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Abstract

An Unhealthy Dietary Pattern-Related Metabolic Signature Is Associated with Cardiometabolic and Mortality Outcomes: A Prospective Analysis of the UK Biobank Cohort †

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Abstract: Background and objectives: An unhealthy dietary pattern (DP) previously identified in the UK Biobank population was positively associated with incident cardiovascular disease (CVD), type 2 diabetes (T2D) and mortality. Differences in individuals' metabolic responses to this DP may help identify novel pathways explaining the observed associations. This study aimed to identify metabolomic signatures characterising adherence to the DP and to investigate prospective associations with cardiometabolic and mortality outcomes. Methods: A cohort of n = 102,862 UK Biobank participants was studied, of which n = 28,123 participants with data on the DP of interest (derived from 2 or more 24 h dietary assessments at baseline) and available metabolomic data (n = 119 metabolites) were used to construct a DP-related metabolic signature score (DPMS) reflecting adherence to the previously identified DP. Metabolomic data were obtained from randomly selected EDTA plasma samples collected at baseline using a high-throughput NMR-based profiling platform. A sparse partial least squares (sPLS) model was used to compute the coefficients needed to calculate the DPMS. Multivariable Cox-proportional hazard models were used to investigate prospective associations between the DPMS and CVD, T2D and mortality outcomes in all participants with available metabolomic data. Results: A DPMS consisting of 46 differential metabolites was calculated, characterised by higher plasma levels of creatinine, saturated fatty acids and sphingomyelins, but lower levels of docosahexaenoic acid, omega 3 and 6 fatty acids and linoleic acids. During an average of 12 years of follow-up, 10,236 cases of total CVD, 5675 cases of T2D and 6367 cases of all-cause mortality were observed in the study sample (mean age 56 years; 55% women). We found significantly positive associations between the DPMS and total CVD events (hazard ratio [HR] per z-score increment = 1.16 [95%CI 1.14–1.18]) and between the T2D (HR per z-score increment = 1.24 [95%CI, 1.22–1.26]) and all-cause mortality (HR per z-score increment = 1.13 [95%CI, 1.10–1.15]). Conclusions: A newly identified metabolic signature reflecting higher adherence to an unhealthy dietary pattern was characterised by metabolites that indicated a poor lipid metabolism. This metabolic signature showed stronger associations with cardiometabolic and mortality outcomes than those observed previously with traditional dietary pattern measurements. Keywords: dietary pattern, plasma metabolomics, cardiometabolic outcomes, mortality, cohort study.

Keywords: dietary pattern; metabolomics; health outcomes; cohort study

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Informed Consent Statement: At recruitment, all participants gave informed consent to participate and be followed-up through data-linkage.

Data Availability Statement: This research was conducted using the UK Biobank resource under application number 14990. Data can be obtained upon application to the UK Biobank.

Conflicts of Interest: The authors declare no conflict of interest.