

Decode

The ME/CFS Study



Overview & Initial Results

30 October 2025

A partnership between



THE UNIVERSITY
of EDINBURGH

**ACTION
FOR
M.E.**



MRC Human
Genetics
Unit

NIHR | National Institute
for Health Research

Summary

1. Why ME/CFS Genetics?
2. How we got here
3. DecodeME results
4. What do they mean?
5. Why a National ME Research Strategy is Essential

Why ME/CFS genetics?

(1) “We estimate that selecting genetically supported targets could double the success rate in clinical development”

(2) Unbiased and comprehensive

Not rooted in necessarily known biology

Can pinpoint relevant bodily system

The support of human genetic evidence for approved drug indications

Matthew R Nelson¹, Hannah Tipney², Jeffery L Painter¹, Judong Shen¹, Paola Nicoletti³, Yufeng Shen^{3,4}, Aris Floratos^{3,4}, Pak Chung Sham^{5,6}, Mulin Jun Li^{6,7}, Junwen Wang^{6,7}, Lon R Cardon⁸, John C Whittaker² & Philippe Sanseau²

SYMPTOMS OF ME/CFS

ME/CFS (myalgic encephalomyelitis/chronic fatigue syndrome) affects several systems throughout the body and commonly develops following infection. Not everyone has the same symptoms or to the same severity, but some common symptoms are listed below.

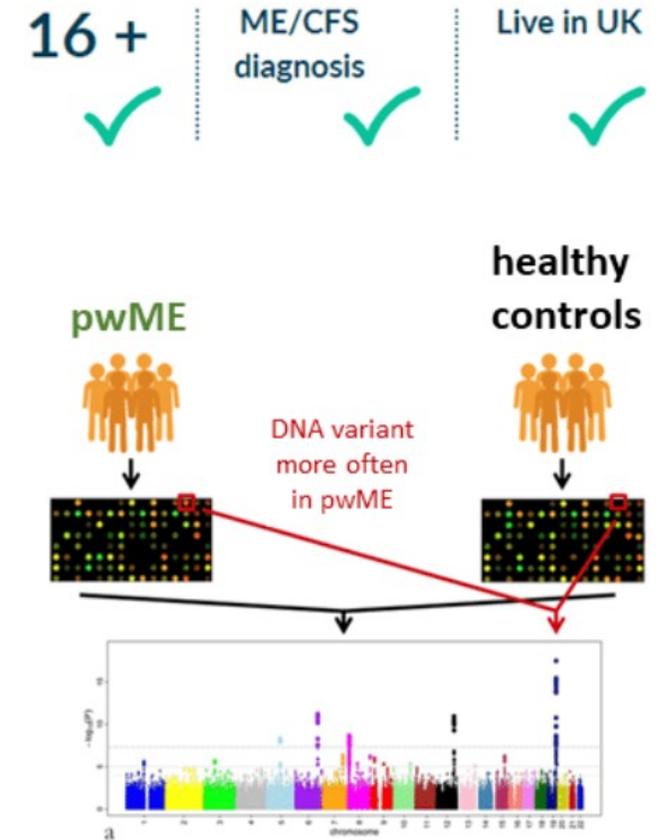
- MUSCLES & JOINTS**
 - Muscle pain
 - Joint pain
 - Post-exertional fatigue
 - Chronic fatigue
- CENTRAL NERVOUS SYSTEM**
 - Brain fog
 - Post-exertional malaise
 - Memory issues
 - Concentration difficulties
 - Headaches
 - Sleep dysfunction
- NEUROENDOCRINE SYMPTOMS**
 - Heat/cold intolerance
 - Marked weight gain/loss
 - Reduced stress tolerance
- THE IMMUNE SYSTEM**
 - Flu-like symptoms
 - New sensitivities
 - Tender lymph nodes
 - Sore throat
- AUTONOMIC SYMPTOMS**
 - Orthostatic intolerance
 - Vertigo
 - Palpitations
 - Irritable bowel syndrome
 - Bladder dysfunction

SCIO - SC036942

How we got here

Objectives:

1. Identify genetic differences in people with ME/CFS, to start to explain the biological mechanisms behind the disease.
 2. Build a clearly defined cohort of people with ME/CFS for future research.
 3. Disseminate the data to academics and industry.
- **Co-produced** with the ME/CFS community.

