

An evaluation of the diet-wide contribution to serum urate levels

Journal:	ВМЈ
Manuscript ID	BMJ.2017.042924
Article Type:	Research
BMJ Journal:	вмл
Date Submitted by the Author:	19-Dec-2017
Complete List of Authors:	Major, Tanya; University of Otago Topless, Ruth; University of Otago, Dalbeth, Nicola; University of Auckland, Merriman, Tony; University of Otago, Biochemistry
Keywords:	uric acid, urate, diet, association

SCHOLARONE™ Manuscripts

An evaluation of the diet-wide contribution to serum urate levels

Tanya J Major¹, Ruth K Topless¹, Nicola Dalbeth², Tony R Merriman^{1*}

Tanya J Major

Job title – Post-Doctoral Fellow

Address – Department of Biochemistry, University of Otago, 710 Cumberland Street, Dunedin 9054, New Zealand.

Ruth K Topless

Job Title – Assistant Research Fellow

Address – Department of Biochemistry, University of Otago, 710 Cumberland Street, Dunedin 9054, New Zealand.

Nicola Dalbeth

Job Title – Professor

Address – Department of Medicine, University of Auckland, 85 Park Rd, Grafton, Auckland 1023, New Zealand.

Tony R Merriman* corresponding author

Job Title – Professor

Address – Department of Biochemistry, University of Otago, 710 Cumberland Street, Dunedin 9054, New Zealand.

E-mail – tony.merriman@otago.ac.nz

Phone - +64 3 479 7846

ABSTRACT

Objective: To systematically test dietary components for association with serum urate and to evaluate the percent variance in serum urate explained by a 'healthy' diet.

Design: Association testing of individual food items in a diet-wide association study (DWAS) and association of composite dietary scores with serum urate levels using cross-sectional data from five cohort studies.

Setting: Atherosclerosis Risk in Communities study (1987 to 1989), Coronary Artery Risk Development in (Young) Adults study (1985), Cardiovascular Health Study (1989 to 1990), Framingham Heart Study (2002 to 2005), and Third National Health and Nutrition Examination Survey (1988 to 1991).

Participants: 18,348 North Americans of European ancestry (9,825 men and 8,523 women) over 18 years of age and without kidney disease, gout, and urate-lowering or diuretic medication use. All participants had serum urate measurements, dietary survey data, information on potential confounders (sex, age, body mass index, average daily calorie intake, and menopausal status), two 'healthy' diet scores, and genome-wide genotypes.

Main Outcome Measures: Average serum urate levels and variance in serum urate levels. Beta-values (95% confidence intervals) and Bonferroni-corrected p-values from covariate-adjusted linear regression analyses, along with regression partial R² values, were used to quantitate association.

Results: Six foods associated with raised serum urate (beer, liquor, wine, tea, shellfish, and soft drinks) and seven foods associated with reduced serum urate (cheese, skim milk, non-citrus fruits, brown bread, margarine, peanuts, and eggs) in sex-specific or combined cohorts. Both a 'Healthy-Eating' and a 'Dietary Approaches to Stop Hypertension (DASH)' diet score were inversely associated with serum urate, but each explained < 0.3% of variance in serum urate. In comparison, in the cohorts tested, 23.9% of variance in serum urate levels was explained by common genome-wide single nucleotide variation.

.st to genetic contributions, diet
.s.

INTRODUCTION

Hyperuricaemia (elevated serum urate concentration) is a central risk factor for gout, and is also associated with chronic kidney disease, hypertension, and metabolic syndrome.[1-4] The balance between hepatic production of urate and intestinal / renal urate excretion pathways determine an individual's serum urate levels.[5] This balance can be modified by both genetic and environmental factors. Familial and twin studies estimating the heritability of serum urate suggest genetic factors explain 25 to 60% of the variability in serum urate levels,[6-13] consistent with estimates from a genome-wide association study of unrelated individuals, which predicted that 25 to 40% of the variability in serum urate levels is controlled by common single nucleotide variants.[14] The remaining 60 to 75% of serum urate variability is therefore explained by genetic factors (common and uncommon) not tagged by common variants, and non-genetic factors such as diet or other environmental exposures.

For centuries diet has been identified as a risk factor for the development of gout.[15 16] Consumption of red meat, shellfish, alcoholic beverages, sugary drinks, and tomatoes have all been associated with increased serum urate levels, and low-fat milk and coffee consumption have been associated with reduced serum urate levels.[17-21] While certain diets (e.g. the Dietary Approaches to Stop Hypertension (DASH)) have been shown to reduce serum urate levels and the risk of gout,[22 23] to date a systematic analysis of the contribution of diet to serum urate levels has not been performed in a sufficiently large data set. Furthermore, the relative contributions of inherited genetic variants and overall diet to variance in serum urate concentrations is unknown. This study aimed to systematically test individual dietary components for association with serum urate in a 'diet-wide association study' (DWAS) and quantify the relative contributions of overall diet and common genome-wide single nucleotide variants in determining serum urate levels.

METHODS

Participants

Demographic, anthropomorphic, and clinical data are presented in Table S1. Information from the baseline visit of the Atherosclerosis Risk in Communities (ARIC; 1987 to 1989; www2.cscc.unc.edu/aric), Coronary Artery Risk Development in (Young) Adults (CARDIA; 1985; www.cardia.dopm.uab.edu), Cardiovascular Heart (CHS; 1989 to 1990; https://chs-nhlbi.org), and Framingham Heart (FHS; 2002 to 2005; www.framinghamheartstudy.org) studies was sourced through the database of Genotypes and Phenotypes (dbGaP; www.ncbi.nlm.nih.gov/gap; project ID #834). Anonymised information from the Third National Health and Nutrition Examination Survey (NHANES III; 1988 to 1991; www.cdc.gov/nchs/nhanes/nhanes3.htm) was also used. These five studies all recruited participants from the United States of America.

Analysis sample-sets of people of European ancestry were developed using consistent exclusion criteria between study cohorts (Figure S1). People without serum urate measurements or genome-wide genotypes were excluded, along with individuals under 18 years of age, people with kidney disease and / or gout, and those taking urate-lowering drugs and / or on diuretic medication. Quality controls for the dietary data were also applied, with participants who answered less than 10% of the food frequency survey excluded, along with individuals whose estimated average daily calorie intake was less than 600 kcal / day or greater than 4,200 kcal / day (inclusive). Participants whose questionnaire answers were deemed unreliable by the study interviewer were also excluded.

Dietary Assessment

During recruitment participants from the five cohorts completed a validated food frequency questionnaire. The ARIC, CHS, and FHS participants completed similar questionnaires in which participants were asked to answer the question "How often, on average, in the past year did you eat [this food]?" by choosing from several frequency

categories (66 questions and 9 answer categories for ARIC, 99 questions and 6 answer categories for CHS, and 126 questions and 9 answer categories for FHS).[24-28] These categorical answers were converted to average serves per week for analysis (Table S2). CARDIA participants answered a specifically designed and validated diet history which assessed their consumption frequency of 100 food items using several questions, "Do you eat [this food]?" if yes, "How much do you usually have?" and "How often do you usually have it?" Answers were then converted to servings per week by the study researchers using the Nutrition Coordinating Centre (NCC; www.ncc.umn.edu) dietary analysis system.[29 30] NHANES III participants were given a questionnaire (60 questions) similar to that of the ARIC, CHS, and FHS studies in which they were asked "How often, in your usual diet over the past month, have you eaten [this food item]?" Answers were given in serves per month and converted to serves per week for analysis (Table S2).[31]

As each study administered a slightly different food frequency questionnaire, with a differing number of questions (60 to 100) and a slightly different list of food items within each question, questionnaires were assessed for between-study comparability. Briefly, questions were grouped together based on food type. Where questions were identical no changes to the data were made. Where questions were not identical between studies (eg. questionnaires asked about any wine consumption vs. separate red wine and white wine consumption) the answers were combined (after serve per week conversion) to create identical questions. If an identical question could not be created the non-matching information was excluded. Additionally, if at least three of the five cohorts did not have identical questions the extra information was also excluded (eg. only CHS and FHS asked about berry consumption, so berries were not included in the DWAS). This resulted in a group of 65 food items with comparable questions within at least three of the five studies (Table S3). Average consumption of each of these 65 food items, per sample-set, is presented in Table S4.

Serum Urate Measurement

Serum urate levels were measured for each participant at recruitment. A standard uricase oxidation assay was used to measure serum urate for the ARIC, CARDIA, and NHANES III studies.[31-34] CHS serum urate levels were measured using a Kodak Ektachem 700 analyser and reagents.[35] For FHS serum urate levels were measured with a phosphotungstic acid reagent autoanalyser.[33 36]

Diet-Wide Association Analysis (DWAS)

For each food item a multivariate linear regression adjusted for sex, age, body mass index, menopausal status, and average daily calorie intake was conducted in the five cohorts separately. Analyses in ARIC, CARDIA, CHS, and FHS were additionally adjusted for whole-genome principal component vectors one to four to account for population stratification and cryptic relatedness (especially within FHS) that may cause confounding. Principal components were calculated using whole-genome genotyping (ARIC: Affymetrix 6.0; CARDIA: Affymetrix 6.0; CHS: Illumina HumanCNV370 duo Beadchip; FHS: Affymetrix 500K and Affymetrix 50K supplemental array; NHANES III: no genotype data available) and the SmartPCA program of EIGENSOFT 2.0, with an output of 10 eigenvectors, no outlier removal, and no population size limit.[37] Regression beta values from the five cohorts were combined using an inverse-variance weighted meta-analysis with a Q-statistic calculated to detect any inter-cohort heterogeneity using the 'metagen' function within the R meta package.[38] A fixed-effect model was used if there was no significant heterogeneity, with a random-effect model used in the presence of heterogeneity ($P_{\rm Q}$ < 0.05). For each regression analysis the partial R^{2} (R_{B}^{2}) attributable to the food item was calculated by comparing the regression R^{2} (R_{AB}^{2}) to the $R^2(R_A^2)$ of a corresponding regression using all the adjusting variables, but not the food item using the 'partial.R2' function with the R asbio package.[39] The diet-wide association analysis was repeated with the inclusion of two scores estimating diet quality (detailed below) as adjusting variables. Each analysis was also repeated in male-only and female-only subsets. Diet-wide significance was set at $P_{\beta} < 7.69 \times 10^{-4}$ after Bonferroni correction for multiple testing (0.05 divided by 65 food items).

Diet Quality Scores

Two diet quality scores were evaluated. The first was a 'Healthy-Eating' score calculated based on the Harvard Healthy Eating Pyramid (2008) and Healthy Eating Plate (2011) guidelines and an adaptation of the methodologies used by Nettleton *et al.*.[40] Food frequency questions (in serves / week) were combined into four categories representing the different levels of the Harvard Healthy Eating Pyramid / Plate[41] – Level 1: red meat, butter, refined grains, potatoes, sugar-sweetened beverages, and desserts / sweets; Level 2: dairy products (excluding butter) and alcohol; Level 3: nuts, seeds, beans, fish, poultry, and eggs; Level 4: vegetables, fruits, and whole grains. Quartiles of these four levels were determined and labelled numerically (0, 1, 2, 3) before being multiplied by a number representing each pyramid level. Level 1 was multiplied by negative two (least favourable), level 2 was multiplied by negative one, level 3 was multiplied by one, and level 4 was multiplied by two (most favourable). These values were summed to create a 'Healthy-Eating' score with a minimum value of -9 and a maximum value of 9, with a larger number indicating 'healthier' dietary habits (Figure S2).

The second diet quality score was the 'Dietary Approaches to Stop Hypertension (DASH)' diet score calculated based on the DASH diet recommendations and a direct replication of the methodologies used previously.[42 43] Food items (in serves per week) were grouped into five food groups representing foods that are emphasised in the DASH diet; fruits, vegetables, nuts / legumes, whole grains, and low-fat dairy products. Two food groups representing foods that are minimised in the DASH diet were also created; red / processed meats and sugar-sweetened beverages. An estimate of the total sodium intake (calculated as part of the food to macro-nutrient conversion protocols performed by each study[24 25 27 29 31]) was included as a third food group that is minimised in the DASH diet. Each food group was classified into quintiles. Those foods that are emphasised in the DASH diet were labelled numerically in ascending order (1, 2, 3, 4, 5) and those foods that are minimised in the DASH diet were labelled in descending order (5, 4, 3, 2, 1). These component scores were summed together to create the final DASH

diet score with a minimum value of 8 and a maximum value of 40, with a larger number indicating 'healthier' dietary habits (Figure S3).

The correlation between diet quality scores was assessed using a Pearson's product-moment correlation test. For each study the two diet quality scores were included in a multivariate linear regression of serum urate levels (separately), adjusted for sex, age, body mass index, menopausal status, and average daily calorie intake, (and whole-genome principal component vectors one to four for ARIC, CARDIA, CHS, and FHS). Regression beta values from each cohort were combined using an inverse-variance weighted meta-analysis with a fixed-effect model if there was no significant heterogeneity, and a random-effect model if there was heterogeneity present ($P_Q < 0.05$). This was repeated in the male-only and female-only subsets. A p-value less than 0.05 was considered statistically significant for these diet quality score analyses. As with the diet-wide analysis the partial \mathbb{R}^2 attributable to the diet quality score was calculated for each regression.

Genetic Analysis

The percentage of variance in serum urate explained by common genetic variants was assessed in two ways. Firstly, the 30 genome-wide significant variants identified by Kottgen *et al.* (2013) in the largest European genome-wide association study[14] were obtained from the whole-genome genotyping data of the ARIC, CARDIA, CHS, and FHS cohorts. Where the specified variant was not directly genotyped, it was imputed on the Sanger Imputation Server (https://imputation.sanger.ac.uk) using a Positional Burrows-Wheeler Transform imputation method.[44] Imputed genotypes were calculated using SHAPEIT2 pre-phased data,[45] and the UK10K plus 1000 genomes phase 3 reference panel. Imputation quality was high for all SNPs analysed (info score \geq 0.58). All variants were in Hardy-Weinberg equilibrium (P > 0.05) within the analysis group, except for rs11264341 in CHS ($P_{\rm HWE} = 0.04$) and rs653178 in ARIC ($P_{\rm HWE} = 2.15 \times 10^{-3}$). A weighted genetic risk score was constructed from these genotypes and assessed for its contribution to serum urate variability. To create the genetic risk score genotypes were

coded (0, 1, 2) to represent the number of risk alleles present, as defined by the effect directions reported by Köttgen *et al.*[14] and were multiplied by the effect size (converted to µmolL⁻¹) estimated by Köttgen *et al.*[14] These weighted variables were summed together, resulting in a genetic risk score with a minimum value of 0 and a maximum value of 236.15. The genetic risk score was associated with serum urate levels using a multivariate linear regression, adjusted for sex, age, body mass index, menopausal status, average daily calorie intake, and the first four eigenvectors from principal component analysis. The resultant regression beta values from each cohort were combined using an inverse-variance weighted meta-analysis and, as with the dietary analyses, the partial R² attributable to the genetic risk score was calculated for each regression. This was repeated in the male-only and female-only subsets.

The second method to assess the contribution of common genetic variants to the variability of serum urate was the generation of heritability estimates under an additive model, and the combined cohort (excluding NHANES III). Briefly, non-imputed wholegenome genotypes for the ARIC, CARDIA, CHS, and FHS cohorts were merged, then filtered to exclude variants deviating from Hardy-Weinberg equilibrium ($P < 1 \times 10^{-6}$), with a variant call rate (< 70%), or a minor allele frequency < 0.01 using PLINK v1.90,[46] before a genetic relationship matrix was created using GCTA v1.26.0.[47] The genetic heritability of serum urate was then calculated using the restricted maximum likelihood (REML) analysis procedure within GCTA v1.26.0. This heritability estimate was adjusted for sex, age, body mass index, menopausal status, average daily calorie intake, and the first four eigenvectors from principal component analysis. Additional estimates were calculated for the male-only and female-only cohorts.

