Supplementary Data 1. Epidemiological characteristics of THL Biobank cohorts.

Supplementary Data 2. Definitions (using ICD-10 codes) of endpoints used in the study, summary data from WHO on disability adjusted life-years in the European region in 2019, and sources for the polygenic scores used in the study.

Supplementary Data 3. All model coefficients computed from the model training in UK Biobank, which were then used to compute the scores for validation in the remainder of UK Biobank and the other two biobanks.

Supplementary Data 4. Prevalence of individuals at high metabolomic risk in biobanks. Threshold for belonging into high-risk group was defined as the top decile of the metabolomic score in the training set of UK Biobank. The prevalence of individuals exceeding those thresholds is reported in each of the validation sets. Alzheimer’s disease and Depressive disorders are omitted for THL because we did not have those endpoints

Supplementary Data 5. Performance of genetic and metabolomic risk prediction models in the three biobanks tested. Only test set samples were used to evaluate performance in UK Biobank. The "*_decile" columns give results of a Cox regression model (hr = hazard ratio, 95ci = 95% confidence interval on hazard ratio, pvalue = two-tailed p-value for hazard ratio ≠ 1) for a binary indictator variable for whether each individual is above the top 10% risk threshold (defined in the UK Biobank training set). The "*_per_sd" columns give the results of a Cox regression for the continuous linear predictor. The auc_* columns give the area under the ROC curve (auc) and it's standard error (auc_se), the delta AUC relative to an age+sex model (delta_auc), and the two-sided p-value for the delta AUC (using DeLong's test). P-values are not adjusted for multiple testing.

Supplementary Data 6. Estimates for interaction between metabolomic and polygenic scores. Estimates and two-tailed p-values are derived from a Cox regression analysis. P-values are not adjusted for multiple testing. Estimates are shown for interaction term `metabolic score * PGS`. HR = Hazard Ratio. SD = Standard deviation, CI = Confidence interval, N = Total number of samples, N cases = Number of cases within samples.

Supplementary Data 7. Individual biomarker correlations between baseline and repeat visits 5 years apart for the 36 biomarkers that were used in the main model training.

Supplementary Data 8. Enrichment of incident disease in high risk groups of different risk scores. Hazard ratios of developing disease for individuals in the top 10% of the multiomic score, the clinical score or the combined score, after 4 and 10 years of follow-up in UK Biobank test set. Estimates, confidence intervals and two-tailed p-values are calculated from a Cox regession analysis. P-values are not adjusted for multiple testing.

Supplementary Data 9. Clinical characteristics between individuals with low and high metabolomic risk score. Low risk group includes individuals whose metabolomic risk is not in the highest decile for any of the 7 scores considered. High risk group includes individuals who have at least one of the 7 metabolic risks in the highest decile. SD = standard deviation. CI = Confidence interval. Two-tailed p-values are calculated using Fisher's exact test (for binary variables) and t-test (for continuous variables) and are not adjusted for multiple testing.

Supplementary Data 10. Details of how the variables used to compute clinical scores were defined in UK Biobank.