Mapping the plasma metabolome to human health and disease

Reading Report

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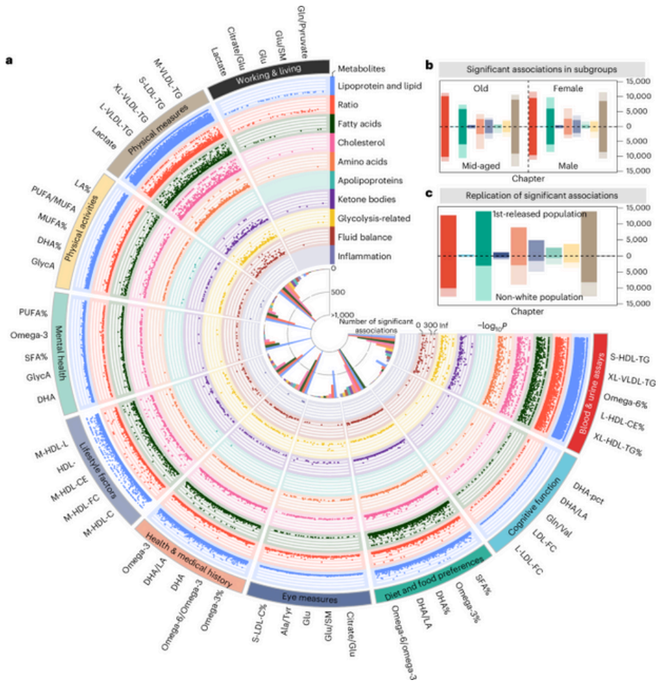
1.Study Overview

- Data Source: UK Biobank (UKB), N = 274,241.
- Dimensions: 313 NMR Metabolites × 1,386 Diseases & 3,142 Traits.
- Follow-up: Median 14.9 years (Prospective Cohort).



- Core Achievement: Created the largest metabolome-phenome "Atlas"; Validated causality using MR.

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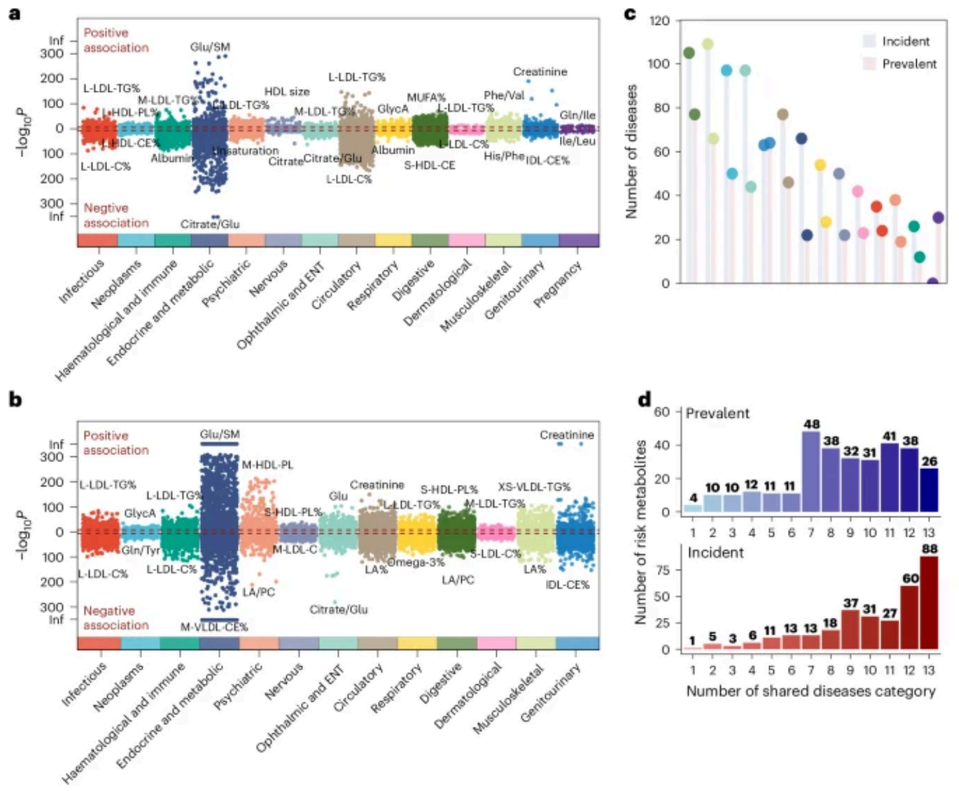
2. Methodology Pipeline

1. **3 Cohorts** (Derivation + 2 Replication sets)

2. **Association Analysis:**

   - Cross-sectional: Logistic Regression.
   - Longitudinal: Cox Proportional-Hazards Model.
   - Outlier Removal → Transformation ->Z-score Standardization

Fig. 2: Atlas of metabolite–disease association analysis results.



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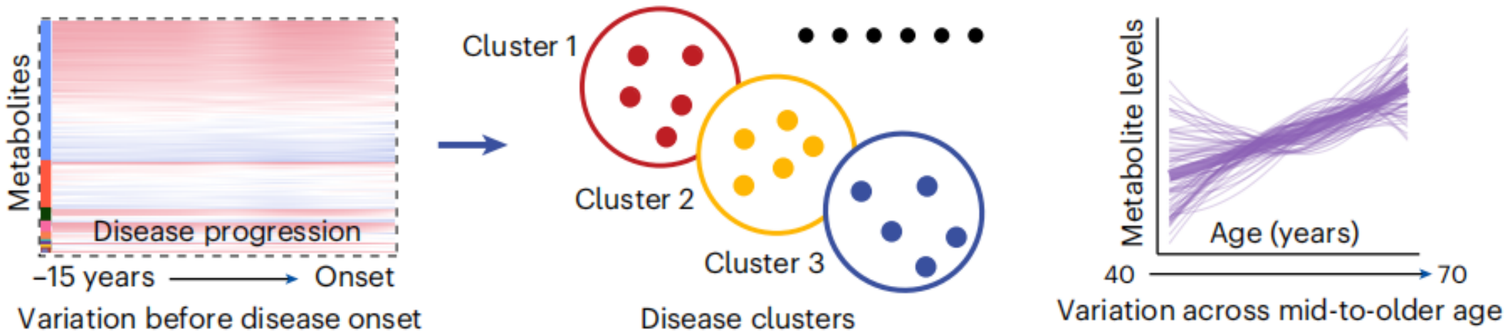
3. Key Result 1 - The "Early Warning" System

Key Finding: 57.5% of metabolites varied >10 years before diagnosis.

Method: Nested Case-Control Study (1:5 matching).

Visualization: Disease Clusters (e.g., Cluster 1: CV diseases) showing similar trajectories.



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4. Key Result 2 - Prediction & Causality

Prediction (AI): LightGBM model for Metabolic Risk Score (MetRS).

Performance: AUC > 0.8 for 81 diseases

(e.g., T2D AUC=0.944, Diabetic Retinopathy AUC=0.940).

Causality (MR): Bidirectional Mendelian Randomization.Result: 454 robust causal pairs

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5.Limitations and future

Limitations:

- 95.1% White ancestry;
- Replication rate in non-white population was low (30-45%);
- may miss early/subclinical stages of chronic diseases.

Future:

- **Pipeline Automation: Build automated Python scripts for outlier filtering (4*IQR) & Z-scoring.**
- **Research Extension: Apply this "Atlas" methodology to Chinese Cohorts .**
- **Specific Interest: Combine Retinal Imaging with Systemic Metabolites.**