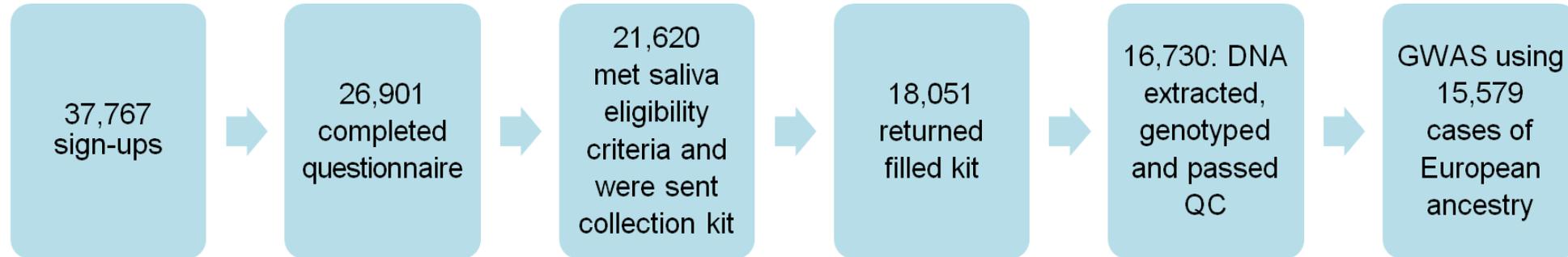


Decode ME
The ME/CFS Study

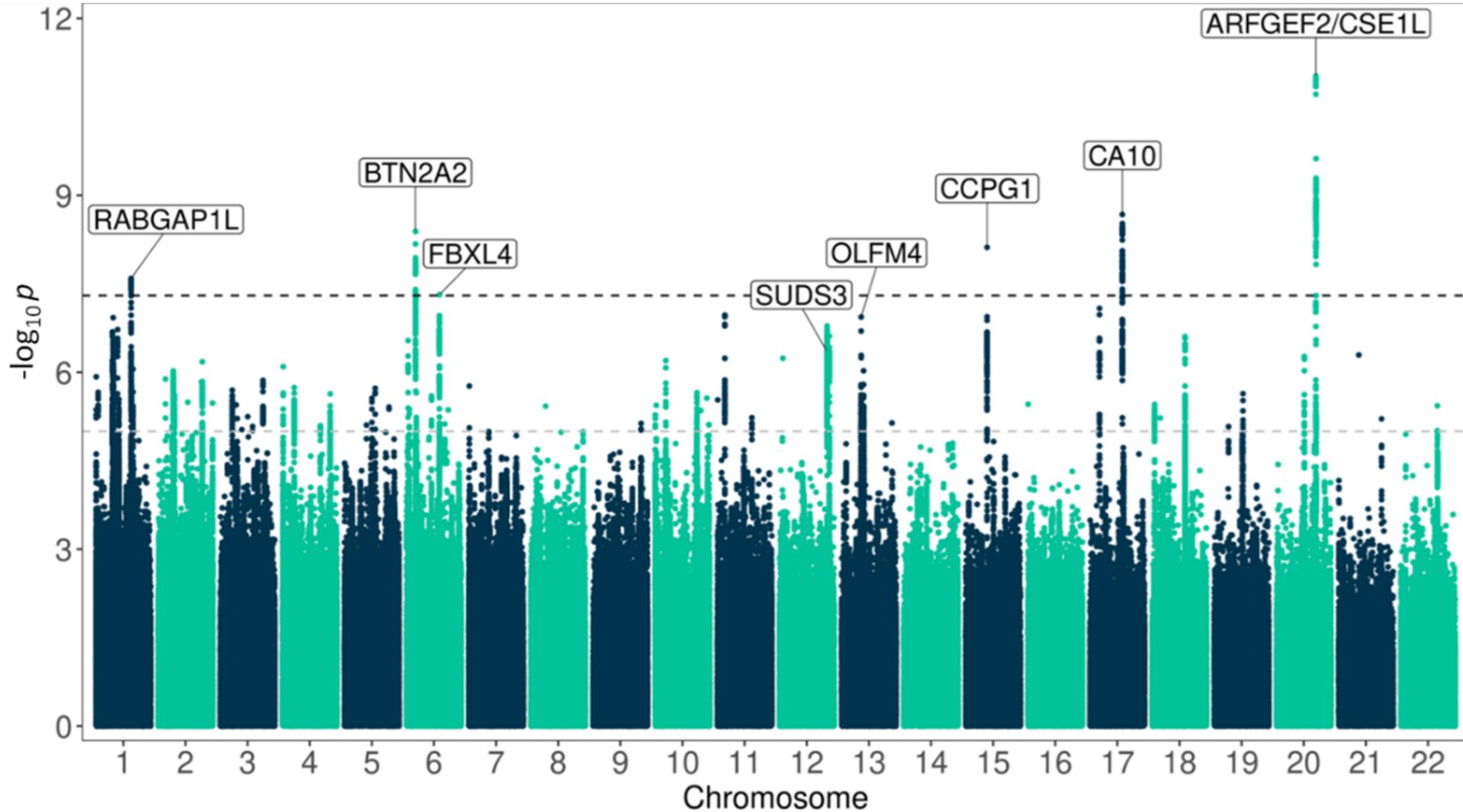
16 +
✓

ME/CFS
diagnosis
✓

Live in UK
✓

