estimates - appear to meet the diagnostic criteria for ME, including experiencing post-exertional malaise
- There are no approved diagnostic tests and no therapies that target the diseases' underlying causes. A major barrier has been their biological heterogeneity and lack of reproducible genetic evidence.

[1] Al-Aly, Z., Davis, H., McCorkell, L. *et al.* Long COVID science, research and policy. *Nat Med* **30**, 2148–2164 (2024). https://doi.org/10.1038/s41591-024-03173-6

- The DecodeME study, the world's largest ME cohort, provides the scale needed to identify reproducible genetic patterns.
- PrecisionLife's combinatorial analytics approach uncovers biological mechanisms that GWAS cannot detect, revealing the full complexity of ME and enabling precision medicine approaches.

What these findings mean:

- Biopharma and research organizations can engage ME and long COVID with more confidence because of increased evidence of the biological pathways and targetable mechanisms underpinning the diseases.
- Repurposed drug trials are likely to benefit from enrichment of genetically matched responders, meaning trial cohorts can be smaller, faster to recruit, and more likely to succeed.
- There is the potential for effective precision medicine therapies to be developed for ME and long COVID patients.

These studies were funded in part by Innovate UK as part of the LOCOME (LOng COvid and Myalgic Encephalomyelitis) project, led by PrecisionLife with contributions from Action for ME and the Human Genetics Unit at the University of Edinburgh and input from the Patient and Public Involvement (PPIE) Group throughout.

This work uses data provided by patients and collected by the NHS as part of their care and support, for which we are also grateful. People with ME and with long Covid and ME shared their views and experiences to help shape the LOCOME project from start to finish. The project's progress was only possible thanks to the thousands of DecodeME participants who generously provided their samples.

About PrecisionLife

PrecisionLife is a UK-based precision medicine company transforming how complex chronic diseases are understood and managed. Its AI-led combinatorial analytics platform identifies the specific mechanisms that drive disease in heterogeneous patient populations – providing insights that often cannot be detected using traditional GWAS methods.

PrecisionLife has undertaken multiple landmark studies in ME and long COVID, including the first large-scale genetic analyses to reveal reproducible disease mechanisms and clinically actionable patient subgroups. Through the LOCOME project, PrecisionLife has now completed the most detailed genetic analysis of ME ever performed, identifying over 250 core genes associated with the disease and revealing clear areas of biological overlap with long COVID.

Across these projects, PrecisionLife is working with partners including Action for ME, the DecodeME team and leading academic researchers to build the evidence base needed for future mechanism-matched diagnostic tests, targeted repurposing trials and precision therapies for people living with ME and long COVID.

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