Research

# The EAT–Lancet planetary health diet and risk of incident chronic kidney disease

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## Abstract

**Background:** Diet may be an important modifiable risk factor for chronic kidney disease (CKD). We explored the association between the EAT–Lancet planetary health diet and the risk of incident CKD.

**Methods:** We obtained data from the UK Biobank cohort on dietary intake, assessed via 24-hour dietary recall questionnaires, for 179 508 participants without CKD at baseline. We evaluated adherence to the EAT–Lancet diet using 4 scoring methods and analyzed its association with incident CKD. We further identified metabolic and proteomic signatures of the EAT–Lancet diet and mediators linking the EAT–Lancet diet to CKD risk.

**Results:** During a median follow-up of 12.1 years, 4819 participants developed incident CKD. Higher EAT–Lancet adherence was inversely associated with CKD risk across all 4 scoring methods: Stubbendorff (adjusted hazard ratio [HR] 0.91, 95% confidence interval [CI] 0.88 to 0.94), Kesse-Guyot (adjusted HR 0.92, 95% CI 0.90 to 0.95), Yi-Xiang (adjusted HR 0.94, 95% CI 0.91 to 0.97), and Knuppel (adjusted HR 0.94, 95% CI 0.92 to 0.97). This association was stronger in participants with low residential green space exposure ($p$ for interaction = 0.008) and those with the rs2010352 GG genotype ($p$ for interaction < 0.001). Metabolic and proteomic signatures (122 metabolites and 143 proteins) of the EAT–Lancet diet were significantly inversely associated with CKD risk and mediated the inverse association between the EAT–Lancet index and incident CKD by 18.0% and 27.2%, respectively. Key mediators included degree of fatty acid unsaturation, glycoprotein acetyls, interleukin -18 receptor 1, and kidney injury molecule 1.

**Interpretation:** The EAT–Lancet diet was associated with lower risk of incident CKD. The related genetic, environmental, proteomic, and metabolic factors identified could inform personalized nutrition strategies.

Chronic kidney disease (CKD) affects nearly 10% of adults globally and is projected to become the fifth leading cause of death by 2040.[1,2] This rising prevalence underscores an urgent public health challenge, with diet emerging as a key modifiable factor for reducing CKD burden.[3]

The EAT–Lancet planetary health diet was proposed to integrate both human health and environmental sustainability.[4] Unlike traditional health-oriented diets such as Dietary Approaches to Stop Hypertension (DASH),[5] the Alternate Mediterranean diet (aMed),[6] Alternative Healthy Eating Index–2010 (AHEI-2010),[7] and healthful Plant-Based Diet Index (hPDI),[8] it defines food group intake within planetary boundaries to help prevent noncommunicable diseases.[4] Although it has been linked to lower risks of diabetes, cancer, and mortality,[9–11] its association with incident CKD remains unclear. Genetic and environmental factors also influence CKD,[12,13] highlighting the need to examine their potential modifying effects.

Advances in proteomics and metabolomics now allow precise characterization of dietary responses and underlying biological pathways. These omics profiles can serve as intermediate phenotypes bridging genetic and environmental exposures with disease risk.[14,15] However, the multi-omics signatures of the EAT–Lancet diet and their role in CKD remain largely unexplored.

To address these gaps, we aimed to investigate the association between adherence to the EAT–Lancet diet and the risk of incident CKD, examine whether this association is modified by genetic and environmental factors, identify proteomic and metabolomic signatures associated with the EAT–Lancet diet, and evaluate their associations with CKD risk and their potential role in mediating the diet–CKD relationship.

## Methods

### Data source and study population

The UK Biobank is a large-scale longitudinal study comprising about 500 000 participants aged 40 to 69 years from England, Scotland, and Wales.[16] At enrolment, participants completed a

touch-screen questionnaire on demographic characteristics, lifestyle, and health, and underwent physical examinations and biological sample collection. Representative subsets of participants provided additional data for metabolic and proteomic analyses.

The study included participants who completed at least 1 online 24-hour dietary recall questionnaire. We excluded participants who had extreme energy intake (male > 4200 or < 600 kcal/d; female > 3600 or < 500 kcal/d); missing baseline CKD status data; and prevalent CKD at baseline (defined as self-reported CKD, estimated glomerular filtration rate [eGFR] < 60 mL/min/1.73 $m^2$, urine albumin-to-creatinine ratio [UACR] ≥ 30 mg/g, or CKD diagnosis before baseline assessment).

### Dietary assessment and EAT–Lancet diet index

Dietary information was collected using the Oxford WebQ Questionnaire, a Web-based 24-hour dietary recall questionnaire.[17] Food item definitions are provided in Appendix 1, Supplementary Table S1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250457/tab-related-content.

Multiple scoring methods have been proposed to quantify adherence to the EAT–Lancet Commission dietary recommendations, though no consensus exists. To ensure robustness in examining associations with incident CKD, we employed 4 established EAT–Lancet diet scores (Box 1).

Higher scores in all 4 methods reflect greater adherence to the EAT–Lancet diet. Among these, the Kesse-Guyot score offers superior ability to capture individual dietary variation by quantifying continuous deviations from recommended cut-off values.[21] This method improves discriminative power in assessing diet adherence[22] and is especially effective for detecting subtle, diet-related differences in metabolic and proteomic profiles. Therefore, unless otherwise stated, we considered the Kesse-Guyot score to be the primary measure of EAT–Lancet diet adherence.

We also calculated other dietary indices — including DASH,[5] aMed,[6] AHEI-2010,[7] and hPDI[8] — and summarized them in Appendix 1, Supplementary Table S5. Dietary components across patterns are compared in Appendix 1, Supplementary Table S6.

### Box 1: EAT–Lancet diet scores

- Knuppel score: Comprises 14 binary-scored components (1 point per recommendation met), yielding a total between 0 and 14 (Appendix 1, Supplementary Table S2, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250457/tab-related-content).[18]
- Stubbendorff score: Uses a 0 to 41 point scale, assigning up to 3 points per component based on adherence level (Appendix 1, Supplementary Table S3).[19]
- Yi-Xiang score: Developed in an Asian cohort, scales intake to a 2500 kcal/d diet, with a total range of 0 to 140 (Appendix 1, Supplementary Table S4).[20]
- Kesse-Guyot score: A continuous metric quantifying deviation from recommended intakes, without upper or lower bounds. It aggregates energy-adjusted departures from cut-offs for each dietary component, capturing both positive and negative deviations (Appendix 1, Supplementary Table S2).[21]

### Outcome assessment

The study outcome was incident CKD, defined using the *International Classification of Diseases, Tenth Revision* (ICD-10) code N18, consistent with previous epidemiologic studies.[23–25] Case identification incorporated data from primary care records, hospital admissions, and death registries to enhance completeness.

We calculated follow-up time from the date of baseline assessment to the date of incident CKD, death, or the end of follow-up (Sept. 30, 2021, for England; July 31, 2021, for Scotland; and Feb. 28, 2018, for Wales), whichever came first.

