

A UK Multi-Omics Infrastructure for MDD and Psychosis

The Mental Health Goals Omics Programme

Co-leads: Prof Gerome Breen (King's College London) · Prof James Walters (Cardiff)

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Office for Life Sciences · delivered by the Medical Research Council (UKRI)





One programme, two arms

MHG Omics Programme

A UK multi-omics infrastructure for psychosis & mood disorders

Co-leads: *Prof Gerome Breen (KCL)* · *Prof James Walters (Cardiff)*

GLAD arm — mood

Lead: *Prof Gerome Breen (KCL)*

- 38k consented, genotyped base
- +12k new blood & multi-omics
- 2,500 followed 3× (2025–30)
- Depression & anxiety

Psychosis arm

Leads: *Prof J. Walters* · *Dr M-E. Lynall*

- ~7,500 cases (first 10 yrs of onset)
- Longitudinal recall sub-cohort
- Built on the Early Intervention Mission
- Early psychosis & ARMS

Shared platform: ~20,000 deeply phenotyped + controls · 35 NHS trusts · harmonised omics, consent & QC · trial-ready



Why now — and why the UK

The gap industry keeps hitting in mental health R&D

- No biosamples linked to longitudinal clinical and digital data at scale
- No harmonised NHS infrastructure to sample and process omics
- No single consented, contactable cohort to recruit and stratify from

The MHG answer — government-backed, built for industry

One consented, contactable, trial-ready resource — built in the NHS, run for industry.

£25m

OLS, via MRC — up to 5 years

35

NHS trusts with new omics
capability

~20,000

deeply phenotyped, + controls



Industry-ready by design

Consent, access and analysis — solved before you arrive

Recontactable

GLAD: all consented for recontact. EIM / psychosis: optional — about 90% opt in.

All industry-consented

Every participant gives permission for industry use of their data

All in DATAMIND TRE

One Trusted Research Environment for every layer — with agentic analysis pipelines enabled

No data-access negotiation from scratch, no bespoke consent, no pipeline build — you plug in.

The GLAD arm

· *led by Prof Gerome Breen (KCL)*



GENETIC LINKS TO

GLAD

ANXIETY & DEPRESSION

WHAT IS THE GLAD STUDY?

For more info, visit
GLADStudy.org.uk

NIHR | BioResource

**JOIN US
IN THE WORLD'S
LARGEST
STUDY**

OF DEPRESSION & ANXIETY
FUNDED BY THE NIHR AND PART OF THE NIHR BIORESOURCE



WE HOPE

400,000

PEOPLE WILL TAKE PART

TAKING PART IS SIMPLE

- YOU FILL IN A SURVEY ONLINE
- WE SEND YOU A DNA TESTING KIT
- YOU SEND BACK A TUBE OF YOUR SALIVA
SO WE CAN LOOK AT YOUR GENETICS



**YOU CAN COMPLETE
THE SURVEY ONLINE**





A running cohort — not a standing start

GLAD — Genetic Links to Anxiety and Depression — is already live and already delivering.

38,000

genotyped participants

30+

validated instruments

Consented

contactable for recall

NHS-linked

records; producing GWAS

Why it matters for delivery: the recruitment engine, consent model and participant base already exist. GLAD-MHG bolts biology onto a proven cohort.



Severe, recurrent depression — at scale

The treatment-experienced patients trials struggle to find

>95%

have recurrent MDD

51%

7+ episodes (vs 6% in UKB)