Study Power

Power to detect an association at the diet-wide significance level ($P_{\beta} = 7.69 \times 10^{-4}$) was calculated as described (Figure S4).[48] All sample-sets were adequately powered (\geq 80%) to detect an effect size (Cohen's f^2) of 0.02. This corresponded to a linear regression partial R^2 value of approximately 1% in each sample-set. The combined

sample-set had power to detect an association with a partial R² of approximately 0.1% (Cohen's $f^2 = 0.002$). Cohen's $f^2 = \frac{R_B^2}{1 - R_{AB}^2}$, where R_B^2 is the partial R^2 corresponding to the est and R²_{AB}

es were performed using R \(\cdots\), individuals with partial or missin. specific food item of interest and R_{AB} is the R² for the entire regression analysis.[49]

All statistical analyses were performed using R v3.2.3 (www.R-project.org). For all regression analyses individuals with partial or missing data were excluded.

RESULTS

Diet-Wide Association Analysis (DWAS)

Thirteen food items were significantly associated with serum urate levels in the full or sex-specific cohorts ($P_{\beta} < 7.69 \times 10^{-4}$; Figure 1, Table 1, and Table S5 to Table S7). Six associated with raised serum urate levels (beer, liquor, wine, tea, soft drink, and shellfish), and seven associated with lower serum urate levels (cheese, skim milk, non-citrus fruit, brown bread, peanuts, margarine, and eggs). In the full cohort wine and soft drinks were only nominally significant ($P_{\beta} < 0.05$, $P_{\beta} > 7.69 \times 10^{-4}$). Both were significantly associated with serum urate in the male-only analysis, along with six other food items (beer, liquor, skim milk, shellfish, peanuts, and eggs). In the female-only subset only three food items (beer, liquor, and brown bread) significantly associated with serum urate (Table 1).

Diet Quality Scores: Association with Serum Urate Levels

Increases in both the 'Healthy-Eating' and DASH diet scores significantly associated with lowered serum urate levels in the full cohort (β = -0.65 µmolL⁻¹, P_{β} = 5.3×10⁻⁶; β = -0.71 µmolL⁻¹, P_{β} = 7.3×10⁻⁵, respectively) and the male-only cohort (β = -0.82 µmolL⁻¹, P_{β} = 1.4×10⁻⁴; β = -0.76 µmolL⁻¹, P_{β} = 6.6×10-3, respectively), but only the DASH diet score was significantly associated with serum urate in the female-only cohort (β = -0.70 µmolL⁻¹, P_{β} = 0.01; Table 2). These diet quality scores were significantly correlated with each other (Cor = 0.71, P_{Cor} < 1.0×10⁻³⁰⁰) and the results of the regression analyses were not significantly different in the full or sex-stratified cohorts (P_{Diff} = 0.77, P_{Diff} = 0.85, and P_{Diff} = 0.65, for the full, male-only, and female-only cohorts respectively).

Given that foods are rarely consumed in isolation, and significant correlations ($P_{\text{Cor}} < 2.4 \times 10^{-5}$) were observed between every food item and at least one other food item (Figure S5), the diet-wide analysis was repeated with adjustment for the diet quality scores to account for confounding due to usual dietary habits. Nine of the eleven food items in the full cohort remained significantly associated (Table S5). Non-citrus fruit was non-significant after adjustment for either of the diet quality scores ($P_{\beta} = 0.10$ and $P_{\beta} = 0.48$), and peanuts maintained a significant association after adjustment for the 'Healthy-Eating'

Table 1. Diet-wide significant associations with serum urate levels in the full or sexspecific cohorts.

E - 4 I4	Full	Cohort		Ma	ale-Only		Fem	ale-Only	
Food Item	β [95% CI]	P_{β}	R ²	β [95% CI]	P_{β}	R^2	β [95% CI]	P_{β}	R ²
Beer	1.55 [1.08; 2.02] ¹	1.05×10 ⁻¹⁰	0.95%	1.33 [1.07; 1.58]	9.16×10 ⁻²⁵	1.23%	1.94 [1.32; 2.55]	6.36×10 ⁻¹⁰	0.47%
Liquor	1.48 [0.80; 2.15] ¹	1.97×10 ⁻⁰⁵	0.39%	1.16 [0.76; 1.56]	1.00×10 ⁻⁰⁸	0.38%	2.04 [1.39; 2.68]	6.87×10 ⁻¹⁰	0.46%
Wine	1.12 $[0.15; 2.09]^1$	0.02	0.17%	1.38 [0.70; 2.05]	6.33×10 ⁻⁰⁵	0.18%	0.83 [-0.50; 2.17] ¹	0.22	0.17%
Tea	0.33 [0.18; 0.49]	1.71×10 ⁻⁰⁵	0.10%	0.33 [0.10; 0.56]	4.23×10 ⁻⁰³	0.10%	0.32 [0.12; 0.53]	1.56×10 ⁻⁰³	0.12%
Soft Drink	0.72 $[0.29; 1.16]^1$	9.97×10 ⁻⁰⁴	0.27%	0.76 [0.48; 1.04]	1.54×10 ⁻⁰⁷	0.32%	0.70 [-0.02; 1.43] ¹	0.06	0.16%
Cheese	-0.59 [-0.87; -0.31]	4.39×10 ⁻⁰⁵	0.07%	-0.62 [-1.05; -0.19]	0.01	0.08%	-0.60 [-0.96; -0.23]	1.36×10 ⁻⁰³	0.06%
Skim Milk	-0.77 [-1.11; -0.42] ¹	1.65×10 ⁻⁰⁵	0.38%	-0.83 [-1.09; -0.58]	1.16×10 ⁻¹⁰	0.54%	-0.57 [-1.01; -0.14] ¹	0.01	0.23%
Shellfish	5.34 [3.30; 7.39]	3.06×10 ⁻⁰⁷	0.15%	6.07 [3.16; 8.98]	4.41×10 ⁻⁰⁵	0.19%	4.43 [1.56; 7.30]	2.49×10 ⁻⁰³	0.11%
Non-Citrus Fruit	-0.29 [-0.45; -0.14]	1.80×10 ⁻⁰⁴	0.06%	-0.38 [-0.62; -0.13]	2.77×10 ⁻⁰³	0.09%	-0.22 [-0.41; -0.03]	0.02	0.03%
Brown Bread	-0.54 [-0.73; -0.35]	1.43×10 ⁻⁰⁸	0.17%	-0.90 [-1.56; -0.23] ¹	0.01	0.20%	-0.51 [-0.78; -0.25]	1.66×10 ⁻⁰⁴	0.14%
*Peanuts	-0.93 [-1.35; -0.52]	8.86×10 ⁻⁰⁶	0.16%	-1.13 [-1.68; -0.57]	6.76×10 ⁻⁰⁵	0.24%	-0.59 [-1.21; 0.02]	0.06	0.06%
Margarine	-0.33 [-0.50; -0.15]	2.40×10 ⁻⁰⁴	0.08%	-0.38 [-1.05; 0.30] ¹	0.27	0.07%	-0.36 [-0.59; -0.12]	3.26×10 ⁻⁰³	0.09%
Eggs	-1.18 [-1.62; -0.74]	1.72×10 ⁻⁰⁷	0.14%	-1.56 [-2.15; -0.98]	1.45×10 ⁻⁰⁷	0.30%	-0.56 [-1.91; 0.79] ¹	0.41	0.01%

 β – inverse-variance weighted meta-analysis beta value, reflecting the change in serum urate level (µmol/L) per one extra serve per week of the food item. 95% CI – 95% confidence intervals of the beta value. P_{β} – p-value for meta-analysis beta value. R^2 – partial R^2 value (R_B^2) converted to a percentage (R^2 * 100). * – indicates not all data-sets were included in the analysis, the number of asterisks represents the number of data-sets missing data. 1 – indicates a random-effect model was used in the meta-analysis due to a heterogeneity P_Q < 0.05.

score ($P_{\beta} = 1.69 \times 10^{-4}$), but not after adjustment for the DASH diet score ($P_{\beta} = 1.12 \times 10^{-3}$). In addition, the non-significant association between serum urate levels and soft drink consumption in the full cohort was significant after adjustment for either of the diet quality scores ($P_{\beta} = 1.31 \times 10^{-8}$ for the 'Healthy-Eating' score and $P_{\beta} = 3.49 \times 10^{-7}$ for the DASH score). Similarly, adjustment for the 'Healthy-Eating' score resulted in significant associations between serum urate and fish or poultry consumption ($P_{\beta} = 1.36 \times 10^{-4}$ and $P_{\beta} = 8.28 \times 10^{-7}$). This was also seen after adjustment for the DASH diet score, with an additional significant association between tomato consumption and serum urate levels ($P_{\beta} = 7.37 \times 10^{-4}$, $P_{\beta} = 7.94 \times 10^{-6}$, and $P_{\beta} = 3.36 \times 10^{-4}$, respectively). In the male-only analysis all eight of the previously associated foods maintained their significance after adjustment for the 'Healthy-Eating' score (Table S6). Peanuts did not maintain their significance after adjustment for the DASH diet score ($P_{\beta} = 1.12 \times 10^{-3}$), but the other seven food items maintained significance (Table S6). In the female-only analysis, only beer and liquor were consistently significant after the diet quality score adjustments (Table S7).

Variance in Serum Urate Explained by Dietary Scores and Inherited Genetic Variants

Individually, the eleven food items associating with serum urate in the full-cohort explained 0.06% to 0.95% of the variation in serum urate levels, and combined they explained 3.07% of the variation (additive effect; Table 1). All 65 food items, collectively, explained 4.12% of variation in serum urate levels (Table S5). The DASH diet score explained more of the variation in serum urate levels in the full cohort (0.22%) than the 'Healthy-Eating' score (0.14%; Table 2), but each diet quality score explained less variation in serum urate than the most strongly associated individual food items (Table 1).

In contrast, 30 variants previously associated with serum urate levels at a genome-wide level of significance in Europeans[14] additively explained 8.5% of the variance in serum urate levels in the full cohort (excluding NHANES III; results not shown) and a weighted serum urate genetic risk score constructed from these 30 variants[14] explained 7.7% of the variance (Table 2). When included in models with either the DASH or 'Healthy-

Table 2. Percent variance in serum urate levels (µmolL⁻¹) explained by dietary and genetic factors.

Cohort	'Hea	althy-Eating	g' Score		D	ASH Diet S	core			Genetic I	Risk Scor	e		Heritabi	lity
Conort	β [95% CI]	P_{β}	R^2	R^2_{GRS}	β [95% CI]	P_{β}	R^2	R^2_{GRS}	β [95% CI]	P_{β}	R^2	R ² _{HES}	R^2_{DASH}	h ² [95% CI]	$P_{h}^{^2}$
Full	-0.65	5.34×10 ⁻⁰⁶	0.1494	0.129/	-0.71	7.33×10 ⁻⁰⁵	0.229/	0.289/	0.98	1.28×10 ⁻²²⁶	7.69%	7.66%	7.67%	23.86%	< 1×10 ⁻¹⁶
[-0.92; -0	[-0.92; -0.37]	3.34^10	0.14/0	0.12/0	$[-1.07; -0.36]^1$	7.55^10 0.22	0.22/0	0.22% 0.28%	[0.92; 1.04]	1.26^10 /.09/0	7.0070	7.0770	[20.20; 27.52]	< 1×10	
Male-Only	-0.82	1 42×10 ⁻⁰⁴	0.179/	0.199/	-0.76	6 57×10 ⁻⁰³	0.109/	0.20%	0.92	3.40×10 ⁻⁸⁴	5.75%	5.73%	5.75%	23.82%	8.19×10 ⁻¹²
Maie-Only	[-1.25; -0.40]	40] 1.42×10 ⁻⁰⁴ 0.17% 0.18%	$\begin{bmatrix} -0.76 \\ [-1.30; -0.21]^1 \end{bmatrix}$ 6.57×10 ⁻⁰³ 0.19% 0.29%		0.29/0	[0.83; 1.02]			3.7370	[16.62; 31.02]					
Famala Only	-0.48	0.23	0.10%	0.06%	-0.70	0.01	0.220/	0.22%	1.04	4.97×10 ⁻¹⁵⁹	10 /110/	10.270/	10.409/	40.30%	< 1×10 ⁻¹⁶
Female Only	$[-1.26; 0.30]^1$	0.23	0.1076	0.00%	$[-1.26; -0.15]^1$	0.01	0.2276	0.2270	[0.96; 1.11]	4.9/^10	10.4170	10.5776	10.40%	[33.54; 47.05]	< 1×10

 β – inverse-variance weighted meta-analysis beta value, reflecting the change in serum urate level (μ mol/L) per one number increase in diet score or genetic risk score. h^2 – heritability estimate converted to a percentage ($h^2 * 100$), 95% CI – 95% confidence intervals of the beta value or h^2 , P_{β} – p-value for meta-analysis beta value. P_b^2 – log-likelihood ratio test p-value for the heritability estimate. R^2 partial R^2 value (R_B^2) converted to a percentage ($R^2 * 100$), R^2_{GRS} – partial R^2 value with additional adjustment for the genetic risk score. R^2_{HES} or R^2_{DASH} – partial R^2 value after additional adjustment for the 'Healthy-Eating' or DASH diet score. 1 – indicates a random-effect model was used in the meta-analysis due to a heterogeneity $P_0 < 0.05$.

.entage variance ex,

c2), whilst the percentag.
.dic risk score fluctuated from a

only cohort to a +0.09% difference in

Genome-wide estimations of serum urate h

c levels in the full cohort (excluding NHANES II),

were 23.8% in the male-only cohort and 40.3% in the fe.

DISCUSSION

Thirteen different food items were significantly associated with serum urate levels. These foods included seven established urate-modifying foods; beer, liquor, wine, soft drinks, cheese, skim milk, and shellfish. The six other foods included two less established urate-modifying foods (tea and non-citrus fruit) and four food items with novel associations – brown bread, peanuts, margarine, and eggs. However, the dietary risk scores explained very little variance in serum urate levels (0.22% by DASH; 0.14% by the 'Healthy-Eating' score) (Table 2). In comparison, the heritability explained by common genetic variants, was estimated to be 23.9%, with a weighted GWAS-identified genetic risk score explaining 7.7% of the variability in serum urate levels (Table 2). Thus, in the datasets analysed here, overall diet explains much less variance in serum urate levels when compared to inherited genetic variants.

The associations observed in this diet-wide study with known, confirmed serum urate-influencing food items were consistent in direction of effect and magnitude with previously reported associations (urate-raising: beer, liquor, and shellfish; urate-lowering: cheese and skim milk).[19 21] Tea consumption was associated with increased serum urate levels in our study, contradictory to a recent meta-analysis that found no evidence for association of tea consumption with serum urate,[50] although the meta-analysis did provide weak evidence for association of green tea consumption with increased serum urate levels. Our study did not distinguish between black and green tea. Additionally, in contrast to other research²⁰ no form of red meat showed a significant association with serum urate in our study. Within the different types of meat analysed only poultry was diet-wide significant effect after adjusting for the diet quality scores.

Due to the diet-wide approach to this analysis, associations with novel and less established foods were identified. Association between peanuts (and/or peanut butter) and decreased serum urate levels has not previously been reported, although a growing pool of evidence has indicated frequent consumption of peanuts associates with a reduced risk of cardiovascular disease, a common comorbidity of hyperuricaemia.[51 52] Egg consumption has previously been associated with reduced urate levels in a Croatian study[53] and protection from hyperuricaemia in a Taiwanese Nutrition and Health Survey.[54] In a third study there was no significant association with the risk of hyperuricaemia in elderly Taiwanese men, although a trend towards protection was evident.[55] Finally, positive association between egg consumption and serum urate levels has been reported in two European cohorts.[56] Certainly the current cumulative evidence is ambiguous regarding a possible role for egg consumption in urate control. Similarly, we observed an association between

non-citrus fruit and reduced serum urate levels. In other studies, consumption of fruit has been inconsistently associated with incident gout, with an increased risk (RR = 1.64) in one analysis[57] and reduced risk in a second analysis.[58] The loss of significance (in the full cohort) when the association of non-citrus fruit with serum urate was adjusted for the two diet quality scores may indicate that greater consumption of fruit is reflective of a healthier diet in general (also inferred from the correlation matrix; Figure S5) and the decrease in serum urate observed here, and in other studies, may be confounded by the healthier diet.