### Statistical analysis

Baseline characteristics are presented as means (standard deviation [SD]) for continuous variables and proportions for categorical variables. We assessed the association between the EAT–Lancet index (per 1-SD increment and by quartiles) and the risk of incident CKD using Cox proportional hazards models, with results expressed as hazard ratios (HRs) and 95% confidence intervals (CIs). A directed acyclic graph depicting the assumed relationships among the EAT–Lancet diet index, CKD risk, and all covariates is provided in Appendix 2, Supplementary Figure S1, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250457/tab-related-content. We performed sensitivity analyses and conducted subgroup analyses to evaluate potential effect modifiers, including genetic factors (genetic risk score and single-nucleotide polymorphisms for CKD) and environmental factors (residential green and blue spaces). We evaluated the credibility of subgroup effect modifications using the Instrument to assess the Credibility of Effect Modification Analyses (ICEMAN) tool.[26]

We constructed metabolic and proteomic signatures using a 2-step analysis: multivariable-adjusted linear regressions followed by the least absolute shrinkage and selection operator (LASSO) model. We calculated signature scores using a weighted sum of identified metabolites and proteins. We derived pathway scores from metabolite categories and protein enrichment. Mediation analysis estimated the proportion of the association between the EAT–Lancet index and incident CKD risk mediated by these signatures and pathways.

We conducted all analyses using R version 4.1.1, with a 2-tailed $p < 0.05$ considered statistically significant. Additional methodologic details regarding dietary assessment and EAT–Lancet diet index, metabolomic and proteomic profiling, genetic and environmental assessment, covariate assessment, and statistical approaches are provided in Appendix 3, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250457/tab-related-content.

### Ethics approval

The study received ethics approval from the North-West Multi-Centre Research Ethics Committee (11/NW/0382), and all participants provided written informed consent.

## Results

### Study participants and population characteristics

The enrolment period for participants spanned from December 2006 to October 2010. Among the 179 508 study participants (Figure 1), the

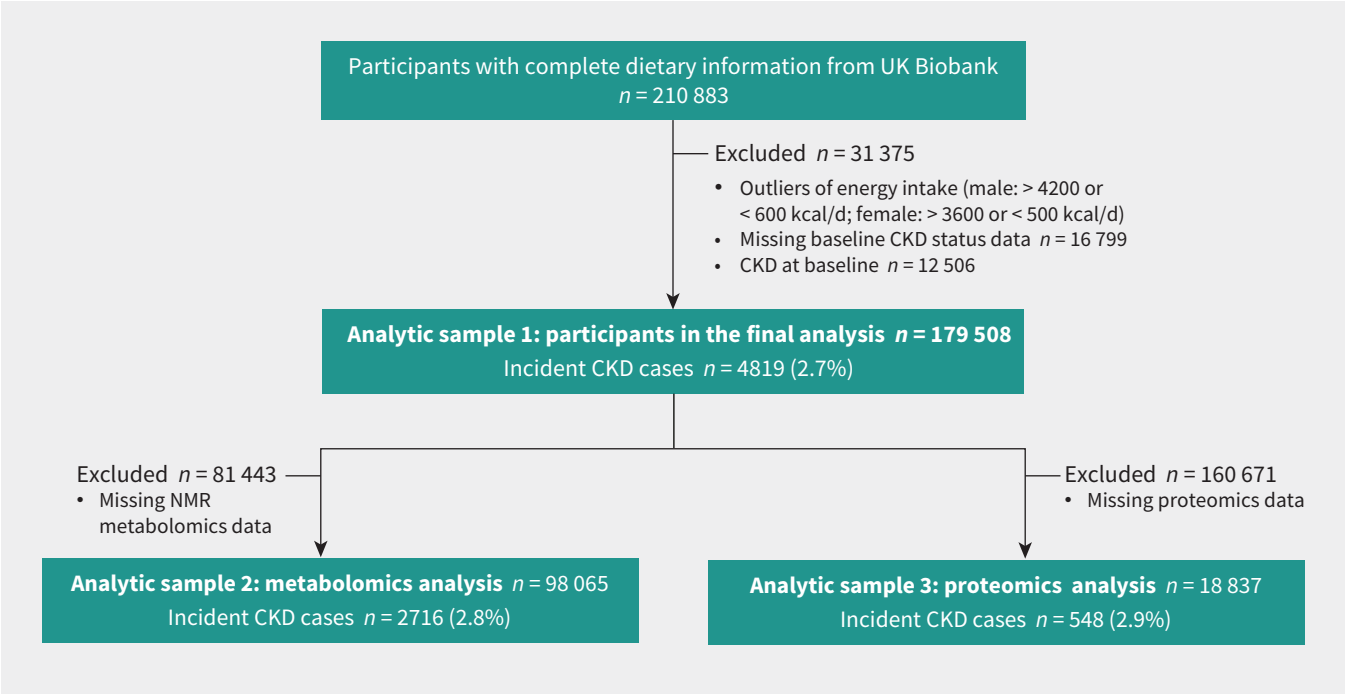


**Figure 1:** Study flow chart of participant selection and analytical cohorts. CKD = chronic kidney disease, NMR = nuclear magnetic resonance.

mean age was 55.9 (SD 7.9) years, 54.6% were female, and 96.0% were White. Those who developed incident CKD were older and less likely to be never-smokers. They also exhibited higher body mass index; lower physical activity, alcohol consumption, eGFR, and EAT–Lancet index scores; and a higher prevalence of hypertension, hypercholesterolemia, and diabetes (Table 1). Participant characteristics were consistent across all analytic samples, as well as between individuals included and those not included in the metabolomics and proteomics analyses (Appendix 1, Supplementary Tables S7 to 9).

## Association between EAT–Lancet Diet adherence and incident CKD

During a median follow-up of 12.1 (interquartile range 11.5 to 12.9) years, 4819 (2.7%) participants developed CKD. The median values for the Yi-Xiang, Knuppel, Stubbendorff, and Kesse-Guyot scores were 50, 9, 21, and 22.9, respectively.

In fully adjusted Cox models, higher scores for each diet index (per 1-SD increase) were associated with a lower risk of incident CKD: Yi-Xiang (adjusted HR 0.94, 95% CI 0.91 to 0.97), Knuppel (adjusted HR 0.94, 95% CI 0.92 to 0.97), Stubbendorff (adjusted HR 0.91, 95% CI 0.88 to 0.94), and Kesse-Guyot (adjusted HR 0.92, 95% CI 0.90 to 0.95) (Table 2). When assessed by quartiles, the Kesse-Guyot score showed a dose–response relationship, with adjusted HRs of 0.90 (95% CI 0.84 to 0.98) for Q2, 0.86 (95% CI 0.79 to 0.93) for Q3, and 0.82 (95% CI 0.76 to 0.90) for Q4 compared with Q1. We observed similar trends for the other scores. Among the 4, Stubbendorff and Kesse-Guyot scores exhibited stronger inverse associations, with a significantly reduced risk already apparent in Q2 (Table 2). Adjusted HRs (95% CIs) for all variables in the multivariable Cox regression models are provided in Appendix 1, Supplementary Tables S10 to 17.

Sensitivity analyses — including further adjustment for a variety of additional food groups and environmental factors, exclusion of early CKD cases or participants with only 1 dietary assessment, use of the last available diet record as the baseline, or complete-case analysis — did not materially alter the results (Appendix 1, Supplementary Table S18). Removing individual EAT–Lancet index components had minimal effect (Appendix 1, Supplementary Table S18). Additionally, in a subsample with repeated eGFR measurements in 2012 and 2013, the inverse association for EAT–Lancet index was consistent when using a biochemical CKD definition (eGFR < 60 mL/min/1.73 $m^2$), supporting the robustness of our primary findings (Appendix 1, Supplementary Table S18).

Exploratory analyses also showed inverse associations between higher diet scores (per 1-SD increase) and CKD risk for DASH (adjusted HR 0.91, 95% CI 0.88 to 0.93), aMed (adjusted HR 0.92, 95% CI 0.90 to 0.95), hPDI (adjusted HR 0.93, 95% CI 0.90 to 0.96), and AHEI-2010 (adjusted HR 0.96, 95% CI 0.93 to 0.99) (Appendix 1, Supplementary Table S19).