30%

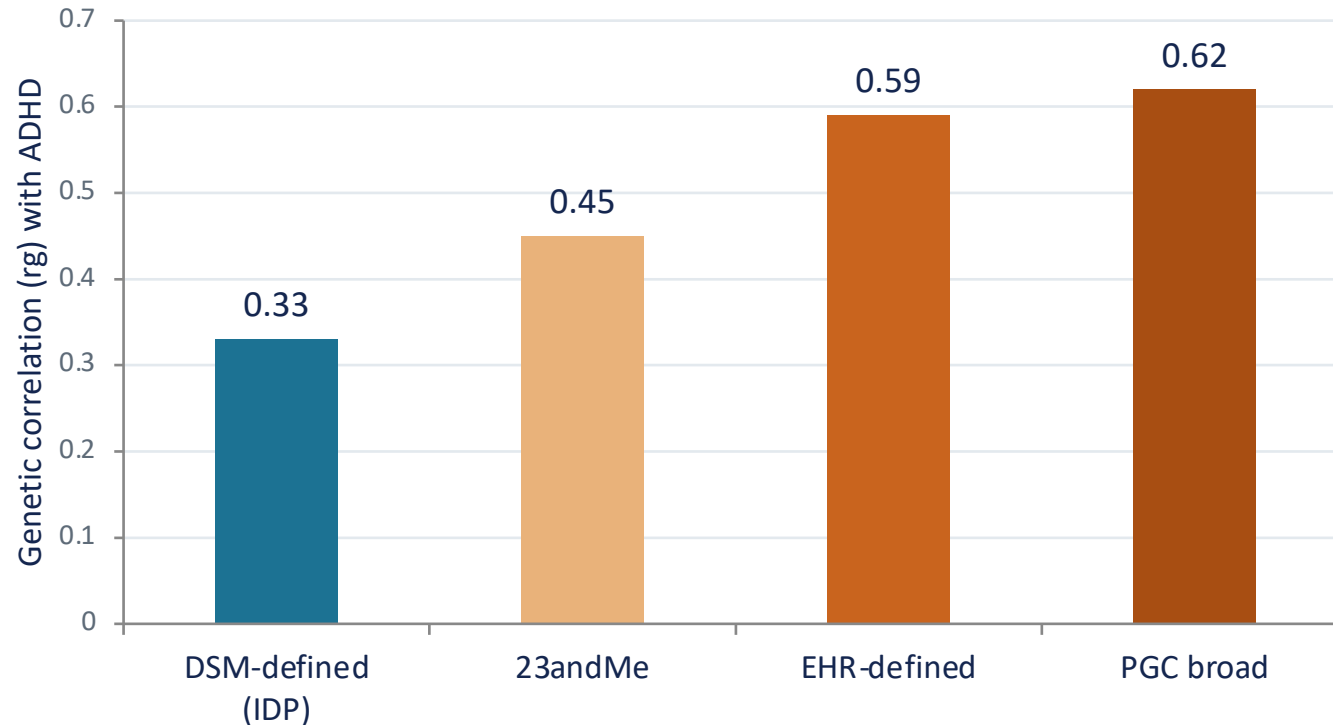
13+ episodes (vs 1.4% in UKB)

If you want highly recurrent, treatment-experienced depression, GLAD has more than any clinical site proposed to recruit — modal onset around age 15.



Identical phenotyping separates MDD from its comorbidities

DSM-defined depression is genetically more specific — cleaner biology for drug discovery



44% vs 76%
of loci lost when ADHD signal is removed — DSM vs broad

Anxiety and neuroticism follow the same pattern — both overlap broad MDD far more than DSM-defined MDD. IDP Consortium · 489,255 individuals · GLAD the largest contributor.



GLAD-MHG adds blood, biology and behaviour

+12,000

new participants — blood & multi-omics

2,500

followed at 0/2M/12M to 2030

Linked NHS

records, including prescribing

From a questionnaire-and-DNA cohort to a longitudinal, multi-layered biology resource

- Multi-omics on blood: WGS, methylation, proteomics, metabolomics
- Continuous digital phenotyping — wearables, passive sensing, voice
- Recruitment via NHS DigiTrials (~9,000 of 12,000 via the England pathway)



Built to answer the questions industry asks

Who responds? Who relapses? Who gets side effects?

Response over time

Co-produced longitudinal assessments capture response, switching and relapse

Side-effect burden

Tolerability and adverse effects tracked across follow-up, linked to prescribing

Voice & app capture

15 minutes at baseline, then short voice check-ins at blood samples to log mood and symptoms beyond questionnaires, relapse, side-effects and episodes

Omics on top

WGS, proteomic and metabolomic layers predict response and tolerability

The voice questionnaire

Phenotype by listening, not ticking — beyond the tyranny of questionnaires

Spoken & open-ended

Verbal responses about lived experience; response to treatments, and side-effects

What tick-boxes miss

Nuance, trajectory and treatment experience — richer subtyping of depression and anxiety

Analysed two ways

From the speech signal computationally, and qualitatively — transcribed and themed

Co-produced

Lived-experience PPI; study materials and digital prompts co-designed

Not just whether someone is ill — but how.