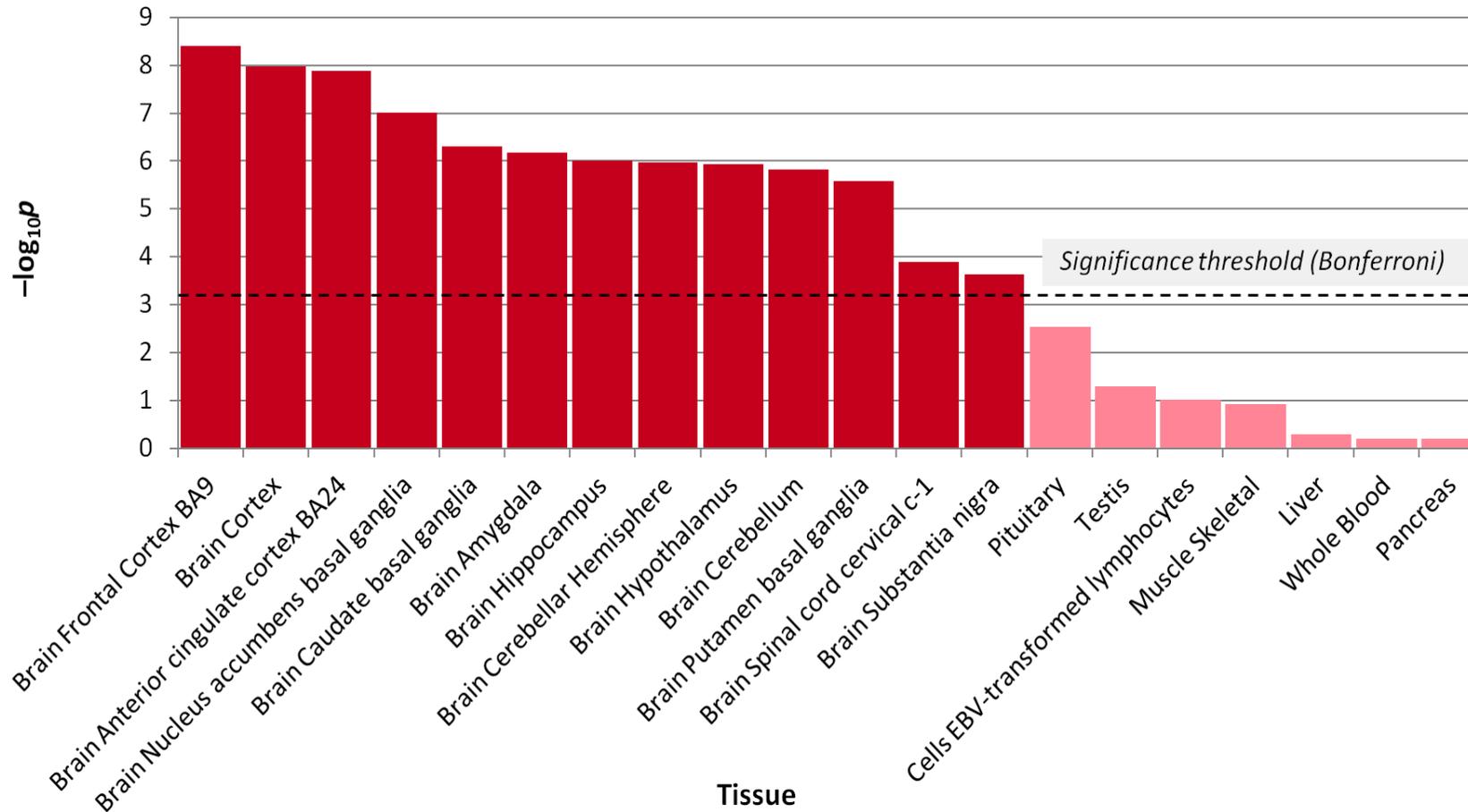


DecodeME discovered **eight genetic signals**



Genome-wide significant

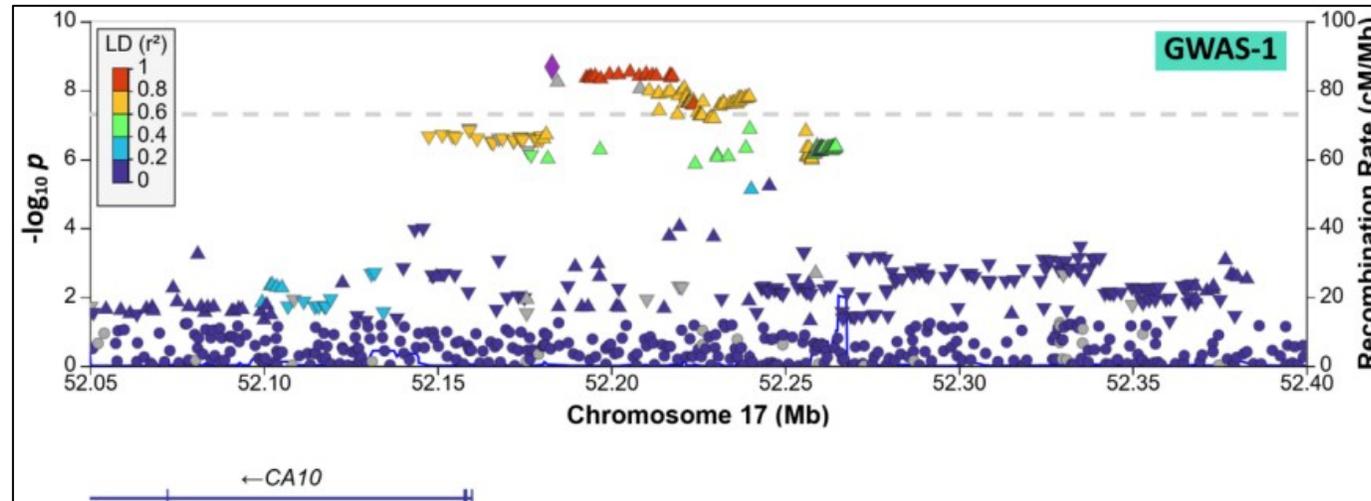
Nervous system involvement



MAGMA gene-tissue analysis shows statistically significant enrichment of ME/CFS-related genes in all 13 brain tissues