## Subgroup analysis

In subgroup analyses of genetic factors, the CKD genetic risk score did not significantly modify the association of incident CKD with either version of the EAT–Lancet index (Kesse-Guyot or Stubbendorff score) or with other dietary patterns (DASH, aMed, AHEI-2010, or hPDI) (Figure 2 and Appendix 2, Supplementary Figure S2). However, the single-nucleotide polymorphism rs2010352-G showed a significant interaction with the EAT–Lancet index on CKD risk ($p$ for interaction < 0.001) (Figure 2 and Appendix 1, Supplementary Table S20), which was rated as moderately credible by the ICEMAN tool (Appendix 4, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250457/tab-related-content).

**Table 1 (part 1 of 2): Baseline characteristics of participants by incident chronic kidney disease status**

| Characteristic | No. (%)* participants | | SMD† |
|---|---|---|---|
| | Developed incident CKD *n* = 4819 | Did not develop incident CKD *n* = 174 689 | |
| Age, yr, mean ± SD | 61.4 ± 6.1 | 55.8 ± 7.9 | 0.804 |
| Sex, female | 2413 (50.1) | 95 585 (54.7) | 0.093 |
| Ethnicity, White | 4633 (96.5) | 167 157 (96.0) | 0.063 |
| Body mass index, mean ± SD | 28.7 ± 5.1 | 26.8 ± 4.5 | 0.403 |
| Townsend deprivation index, mean ± SD | −1.6 ± 2.9 | −1.6 ± 2.9 | 0.016 |
| Smoking status | | | 0.161 |
| Current | 374 (7.8) | 13 563 (7.8) | |
| Never | 2377 (49.3) | 99 472 (56.9) | |
| Previous | 2053 (42.6) | 61 225 (35.0) | |
| Optimal physical activity | 2463 (51.1) | 95 552 (54.7) | 0.129 |
| Medical condition | | | |
| Hypertension | 3524 (73.1) | 86 667 (49.6) | 0.498 |
| High cholesterol | 1727 (35.8) | 25 949 (14.9) | 0.497 |
| Diabetes | 621 (12.9) | 6548 (3.7) | 0.336 |
| Alcohol consumption, g/d | | | 0.137 |
| < 5 | 2330 (48.4) | 73 489 (42.1) | |
| 5–15 | 779 (16.2) | 28 464 (16.3) | |
| ≥ 15 | 1710 (35.5) | 72 736 (41.6) | |
| Vitamin and mineral supplements | 1713 (35.5) | 61 883 (35.4) | 0.036 |
| Diet variation‡ | | | 0.073 |
| Never or rarely | 1605 (33.3) | 62 141 (35.6) | |
| Often | 451 (9.4) | 13 279 (7.6) | |
| Sometimes | 2755 (57.2) | 98 913 (56.6) | |
| Energy, kcal/d, mean ± SD | 2026.6 ± 560.8 | 2051.6 ± 554.8 | 0.045 |
| eGFR, mL/min/1.73 $m^2$, mean ± SD | 82 ± 12.4 | 96.1 ± 11.4 | 1.18 |
| UACR, mg/g, mean ± SD | 9.3 ± 5.9 | 9.1 ± 5.7 | 0.04 |
| EAT–Lancet planetary health diet, mean ± SD | | | |
| Yi-Xiang score | 48.6 ± 12.2 | 49.7 ± 12.6 | 0.086 |
| Knuppel score | 8.6 ± 1.3 | 8.8 ± 1.3 | 0.095 |
| Stubbendorff score | 20.7 ± 3.9 | 21.3 ± 4.1 | 0.13 |
| Kesse-Guyot score | 20.9 ± 33.9 | 24.9 ± 34.3 | 0.118 |

For environmental factors, stronger inverse associations between the EAT–Lancet index (per 1-SD increase in Kesse-Guyot score) and CKD were observed among participants with lower residential green space (1000-m buffer: $p$ for interaction = 0.008; 300-m buffer: $p$ for interaction = 0.09) and lower blue space at 300 m ($p$ for interaction = 0.1) (Figure 2). We noted similar trends for the Stubbendorff-based score (Appendix 2, Supplementary Figure S2). The interaction with residential green space (1000-m buffer) was considered moderately credible per ICEMAN (Appendix 4). No environmental factors significantly modified associations between CKD risk and the other dietary patterns (Figure 2).

We observed no significant effect modification for age, sex, race, Townsend deprivation index, physical activity, or history of diabetes on the association between the EAT–Lancet index and CKD (all $p$ for interaction > 0.05; Appendix 2, Supplementary Figures S2 and S3).

## Metabolic and proteomic signatures of the EAT–Lancet planetary health diet

Linear regression followed by Bonferroni correction identified 146 metabolites significantly associated with the EAT–Lancet index (Kesse-Guyot score) (Appendix 1, Supplementary Table S21). LASSO regression refined these to 122 key metabolites, primarily comprising lipoprotein subclasses and fatty acids (Appendix 1, Supplementary Table S22; Appendix 2, Supplementary Figure S4). Descriptive statistics of the resulting metabolic signature score are detailed in Appendix 1, Supplementary Table S23.

**Table 1 (part 2 of 2): Baseline characteristics of participants by incident chronic kidney disease status**

| Characteristic | No. (%)* participants | | SMD† |
|---|---|---|---|
| | Developed incident CKD *n* = 4819 | Did not develop incident CKD *n* = 174 689 | |
| Dietary component, g/d, mean ± SD | | | |
| Fruits | 214.3 ± 168.2 | 213.5 ± 168.7 | 0.004 |
| Vegetables | 177.9 ± 157.3 | 184.2 ± 156.5 | 0.04 |
| Tubers and starchy vegetables | 110.8 ± 100.3 | 95.7 ± 93.2 | 0.156 |
| Total grains | 203.2 ± 112.3 | 213.7 ± 115.8 | 0.092 |
| Legumes | 22.2 ± 35.8 | 22.5 ± 36.1 | 0.007 |
| Nuts | 5.8 ± 13.6 | 6.8 ± 15.0 | 0.069 |
| Dairy | 263.2 ± 147.3 | 261.6 ± 147.8 | 0.011 |
| Poultry | 35.1 ± 54.6 | 34.4 ± 51.9 | 0.013 |
| Eggs | 21.9 ± 40.9 | 21.0 ± 39.8 | 0.021 |
| Red meat | 43 ± 52.5 | 39.4 ± 52.1 | 0.068 |
| Fish | 30.5 ± 48.1 | 32.2 ± 47.5 | 0.035 |
| Added sugar | 65 ± 37.4 | 64.4 ± 35.3 | 0.017 |
| Saturated fat | 26.9 ± 11.6 | 26.8 ± 11.5 | 0.007 |
| Unsaturated fat | 38.4 ± 15.5 | 39.1 ± 15.5 | 0.046 |
| Green space, %, mean ± SD§ | | | |
| 300 m buffer | 68.6 ± 14.2 | 67.7 ± 14.9 | 0.061 |
| 1000 m buffer | 71.5 ± 13.7 | 70.5 ± 14.4 | 0.076 |
| Blue space, %, mean ± SD§ | | | |
| 300 m buffer | 0.6 ± 1.1 | 0.6 ± 1.1 | 0.024 |
| 1000 m buffer | 1.0 ± 1.2 | 1.0 ± 1.3 | 0.033 |

CKD = chronic kidney disease, eGFR = estimated glomerular filtration rate, SMD = standardized mean difference, SD = standard deviation, UACR = urine albumin to creatinine ratio.