Several studies have used food frequency data to estimate the effect of individual dietary habits on serum urate levels, similar to the 'Healthy-Eating' score and DASH diet score analyses presented here, with varying results. Heidemann et al. [59] used a factor analysis to create two indicators of dietary habits in a group of German individuals. This study showed that individuals whose diet was characterised by high intake of refined grains, processed meats, eggs, and sugar-sweetened beverages (processed food dietary pattern) had significantly higher urate levels than people who did not commonly eat these foods. However, when this analysis was reversed, using a diet score that represented a health conscious dietary pattern (characterised by a high intake of fruit, vegetables, and whole grains), no association with serum urate was seen. [59] Similarly, Tsai et al. [60] assessed the association between estimates of three dietary patterns and serum urate levels in Taiwanese individuals, finding no significant association between estimates of a urate-raising dietary pattern (consuming high levels of seafood, meat, sugar-sweetened beverages, and organ meats), a fish and fried food dietary pattern, or a vegetable and fruit dietary pattern. They posited that other clinical factors such as obesity and concomitant medications are more important than diet in determining serum urate levels, [60] a suggestion supported by the greater effect of genetics versus diet observed here.

Our results using the DASH diet score compare well to the Juraschek *et al.* randomised control trial that demonstrated an average reduction of serum urate of 21 μ molL⁻¹ (0.35 mg/dL) when comparing the DASH diet to an 'average American diet' in individuals with pre- or Stage 1-hypertension.[22] There was a greater reduction of 77 μ molL⁻¹ (1.29 mg/dL) in participants with hyperuricaemia (although there were very few hyperuricaemic subjects (n = 8)). In our analysis the DASH dietary scores could vary from 8 to 40, with each unit increase in score associated with a 0.71 μ mol/L decrease in serum urate. This corresponds with a decrease of 22.7 μ mol/L between the least DASH-like diet, similar to the decrease of 21 μ molL⁻¹ reported by Juraschek *et*

al..[22] Certainly, if a DASH diet is able to be maintained outside the research setting our and Juraschek *et al.*'s data[22] indicate that, relative to a non-DASH diet, a clinically-relevant decrease in serum urate levels can be achieved. However, implementation of the DASH diet may not be straightforward; although this diet was reported two decades ago,[42] the barriers to implementing this diet both at the population level and primary care setting are yet to be overcome.[61]

There are limitations to our study. The primary limitation is the use of differing food frequency questionnaires between studies, which led to methodological challenges when combining the studyspecific effects and may have led to the study participants giving information of variable accuracy between studies. To circumvent these issues the food frequency data were carefully inspected for between-study comparability and several quality-controls were applied to the data before use. Adjustment for estimated average daily calorie intake was also consistently performed during analysis to further minimise any bias or inaccuracies caused by these differing questionnaires. However, variability in reporting accuracy may have contributed to several food items (16 out of 65 in the full cohort) producing a significant heterogeneity p-value during meta-analysis. Given that data were collected at different times (1985 to 2002) food compositions may also have changed, resulting in unintentional combining of non-comparable food items in this analysis and contributing to the significant heterogeneity p-values. This situation may be particularly important when processed foods are being assessed (such as cereals, bread, mayonnaise / dressing).[62] This is also an important consideration in generalisation of results to the present-day or to other countries. This study population was individuals of European ancestry living in the United States of America, and the dietary and genetic analysis may not be generalisable to other populations. Additionally, as with any large-scale set of analyses the likelihood of finding a falsely significant result increases with every extra test added. With the application of a Bonferroni correction to account for this multipletesting effect this likelihood is reduced. However, it is possible that some of the food items that were nominally significant (P < 0.05) may have a real effect undetected in this study (type II error). Finally, measurement error of dietary intake [63] will contribute to suppressed R² estimates of the contribution of diet to variance in serum urate levels relative to that of the genetic R² estimates. which will have minimal measurement error. The study population did not include those with a diagnosis of gout or those on urate-lowering therapy, and therefore, these results cannot be generalized to people with gout.

This study has identified an association between an increased healthy eating score and reduced urate. Our data are important in demonstrating the relative contributions of overall diet and inherited

FIGURE LEGEND

Figure 1. Manhattan plot of –log10(p-values) for 65 food items associated with serum urate levels.

Green dots indicate a serum urate-raising effect; orange dots indicate a serum urate-lowering effect. Red line -Bonferroni corrected multiple-testing significance threshold ($P_{\beta} < 7.69 \times 10^{-4}$). Blue dashed line – nominal significance level $(P_{\beta} < 0.05)$. * – indicates not all data-sets were included in the analysis, the number of asterisks represents the Output
 of data-sets missing data. number of data-sets missing data.

ACKNOWLEDGMENTS

The ARIC study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts N01-HC-55015, N01-HC-55016, N01-HC-55018, N01-HC-55019, N01-HC-55020, N01-HC-55021, N01-HC-55022, R01HL087641, R01HL59367, and R01HL086694; National Human Genome Research Institute contract U01HG004402; and National Institutes of Health contract HHSN268200625226C. Infrastructure was partly supported by Grant Number UL1RR025005, a component of the National Institutes of Health and NIH Roadmap for Medical Research. The FHS and the Framingham SHARe project are conducted and supported by the National Heart, Lung, and Blood Institute in collaboration with Boston University. The Framingham SHARe data used for the analyses described in this manuscript were obtained through dbGaP. The CHS research reported in this article was supported by contract numbers N01-HC-85079, N01-HC-85080, N01-HC-85081, N01-HC-85082, N01-HC-85083, N01-HC-85084, N01-HC-85085, N01-HC-85086, N01-HC-35129, N01 HC-15103, N01 HC-55222, N01-HC-75150, N01-HC-45133, N01-HC-85239 and HHSN268201200036C; grant numbers U01 HL080295 from the National Heart, Lung, and Blood Institute and R01 AG-023629 from the National Institute on Aging, with additional contribution from the National Institute of Neurological Disorders and Stroke. A full list of principal CHS investigators and institutions can be found at http://www.chs-nhlbi.org/pi.htm. The Coronary Artery Risk Development in Young Adults Study (CARDIA) is conducted and supported by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with the University of Alabama at Birmingham (N01-HC95095 & N01-HC48047), University of Minnesota (N01-HC48048), Northwestern University (N01-HC48049), and Kaiser Foundation Research Institute (N01-HC48050). The authors thank the staff, participants, and funding bodies of the ARIC, CARDIA, CHS, FHS, and NHANES III studies for their important contributions. This manuscript was not prepared in collaboration with, nor approved by, investigators of the ARIC, CARDIA, CHS, FHS, or NHANES III studies and does not necessarily reflect the opinions or views of these studies or their institutions / funding bodies (Boston University, or the National Heart, Lung and Blood Institute). For data from NHANES III, the Centres for Disease Control and Prevention (CDC) and National Centre for Health Statistics (NCHS) (Hyattsville, MD) are thanked.

COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted

work; ND has received consulting fees, speaker fees, or grants from the following companies who have developed or marketed urate-lowering therapies for management of gout: Takeda, Ardea Biosciences / AstraZeneca, Cymabay / Kowa, Crealta / Horizon. TRM has received grants from Ardea Biosciences / AstraZeneca and Ironwood Pharmaceuticals. TJM and RKGT have had no financial relationships with any organisations that might have an interest in the submitted work in the previous three years and; no other relationships or activities that could appear to have influenced the submitted work.

FUNDING

This work was supported by the Health Research Council of New Zealand and the University of Otago. The Sponsors had no role in design, carrying out and reporting of the study.

CONTRIBUTORSHIP STATEMENT

TJM, ND and TRM conceived the study. TJM and RKT managed and analysed data. TJM and TRM wrote the manuscript. ND and RKT commented on drafts. All authors approved the final manuscript.

TRANSPARENCY DECLARATION

TRM (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

REFERENCES

- 1. Choi HK, Ford ES. Prevalence of the metabolic syndrome in individuals with hyperuricemia. *Am J Med* 2007;120:442-7.
- 2. Niskanen LK, Laaksonen DE, Nyyssonen K, et al. Uric acid level as a risk factor for cardiovascular and all-cause mortality in middle-aged men: A prospective cohort study. *Arch Intern Med* 2004;164:1546-51.
- 3. Winnard D, Wright C, Jackson G, et al. Gout, diabetes and cardiovascular disease in the Aotearoa New Zealand adult population: co-prevalence and implications for clinical practice. *NZ Med J* 2013;126:53-64.
- 4. Zhu Y, Pandya BJ, Choi HK. Comorbidities of gout and hyperuricemia in the US general population: NHANES 2007-2008. *Am J Med* 2012;125:679-87.
- 5. Dalbeth N, Merriman TR, Stamp LK. Gout. Lancet 2016;388:2039-52.
- 6. Duan H-P, Pang Z-C, Zhang D-F, et al. Heritability of serum uric acid in adult twins. *Zhonghua Liu Xing Bing Xue Za Zhi* 2010;31:384-88.
- 7. Friedlander Y, Kark J, Stein Y. Family resemblance for serum uric acid in a Jerusalem sample of families. *Hum Genet* 1988;79:58-63.
- 8. Gulbrandsen C, Morton N, Rao D, et al. Determinants of plasma uric acid. *Hum Genet* 1979;50:307-12.
- 9. Kalousdian S, Fabsitz R, Havlik R, et al. Heritability of clinical chemistries in an older twin cohort: the NHLBI Twin Study. *Genet Epidemiol* 1987;4:1-11.
- 10. Krishnan E, Lessov-Schlaggar CN, Krasnow RE, Swan GE. Nature versus nurture in gout: A twin study. *Am J Med* 2012;125:499-504.
- 11. Rice T, Vogler GP, Perry TS, et al. Heterogeneity in the familial aggregation of fasting serum uric acid level in five North American populations: the lipid research clinics family study. *Am J Med Genet* 1990;36:219-25.
- 12. Voruganti VS, Goring HH, Mottl A, et al. Genetic influence on variation in serum uric acid in American Indians: the strong heart family study. *Hum Genet* 2009;126:667-76.
- 13. Wilk JB, Djousse L, Borecki I, et al. Segregation analysis of serum uric acid in the NHLBI Family Heart Study. *Hum Genet* 2000;106:355-59.
- 14. Köttgen A, Albrecht E, Teumer A, et al. Genome-wide association analyses identify 18 new loci associated with serum urate concentrations. *Nat Genet* 2013;45:145-54.
- 15. Nuki G, Simkin PA. A concise history of gout and hyperuricemia and their treatment. *Arthritis Res Ther* 2006;8:S1
- 16. Porter R, Rousseau GS. Gout: The patrician malady. Great Britain: Yale University Press, 1998.
- 17. Choi HK, Curhan G. Coffee, tea, and caffeine consumption and serum uric acid level: The Third National Health and Nutrition Examination Survey. *Arthritis Rheum* 2007;57:816-21.
- 18. Choi JW, Ford ES, Gao X, Choi HK. Sugar-sweetened soft drinks, diet soft drinks, and serum uric acid level: The Third National Health and Nutrition Examination Survey. *Arthritis Rheum* 2008;59:109-16.
- 19. Choi HK, Liu S, Curhan G. Intake of purine-rich foods, protein, and dairy products and relationship to serum levels of uric acid: the Third National Health and Nutrition Examination Survey. *Arthritis Rheum* 2005;52:283-9.
- 20. Flynn TJ, Cadzow M, Dalbeth N, et al. Positive association of tomato consumption with serum urate: support for tomato consumption as an anecdotal trigger of gout flares. *BMC Musculoskel Dis* 2015;16:196.
- 21. Choi HK, Curhan G. Beer, liquor, and wine consumption and serum uric acid level: the Third National Health and Nutrition Examination Survey. Arthritis Rheum 2004;51:1023-9.
- 22. Juraschek SP, Gelber AC, Choi HK, et al. Effects of the dietary approaches to Stop hypertension (DASH) diet and sodium intake on serum uric acid. *Arthritis Rheumatol* 2016;68:3002-9.

- 23. Rai SK, Fung TT, Lu N, et al. The Dietary Approaches to Stop Hypertension (DASH) diet, Western diet, and risk of gout in men: prospective cohort study. *BMJ* 2017;357:j1794.
- 24. Kumanyika S, Tell GS, Fried L, et al. Picture-sort method for administering a food frequency questionnaire to older adults. *J Am Diet Assoc* 1996;96:137-44.
- 25. Rimm EB, Giovannucci EL, Stampfer MJ, et al. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. *Am J Epidemiol* 1992;135:1114-26.
- 26. Salvini S, Hunter DJ, Sampson L, et al. Food-based validation of a dietary questionnaire: The effects of week-to-week variation in food consumption. *Int J Epidemiol* 1989;18:858-67.
- 27. Stevens J, Metcalf PA, Dennis BH, et al. Reliability of a food frequency questionnaire by ethnicity, gender, age and education. *Nutr Res* 1996;16:735-45.
- 28. Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol* 1985;122:51-65.
- 29. McDonald A, Van Horn L, Slattery M, et al. The CARDIA dietary history: development, implementation, and evaluation. *J Am Diet Assoc* 1991;91:1104-12.
- 30. Schakel SF, Buzzard IM, Gebhardt SE. Procedures for estimating nutrient values for food composition databases. *Journal of Food Composition and Analysis* 1997;10:102-14.
- 31. National Center for Health Statistics. Plan and operation of the Third National Health and Nutritional Examination Survey, 1988-94. Series 1: programs and collection procedures. *Vital Health Stat* 1994;1:1-407
- 32. ARIC Investigators. The Atherosclerosis Risk in Communities (ARIC) study: design and objectives. *Am J Epidemiol* 1989;129:687-702.
- 33. Henry R, Sobel C, Kim J. A modified carbonate-phosphotungstate method for the determination of uric acid and comparison with the spectrophotometric uricase method. *Am J Clin Pathol* 1957;28:152-60.
- 34. Jiang Y, Liu O, Xu G. Assessment of the trueness and inter-laboratory precision of routine uric acid assays using 4 frozen pooled serum samples measured by the Japan Society of Clinical Chemistry's HPLC method. *Ann Lab Med* 2014;34:104-10.
- 35. Cushman M, Cornell ES, Howard PR, et al. Laboratory methods and quality assurance in the Cardiovascular Health Study. *Clin Chem* 1995;41:264-70.
- 36. Crowley LV. Determination of uric acid an automated analysis based on a carbonate method. *Clin Chem* 1964;10:838-44.
- 37. Patterson N, Price AL, Reich D. Population structure and eigenanalysis. *PLoS Genet* 2006;2:e190.
- 38. Schwarzer G. Meta: An R package for meta-analysis. *R news* 2007;7:40-45.
- 39. Aho KA. Foundational and applied statistics for biologists using R. CRC Press, 2013.
- 40. Nettleton JA, Hivert M-F, Lemaitre RN, et al. Meta-analysis investigating associations between healthy diet and fasting glucose and insulin levels and modification by loci associated with glucose homeostasis in data from 15 cohorts. *Am J Epidemiol* 2013;177:103-15.
- 41. Department of Nutrition Harvard. The Nutrition Source: Harvard T.H. Chan School of Public Health. Secondary The Nutrition Source: Harvard T.H. Chan School of Public Health 2015. http://www.hsph.harvard.edu/nutritionsource/healthy-eating-plate/.
- 42. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. *New Eng J Med* 1997;336:1117-24.
- 43. Fung TT, Chiuve SE, McCullough ML, et al. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. *Arch Intern Med* 2008;168:713-20.
- 44. Durbin R. Efficient haplotype matching and storage using the positional Burrows–Wheeler transform (PBWT). *Bioinformatics* 2014;30:1266-72.
- 45. Delaneau O, Marchini J, Zagury J-F. A linear complexity phasing method for thousands of genomes. *Nat Methods* 2012;9:179-81.