What industry gets from the mood arm

Recall-by-genotype

Re-contact consented participants by genotype or biology for targeted studies

Stratified trial recruitment

Enrich for severity, treatment-resistance or molecular subtype before first contact

Biomarker discovery → validation

Proteomic & metabolomic signatures tied to response and side-effect endpoints

One front door

Access via Datamind and the MHG Alliance Team — consented, QC'd, contactable, governed

Same consent, QC and analytic standards as the psychosis arm — one interoperable resource.

Over to the psychosis arm

Led by Prof James Walters (Cardiff) & Dr Mary-Ellen Lynall (Cambridge)

Presented by Prof Graham Murray (University of Cambridge)

Same platform. Same standards. A different disorder.





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Psychosis arm

Leads: *Prof J. Walters* · *Dr M-E. Lynall*

- 7,500 cases (first 10 yrs of onset)
- Longitudinal recall ~90%
- Built on the Early Intervention Mission
- Early psychosis & ARMS

Shared platform: ~20,000 deeply phenotyped + controls · 35 NHS trusts · harmonised omics, consent & QC · trial-ready



MHG has extended the Early Intervention Mission

The Early Intervention Mission (NIHR MH-TRC) — CI Prof Graham Murray — scaled up across Cardiff, Cambridge and Edinburgh.

2,000 → 7,500
cases recruited

3 → 10 yrs
within 10 years of onset

to Mar 2030
extended from Jan 2028

What the extension adds

- Repeat blood samples — a longitudinal cohort following biology over time
- The psychosis arm of a national multi-omics dataset (Cardiff · Cambridge · Edinburgh)
- Optional linkage to wider health and administrative records

830 patients recruited so far — recruiting to a target of 7,500.

A national footprint

GLAD and EIM / Psychosis sites across the UK

● GLAD — 11 sites

● **EIM / Psychosis — 27 sites**

Co-located hubs sit side by side across England, Scotland, Wales and Northern Ireland.

Also recruiting nationally online, via NHS DigiTrials.

838 psychosis patients recruited so far.





Aims — precision medicine in early psychosis

Who responds? Who relapses? Who gets side effects?

Stratify risk

Risk stratification, tailored prevention and early intervention

Representative cohort

Psychosis within 10 years of onset – widespread geographical sampling and ensuring hard to reach groups take part

Refine existing tools

Move personalised-psychiatry approaches closer to routine practice

Build new tools

WGS, proteomic and metabolomic layers to predict response and tolerability

Two arms, one resource

Psychosis and mood, on a single trial-ready platform

~20,000

deeply phenotyped + controls

35

NHS trusts

Industry facing

MHG Alliance Team

- GLAD consented for recontact & industry use; EIM recontact optional (~90% opt in)
- All data in the DATAMIND TRE — agentic analysis pipelines enabled
- Harmonised omics, consent and QC; predictive pipelines for response, relapse and stratification

Psychosis arm: eim@psychiatry.cam.ac.uk GLAD: gladadmin@kcl.ac.uk

Programme enquiries: DIGIT-MHG@kcl.ac.uk



Omics data scope

Omics layer	Main cohort — baseline 19000 cases + 1000 controls	Longitudinal — baseline 4500 cases + 500 controls	Longitudinal — 12 months
Genomics	SNP array	SNP array	Long-read sequencing
Proteomics	Olink Target 96 (92 proteins)	Olink Reveal (1,000 proteins)	Olink Reveal (1,000 proteins)
Metabolomics	Nightingale (~250)	Nightingale (~250)	Nightingale (~250)
Cellular (PBMC)	—	Immunophenotyping (n=150) iPSC lines (n=100)	Immunophenotyping (n=150) iPSC lines (n=100)

Harmonised with the mood arm — shared assays, consent and QC make the two arms one interoperable dataset.



Where industry can partner

Across both arms — mood and psychosis

Extended omics on stored samples

Further proteomic, metabolomic or genomic assays beyond current scope

PBMC & iPSC platform

Patient-derived cells for mechanistic and drug-discovery work

Biomarker discovery & validation

Candidate markers for risk, prognosis and treatment response

Deeper phenotyping on recall

Re-contact consenting participants for targeted follow-up

Integration with linked data

Molecular data joined to questionnaires and NHS records

Wearables & digital measures

Continuous activity, sleep and physiology linked to molecular profiles

Thank you

The Mental Health Goals Omics Programme

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