*Unless indicated otherwise.
†Values < 0.1 indicate no clinically meaningful difference between groups.
‡Diet variation: Based on the question, "Does your diet vary much from week to week?" (response options: never or rarely, sometimes, often).
§Green/Blue space, %: Proportion of all land-use types within a residential buffer that is classified as "Greenspace"/"Water."

This score showed a significant positive correlation with the EAT–Lancet index (Spearman $r$ = 0.2, $p$ < 0.001; Appendix 2, Supplementary Figure S5).

Similarly, 420 proteins were significantly associated with the index after Bonferroni correction, with LASSO regression narrowing these to 143 key plasma proteins (Appendix 1, Supplementary Tables S24 and S25; Appendix 2, Supplementary Figure S4). Kyoto Encyclopedia of Genes and Genomes enrichment analysis indicated their involvement in cytokine–cytokine receptor interactions, phagosome formation, cell adhesion molecules, and complement and coagulation cascades (Appendix 1, Supplementary Table S26). Detailed descriptive statistics of the resulting proteomic signature score are provided in Appendix 1, Supplementary Table S23. The proteomic signature score was positively correlated with the EAT–Lancet index (Spearman $r$ = 0.3, $p$ < 0.001; Appendix 2, Supplementary Figure S5).

Metabolomic and proteomic profiles were also established for the DASH, aMed, hPDI, and AHEI-2010 diets (Appendix 1, Tables S27 to 34). Notably, 68 metabolites and 45 proteins were shared between the EAT–Lancet index and all other dietary patterns (Appendix 2, Supplementary Figure S6).

## Association of metabolic and proteomic signature scores of the EAT–Lancet index with incident CKD risk

In the metabolic and proteomic cohorts, 2716 (2.8%) and 548 (2.9%) participants developed CKD, respectively. As shown in Figure 3A and 3B, both the metabolic and proteomic signature scores of the EAT–Lancet index exhibited significant inverse linear associations with CKD risk. Each 1-SD increase in the metabolic signature score was associated with an 11% lower risk of CKD (adjusted HR 0.89, 95% CI 0.85 to 0.93) (Figure 3A). Similarly, each 1-SD increase in the proteomic signature score was associated with a 20% risk reduction (adjusted HR 0.80, 95% CI 0.73 to 0.89) (Figure 3B). Furthermore, participants with high metabolic or proteomic signature scores showed a lower cumulative incidence of CKD than those with high EAT–Lancet index scores (Figure 3C and 3D).

## Mediation analysis

The metabolic signature score significantly mediated 18.0% of the total effect of the EAT–Lancet index on CKD risk ($p$ < 0.001; Figure 4A). Pathway-specific analysis identified 3 major mediating metabolic categories: fatty acids (12.0%), inflammation

**Table 2: Association between EAT–Lancet planetary health diet adherence, assessed by 4 scoring methods (Yi-Xiang, Knuppel, Stubbendorff, and Kesse-Guyot score), and incident chronic kidney disease risk**

| EAT–Lancet index | Total | No. (%) events | Model 1* HR (95% CI) | Model 2† HR (95% CI) |
|---|---|---|---|---|
| **Yi-Xiang score** | | | | |
| Per 1-SD increment | 179 508 | 4819 (2.7) | 0.91 (0.89–0.94) | 0.94 (0.91–0.97) |
| Quartiles | | | | |
| Q1 (0–40) | 42 822 | 1242 (2.9) | Ref. | Ref. |
| Q2 (41–49) | 45 915 | 1358 (3.0) | 0.97 (0.90–1.05) | 0.99 (0.92–1.07) |
| Q3 (50–57) | 42 017 | 1087 (2.6) | 0.86 (0.79–0.93) | 0.89 (0.82–0.97) |
| Q4 (58–140) | 48 754 | 1132 (2.3) | 0.78 (0.72–0.85) | 0.84 (0.77–0.91) |
| **Knuppel score** | | | | |
| Per 1-SD increment | 179 508 | 4819 (2.7) | 0.91 (0.88–0.94) | 0.94 (0.92–0.97) |
| Quartiles | | | | |
| Q1 (0–7) | 28 898 | 860 (3.0) | Ref. | Ref. |
| Q2 (8) | 46 471 | 1342 (2.9) | 0.94 (0.86–1.03) | 0.96 (0.88–1.05) |
| Q3 (9) | 54 300 | 1472 (2.7) | 0.88 (0.81–0.96) | 0.92 (0.85–1.01) |
| Q4 (10–14) | 49 839 | 1145 (2.3) | 0.76 (0.69–0.83) | 0.85 (0.77–0.93) |
| **Stubbendorff score** | | | | |
| Per 1-SD increment | 179 508 | 4819 (2.7) | 0.87 (0.84–0.89) | 0.91 (0.88–0.94) |
| Quartiles | | | | |
| Q1 (0–17) | 33 043 | 1013 (3.1) | Ref. | Ref. |
| Q2 (18–20) | 44 807 | 1283 (2.9) | 0.88 (0.81–0.96) | 0.91 (0.84–0.99) |
| Q3 (21–23) | 49 152 | 1355 (2.8) | 0.84 (0.78–0.92) | 0.91 (0.83–0.98) |
| Q4 (24–41) | 52 506 | 1168 (2.2) | 0.69 (0.64–0.76) | 0.78 (0.71–0.85) |
| **Kesse-Guyot score** | | | | |
| Per 1-SD increment | 179 508 | 4819 (2.7) | 0.89 (0.86–0.91) | 0.92 (0.90–0.95) |
| Quartiles | | | | |
| Q1 (< 3.8) | 44 877 | 1414 (3.2) | Ref. | Ref. |
| Q2 (3.8 to < 22.9) | 44 877 | 1238 (2.8) | 0.89 (0.82–0.96) | 0.90 (0.84–0.98) |
| Q3 (22.9 to < 43.7) | 44 877 | 1115 (2.5) | 0.81 (0.74–0.87) | 0.86 (0.79–0.93) |
| Q4 (≥ 43.7) | 44 877 | 1052 (2.3) | 0.74 (0.68–0.80) | 0.82 (0.76–0.90) |

Note: CI = confidence interval, HR = hazard ratio, Ref. = reference, SD = standard deviation.
*Model 1: Adjusted for age, sex, race, body mass index, Townsend deprivation index, smoking status, physical activity, comorbidities (hypertension, diabetes, and high cholesterol), alcohol consumption, vitamin and mineral supplements, diet variation, and total energy.
†Model 2: Adjusted for covariates in Model 1, as well as genetic risk score for chronic kidney disease, and baseline renal function (estimated glomerular filtration rate and urine albumin-to-creatinine ratio).

(8.6%), and fluid balance (2.9%) (Figure 4B). Key mediators included the degree of unsaturation (the number of carbon–carbon double bonds in fatty acids), glycoprotein acetyls, and docosahexaenoic acid (DHA) (Appendix 1, Supplementary Table S35; Appendix 2, Supplementary Figure S7).

The proteomic signature score mediated a more substantial proportion of the association, accounting for 27.2% of the total effect ($p < 0.001$; Figure 4C). Key mediating pathways included cytokine–cytokine receptor interaction (15.1%), efferocytosis (16.5%), and lysosome function (6.6%) (Figure 4D). Major protein mediators were hepatitis A virus cellular receptor 1 (HAVCR1), interleukin-18 receptor 1 (IL18R1), and pro-transforming growth factor α (Appendix 1, Supplementary Table S36; Appendix 2, Supplementary Figure S7).

## Interpretation

In this large prospective cohort study, greater adherence to the EAT–Lancet planetary health diet was significantly associated with a reduced risk of incident CKD. This protective association was particularly evident among individuals with low residential green space exposure and specific genetic variants.