- 46. Chang CC, Chow CC, Tellier LC, et al. Second-generation PLINK: rising to the challenge of larger and richer datasets. *Gigascience* 2015;4:7.
- 47. Yang J, Lee SH, Goddard ME, Visscher PM. GCTA: a tool for genome-wide complex trait analysis. *Am J Hum Genet* 2011;88:76-82.
- 48. Cohen J. Statistical power analysis for the behavioral sciences. 2nd Edition ed. United States of America: Lawrence Erlbaum Associates, 1988.
- 49. Selya AS, Rose JS, Dierker LC, et al. A practical guide to calculating Cohen's f2, a measure of local effect size, from PROC MIXED. *Front Psychol* 2012;3:111.
- 50. Zhang Y, Cui Y, Li X-a, et al. Is tea consumption associated with the serum uric acid level, hyperuricemia or the risk of gout? A systematic review and meta-analysis. *BMC Musculoskel Dis* 2017;18:95.
- 51. Kuo C-F, Grainge MJ, Mallen C, et al. Comorbidities in patients with gout prior to and following diagnosis: case-control study. *Ann Rheum Dis* 2016;75:210-7.
- 52. Luo C, Zhang Y, Ding Y, et al. Nut consumption and risk of type 2 diabetes, cardiovascular disease, and all-cause mortality: a systematic review and meta-analysis. *Am J Clin Nutr* 2014;100:256-69.
- 53. Jerončić I, Mulić R, Klišmanić Z, et al. Interactions between genetic variants in glucose transporter type 9 (SLC2A9) and dietary habits in serum uric acid regulation. *Croatian Med J* 2010;51:40-47.
- 54. Chuang S-Y, Lee S-C, Hsieh Y-T, Pan W-H. Trends in hyperuricemia and gout prevalence: Nutrition and Health Survey in Taiwan from 1993-1996 to 2005-2008. *Asia Pac J Clin Nutr* 2011;20:301-8.
- 55. Chang WC. Dietary intake and the risk of hyperuricemia, gout and chronic kidney disease in elderly Taiwanese men. *Aging Male* 2011;14:195-202.
- 56. Zykova SN, Storhaug HM, Toft I, et al. Cross-sectional analysis of nutrition and serum uric acid in two Caucasian cohorts: the AusDiab Study and the Tromso study. *Nutr J* 2015;14:49.
- 57. Choi HK, Curhan G. Soft drinks, fructose consumption, and the risk of gout in men: A prospective cohort study. *BMJ* 2008;336:309-12.
- 58. Williams PT. Effects of diet, physical activity and performance, and body weight on incident gout in ostensibly healthy, vigorously active men. *Am J Clin Nutr* 2008;87:1480-7.
- 59. Heidemann C, Scheidt-Nave C, Richter A, Mensink G. Dietary patterns are associated with cardiometabolic risk factors in a representative study population of German adults. *Br J Nutr* 2011;106:1253-62.
- 60. Tsai Y-T, Liu J-P, Tu Y-K, et al. Relationship between dietary patterns and serum uric acid concentrations among ethnic Chinese adults in Taiwan. *Asia Pac J Clin Nutr* 2012;**21**:263-70.
- 61. Steinberg D, Bennett GG, Svetkey L. The DASH diet, 20 years later. JAMA 2017;317:1529-30.
- 62. Johnson RJ. The Fat Switch. Second Edition ed. United States of America: mercola.com, 2012.
- 63. Freedman LS, Schatzkin A, Midthune D, Kipnis V. Dealing with dietary measurement error in nutritional cohort studies. *J Natl Cancer Inst* 2011;**103**:1086-92.
- 64. Dalbeth N, Petrie KJ, House M, et al. Illness perceptions in patients with gout and the relationship with progression of musculoskeletal disability. *Arthritis Care Res* 2011;63:1605-12.
- 65. Duyck SD, Petrie KJ, Dalbeth N. "You Don't Have to Be a Drinker to Get Gout, But It Helps": A Content Analysis of the Depiction of Gout in Popular Newspapers. *Arthritis Care Res* 2016;68:1721-5.
- 66. Spaetgens B, Pustjens T, Scheepers LE, et al. Knowledge, illness perceptions and stated clinical practice behaviour in management of gout: a mixed methods study in general practice. *Clin Rheumatol* 2016;35:2053-61.

67. Spencer K, Carr A, Doherty M. Patient and provider barriers to effective management of gout in general practice: a qualitative study. *Ann Rheum Dis* 2012;71:1490-5.

Confidential: Tother only

SUPPLEMENTAL MATERIAL

Aluation of the dic.

Aya J Major[†], Ruth K Tople.

Table S1. Demographic, anthropomorphic, and clinical summary for the five datasets.

Takal Darki da anta	ARIC	CARDIA	CHS	FHS	NHANES III
Total Participants	7228	1413	2101	3040	4566
7/):	F	Baseline Informatio	n		
Sex (% Female)	3681 (50.93%)	807 (57.11%)	1251 (59.54%)	1654 (54.41%)	2432 (53.26%)
Menopause Status (% of females))	2078 (56.45%)	2 (0.25%)	1116 (89.21%)	210 (12.70%)	1032 (11.60%)
Age (Years)	54 ± 6	26 ± 3	72 ± 5	40 ± 9	53 ± 19
BMI (kg/m ²)	26.47 ± 4.49	23.57 ± 3.86	25.84 ± 4.15	26.52 ± 5.30	26.07 ± 5.04
Serum Urate (µmolL ⁻¹)	342.13 ± 81.43	312.10 ± 79.47	315.11 ± 78.10	307.40 ± 85.73	309.23 ± 79.63
SNPs Genotyped	837,177	718,694	327,014	549,726	-
Average Calorie Intake (kcal/day)	$1,642.22 \pm 601.98$	$2,344.62 \pm 801.95$	$1,815.18 \pm 641.99$	$2,075.25 \pm 684.15$	$2,001.69 \pm 768.60$
	Self-	Reported Comorbi	dities		
Diabetes	273 (3.78%)	25 (0.69%)	127 (6.04%)	32 (1.05%)	237 (5.19%)
High Blood Pressure	1450 (20.06%)	333 (9.19%)	574 (27.32%)	58 (1.91%)	1019 (22.32%)
High Cholesterol	1517 (20.99%)	78 (2.15%)	469 (22.32%)	237 (7.80%)	1030 (22.56%)
Heart Problems	325 (4.50%)	218 (6.02%)	382 (18.18%)	68 (2.24%)	355 (7.77%)

Values are shown as the mean ± standard deviation, or as the number of participants (percentage).

Table S2. Food frequency questionnaire answer categories and serves per week conversion factor.

NT.	ARIO		CARDIA		CARDIA CHS FHS		FHS		NHANES III	
No.	Category	Conversion	Category	Conversion	Category	Conversion	Category	Conversion	Category	Conversion
1	Almost never	0	Serves/week	-	Never	0	Never, or < 1/month	0	Times/month	Divided by 4.33 (average weeks/month)
2	1-3 serves/month	0.47			5-10 times/month	0.14	1-3 serves/month	0.47		
3	1 serve/week	1			1-3 times/month	0.47	1 serve/week	1		
4	2-4 serves/week	3			1-4 times/week	2.5	2-4 serves/week	3		
5	5-6 serves/week	5.5			Almost every day	6	5-6 serves/week	5.5		
6	1 serve/day	7					1 serve/day	7		
7	2-3 serves/day	17.5					2-3 serves/day	17.5		
8	4-6 serves/day	35					4-5 serves/day	31.5		
9	>6 serves/day	42					≥ 6 serves/day	42		

CHS and NHANES III did not specify portion size. ARIC, CARDIA, and FHS did not specify the same portion sizes. Portion size was not considered in this study. Category

[–] possible answers as designated by the study questionnaire. Conversion – number of serves per week corresponding to the average category answer.

Table S3. Summary of 65 comparable food items and their study-specific food frequency questions.

Food Item	ARIC	CARDIA	CHS	FHS	NHANES III
	UA		Alcohol		
Beer	Beer	Beer/Ales	Beer	Beer	Beer/Lite Beer
Liquor	Hard Liquor	Distilled Liquor; Cordial and Liqueur	Liquor	Liquor/Whiskey/Gin	Hard Liquor/Tequila/Gin/ Whiskey
Wine	Wine	Wine	Wine	Red Wine; White Wine	Wine/Wine Coolers/ Champagne
		70.	Beverages		
Citrus Juice	Orange Juice/Grapefruit Juice	Citrus Juice	Orange Juice/Grapefruit Juice	Orange Juice; Grapefruit Juice	Orange Juice/Grapefruit Juice/Tangerine Juice
Non-Citrus Juice	Fruit Punch	Non-Citrus Fruit Juice; Fruit Drinks; Flavoured Water	Tang/Breakfast Drinks; Other Fruit Juice/Fruit Drink	Apple Juice/Cider; Other Fruit Juice/Fruit Drink	Apple Juice/Grape Juice/ Cranberry Juice/Other Fruit Juice; Hi-C/Tang/ Hawaiian Punch/ Kool-Aid; Fruit Drink/Fruit Pop
Coffee	Coffee	Coffee	Coffee	Coffee	Coffee
**Decaffeinated Coffee	-	Coffee Substitutes	Decaffeinated Coffee	Decaffeinated Coffee	-
Tea	Hot Tea/Iced Tea	Tea	Hot Tea/Iced Tea	Non-Herbal Tea	Tea
Diet Soft Drink	Diet Soft Drink	Diet Soft Drinks; Unsweetened Soft Drinks	Diet Soft Drinks	Diet Cola; Diet Soft Drink	Diet Cola/Diet Soda
Soft Drink	Regular Soft Drink	Sweetened Soft Drinks	Regular Soft Drinks	Cola; Soft Drink	Cola/Soda
		Da	airy Products		
Butter	Butter (as spread)	Butter; Reduced Fat Butter	Butter (as spread)	Butter (as spread)	Butter (as spread)
Cheese	Cheese; Cottage Cheese/ Ricotta	Cheese/Processed Cheese/ Cottage Cheese/Ricotta	Cheese/Cheese Spread; Cottage Cheese	Cheddar Cheese/American Cheese; Cottage Cheese/ Ricotta; Cream Cheese	American Cheese/Swiss Cheese/Cheddar Cheese/ Cottage Cheese
**Cream	-	Cream/Sour Cream	Cream	Cream; Sour Cream	-
Ice Cream	Ice Cream	Ice Cream/Frozen Shakes	Ice Cream	Ice Cream	Ice Cream/Ice Milk/ Milkshakes
**Flavoured Milk	-	Flavoured Milk; Flavoured Milk Powder	-	Sherbet Milk/Ice Milk	Chocolate Milk/Hot Cocoa
Skim Milk	Skim Milk/Low-fat Milk	Reduced-Fat Milk; Low-Fat Milk/Fat-Free Milk	2% Milk; Skim Milk/1% Milk/Buttermilk	Skim Milk/Low-fat Milk	2% Milk/Low-fat Milk/ 1% Milk/Skim Milk/Non-Fat Milk/Buttermilk

Whole Milk	Whole Milk	Whole Milk	Whole Milk	Whole Milk	Whole Milk/Regular Milk
Yoghurt	Yoghurt	Yoghurt	Flavoured Yoghurt	Yoghurt	Yoghurt/Frozen Yoghurt
		I	Desserts/Sweets		
Cake/Pie	Doughnuts; Danish/Sweet Roll/Coffee Cake/Pastries; Cake/Brownie; Cookies; Pie	Cake/Cookies/Pies/ Pastries/Danish/ Doughnuts/Cobblers	Doughnuts/Cookies/Cakes/ Pastry; Pumpkin Pie/Sweet Potato Pie; Other Pies	Cookies; Brownies; Doughnuts; Cake; Sweet Roll/Coffee Cake/Pastry; Pie	Cakes/Cookies/Brownies/ Pies/Doughnuts/Pastries
Candy	Non-Chocolate Candy; Jam/Jelly	Non-Chocolate Candy; Syrup/Honey/Jam/Jelly	Non-Chocolate Candy/ Jelly/Honey/Brown Sugar	Non-Chocolate Candy; Jams/ Jellies/Syrup/Honey/Preserves	-
Chocolate	Chocolate Bar/Chocolate Pieces	Chocolate Candy	Chocolate Candy	Chocolate Bars/Chocolate Pieces; Chocolate Candy	Chocolate Candy/Fudge
Muffins/Corn Bread	Biscuits/Cornbread; Muffins	Quick Breads/Corn Muffins/Pancakes/Waffles/ Croissant/Tortilla	Biscuits/Muffins/Burger Rolls; Corn Bread/Corn Muffins/Corn Tortillas	English Muffins/Rolls/ Bagels; Muffins/Biscuits; Pancakes/ Waffles	Corn Bread/Corn Muffins/Co Tortillas
			Fish/Seafood		
Fish	Dark Meat Fish; Other Fish; Canned Tuna Fish	Fresh Fish/Smoked Fish	Baked Fish/Broiled Fish; Tuna Fish/Tuna Salad/Tuna Casserole	Dark-Meat Fish; Other Fish; Canned Tuna Fish	Fish Fillets/Fish Sticks/ Fish Sandwiches/Tuna
Shellfish	Shrimp/Lobster/Scallops	Shellfish	Shell Fish/Shrimp/ Lobster/Crab/Oysters	Shrimp, Lobster, Scallops	Shrimp/Clams/Oysters/ Crab/Lobsters
Citrus Fruit	Oranges	Oranges/Grapefruit/ Tangerine/ Lemon	Fruit Oranges; Grapefruit; Lemon	Oranges; Grapefruit	Oranges/Grapefruit/ Tangerin
Non-Citrus Fruit	Apples/Pears; Bananas; Peaches/ Apricots/Plums; Other Fruit	Non-Citrus Fruits	Apples/Applesauce/ Pears; Bananas; Strawberries; Cantaloupe; Watermelon; Apricots/Peaches/ Nectarines; Other Fruits	Apples/Pears; Bananas; Strawberries; Blueberries; Cantaloupe; Watermelon; Peaches/Apricots/Plums; Raisins/Grapes; Prunes	Apple/Banana/Pear/Berries Cherries/Grapes/ Plum/Othe Fruits; Cantaloupe/Honeyder Watermelon; Peach/ Nectarine/Apricot
**Apple/Pear	Apples/Pears	-	Apples/Applesauce/Pears	Apples/Pears	-
**Banana	Bananas	-	Bananas	Bananas	-
**Melon	-	-	Cantaloupe; Watermelon	Cantaloupe; Watermelon	Cantaloupe/Honeydew/ Watermelon
	Peaches/Apricots/Plums		Apricots/Nectarines/Peaches	Peaches/Apricots/Plums	Peach/Nectarine/Apricot