Nervous system involvement

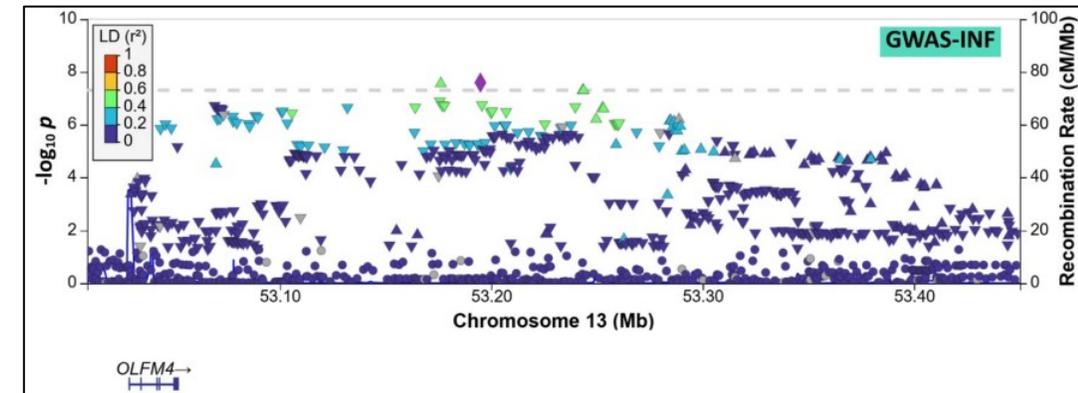
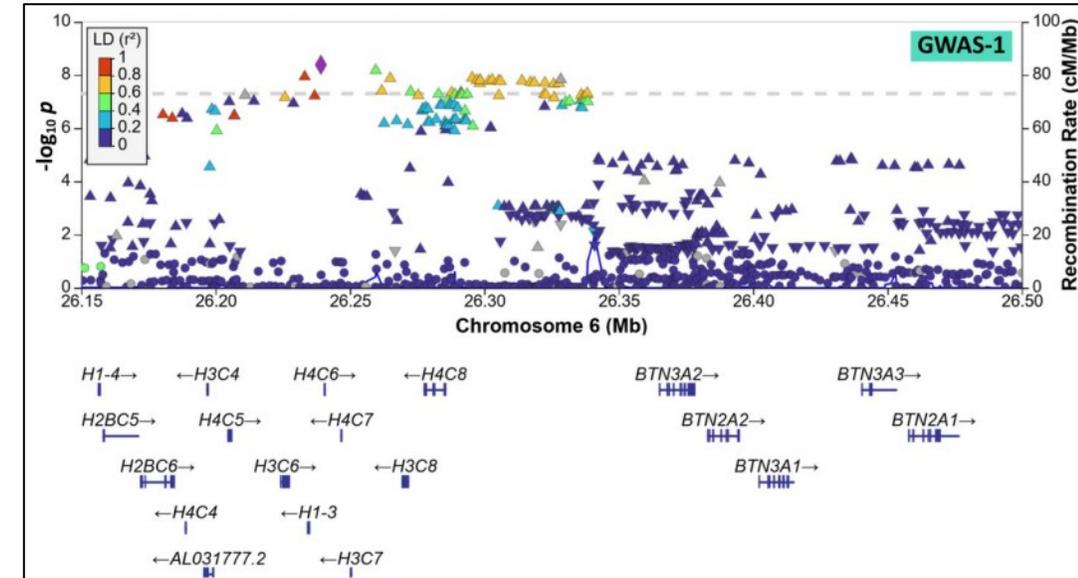
- One association points to the nervous system
It had previously been found among people experiencing **chronic pain**.



Immune system involvement

- Two signals likely relate to the **body's response to infection**

These reflect most people's report of an **infection before first onset** of symptoms.



Shared genetics among Infection Associated and other Chronic Illnesses

- Long COVID (*BPTF*) & ME/CFS (*OLFM4, RABGAP1L/GPR52*) overlap with Fibromyalgia risk loci Kerrebijen et al. 2025
- “We also identified overlap in the genes associated with Fatigue Dominant long COVID and ME/CFS” Taylor et al. PrecisionLife, J Transl Med (2023)

What are the implications of these results for people with ME/CFS?

Genes are one part of the puzzle

- Does having these genetic differences mean I definitely have ME/CFS? (No)
- If I don't carry these genetic differences, does this mean I won't get ME/CFS? (No)
- What does this mean for treatment and testing? (Nothing immediately)

Future Research

- What specific genes contribute to ME/CFS, and how?
- How can we now accelerate towards effective treatments and diagnostics?

A National ME Research Strategy is Essential

FOUR reasons why ME/CFS proposals more rarely meet funding criteria:

- (1) Less funding has generated less evidence,
- (2) More disagreement (myriad hypotheses),
- (3) Aversion to addressing ME/CFS's complexity and clinical heterogeneity, and
- (4) Stigma, including due to it being a female-biased disease

THREE reasons why ME/CFS deserves a National Strategy:

- (1) High prevalence: 0.92% of females and 0.25% of males
- (2) Substantial health, social and economic burden of disease
- (3) Future proofing: probability of another deadly pandemic over the next 25 years is 47–57%.

The UK PRIME network is being set up to help address these issues.

DecodeME Co-production

People with lived experience of ME

- **Andy Devereux-Cooke**
- Sian Leary
- Simon McGrath
- Emma Northwood
- Anna Redshaw
- Charles Shepherd
- Pippa Stacey
- Claire Tripp
- Jim Wilson

External partners

- Hot Tin Roof
- Itineris
- Gemini-Print
- UK Biocentre
- ThermoFisher/
Affymetrix

Action for M.E.

- **Sonya Chowdhury**
- Isabel Lewis
- Ruth Richardson
- Cliff Murray
- Nicola Riddick
- Claire Dransfield

25% M.E. Group

- Helen Baxter

UoE PR/Comms team

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- Shane Canning

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- Silvia Shen
- Sarah Brown

DecodeME UoE Team

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- Joshua Dibble
- Sumy Baby
- David Perry
- Anne Connolly
- Ewan McDowall
- Gemma Samms
- Andrew Bretherick
- Jareth C. Wolfe
- Øyvind Almelid
- Hannes Becher

and many others