Greater adherence to the EAT–Lancet diet — assessed using 4 different scoring methods — was consistently associated with a

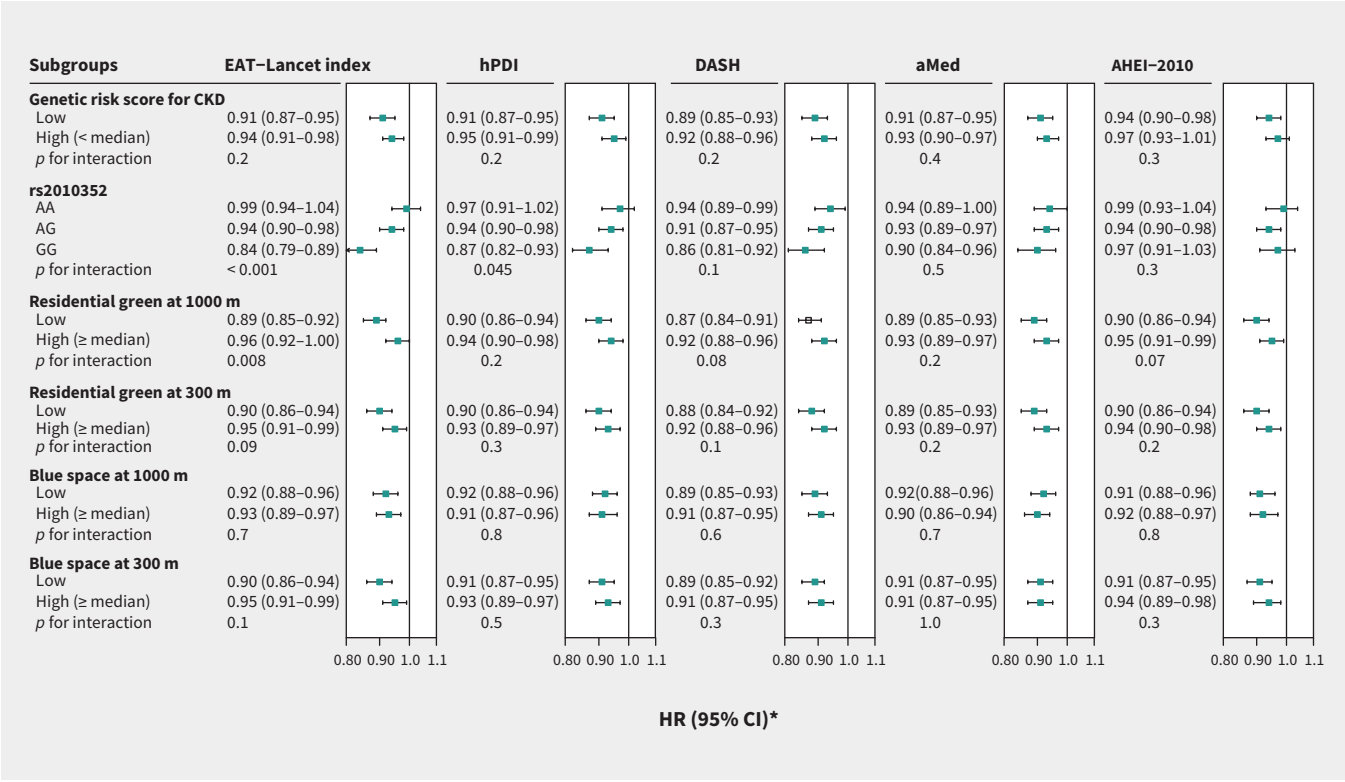


**Figure 2:** Subgroup analyses of associations between dietary patterns (per 1 standard deviation increase) and chronic kidney disease (CKD) risk, stratified by genetic and environmental factors, adjusted for age, sex, race, body mass index, Townsend deprivation index, smoking status, physical activity, comorbidities (hypertension, diabetes, and high cholesterol), alcohol consumption (adjusted for EAT–Lancet index, Dietary Approaches to Stop Hypertension [DASH], and healthful Plant-Based Diet Index [hPDI]), vitamin and mineral supplements, diet variation, total energy, genetic risk score for CKD (not adjusted when stratified by genetic factors), and baseline renal function (estimated glomerular filtration rate and urine albumin-to-creatinine ratio). The EAT–Lancet index was defined by the Kesse-Guyot score. Note: AHEI-2010 = Alternative Healthy Eating Index–2010, aMed = Alternate Mediterranean diet, CI = confidence interval, HR = hazard ratio. *Unless otherwise specified.

reduced risk of incident CKD. The Kesse-Guyot scores showed slightly stronger inverse associations, which may be attributable to their continuous and unbounded scoring systems that better capture individual variations in dietary intake. Notably, the magnitude of risk reduction associated with the EAT–Lancet diet was comparable to that of established dietary patterns such as DASH, aMed, and hPDI, and slightly stronger than that of AHEI-2010.

A key commonality among these dietary patterns is their emphasis on higher consumption of vegetables, fruits, and nuts, and reduced intake of red meat — components consistently associated with lower CKD risk in previous studies.[27–29] A distinctive aspect of the EAT–Lancet diet is its specific limitation of added sugars and fats, which may further mitigate kidney risk through modulation of inflammation and oxidative stress pathways.[30,31] These results underscore the potential of the EAT–Lancet diet as an effective dietary strategy for CKD prevention.

Subgroup analyses showed that the association between adherence to the EAT–Lancet diet and reduced risk of CKD was modified by specific genetic and environmental factors. A significant interaction was observed with the rs2010352 genetic variant, located near the AK6 gene involved in adenosine metabolism.[32] This variant may influence adenosine signalling, potentially modulating diet-induced inflammation, oxidative stress, and fibrosis, thereby affecting CKD risk.[33] This suggests that individuals with different AK6 genotypes may respond differently to the EAT–Lancet diet, highlighting a potential role for genetically informed dietary recommendations. Additionally, residential green space exposure modified this association, with a stronger protective effect of the diet observed among individuals with lower green space availability. This may indicate a compensatory role of diet in mitigating environmental risks. Notably, no interaction was found with overall genetic risk score for CKD or with socioeconomic status (as measured by Townsend deprivation index), supporting the idea that the benefits of the EAT–Lancet diet could be broadly applicable across genetic backgrounds and that green space may exert an independent environmental effect. These findings highlight the potential for targeted dietary strategies based on genetic and environmental contexts.

We identified 122 metabolites and 143 proteins significantly associated with EAT–Lancet adherence. Notably, while many biomarkers (e.g., ghrelin upregulation and very low-density lipoprotein lipid reduction) were shared with other healthy diets such as DASH and aMed — helping explain their similar protective effects[24,34] — 23 biomarkers were unique to the EAT–Lancet diet. These included complement component 3 and endoglin, which may identify individuals most likely to benefit from this dietary pattern.[35,36] Integration of these omics signatures with