	Dark Bread/Whole Grain	Whole Grain Bread/Whole Grain	Dark Bread/Whole		Dark Bread/Whole
Brown Bread	Bread	Rolls	Wheat/Rye/Pumpernickel	Dark Bread	Wheat/Rye/Pumpernickel
White Bread	White Bread; Crackers	White Bread/Plain Rolls; Crackers	White Bread/Bagels/ Crackers	White Bread; Crackers/ Triskets/Wheat Thins	White Bread/Rolls/ Bagels/Crackers
Cold Cereal	Cold Breakfast Cereal	Ready-To-Eat Cereal	Bran Cereal/Granola Cereal; Cold Cereal; Fortified Cereal	Cold Breakfast Cereal	Bran Cereal; Fortified Cereal; Cold Cereals
*Cooked Cereal	Cooked Cereal/Oatmeal/ Grits/Cream of Wheat	-	Cooked Cereal	Cooked Oatmeal; Cooked Breakfast Cereal	Cooked Cereals/Oatmeal/ Cream of Wheat/Cream of Rice/Grits
Pasta	Spaghetti/Noodles/Other Pasta	Pasta; Whole Grain Pasta	Spaghetti/Lasagne/Pasta	Pasta/Spaghetti/Noodles	Spaghetti/Pasta
*Rice	Rice	-	Rice	Brown Rice; White Rice	Rice
		//X 。 I	Legumes/Nuts		
Legumes	Beans/Lentils/Pinto Beans/Baked Beans	Legumes/Dried Beans	Baked Beans/Pinto Beans/ Kidney Beans	Beans/Lentils/Dried Beans	Beans/Lentils/Chickpeas
*Nuts	Nuts	Nuts/Seeds		Nuts	-
*Peanuts	Peanut Butter	Nut Butter/Seed Butter	Peanuts/Peanut Butter	Peanut Butter	-
			Meat		
*Bacon	Bacon	Cured Pork; Lean Cured Pork	Bacon	Bacon	-
Beef/Pork/Lamb	Beef/Pork/Lamb	Beef; Lean Beef; Lamb; Lean Lamb; Pork; Lean Pork	Beef; Pork	Beef/Pork/Lamb	Beef; Pork/Ham
**Hamburger	Hamburger	-	Hamburger/ Cheeseburger/Meat Loaf	Hamburger	-
**Hotdog	Hotdogs	-	Hotdogs	Hotdogs	-
Organ Meats	Liver	Organ Meat	Liver/Chicken Liver	Liver	Liver/Organ Meats
*Sausage/Lunch	Processed Meat/Sausage/	Cold Cuts/Sausage; Lean Cold	Liverwurst; Ham/Lunch Meat;	Processed Meats/Sausage/	_
Meat	Salami/Bologna	Cuts/Lean Sausage	Sausage	Salami/Bologna	
Poultry	Chicken/Turkey	Poultry; Lean Poultry	Chicken/Turkey	Chicken/Turkey	Chicken/Turkey
			Vegetables		
*Cabbage/	Cabbage/Cauliflower/ Brussel	_	Cauliflower/Brussel Sprouts;	Cabbage/Coleslaw; Cauliflower;	Brussel Sprouts/ Cauliflower;
Cauliflower	Sprout		Coleslaw/ Cabbage/Sauerkraut	Brussel Sprouts	Cabbage/ Coleslaw/Sauerkraut
*Broccoli	Broccoli	-	Broccoli	Broccoli	Broccoli
*Carrot	Carrots	-	Carrots	Carrots	Carrots
**Corn	Corn	-	Corn	Corn	-
**Lettuce	-	-	Green Salad	Iceberg Lettuce/Lettuce Head; Romaine Lettuce/Leaf Lettuce	Tossed Salad

**Peas	Peas/Lima Beans	-	Peas	Peas/Lima Beans	-
Potato	Mashed Potato; French Fried Potato	Baked Potato/Boiled Potato; Fried Potato/French Fries	Boiled Potato/Baked Potato; French Fries/Fried Potatoes	Baked Potato/Boiled Potato/Mashed Potato; French Fried Potato	Baked Potato/Mashed Potato/French-Fried Potato
Spinach	Spinach/Collards/ Greens	Leafy Green Vegetables	Spinach; Mustard Greens/ Turnip Greens/Collards	Spinach; Kale/Mustard/ Chard Greens	Spinach/Greens/Collards/ Kale
**String Beans	String Beans/Green Beans	-	String Beans/Green Beans	String Beans	-
Tomato	Tomatoes/Tomato Juice	Tomatoes/Tomato Sauce	Tomatoes/Tomato Juice	Tomatoes; Tomato Juice	Tomatoes/Tomato Juice/Salsa
Winter Squash	Dark Yellow Winter Squash; Sweet Potato	Pumpkin/Sweet Potato/Winter Squash	Winter Squash/Baked Squash; Sweet Potato/Yam	Yellow Winter Squash; Yams/Sweet Potato	Sweet Potatoes/Yams/ Orange Squash/Pumpkin
		Otl	ner Food Items		
**Creamer	-	Non-Dairy Cream	Non-Dairy Creamer	Non-Dairy Coffee Whitener	-
Margarine	Margarine/Butter Blend (as spread)	Margarine; Reduced-Fat Margarine	Margarine (as spread)	Margarine (as spread)	Margarine (as spread)
*Mayonnaise/ Dressing	-	Salad Dressing/Mayonnaise	Salad Dressing/Mayonnaise	Mayonnaise/Creamy Salad Dressing; Italian Dressing/ Vinegar Dressing	Mayonnaise/Salad Dressing
Eggs	Eggs	Eggs	Eggs	Eggs	Eggs
**Fried Food	Fried Food	Fried Fruits; Fried Vegetables; Fried Chicken; Fried Fish; Fried Shellfish	Fried Chicken; Fried Fish	-	-
Chips/Popcorn	Potato Chips/Corn Chips; Popcorn	Snack Chips; Popcorn; Flavoured Popcorn; Potato Chips/Onion Rings/Savoury Snacks	Salty Snacks/Chips/Popcorn	Potato Chips/Corn Chips; Popcorn	Potato Chips/Corn Chips/ Pretzels/Popcorn
*Condiments	Catsup/Hot Sauce/Soy Sauce/Steak Sauce	Catsup/Barbeque Sauce/ Mustard	Red Chilli Sauce/Taco Sauce/Salsa Picante	Red Chilli Sauce; Mustard	-
*Table Sugar	Sugar Added to Food/ Beverages	Sugar	Sugar Added to Cereal/ Beverages	Sugar Added to Food/ Beverages	-

^{/ –} indicates items were asked about together on the questionnaire.; – indicates questions that were combined before analysis to make food items comparable between studies. * – indicates not all data-sets had a comparable question, the number of asterisks represents the number of data-sets missing data.

Table S4. Summary of the mean ± standard deviation consumption frequency for 65 food items after conversion to serves/week.

E - 4 14	AR	RIC	CAR	RDIA	Cl	HS	FI	IS	NHAN	ES III
Food Item	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
					Alcohol					
Beer	2.82 ± 6.75	0.46 ± 2.09	0.73 ± 1.05	0.27 ± 0.48	1.58 ± 5.20	0.24 ± 1.91	4.68 ± 7.24	1.11 ± 2.60	1.55 ± 3.63	0.44 ± 1.70
Liquor	1.67 ± 4.25	0.81 ± 2.37	0.17 ± 0.44	0.10 ± 0.28	1.89 ± 5.18	1.07 ± 3.46	1.17 ± 3.30	0.55 ± 1.60	0.73 ± 2.58	0.31 ± 1.11
Wine	0.59 ± 1.77	0.68 ± 1.99	0.15 ± 0.30	0.21 ± 0.35	0.80 ± 2.61	0.61 ± 2.12	1.94 ± 3.79	2.13 ± 3.74	0.36 ± 1.27	0.43 ± 1.27
)		Beverages					
Citrus Juice	3.72 ± 4.58	3.72 ± 4.11	1.08 ± 1.57	0.75 ± 0.94	3.22 ± 2.50	3.45 ± 2.57	3.40 ± 4.41	2.81 ± 4.12	2.86 ± 3.39	3.03 ± 3.46
Non-Citrus Juice	1.04 ± 2.76	0.79 ± 2.64	0.66 ± 1.09	0.56 ± 0.85	1.30 ± 2.15	1.28 ± 2.19	3.90 ± 5.77	2.71 ± 4.50	2.39 ± 5.05	2.44 ± 4.03
Coffee	15.65 ± 14.47	13.59 ± 14.08	1.83 ± 2.98	1.70 ± 2.95	3.16 ± 2.78	2.88 ± 2.85	10.23 ± 9.75	8.20 ± 8.65	10.43 ± 15.04	8.25 ± 12.84
**Decaffeinated Coffee	=	-	0.00 ± 0.00	0.00 ± 0.02	2.43 ± 2.73	2.47 ± 2.74	0.76 ± 2.79	1.55 ± 4.53	-	-
Tea	4.05 ± 7.37	4.62 ± 7.83	0.98 ± 7.58	0.89 ± 3.09	1.87 ± 2.27	2.29 ± 2.42	1.38 ± 3.90	2.78 ± 5.41	3.08 ± 6.48	3.45 ± 6.75
Diet Soft Drink	3.47 ± 6.31	4.28 ± 7.12	0.42 ± 1.16	0.76 ± 1.65	1.08 ± 1.87	1.06 ± 1.83	3.91 ± 8.29	4.25 ± 8.20	2.32 ± 5.44	3.29 ± 6.69
Soft Drink	2.94 ± 5.23	1.87 ± 4.82	0.94 ± 1.43	0.50 ± 1.07	0.99 ± 1.74	0.50 ± 1.26	3.73 ± 6.40	1.57 ± 4.17	3.36 ± 6.54	2.45 ± 6.27
				D	airy Products					
Butter	2.62 ± 5.45	2.46 ± 5.35	1.77 ± 2.13	1.42 ± 1.94	1.37 ± 2.17	1.09 ± 2.04	2.55 ± 4.08	2.45 ± 4.09	1.13 ± 2.70	1.02 ± 2.64
Cheese	3.54 ± 3.82	3.95 ± 3.98	0.55 ± 0.56	0.56 ± 0.59	2.55 ± 2.37	2.83 ± 2.64	5.25 ± 5.12	5.44 ± 5.20	2.80 ± 2.67	2.70 ± 2.59
**Cream	-	-	0.35 ± 0.64	0.35 ± 0.57	0.62 ± 1.65	0.44 ± 1.42	4.65 ± 7.16	4.65 ± 7.85	-	-
Ice Cream	2.10 ± 3.61	1.38 ± 2.43	0.27 ± 0.37	0.22 ± 0.34	1.53 ± 1.69	1.23 ± 1.58	1.15 ± 1.57	1.01 ± 1.45	1.49 ± 3.03	1.09 ± 1.71
**Flavoured Milk	-	-	0.04 ± 0.26	0.06 ± 0.40	-		0.24 ± 0.68	0.25 ± 0.84	0.42 ± 1.50	0.43 ± 1.69
Skim Milk	5.57 ± 7.09	5.09 ± 6.28	1.22 ± 1.62	1.01 ± 1.36	4.10 ± 3.34	4.23 ± 3.20	4.68 ± 6.43	5.58 ± 6.62	6.79 ± 5.89	6.85 ± 6.71
Whole Milk	1.80 ± 4.40	0.94 ± 3.16	0.39 ± 0.94	0.18 ± 0.67	3.23 ± 3.71	2.56 ± 3.40	1.03 ± 3.23	0.48 ± 2.19	5.92 ± 5.90	5.41 ± 6.17
Yoghurt	0.36 ± 1.26	0.86 ± 1.99	0.12 ± 0.27	0.15 ± 0.24	0.51 ± 1.20	0.87 ± 1.53	1.06 ± 2.04	1.70 ± 2.30	0.47 ± 1.33	0.90 ± 1.84
				De	esserts/Sweets					
Cake/Pie	6.36 ± 6.68	5.00 ± 5.57	0.24 ± 0.44	0.19 ± 0.36	2.88 ± 2.62	2.16 ± 2.29	4.85 ± 5.63	3.60 ± 4.17	3.11 ± 3.24	2.65 ± 2.99
Candy	0.99 ± 2.42	0.96 ± 2.09	0.45 ± 0.57	0.26 ± 0.35	1.57 ± 1.94	1.21 ± 1.66	1.84 ± 2.78	2.04 ± 3.27	-	-
Chocolate	1.77 ± 2.72	1.91 ± 3.29	0.14 ± 0.32	0.17 ± 0.41	0.78 ± 1.28	0.79 ± 1.36	2.09 ± 3.12	2.11 ± 3.28	1.00 ± 1.87	1.02 ± 1.88
Muffins/Corn Bread	1.16 ± 2.28	0.95 ± 1.78	0.07 ± 0.21	0.07 ± 0.20	1.87 ± 2.02	1.68 ± 1.94	3.20 ± 2.90	2.84 ± 2.76	0.65 ± 1.38	0.56 ± 1.26
]	Fish/Seafood				/ / .	
Fish	1.62 ± 1.78	1.95 ± 2.08	0.37 ± 0.54	0.30 ± 0.47	1.93 ± 1.83	2.46 ± 2.24	1.89 ± 1.97	1.86 ± 1.87	1.01 ± 1.13	0.96 ± 1.01
Shellfish	0.25 ± 0.43	0.23 ± 0.40	0.21 ± 0.40	0.15 ± 0.28	0.35 ± 0.66	0.33 ± 0.65	0.40 ± 0.55	0.37 ± 0.47	0.33 ± 0.55	0.26 ± 0.45

Fruit

Citrus Fruit	1.46 ± 2.48	1.78 ± 2.65	0.35 ± 0.61	0.30 ± 0.49	4.31 ± 3.65	5.28 ± 4.27	1.20 ± 2.31	1.42 ± 2.26	1.25 ± 2.23	1.57 ± 2.56
Non-Citrus Fruit	7.83 ± 7.00	9.89 ± 7.83	0.96 ± 1.19	1.05 ± 1.02	13.55 ± 7.55	16.46 ± 8.67	6.40 ± 6.25	8.52 ± 8.10	4.80 ± 4.67	5.60 ± 5.01
**Apple/Pear	2.90 ± 3.76	3.40 ± 3.99	-	-	2.64 ± 2.15	3.28 ± 2.25	1.73 ± 2.56	1.96 ± 2.48	-	-
**Banana	2.26 ± 2.68	2.53 ± 2.68	-	-	3.44 ± 2.26	3.52 ± 2.27	1.79 ± 2.24	1.80 ± 2.32	-	-
**Melon	-/-	-	-	-	2.45 ± 2.79	3.45 ± 3.29	0.73 ± 1.09	1.24 ± 2.37	0.62 ± 1.33	0.82 ± 1.55
*Peach	0.86 ± 1.65	1.07 ± 1.90	-	-	2.69 ± 2.68	3.18 ± 3.01	0.41 ± 0.87	0.69 ± 1.66	0.76 ± 1.61	0.92 ± 1.79
					Grains					
Brown Bread	6.17 ± 7.42	6.08 ± 6.39	1.05 ± 1.16	0.80 ± 0.86	2.82 ± 2.36	3.01 ± 2.41	3.41 ± 4.89	3.50 ± 4.97	3.08 ± 4.15	3.39 ± 4.14
White Bread	6.07 ± 7.99	4.02 ± 6.07	1.97 ± 1.74	1.34 ± 1.19	2.96 ± 2.54	2.31 ± 2.39	5.31 ± 6.46	4.85 ± 6.24	5.82 ± 5.45	4.82 ± 4.90
Cold Cereal	3.53 ± 4.55	3.08 ± 3.63	0.62 ± 1.05	0.42 ± 0.64	5.80 ± 4.91	4.97 ± 4.50	2.27 ± 2.99	2.34 ± 2.74	2.81 ± 3.29	2.67 ± 3.00
*Cooked Cereal	0.95 ± 2.07	1.08 ± 1.91	-	-	1.48 ± 1.97	1.72 ± 2.10	0.66 ± 1.52	0.90 ± 1.66	0.80 ± 1.70	0.85 ± 1.73
Pasta	1.00 ± 1.26	1.07 ± 1.21	0.43 ± 0.52	0.30 ± 0.39	0.87 ± 1.07	0.82 ± 0.98	2.10 ± 1.58	1.95 ± 1.64	0.64 ± 0.83	0.66 ± 0.80
*Rice	1.01 ± 1.52	1.22 ± 1.49	-	-	1.45 ± 1.43	1.61 ± 1.36	1.67 ± 1.72	1.49 ± 1.68	0.92 ± 1.25	0.98 ± 1.29
				L	egumes/Nuts					
Legumes	0.89 ± 1.34	0.66 ± 1.01	0.13 ± 0.27	0.11 ± 0.26	1.20 ± 1.36	1.01 ± 1.27	0.68 ± 1.14	0.80 ± 1.56	1.07 ± 1.34	0.96 ± 1.36
**Nuts	1.07 ± 2.01	0.86 ± 1.88	0.57 ± 1.03	0.43 ± 0.93	-	-	1.37 ± 3.12	1.25 ± 2.44	-	-
Peanuts	2.12 ± 3.72	1.81 ± 2.90	0.33 ± 0.72	0.21 ± 0.41	1.57 ± 1.88	1.38 ± 1.72	1.61 ± 2.56	1.67 ± 2.50	-	-
					Meat					
Bacon	1.15 ± 2.02	0.72 ± 1.28	0.28 ± 0.39	0.16 ± 0.25	0.99 ± 1.40	0.62 ± 1.10	0.77 ± 1.31	0.46 ± 0.95	-	-
Beef/Pork/Lamb	3.63 ± 3.12	2.99 ± 2.59	1.47 ± 1.21	0.81 ± 0.90	2.34 ± 2.16	2.14 ± 2.20	3.13 ± 2.34	2.42 ± 2.04	3.70 ± 2.77	3.01 ± 2.49
**Hamburger	1.71 ± 1.65	1.13 ± 1.12	-	-	1.24 ± 1.29	0.91 ± 1.04	1.19 ± 1.14	0.76 ± 0.88	-	-
**Hotdog	0.78 ± 1.23	0.44 ± 0.73	-	-	0.56 ± 0.88	0.43 ± 0.78	0.56 ± 0.79	0.28 ± 0.46	-	-
Organ Meats	0.19 ± 0.19	0.17 ± 0.18	0.02 ± 0.08	0.02 ± 0.08	0.29 ± 0.63	0.23 ± 0.51	0.01 ± 0.09	0.02 ± 0.11	0.09 ± 0.25	0.07 ± 0.22
Sausage/Lunch Meat	1.80 ± 2.64	0.89 ± 1.71	0.63 ± 0.74	0.32 ± 0.46	1.78 ± 2.16	1.09 ± 1.70	1.30 ± 1.73	0.68 ± 1.46	-	-
Poultry	2.17 ± 2.01	2.44 ± 2.11	0.77 ± 0.79	0.58 ± 0.64	1.28 ± 1.28	1.66 ± 1.41	3.74 ± 2.76	3.61 ± 2.85	1.77 ± 1.45	2.00 ± 1.62
					Vegetables			•		
*Cabbage/Cauliflower	1.05 ± 1.44	1.33 ± 1.69	-	-	2.08 ± 1.90	2.58 ± 2.15	0.73 ± 1.16	0.86 ± 1.42	1.26 ± 1.50	1.28 ± 1.55
*Broccoli	1.18 ± 1.44	1.80 ± 2.21	-	-	1.30 ± 1.35	1.89 ± 1.56	1.19 ± 1.37	1.50 ± 1.58	0.91 ± 1.24	1.17 ± 1.38
*Carrot	1.19 ± 1.92	1.50 ± 1.96	-	-	2.02 ± 1.65	2.25 ± 1.71	2.10 ± 2.48	2.90 ± 3.73	1.64 ± 1.87	1.88 ± 2.05
**Corn	1.12 ± 1.23	0.87 ± 1.02	-	-	1.22 ± 1.34	1.14 ± 1.34	1.06 ± 1.14	1.01 ± 1.23	-	-
**Lettuce	-	-	-	-	3.08 ± 2.17	3.37 ± 2.16	3.94 ± 3.85	5.17 ± 5.32	2.28 ± 2.21	2.64 ± 2.30
**Peas	1.23 ± 1.33	0.99 ± 1.31	-	-	1.37 ± 1.33	1.53 ± 1.33	0.77 ± 1.11	0.74 ± 1.07	-	-
Potato	3.55 ± 2.59	2.91 ± 2.27	0.20 ± 0.23	0.17 ± 0.20	3.35 ± 2.32	3.00 ± 2.12	2.63 ± 2.00	1.98 ± 1.69	3.23 ± 2.57	2.99 ± 2.51
Spinach	0.71 + 1.00	0.77 + 1.26	0.27 . 0.62	0.54 : 1.01	1.00 . 1.00	4 50 . 0 00				
Spinacii	0.71 ± 1.08	0.77 ± 1.26	0.37 ± 0.63	0.54 ± 1.01	1.26 ± 1.96	1.79 ± 2.32	0.94 ± 1.73	1.47 ± 2.42	0.65 ± 1.15	0.66 ± 1.17