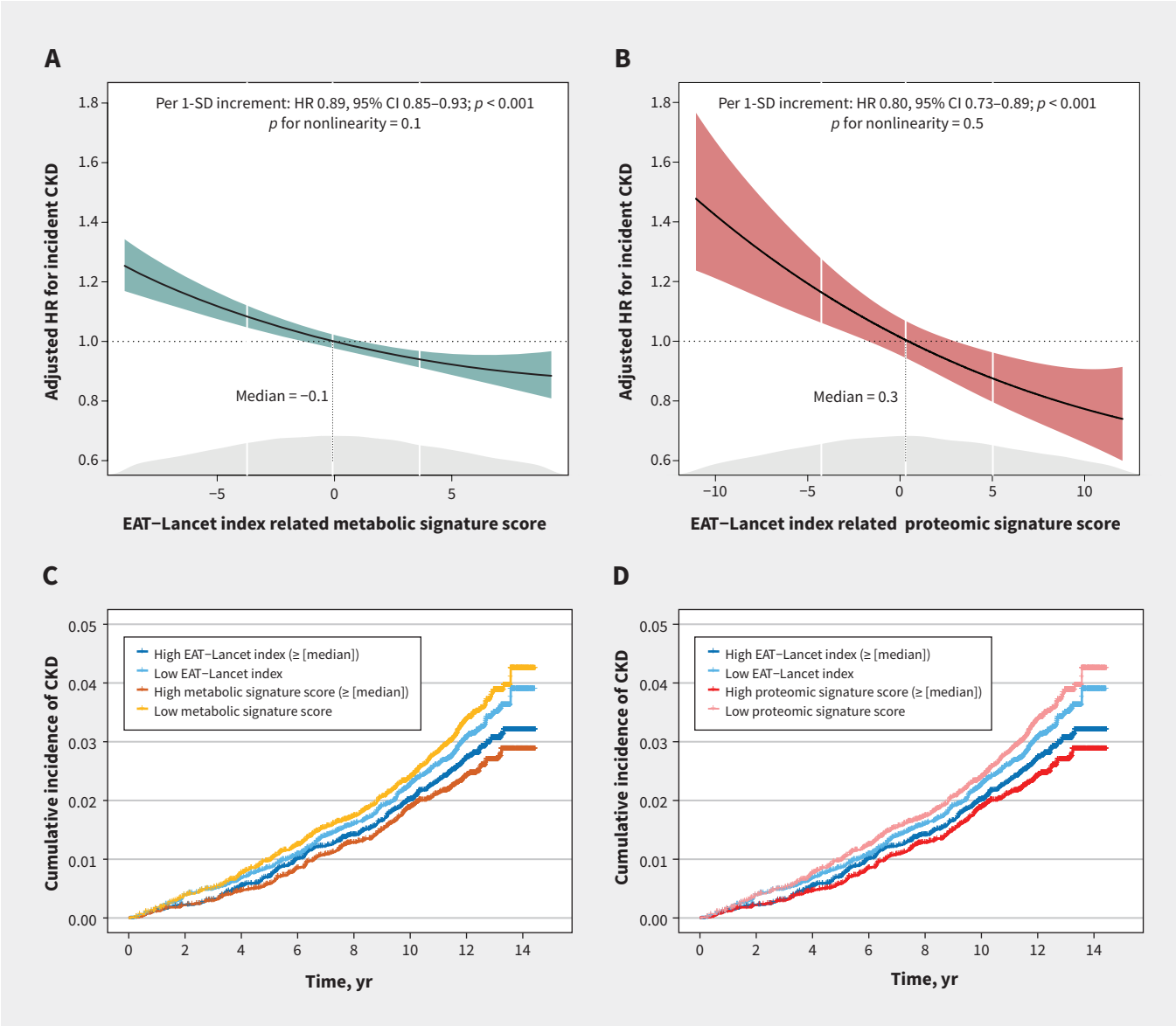


**Figure 3:** Dose–response curves show the association between the metabolic (A) and proteomic (B) signature scores of the EAT–Lancet diet and the risk of chronic kidney disease (CKD). The reference point (hazard ratio [HR] 1) corresponds to the median value of each score. Cumulative incidence of CKD by dichotomized exposure levels (low v. high, using the median as cut-off) for the EAT–Lancet diet, metabolic signature score (C), and proteomic signature score (D). Median values were 22.9 for the EAT–Lancet diet (Kesse-Guyot score), −0.1 for the metabolic score, and 0.3 for the proteomic score. Note: CI = confidence interval, SD = standard deviation.

dietary data offers a promising approach to personalizing nutrition strategies for CKD prevention.

The association between the EAT–Lancet diet and a reduced risk of CKD was partially mediated — accounting for about 18% to 27% of the protective effect — through specific metabolomic and proteomic pathways.

Three major metabolite categories were identified as mediators: anti-inflammatory fatty acids (e.g., DHA), inflammatory markers, and fluid balance regulators. These align closely with established CKD pathophysiology.[37,38] Polyunsaturated fatty acids such as DHA are known to attenuate renal inflammation and oxidative stress, both key drivers of CKD progression.[39] Inflammatory glycoproteins reflect subclinical immune activation, commonly elevated in CKD,[38] while fluid-regulating metabolites help maintain vascular and tubular homeostasis.[40,41] The EAT–Lancet diet, rich in unsaturated fats, polyphenols, and high-quality protein, may directly modulate these metabolic pathways, thereby mitigating renal damage.[42–44]

Four key biological pathways mediated the diet–CKD association: cytokine–cytokine receptor interaction, efferocytosis, lysosomal function, and phagosomal regulation. These are critically implicated in CKD pathogenesis. For example, cytokine receptors (e.g., IL18R1) modulate inflammatory responses that promote fibrosis,[45] while efferocytosis-related proteins (e.g., HAVCR1 or kidney injury molecule-1) are involved in clearing damaged cells and the renal fibrosis process.[46] Lysosomal and phagosomal pathways maintain cellular homeostasis and are often impaired in CKD.[47] The EAT–Lancet diet, through its anti-inflammatory and lipid-modifying