**String Beans	1.86 ± 1.99	1.89 ± 2.03	-	-	1.65 ± 1.40	1.91 ± 1.40	0.79 ± 0.95	1.01 ± 1.23	-	=
Tomato	1.90 ± 2.27	2.04 ± 2.42	0.28 ± 0.36	0.35 ± 0.51	1.70 ± 1.88	1.93 ± 2.01	2.31 ± 2.66	2.69 ± 3.00	2.66 ± 2.50	2.59 ± 2.49
Winter Squash	0.49 ± 0.86	0.50 ± 0.82	0.30 ± 0.64	0.38 ± 0.82	1.07 ± 1.31	1.28 ± 1.60	0.59 ± 0.95	0.86 ± 1.18	0.34 ± 0.70	0.34 ± 0.68
	· () ,			Oth	er Food Items					
**Creamer		-	0.19 ± 0.83	0.15 ± 0.64	0.91 ± 1.96	0.79 ± 1.88	1.01 ± 4.06	1.29 ± 4.61	-	-
Margarine	8.41 ± 8.05	8.85 ± 7.94	1.63 ± 1.94	1.29 ± 1.72	3.16 ± 2.54	3.22 ± 2.52	2.38 ± 3.79	2.58 ± 4.21	4.27 ± 4.69	4.52 ± 4.76
*Mayonnaise/Dressing	-	1-	0.74 ± 1.15	0.61 ± 1.20	2.59 ± 2.23	2.82 ± 2.24	3.55 ± 3.74	4.20 ± 4.00	3.38 ± 3.31	3.43 ± 3.29
Eggs	2.32 ± 2.99	1.62 ± 1.92	0.06 ± 0.17	0.09 ± 0.21	1.60 ± 1.57	1.27 ± 1.39	2.20 ± 2.91	1.87 ± 2.51	1.70 ± 2.16	1.22 ± 1.62
**Fried Food	3.16 ± 3.31	2.00 ± 2.80	0.00 ± 0.01	0.00 ± 0.00	2.35 ± 2.33	1.67 ± 2.10	-	-	-	-
Chips/Popcorn	1.50 ± 2.45	1.16 ± 1.98	0.33 ± 0.46	0.26 ± 0.42	0.75 ± 1.24	0.64 ± 1.19	2.51 ± 2.74	2.28 ± 2.70	1.83 ± 2.26	1.70 ± 2.08
*Condiments	1.93 ± 2.57	1.17 ± 1.82	1.15 ± 1.15	0.71 ± 1.22	0.17 ± 0.55	0.14 ± 0.52	1.83 ± 3.15	1.83 ± 3.05	-	-
Table Sugar	1.41 ± 3.01	0.83 ± 1.79	1.06 ± 2.51	0.57 ± 1.27	2.88 ± 3.91	1.67 ± 3.11	7.16 ± 11.74	6.37 ± 12.96	-	-

All values are presented as mean ± standard deviation in serves per week. * – indicates not all data-sets were included in the analysis, the number of asterisks represents the number of data-sets missing data for this food item.

Table S5. Diet-wide association study results for the original and diet quality score adjusted analyses in the full cohort.

	No	Diet Score Adj	ustment		'Не	althy-Eating	Score Adju	sted	DA	SH Diet Sco	re Adjus	ted
Food Items	β [95% CI]	P_{β}	\mathbb{R}^2	P_{Q}	β [95% CI]	P_{β}	\mathbb{R}^2	P_{Q}	β [95% CI]	P_{β}	R ²	P_{Q}
		/\			Alcoh	ol						
Beer	1.55 [1.08; 2.02]	1.05×10 ⁻¹⁰	0.95%	0.02	1.51 [1.03; 1.98]	3.72×10 ⁻¹⁰	0.88%	0.02	1.49 [1.04; 1.94]	9.32×10 ⁻¹¹	0.89%	0.03
Liquor	1.48 [0.80; 2.15]	1.97×10 ⁻⁰⁵	0.39%	0.02	1.41 [0.73; 2.10]	4.98×10 ⁻⁰⁵	0.35%	0.02	1.41 [0.78; 2.05]	1.25×10 ⁻⁰⁵	0.37%	0.04
Wine	1.12 [0.15; 2.09]	0.02	0.17%	0.01	1.15 [0.19; 2.12]	0.02	0.18%	0.01	1.21 [0.21; 2.22]	0.02	0.20%	0.01
					Bevera	ges						
Citrus Juice	0.25 [-0.01; 0.51]	0.06	0.04%	0.69	0.23 [-0.03; 0.49]	0.08	0.03%	0.70	0.22 [-0.04; 0.48]	0.10	0.03%	0.70
Non-Citrus Juice	-0.07 [-0.61; 0.48]	0.81	0.01%	0.02	-0.11 [-0.67; 0.45]	0.70	0.01%	0.02	-0.18 [-0.78; 0.41]	0.55	0.01%	0.01
Coffee	0.11 [-0.14; 0.37]	0.38	0.01%	3.48×10 ⁻⁰⁴	0.08 [-0.16; 0.31]	0.53	0.01%	1.43×10-03	0.08 [-0.16; 0.31]	0.53	0.02%	1.25×10-03
**Decaffeinate d Coffee	-0.35 [-0.87; 0.17]	0.19	0.06%	0.24	-0.30 [-0.82; 0.22]	0.26	0.05%	0.32	-0.26 [-0.78; 0.26]	0.33	0.04%	0.43
Tea	0.33 [0.18; 0.49]	1.71×10 ⁻⁰⁵	0.10%	0.44	0.34 [0.18; 0.49]	1.51×10 ⁻⁰⁵	0.10%	0.46	0.34 [0.18; 0.49]	1.67×10 ⁻⁰⁵	0.10%	0.49
Diet Soft Drink	-0.08 [-0.24; 0.07]	0.29	0.01%	0.56	-0.07 [-0.22; 0.09]	0.39	0.01%	0.56	-0.07 [-0.22; 0.09]	0.39	0.01%	0.57
Soft Drink	0.72 [0.29; 1.16]	9.97×10 ⁻⁰⁴	0.27%	0.02	0.61 [0.40; 0.82]	1.31×10 ⁻⁰⁸	0.19%	0.07	0.55 [0.34; 0.77]	3.49×10 ⁻⁰⁷	0.16%	0.05
					Dairy Pro	ducts			1			
Butter	-0.02 [-0.26; 0.23]	0.89	< 0.01%	0.30	-0.12 [-0.37; 0.12]	0.33	< 0.01%	0.45	-0.10 [-0.34; 0.14]	0.42	< 0.01%	0.37
Cheese	-0.59 [-0.87; -0.31]	4.39×10 ⁻⁰⁵	0.07%	0.18	-0.60 [-0.88; -0.31]	3.51×10 ⁻⁰⁵	0.07%	0.22	-0.57 [-0.86; -0.29]	6.96×10 ⁻⁰⁵	0.06%	0.27
**Cream	0.14 [-0.15; 0.42]	0.34	0.02%	0.65	0.08 [-0.21; 0.37]	0.59	< 0.01%	0.89	0.07 [-0.21; 0.36]	0.62	< 0.01%	0.83
Ice Cream	0.31 [-0.58; 1.20]	0.49	< 0.01%	0.03	-0.04 [-0.45; 0.37]	0.85	< 0.01%	0.12	0.04 [-0.38; 0.45]	0.87	< 0.01%	0.08

**Flavoured Milk	0.03 [-1.09; 1.14]	0.96	< 0.01%	0.62	-0.03 [-1.15; 1.09]	0.96	< 0.01%	0.60	0.05 [-1.06; 1.17]	0.92	< 0.01%	0.59
Skim Milk	-0.77 [-1.11; -0.42]	1.65×10 ⁻⁰⁵	0.38%	0.03	-0.76 [-1.10; -0.43]	8.10×10 ⁻⁰⁶	0.40%	0.04	0.50	3.45×10 ⁻¹⁰	0.25%	0.26
Whole Milk	-0.36 [-0.66; -0.05]	0.02	0.03%	0.26	-0.51 [-0.82; -0.21]	1.06×10 ⁻⁰³	0.06%	0.61	-0.52 [-0.82; -0.21]	9.11×10 ⁻⁰⁴	0.06%	0.51
Yoghurt	-0.30 [-0.89; 0.29]	0.32	0.01%	0.19	-0.13 [-0.73; 0.47]	0.67	< 0.01%	0.21	0.26 [-0.36; 0.89]	0.41	< 0.01%	0.15
					Desserts/S	weets						
Cake/Pie	-0.27 [-0.49; -0.04]	0.02	0.01%	0.11	-0.38 [-0.61; -0.14]	1.44×10 ⁻⁰³	0.03%	0.29	-0.33 [-0.56; -0.10]	4.74×10 ⁻⁰³	0.02%	0.15
*Candy	-0.26 [-0.76; 0.24]	0.31	0.01%	0.62	-0.36 [-0.86; 0.14]	0.16	0.01%	0.58	-0.26 [-0.76; 0.24]	0.31	0.01%	0.84
Chocolate	0.40 [-0.49; 1.30]	0.38	< 0.01%	0.02	0.18 [-0.65; 1.01]	0.67	< 0.01%	0.03	0.25 [-0.60; 1.09]	0.57	< 0.01%	0.03
Muffins/Corn Bread	-0.53 [-1.04; -0.02]	0.04	0.01%	0.05	-0.83 [-1.82; 0.16]	0.10	0.01%	0.03	-0.57 [-1.08; -0.06]	0.03	0.01%	0.06
					Fish/Seaf	ood						
Fish	0.56 [-0.04; 1.17]	0.07	0.02%	0.43	1.25 [0.61; 1.89]	1.36×10 ⁻⁰⁴	0.08%	0.20	1.07 [0.45; 1.69]	7.37×10 ⁻⁰⁴	0.07%	0.29
Shellfish	5.34 [3.30; 7.39]	3.06×10 ⁻⁰⁷	0.15%	0.24	5.79 [3.73; 7.84]	3.35×10 ⁻⁰⁸	0.18%	0.30	5.53 [3.48; 7.58]	1.21×10 ⁻⁰⁷	0.17%	0.28
					Fruit							
Citrus Fruit	-0.29 [-0.68; 0.09]	0.14	0.01%	0.23	-0.02 [-0.42; 0.38]	0.93	< 0.01%	0.11	0.05 [-0.35; 0.45]	0.81	< 0.01%	0.12
Non-Citrus Fruit	-0.29 [-0.45; -0.14]	1.80×10 ⁻⁰⁴	0.06%	0.30	-0.15 [-0.32; 0.03]	0.10	0.01%	0.32	-0.07 [-0.24; 0.11]	0.48	< 0.01%	0.50
**Apple/Pear	-0.38 [-0.74; -0.01]	0.04	0.03%	0.09	-0.10 [-0.50; 0.29]	0.60	< 0.01%	0.26	0.02 [-0.37; 0.42]	0.91	< 0.01%	0.51
**Banana	-0.66 [-1.14; -0.18]	0.01	0.05%	0.97	-0.42 [-0.92; 0.08]	0.10	0.02%	0.75	-0.22 [-0.73; 0.29]	0.40	< 0.01%	0.77
**Melon	-0.13 [-0.79; 0.53]	0.70	< 0.01%	0.17	0.29 [-0.40; 0.98]	0.41	< 0.01%	0.41	0.31 [-0.37; 0.99]	0.37	0.01%	0.37
*Peach	-0.24 [-1.20; 0.72]	0.62	< 0.01%	0.04	-0.03 [-0.60; 0.55]	0.93	< 0.01%	0.11	0.05 [-0.53; 0.63]	0.87	< 0.01%	0.11
					Grain	s						
Brown Bread	-0.54 [-0.73; -0.35]	1.43×10 ⁻⁰⁸	0.17%	0.19	-0.47 [-0.67; -0.26]	6.60×10 ⁻⁰⁶	0.09%	0.44	-0.42 [-0.63; -0.22]	4.48×10 ⁻⁰⁵	0.07%	0.81