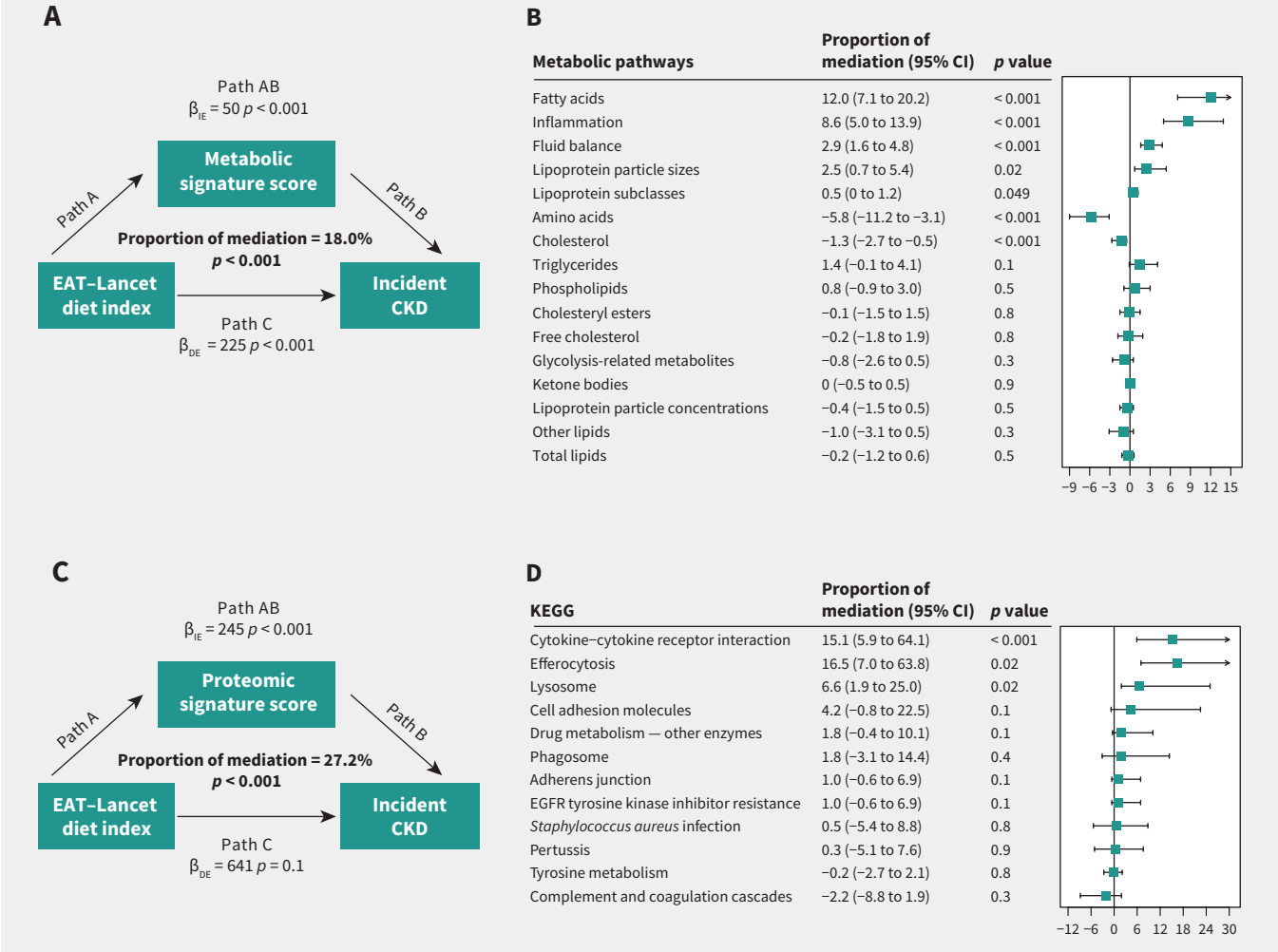


**Figure 4:** Mediation analysis of the association between the EAT–Lancet index and chronic kidney disease (CKD) risk through (A) overall metabolic signature score, (B) specific metabolic pathways, (C) overall proteomic signature score, and (D) specific proteomic pathways. $\beta_{IE}$ represents the indirect effect of the metabolic or proteomic signature or pathways on incident CKD; $\beta_{DE}$ indicates the direct effect of the EAT–Lancet index. Models were adjusted for age, sex, race, body mass index, Townsend deprivation index, smoking status, physical activity, comorbidities (hypertension, diabetes, and high cholesterol), alcohol consumption, vitamin and mineral supplements, diet variation, total energy intake, genetic risk score for CKD, and baseline renal function (estimated glomerular filtration rate [eGFR] and urine albumin-to-creatinine ratio). The EAT–Lancet index was defined using the Kesse-Guyot score. Note: CI = confidence interval, KEGG = Kyoto Encyclopedia of Genes and Genomes.

components, may enhance efferocytic capacity and restore lysosomal function, thereby preserving kidney integrity.[48–50]

Collectively, these multi-omics mechanisms reflect the diet's potential to simultaneously target inflammation, lipid metabolism, and cellular clearance processes — highlighting its potential role in personalized CKD prevention strategies.

Our findings offer several clinically relevant implications for both clinicians and patients. The EAT–Lancet diet may provide a practical, evidence-based dietary framework for CKD prevention, with clearly defined recommendations across 14 food groups that facilitate clinical application and patient adherence. Its benefits seem particularly pronounced among high-risk subgroups — such as individuals with specific genetic variants (e.g., rs2010352) or limited residential green space — enabling more personalized and stratified dietary guidance.

The multi-omics biomarkers identified in this study further enhance personalization by offering objective tools to monitor metabolic and proteomic responses, potentially allowing clinicians to track adherence and tailor dietary advice based on individual physiologic profiles. Importantly, the EAT–Lancet diet aligns with broader chronic disease prevention goals, supporting overall health beyond CKD.[4] These insights reinforce the value of integrating planetary health principles with precision nutrition, paving the way for functionally enriched foods and targeted dietary strategies that benefit high-risk individuals across multiple disease domains.

## Limitations

Although the dietary assessment method used has been extensively validated,[17] the reliance on 24-hour dietary questionnaires may introduce recall bias and might not fully represent long-term dietary patterns. However, sensitivity analyses excluding participants with only 1 dietary assessment yielded consistent results among those with repeated measures (median 3) (Appendix 1,

Supplementary Table S18), supporting the robustness of our findings. Despite adjustment for numerous confounders, residual confounding may persist owing to unmeasured health-seeking behaviours. Moreover, self-reported measures of smoking, alcohol use, and physical activity are susceptible to social desirability bias, potentially leading to nondifferential misclassification. While ICD-10 codes have demonstrated high specificity (≥ 0.90) in identifying CKD patients in validation studies,[51] their sensitivity is variable and some patients with CKD may have been missed. This could potentially lead to an underestimation of the true association between EAT–Lancet diet adherence and CKD risk. Finally, the UK Biobank cohort is predominantly White and older, limiting generalizability to other ethnic and age groups.

## Conclusion

Adherence to the EAT–Lancet diet is associated with a lower risk of incident CKD, particularly in individuals with low green-space exposure and specific genetic variants. The protective effect is partially mediated through multi-omic pathways related to inflammation, lipid metabolism, and cellular homeostasis. These findings support the adoption of planetary health diets in CKD prevention and underscore the value of personalized nutrition strategies that incorporate genetic, environmental, and molecular profiling.