White Bread	[-0.13	.04 3; 0.21]	0.63	< 0.01%	0.91	-0.08 [-0.26; 0.10]	0.38	< 0.01%	0.79	-0.08 [-0.26; 0.09]	0.35	< 0.01%	0.93
Cold Cereal		0.75 2; -0.18]	0.01	0.08%	0.02	-0.73 [-1.26; -0.19]	0.01	0.09%	0.03	-0.57 [-1.09; -0.05]	0.03	0.05%	0.05
*Cooked Cereal		0.77 4; 0.61]	0.27	0.01%	8.83×10 ⁻⁰⁴	-0.50 [-1.87; 0.86]	0.47	< 0.01%	1.37×10 ⁻⁰³	-0.32 [-1.59; 0.94]	0.61	< 0.01%	4.66×10 ⁻⁰³
Pasta		0.22 9; 0.64]	0.61	< 0.01%	0.84	-0.16 [-1.02; 0.70]	0.72	< 0.01%	0.71	-0.07 [-0.94; 0.80]	0.87	< 0.01%	0.73
*Rice		.24 5; 0.94]	0.50	0.01%	0.22	0.52 [-0.18; 1.22]	0.15	0.03%	0.25	0.66 [-0.05; 1.37]	0.07	0.04%	0.34
				YA		Legumes/N	Vuts						
Legumes		.93 2; 2.39]	0.21	0.04%	0.03	1.40 [-0.17; 2.96]	0.08	0.08%	0.02	1.55 [0.11; 2.99]	0.03	0.10%	0.04
**Nuts	[-1.12	0.56 2; 0.01]	0.05	0.03%	0.07	-0.40 [-0.98; 0.18]	0.18	0.01%	0.07	-0.27 [-0.85; 0.32]	0.37	0.01%	0.14
*Peanuts).93 5; -0.52]	8.86×10 ⁻⁰⁶	0.16%	0.28	-0.80 [-1.22; -0.39]	1.69×10 ⁻⁰⁴	0.11%	0.39	-0.71 [-1.14; -0.28]	12×10 ⁻⁰³	0.08%	0.58
						Meat							
*Bacon		-0.34 [-1.16; 0.47]	0.41	< 0.01%	0.38	-0.56 [-1.37; 0.26]	0.18	0.01%	0.20	-0.94 [-1.78; -0.11]	0.03	0.04%	0.16
Beef/Pork/La	ımb	0.68 [-0.14; 1.51]	0.10	0.05%	0.02	0.55 [-0.28; 1.37]	0.19	0.03%	0.03	0.30 [-0.61; 1.21]	0.52	0.01%	0.01
**Hamburg	ger	0.90 [-0.11; 1.90]	0.08	0.02%	0.34	0.59 [-0.43; 1.60]	0.26	0.01%	0.23	0.14 [-0.89; 1.18]	0.79	< 0.01%	0.29
**Hotdog		0.18 [-1.19; 1.55]	0.80	< 0.01%	0.22	-0.14 [-1.51; 1.24]	0.84	< 0.01%	0.32	-0.65 [-2.05; 0.74]	0.36	0.01%	0.55
Organ Mea	its	-5.36 [-9.44; -1.28]	0.01	0.03%	0.69	-5.41 [-9.48; -1.34]	0.01	0.03%	0.68	-6.02 [-10.10; - 1.94]	3.83×10 ⁻⁰³	0.03%	0.67
*Sausage/Luncl	n Meat	0.11 [-0.50; 0.72]	0.72	< 0.01%	0.16	-0.09 [-0.70; 0.52]	0.78	< 0.01%	0.34	-0.36 [-0.99; 0.26]	0.26	0.01%	0.54
Poultry		0.85 [0.35; 1.35]	8.31×10 ⁻⁰⁴	0.08%	0.15	1.32 [0.80; 1.85]	8.28×10 ⁻⁰⁷	0.17%	0.21	1.16 [0.65; 1.67]	7.94×10 ⁻⁰⁶	0.15%	0.21
						Vegetabl	es						
*Cabbage/ Cauliflower	[-0.62	.06 2; 0.73]	0.87	< 0.01%	0.73	0.66 [-0.05; 1.36]	0.07	0.03%	1.00	0.64 [-0.06; 1.34]	0.07	0.03%	0.99
*Broccoli		.00 3; 0.64]	0.99	< 0.01%	0.17	0.55 [-0.12; 1.22]	0.11	0.02%	0.52	0.63 [-0.04; 1.30]	0.06	0.03%	0.40

*Carrot	-0.62 [-1.63; 0.39]	0.23	0.01%	0.01	-0.01 [-0.49; 0.47]	0.96	< 0.01%	0.08	0.12 [-0.36; 0.60]	0.62	< 0.01%	0.05
**Corn	-0.76 [-1.80; 0.29]	0.16	0.02%	0.43	-0.42 [-1.47; 0.64]	0.44	0.01%	0.41	-0.46 [-1.51; 0.59]	0.39	0.01%	0.50
**Lettuce	0.09 [-0.30; 0.49]	0.64	< 0.01%	0.92	0.34 [-0.08; 0.76]	0.11	0.02%	0.58	0.38 [-0.03; 0.79]	0.07	0.03%	0.78
**Peas	-0.56 [-1.52; 0.41]	0.26	0.01%	0.42	-0.15 [-1.13; 0.84]	0.77	< 0.01%	0.45	-0.17 [-1.15; 0.81]	0.73	< 0.01%	0.56
Potato	0.74 [0.28; 1.20]	1.61×10^{-03}	0.09%	0.80	0.67 [0.20; 1.13]	4.76×10 ⁻⁰³	0.07%	0.78	0.58 [0.12; 1.04]	0.01	0.06%	0.69
Spinach	0.26 [-0.38; 0.91]	0.42	0.01%	0.06	0.77 [0.09; 1.44]	0.03	0.03%	0.09	0.87 [0.20; 1.54]	0.01	0.04%	0.07
**String Beans	-0.14 [-0.86; 0.57]	0.70	< 0.01%	0.28	0.29 [-0.45; 1.03]	0.45	< 0.01%	0.48	0.27 [-0.47; 1.00]	0.48	< 0.01%	0.50
Tomato	0.45 [0.04; 0.87]	0.03	0.03%	0.83	0.71 [0.28; 1.13]	1.18×10 ⁻⁰³	0.07%	0.63	0.78 [0.35; 1.21]	3.36×10 ⁻⁰⁴	0.09%	0.48
Winter Squash	-0.65 [-1.72; 0.42]	0.23	< 0.01%	0.09	0.00 [-1.10; 1.10]	1.00	< 0.01%	0.05	0.18 [-0.92; 1.27]	0.75	< 0.01%	0.12
					Other Food	Items						
**Creamer	0.05 [-0.43; 0.53]	0.85	< 0.01%	0.14	0.01 [-0.47; 0.49]	0.97	< 0.01%	0.13	0.00 [-0.48; 0.48]	1.00	< 0.01%	0.14
Margarine	-0.33 [-0.50; -0.15]	2.40×10 ⁻⁰⁴	0.08%	0.10	-0.33 [-0.50; -0.15]	2.54×10 ⁻⁰⁴	0.08%	0.09	-0.32 [-0.50; -0.15]	2.61×10 ⁻⁰⁴	0.08%	0.11
*Mayonnaise/ Dressing	-0.04 [-0.43; 0.36]	0.85	< 0.01%	0.75	0.04 [-0.36; 0.43]	0.86	< 0.01%	0.66	0.02 [-0.38; 0.41]	0.92	< 0.01%	0.71
Eggs	-1.18 [-1.62; -0.74]	1.72×10 ⁻⁰⁷	0.14%	0.53	-1.16 [-1.60; -0.71]	3.31×10 ⁻⁰⁷	0.13%	0.42	-1.34 [-1.78; -0.89]	4.56×10 ⁻⁰⁹	0.18%	0.16
**Fried Food	0.38 [-0.15; 0.91]	0.16	0.03%	0.28	0.28 [-0.25; 0.81]	0.30	0.02%	0.29	0.15 [-0.39; 0.69]	0.59	0.01%	0.33
Chips/Popcorn	0.26 [-0.20; 0.73]	0.27	0.01%	0.11	0.18 [-0.29; 0.65]	0.46	< 0.01%	0.17	0.12 [-0.35; 0.59]	0.61	< 0.01%	0.17
*Condiments	0.49 [-0.01; 0.99]	0.06	0.02%	0.23	0.54 [0.03; 1.04]	0.04	0.03%	0.31	0.52 [0.02; 1.02]	0.04	0.02%	0.43
*Table Sugar	0.90 [0.07; 1.74]	0.03	0.11%	4.36×10 ⁻⁰⁴	0.65 [-0.02; 1.32]	0.06	0.06%	0.01	0.68 [-0.03; 1.40]	0.06	0.08%	0.01

 β – inverse-variance weighted meta-analysis beta value, reflecting the change in serum urate level (μ mol/L) per one extra serve per week of the food item. 95% CI – 95% confidence intervals of the beta value. P_{β} – p-value for meta-analysis beta value, p-values in italics were nominally significant (P_{β} < 0.05; P_{β} > 7.69×10⁻⁰⁴), p-values in italics

.99×10⁻⁰⁴), R² – partial R² value (R²₈) converted to a pc.
.andom-effect model was used in the meta-analysis. * – indicate.
.tu-sets missing data. and bold were diet-wide significant ($P_B < 7.69 \times 10^{-04}$). R^2 – partial R^2 value (R_B^2) converted to a percentage ($R^2 * 100$). P_Q – p-value for the heterogeneity Q-statistic generated during the meta-analysis, if $P_Q < 0.05$ a random-effect model was used in the meta-analysis. * – indicates not all data-sets were included in the analysis, the number of asterisks represents the number of data-sets missing data.

Table S6. Diet-wide association results for the original and diet quality score adjusted analyses in the male-only cohort.

	ľ	No Diet Score A	Adjustment		'Hea	althy-Eating' S	Score Adjust	ed	DA	SH Diet Scor	re Adjusted	ı
Food Items	β [95% CI]	P_{β}	\mathbb{R}^2	P_{Q}	β [95% CI]	P_{β}	R ²	P_{Q}	β [95% CI]	P_{β}	\mathbb{R}^2	P_{Q}
		/\			Alcohol							
Beer	1.33 [1.07; 1.58]	9.17×10 ⁻²⁵	1.23%	0.12	1.29 [1.03; 1.54]	7.65×10 ⁻²³	1.13%	0.26	1.28 [1.02; 1.53]	8.17×10 ⁻²³	1.16%	0.25
Liquor	1.16 [0.76; 1.56]	1.00×10 ⁻⁰⁸	0.38%	0.10	1.11 [0.71; 1.51]	4.43×10 ⁻⁰⁸	0.34%	0.13	1.12 [0.72; 1.52]	3.05×10 ⁻⁰⁸	0.37%	0.20
Wine	1.38 [0.70; 2.05]	6.33×10 ⁻⁰⁵	0.18%	0.15	1.46 [0.79; 2.14]	2.12×10 ⁻⁰⁵	0.19%	0.11	1.53 [0.85; 2.21]	9.21×10 ⁻⁰⁶	0.21%	0.09
					Beverages							
Citrus Juice	0.30 [-0.08; 0.67]	0.12	0.03%	0.44	0.29 [-0.08; 0.66]	0.12	0.03%	0.46	0.30 [-0.07; 0.67]	0.11	0.04%	0.53
Non-Citrus Juice	0.22 [-0.16; 0.60]	0.26	0.02%	0.36	0.18 [-0.19; 0.56]	0.34	0.01%	0.32	0.17 [-0.21; 0.54]	0.38	0.01%	0.29
Coffee	0.03 [-0.22; 0.28]	0.83	0.02%	0.04	-0.08 [-0.19; 0.04]	0.19	0.02%	0.11	-0.07 [-0.19; 0.04]	0.21	0.02%	0.09
**Decaffeinated Coffee	-0.70 [-1.76; 0.36]	0.19	0.06%	0.96	-0.57 [-1.63; 0.49]	0.29	0.04%	0.94	-0.52 [-1.58; 0.54]	0.34	0.03%	0.99
Tea	0.33 [0.10; 0.56]	4.23×10 ⁻⁰³	0.10%	0.82	0.34 [0.11; 0.56]	3.89×10 ⁻⁰³	0.10%	0.77	0.34 [0.11; 0.56]	3.88×10 ⁻⁰³	0.09%	0.82
Diet Soft Drink	-0.25 [-0.49; 0.00]	0.05	0.05%	0.55	-0.22 [-0.47; 0.03]	0.08	0.03%	0.58	-0.23 [-0.48; 0.02]	0.07	0.03%	0.53
Soft Drink	0.76 [0.48; 1.04]	1.54×10 ⁻⁰⁷	0.32%	0.78	0.67 [0.38; 0.97]	7.84×10 ⁻⁰⁶	0.23%	0.60	0.65 [0.35; 0.95]	2.24×10 ⁻⁰⁵	0.21%	0.33
					Dairy Produ	cts						
Butter	-0.08 [-0.44; 0.27]	0.64	< 0.01%	0.50	-0.18 [-0.54; 0.18]	0.32	0.01%	0.40	-0.15 [-0.51; 0.20]	0.40	0.01%	0.40
Cheese	-0.62 [-1.05; -0.19]	0.01	0.08%	0.47	-0.64 [-1.07; -0.21]	3.41×10 ⁻⁰³	0.09%	0.58	-0.62 [-1.05; -0.19]	4.48×10 ⁻⁰³	0.08%	0.55
**Cream	0.28 [-0.22; 0.78]	0.27	0.04%	0.73	0.09 [-0.42; 0.60]	0.74	< 0.01%	0.85	0.16 [-0.34; 0.66]	0.53	0.02%	0.79
Ice Cream	-0.05 [-0.56; 0.47]	0.85	< 0.01%	0.37	-0.12 [-0.64; 0.40]	0.64	< 0.01%	0.42	-0.07 [-0.59; 0.44]	0.78	< 0.01%	0.38

**Flavoured Milk	0.14 [-1.66; 1.93]	0.88	< 0.01%	0.41	0.02 [-1.78; 1.82]	0.99	< 0.01%	0.38	0.19 [-1.60; 1.99]	0.83	< 0.01%	0.30
Skim Milk	-0.83 [-1.09; -0.58]	1.16×10 ⁻¹⁰	0.54%	0.22	-0.86 [-1.11; -0.60]	3.71×10 ⁻¹¹	0.57%	0.17	-0.76 [-1.02; -0.49]	2.24×10 ⁻⁰⁸	0.40%	0.68
Whole Milk	-0.59 [-0.99; -0.19]	3.69×10 ⁻⁰³	0.10%	0.98	-0.72 [-1.13; -0.31]	5.21×10 ⁻⁰⁴	0.16%	0.98	-0.73 [-1.14; -0.33]	3.99×10 ⁻⁰⁴	0.16%	0.94
Yoghurt	-0.51 [-1.57; 0.54]	0.34	0.01%	0.98	-0.20 [-1.27; 0.87]	0.71	< 0.01%	0.96	0.20 [-0.90; 1.31]	0.72	< 0.01%	0.75
					Desserts/Swe	ets						
Cake/Pie	-0.17 [-0.48; 0.14]	0.28	0.01%	0.33	-0.27 [-0.59; 0.04]	0.09	0.02%	0.34	-0.22 [-0.53; 0.09]	0.17	0.01%	0.26
*Candy	-0.08 [-0.82; 0.66]	0.83	< 0.01%	0.67	-0.14 [-0.88; 0.61]	0.72	< 0.01%	0.71	0.00 [-0.75; 0.74]	0.99	< 0.01%	0.87
Chocolate	0.53 [-0.11; 1.17]	0.11	0.04%	0.17	0.39 [-0.26; 1.03]	0.24	0.02%	0.17	0.45 [-0.19; 1.09]	0.17	0.03%	0.13
Muffins/Corn Bread	-0.06 [-0.78; 0.66]	0.87	< 0.01%	0.72	-0.13 [-0.85; 0.59]	0.73	< 0.01%	0.63	-0.12 [-0.84; 0.60]	0.75	< 0.01%	0.69
					Fish/Seafood	d						
Fish	0.66 [-0.26; 1.58]	0.16	0.03%	0.73	1.40 [0.43; 2.38]	4.86×10 ⁻⁰³	0.10%	0.40	1.18 [0.24; 2.13]	0.01	0.08%	0.63
Shellfish	6.07 [3.16; 8.98]	4.41×10 ⁻⁰⁵	0.19%	0.56	6.68 [3.76; 9.60]	7.27×10 ⁻⁰⁶	0.22%	0.70	6.25 [3.33; 9.16]	2.63×10 ⁻⁰⁵	0.21%	0.63
					Fruit							
Citrus Fruit	-0.28 [-0.89; 0.32]	0.36	0.01%	0.47	0.01 [-0.62; 0.64]	0.97	< 0.01%	0.24	0.04 [-0.60; 0.67]	0.91	< 0.01%	0.22
Non-Citrus Fruit	-0.38 [-0.62; -0.13]	2.77×10 ⁻⁰³	0.09%	0.06	-0.21 [-0.49; 0.07]	0.14	0.02%	0.26	-0.17 [-0.46; 0.12]	0.26	0.01%	0.70
**Apple/Pear	-0.46 [-1.01; 0.08]	0.09	0.05%	0.14	-0.21 [-0.80; 0.37]	0.48	0.01%	0.51	-0.13 [-0.71; 0.46]	0.67	< 0.01%	0.41
**Banana	-0.75 [-1.46; -0.03]	0.04	0.07%	0.35	-0.44 [-1.20; 0.31]	0.25	0.02%	0.53	-0.29 [-1.06; 0.48]	0.46	0.01%	0.74
**Melon	0.29 [-0.99; 1.56]	0.66	0.01%	0.56	0.91 [-0.42; 2.23]	0.18	0.04%	0.74	0.86 [-0.46; 2.18]	0.20	0.04%	0.61
*Peach	-0.25 [-2.21; 1.71]	0.80	0.01%	0.01	0.21 [-1.88; 2.30]	0.84	< 0.01%	0.01	0.37 [-1.78; 2.52]	0.74	< 0.01%	4.93×10 ⁻⁰³
					Grains							
Brown Bread	-0.90 [-1.56; -0.23]	0.01	0.20%	0.02	-0.49 [-0.78; -0.21]	7.57×10 ⁻⁰⁴	0.10%	0.16	-0.46 [-0.75; -0.18]	1.53×10 ⁻⁰³	0.09%	0.13