## References


1. Kalantar-Zadeh K, Jafar TH, Nitsch D, et al. Chronic kidney disease. *Lancet* 2021;398:786-802.
2. Foreman KJ, Marquez N, Dolgert A, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016-40 for 195 countries and territories. *Lancet* 2018;392:2052-90.
3. Kramer H. Diet and chronic kidney disease. *Adv Nutr* 2019;10 (Suppl 4): S367-79.
4. Willett W, Rockström J, Loken B, et al. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. *Lancet* 2019;393:447-92.
5. Sotos-Prieto M, Bhupathiraju SN, Mattei J, et al. Association of changes in diet quality with total and cause-specific mortality. *N Engl J Med* 2017;377:143-53.
6. Fung TT, Hu FB, McCullough ML, et al. Diet quality is associated with the risk of estrogen receptor-negative breast cancer in postmenopausal women. *J Nutr* 2006;136:466-72.
7. Chiuve SE, Fung TT, Rimm EB, et al. Alternative dietary indices both strongly predict risk of chronic disease. *J Nutr* 2012;142:1009-18.
8. Heianza Y, Zhou T, Sun D, et al. Healthful plant-based dietary patterns, genetic risk of obesity, and cardiovascular risk in the UK biobank study. *Clin Nutr* 2021;40:4694-701.
9. Chen H, Wang X, Ji JS, et al. Plant-based and planetary-health diets, environmental burden, and risk of mortality: a prospective cohort study of middle-aged and older adults in China. *Lancet Planet Health* 2024; 8:e545-53.
10. Zhang S, Stubbendorff A, Olsson K, et al. Adherence to the EAT-Lancet diet, genetic susceptibility, and risk of type 2 diabetes in Swedish adults. *Metabolism* 2023;141:155401.
11. Laine JE, Huybrechts I, Gunter MJ, et al. Co-benefits from sustainable dietary shifts for population and environmental health: an assessment from a large European cohort study. *Lancet Planet Health* 2021;5:e786-96.
12. Liu M, Ye Z, He P, et al. Relations of residential green and blue spaces with new-onset chronic kidney disease. *Sci Total Environ* 2023;869:161788.
13. Zhang Y, Zhang Y, Ye Z, et al. Mobile phone use, genetic susceptibility and new-onset chronic kidney diseases. *Int J Public Health* 2023; 68:1605358.
14. Ye Z, Zhang Y, Zhang Y, et al. Large-scale proteomics improve prediction of chronic kidney disease in people with diabetes. *Diabetes Care* 2024;47:1757-63.
15. Yang S, Ye Z, He P, et al. Plasma proteomics for risk prediction of Alzheimer's disease in the general population. *Aging Cell* 2024;23:e14330.
16. Sudlow C, Gallacher J, Allen N, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med* 2015;12:e1001779.
17. Liu B, Young H, Crowe FL, et al. Development and evaluation of the Oxford WebQ, a low-cost, web-based method for assessment of previous 24 h dietary intakes in large-scale prospective studies. *Public Health Nutr* 2011;14: 1998-2005.
18. Knuppel A, Papier K, Key TJ, et al. EAT-Lancet score and major health outcomes: the EPIC-Oxford study. *Lancet* 2019;394:213-4.
19. Stubbendorff A, Sonestedt E, Ramne S, et al. Development of an EAT-Lancet index and its relation to mortality in a Swedish population. *Am J Clin Nutr* 2022;115:705-16.
20. Ye YX, Geng TT, Zhou YF, et al. Adherence to a planetary health diet, environmental impacts, and mortality in Chinese adults. *JAMA Netw Open* 2023;6:e2339468.
21. Kesse-Guyot E, Rebouillat P, Brunin J, et al. Environmental and nutritional analysis of the EAT-Lancet diet at the individual level: insights from the NutriNet-Santé study. *J Clean Prod* 2021;296:126555.
22. Lu X, Wu L, Shao L, et al. Adherence to the EAT-Lancet diet and incident depression and anxiety. *Nat Commun* 2024;15:5599.
23. Cheng X, Song C, Ouyang F, et al. Systolic blood pressure variability: risk of cardiovascular events, chronic kidney disease, dementia, and death. *Eur Heart J* 2025;46:2673-87.
24. Geng TT, Chen JX, Lu Q, et al. Nuclear magnetic resonance-based metabolomics and risk of CKD. *Am J Kidney Dis* 2024;83:9-17.
25. Liu M, Zhang Y, Ye Z, et al. Inflammatory bowel disease with chronic kidney disease and acute kidney injury. *Am J Prev Med* 2023;65:1103-12.
26. Schandelmaier S, Briel M, Varadhan R, et al. Development of the Instrument to assess the Credibility of Effect Modification Analyses (ICEMAN) in randomized controlled trials and meta-analyses. *CMAJ* 2020;192:E901-6.
27. Wang K, Qian D, Hu Y, et al. Nut consumption and effects on chronic kidney disease and mortality in the United States. *Am J Nephrol* 2022;53: 503-12.
28. Mirmiran P, Yuzbashian E, Aghayan M, et al. A prospective study of dietary meat intake and risk of incident chronic kidney disease. *J Ren Nutr* 2020;30:111-8.
29. Jhee JH, Kee YK, Park JT, et al. A diet rich in vegetables and fruit and incident CKD: a community-based prospective cohort study. *Am J Kidney Dis* 2019; 74:491-500.
30. Andres-Hernando A, Orlicky DJ, Cicerchi C, et al. High fructose corn syrup accelerates kidney disease and mortality in obese mice with metabolic syndrome. *Biomolecules* 2023;13:780.
31. Muramatsu H, Akimoto N, Hashimoto M, et al. Influence of polyunsaturated fatty acid intake on kidney functions of rats with chronic renal failure. *Mar Drugs* 2021;19:692.
32. SNP-National Center for Biotechnology Information (NCBI) [website]. Bethesda (MD): National Library of Medicine. Available: https://www.ncbi.nlm.nih.gov/snp/ (accessed 2025 Aug. 15).
33. Oyarzún C, Garrido W, Alarcón S, et al. Adenosine contribution to normal renal physiology and chronic kidney disease. *Mol Aspects Med* 2017;55:75-89.
34. Deboer MD, Zhu X, Levasseur PR, et al. Ghrelin treatment of chronic kidney disease: improvements in lean body mass and cytokine profile. *Endocrinology* 2008;149:827-35.
35. Gerrits T, Brouwer IJ, Dijkstra KL, et al. Endoglin is an important mediator in the final common pathway of chronic kidney disease to end-stage renal disease. *Int J Mol Sci* 2022;24:646.
36. Bao X, Borné Y, Muhammad IF, et al. Complement C3 and incident hospitalization due to chronic kidney disease: a population-based cohort study. *BMC Nephrol* 2019;20:61.
37. Waters DD, Vogt L. Lipids, inflammation, and chronic kidney disease: a SHARP perspective. *Kidney Int* 2018;93:784-6.
38. Kettunen J, Ritchie SC, Anufrieva O, et al. Biomarker glycoprotein acetyls is associated with the risk of a wide spectrum of incident diseases and stratifies mortality risk in angiography patients. *Circ Genom Precis Med* 2018;11:e002234.
39. Ong KL, Marklund M, Huang L, et al. Association of omega 3 polyunsaturated fatty acids with incident chronic kidney disease: pooled analysis of 19 cohorts. *BMJ* 2023;380:e072909.
40. John B, Tan BK, Dainty S, et al. Plasma volume, albumin, and fluid status in peritoneal dialysis patients. *Clin J Am Soc Nephrol* 2010;5:1463-70.
41. Fischer K, Kettunen J, Würtz P, et al. Biomarker profiling by nuclear magnetic resonance spectroscopy for the prediction of all-cause mortality: an observational study of 17 345 persons. *PLoS Med* 2014;11:e1001606.
42. Qi J, Spinelli JJ, Dummer T, et al. Metabolomics and cancer preventive behaviors in the BC Generations Project. *Sci Rep* 2021;11:12094.

43. Zhubi-Bakija F, Bajraktari G, Bytyçi I, et al. The impact of type of dietary protein, animal versus vegetable, in modifying cardiometabolic risk factors: a position paper from the International Lipid Expert Panel (ILEP). *Clin Nutr* 2021;40:255-76.
44. Whelan J, Fritsche K. Linoleic acid. *Adv Nutr* 2013;4:311-2.
45. Hao Y, Reyes LT, Morris R, et al. Changes of protein levels in human urine reflect the dysregulation of signaling pathways of chronic kidney disease and its complications. *Sci Rep* 2020;10:20743.
46. Tutunea-Fatan E, Arumugarajah S, Suri RS, et al. Sensing dying cells in health and disease: the importance of kidney injury molecule-1. *J Am Soc Nephrol* 2024;35:795-808.
47. Kimura T, Isaka Y, Yoshimori T. Autophagy and kidney inflammation. *Autophagy* 2017;13:997-1003.
48. Wang R, Yao L, Lin X, et al. Exploring the potential mechanism of *Rhodomyrtus tomentosa* (Ait.) Hassk fruit phenolic rich extract on ameliorating nonalcoholic fatty liver disease by integration of transcriptomics and metabolomics profiling. *Food Res Int* 2022;151:110824.
49. Yoshimura A, Yamaguchi T, Kugita M, et al. High levels of dietary lard or sucrose may aggravate lysosomal renal injury in non-obese, streptozotocin-injected CD-1 mice provided isocaloric diets. *J Nutr Sci Vitaminol (Tokyo)* 2021;67:243-8.
50. Yum HW, Na HK, Surh YJ. Anti-inflammatory effects of docosahexaenoic acid: implications for its cancer chemopreventive potential. *Semin Cancer Biol* 2016;40-41:141-59.
51. Grams ME, Plantinga LC, Hedgeman E, et al. Validation of CKD and related conditions in existing data sets: a systematic review. *Am J Kidney Dis* 2011;57:44-54.



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