White Bread	-0.09 [-0.32; 0.15]	0.46	< 0.01%	0.97	-0.22 [-0.47; 0.03]	0.08	0.04%	0.87	-0.20 [-0.44; 0.05]	0.11	0.03%	0.96
Cold Cereal	-0.60 [-0.98; -0.22]	1.94×10 ⁻⁰³	0.09%	0.18	-0.59 [-0.97; -0.20]	2.64×10 ⁻⁰³	0.09%	0.35	-0.48 [-0.87; -0.09]	0.02	0.05%	0.41
*Cooked Cereal	-0.86 [-1.68; -0.04]	0.04	0.05%	0.09	-0.61 [-1.44; 0.23]	0.15	0.02%	0.21	-0.56 [-1.40; 0.28]	0.19	0.02%	0.32
Pasta	-0.09 [-1.38; 1.20]	0.89	< 0.01%	0.77	-0.01 [-1.30; 1.29]	0.99	< 0.01%	0.76	0.12 [-1.18; 1.42]	0.85	< 0.01%	0.82
*Rice	0.15 [-1.80; 2.10]	0.88	< 0.01%	0.03	0.63 [-0.43; 1.68]	0.24	0.02%	0.07	0.71 [-0.35; 1.77]	0.19	0.02%	0.11
					Legumes/Nu	ts						
Legumes	1.79 [0.62; 2.96]	2.77×10 ⁻⁰³	0.12%	0.11	2.34 [1.15; 3.54]	1.25×10 ⁻⁰⁴	0.18%	0.25	2.36 [1.17; 3.56]	1.09×10 ⁻⁰⁴	0.19%	0.37
**Nuts	-1.02 [-2.84; 0.80]	0.27	0.05%	0.03	-0.47 [-1.30; 0.35]	0.26	0.02%	0.10	-0.36 [-1.19; 0.46]	0.39	0.01%	0.12
*Peanuts	-1.13 [-1.68; -0.57]	6.76×10 ⁻⁰⁵	0.24%	0.35	-1.02 [-1.58; -0.45]	4.10×10 ⁻⁰⁴	0.18%	0.58	-0.96 [-1.54; -0.38]	1.12×10 ⁻⁰³	0.15%	0.81
					Meat							
*Bacon	-0.81 [-1.83; 0.22]	0.12	0.03%	0.74	-0.95 [-1.97; 0.08]	0.07	0.05%	0.72	-1.24 [-2.29; -0.19]	0.02	0.09%	0.80
Beef/Pork/Lamb	0.72 [-0.39; 1.82]	0.20	0.06%	0.05	0.52 [-0.07; 1.11]	0.09	0.03%	0.08	0.36 [-0.87; 1.58]	0.57	0.02%	0.03
**Hamburger	0.64 [-0.65; 1.93]	0.33	0.01%	0.33	0.37 [-0.93; 1.68]	0.58	< 0.01%	0.29	0.03 [-1.30; 1.36]	0.96	< 0.01%	0.30
**Hotdog	-0.15 [-1.84; 1.54]	0.86	< 0.01%	0.10	-0.41 [-2.11; 1.28]	0.63	< 0.01%	0.20	-0.78 [-2.50; 0.94]	0.37	0.01%	0.41
Organ Meats	-7.92 [-13.74; -2.10]	0.01	0.07%	0.21	-7.71 [-13.53; -1.89]	0.01	0.07%	0.23	-8.10 [-13.92; -2.27]	0.01	0.08%	0.23
*Sausage/Lunch Meat	-0.13 [-0.91; 0.66]	0.75	< 0.01%	0.19	-0.29 [-1.08; 0.49]	0.47	< 0.01%	0.27	-0.51 [-1.31; 0.30]	0.22	0.02%	0.18
Poultry	1.13 [0.35; 1.92]	4.63×10 ⁻⁰³	0.10%	0.37	1.73 [0.91; 2.55]	3.71×10 ⁻⁰⁵	0.21%	0.24	1.44 [0.64; 2.24]	4.02×10 ⁻⁰⁴	0.17%	0.35
					Vegetables							
*Cabbage/ Cauliflower	-0.30 [-1.36; 0.75]	0.58	< 0.01%	0.88	0.33 [-0.79; 1.44]	0.56	0.01%	0.99	0.21 [-0.89; 1.31]	0.71	< 0.01%	0.97
*Broccoli	-0.06 [-1.17; 1.05]	0.92	< 0.01%	0.20	0.71 [-0.48; 1.89]	0.24	0.02%	0.42	0.69 [-0.49; 1.87]	0.25	0.02%	0.44

*Carrot	-0.74 [-2.18; 0.70]	0.31	0.02%	0.03		0.05 [-0.75; 0.86]	0.90	< 0.01%	0.05	-0.17 [-1.70; 1.35]	0.82	< 0.01%	0.03		
**Corn	-1.04 [-2.55; 0.46]	0.18	0.03%	0.54		-0.66 [-2.19; 0.87]	0.40	0.01%	0.74	-0.65 [-2.17; 0.87]	0.40	0.01%	0.70		
**Lettuce	0.41 [-0.31; 1.14]	0.27	0.03%	0.64		1.06 [0.28; 1.84]	0.01	0.14%	0.88	0.92 [0.16; 1.69]	0.02	0.13%	0.83		
**Peas	-0.91 [-2.35; 0.53]	0.22	0.03%	0.18		-0.43 [-1.90; 1.05]	0.57	0.01%	0.30	-0.47 [-1.93; 0.99]	0.53	0.01%	0.25		
Potato	0.75 [0.09; 1.41]	0.02	0.07%	0.48		0.65 [-0.01; 1.32]	0.05	0.05%	0.52	0.60 [-0.06; 1.26]	0.07	0.05%	0.51		
Spinach	0.12 [-1.00; 1.25]	0.83	< 0.01%	0.13		0.85 [-0.32; 2.02]	0.16	0.02%	0.26	0.85 [-0.32; 2.01]	0.15	0.02%	0.21		
**String Beans	0.27 [-0.78; 1.32]	0.62	< 0.01%	0.07		0.64 [-0.45; 1.72]	0.25	0.03%	0.23	0.59 [-0.48; 1.66]	0.28	0.03%	0.19		
Tomato	0.69 [0.04; 1.34]	0.04	0.06%	0.18		1.03 [0.37; 1.70]	2.38×10 ⁻⁰³	0.12%	0.42	0.99 [0.33; 1.65]	3.38×10 ⁻⁰³	0.12%	0.39		
Winter Squash	-0.90 [-3.81; 2.01]	0.54	0.02%	0.04		0.02 [-2.87; 2.90]	0.99	< 0.01%	0.05	-0.30 [-2.03; 1.44]	0.74	< 0.01%	0.11		
	[-3.81; 2.01]														
**Creamer	0.28 [-0.55; 1.11]	0.50	0.02%	0.36		0.18 [-0.65; 1.01]	0.67	0.01%	0.40	0.22 [-0.61; 1.05]	0.60	0.01%	0.39		
Margarine	-0.38 [-1.05; 0.30]	0.27	0.07%	0.02		-0.39 [-1.04; 0.26]	0.24	0.07%	0.03	-0.37 [-1.01; 0.27]	0.26	0.06%	0.03		
*Mayonnaise/ Dressing	-0.03 [-0.65; 0.60]	0.93	< 0.01%	0.74		0.15 [-0.48; 0.78]	0.64	0.01%	0.89	0.06 [-0.57; 0.69]	0.85	< 0.01%	0.82		
Eggs	-1.56 [-2.15; -0.98]	1.45×10 ⁻⁰⁷	0.30%	0.23		-1.50 [-2.08; -0.91]	5.23×10 ⁻⁰⁷	0.29%	0.36	-1.69 [-2.28; -1.10]	1.99×10 ⁻⁰⁸	0.38%	0.25		
**Fried Food	0.20 [-0.50; 0.89]	0.58	0.01%	0.73		0.16 [-0.53; 0.85]	0.65	< 0.01%	0.66	0.08 [-0.63; 0.78]	0.83	< 0.01%	0.68		
Chips/Popcorn	0.16 [-0.51; 0.83]	0.64	< 0.01%	0.75		0.06 [-0.61; 0.73]	0.86	< 0.01%	0.69	0.04 [-0.63; 0.71]	0.90	< 0.01%	0.64		
*Condiments	0.17 [-0.52; 0.86]	0.63	< 0.01%	0.40		0.28 [-0.41; 0.98]	0.42	< 0.01%	0.43	0.23 [-0.46; 0.92]	0.51	< 0.01%	0.52		
*Table Sugar	0.81 [-0.08; 1.69]	0.08	0.13%	0.01		0.56 [-0.24; 1.35]	0.17	0.07%	0.03	0.66 [-0.18; 1.50]	0.13	0.09%	0.02		

 β – inverse-variance weighted meta-analysis beta value, reflecting the change in serum urate level (μ mol/L) per one extra serve per week of the food item. 95% CI – 95% confidence intervals of the beta value. P_{β} – p-value for meta-analysis beta value, p-values in italics were nominally significant (P_{β} < 0.05; P_{β} > 7.69×10⁻⁰⁴), p-values in italics

.59×10^{nb}), \mathbb{R}^2 – partial \mathbb{R}^2 value (\mathbb{R}^2_0) converted to a p... andom-effect model was used in the meta-analysis: * – indicate. atta-sets missing data and bold were diet-wide significant ($P_B < 7.69 \times 10^{-04}$). R^2 – partial R^2 value (R_B^2) converted to a percentage ($R^2 * 100$). P_Q – p-value for the heterogeneity Q-statistic generated during the meta-analysis, if $P_Q < 0.05$ a random-effect model was used in the meta-analysis. * – indicates not all data-sets were included in the analysis, the number of asterisks represents the number of data-sets missing data.

Table S7. Diet-wide association results for the original and diet score adjusted analyses in the female-only cohort.

		No Diet Score	e Adjustment	t	'Не	althy-Eating	Score Adjus	ted	DA	SH Diet Sco	re Adjuste	d
Food Items	β [95% CI]	P_{β}	\mathbb{R}^2	P_{Q}	β [95% CI]	P_{β}	R ²	P_{Q}	β [95% CI]	P_{β}	R ²	P_{Q}
					Alcohol							
Beer	1.94 [1.32; 2.55]	6.36×10 ⁻¹⁰	0.47%	0.26	1.91 [1.29; 2.52]	1.31×10 ⁻⁰⁹	0.44%	0.24	1.89 [1.27; 2.51]	2.58×10 ⁻⁰⁹	0.43%	0.26
Liquor	2.04 [1.39; 2.68]	6.87×10 ⁻¹⁰	0.46%	0.13	1.94 [1.29; 2.59]	4.86×10 ⁻⁰⁹	0.43%	0.09	1.91 [1.27; 2.56]	6.96×10 ⁻⁰⁹	0.42%	0.14
Wine	0.83 [-0.50; 2.17]	0.22	0.17%	0.01	0.84 [-0.47; 2.16]	0.21	0.18%	0.01	0.94 [-0.37; 2.25]	0.16	0.19%	0.01
				/	Beverage	S						
Citrus Juice	0.19 [-0.16; 0.55]	0.29	0.02%	0.98	0.18 [-0.17; 0.54]	0.32	0.02%	0.96	0.13 [-0.23; 0.49]	0.47	0.02%	0.86
Non-Citrus Juice	-0.06 [-0.44; 0.32]	0.76	< 0.01%	0.15	-0.07 [-0.45; 0.32]	0.74	< 0.01%	0.15	-0.15 [-0.54; 0.23]	0.44	< 0.01%	0.11
Coffee	0.05 [-0.22; 0.31]	0.72	0.01%	0.02	0.02 [-0.22; 0.27]	0.84	0.01%	0.04	0.01 [-0.23; 0.25]	0.93	0.02%	0.04
**Decaffeinated Coffee	-0.18 [-0.73; 0.37]	0.52	0.04%	0.14	-0.16 [-0.71; 0.39]	0.57	0.03%	0.22	-0.13 [-0.68; 0.43]	0.65	0.03%	0.29
Tea	0.32 [0.12; 0.53]	1.56×10 ⁻⁰³	0.12%	0.08	0.33 [0.13; 0.53]	1.35×10 ⁻⁰³	0.11%	0.10	0.33 [0.12; 0.53]	1.53×10 ⁻⁰³	0.12%	0.10
Diet Soft Drink	0.06 [-0.14; 0.25]	0.56	< 0.01%	0.80	0.06 [-0.14; 0.25]	0.55	< 0.01%	0.84	0.07 [-0.12; 0.27]	0.47	< 0.01%	0.81
Soft Drink	0.70 [-0.02; 1.43]	0.06	0.16%	4.56×10 ⁻⁰³	0.61 [-0.04; 1.27]	0.07	0.11%	0.02	0.41 [0.10; 0.71]	0.01	0.08%	0.06
					Dairy Produ	icts						
Butter	0.06 [-0.27; 0.39]	0.71	< 0.01%	0.19	-0.03 [-0.36; 0.31]	0.86	< 0.01%	0.65	-0.02 [-0.35; 0.31]	0.91	< 0.01%	0.51
Cheese	-0.60 [-0.96; -0.23]	1.36×10 ⁻⁰³	0.06%	0.49	-0.61 [-0.98; -0.25]	1.06×10 ⁻⁰³	0.06%	0.51	-0.58 [-0.94; -0.21]	2.14×10 ⁻⁰³	0.05%	0.60
**Cream	0.04 [-0.29; 0.37]	0.81	< 0.01%	0.86	0.10 [-0.24; 0.44]	0.56	< 0.01%	0.90	0.03 [-0.30; 0.36]	0.85	< 0.01%	0.93
Ice Cream	0.35 [-0.34; 1.03]	0.32	0.04%	0.08	0.18 [-0.51; 0.88]	0.60	0.03%	0.29	0.30 [-0.41; 1.01]	0.40	0.04%	0.27

**Flavoured Milk	-0.27 [-1.64; 1.10]	0.70	< 0.01%	0.31	-0.31 [-1.69; 1.06]	0.65	< 0.01%	0.31	-0.27 [-1.64; 1.10]	0.69	< 0.01%	0.30
Skim Milk	-0.57 [-1.01; -0.14]	0.01	0.23%	0.04	-0.51 [-0.74; -0.27]	1.72×10 ⁻⁰⁵	0.25%	0.05	-0.40 [-0.64; -0.16]	1.07×10 ⁻⁰³	0.13%	0.10
Whole Milk	0.14 [-0.33; 0.61]	0.56	0.01%	0.15	-0.07 [-0.55; 0.41]	0.78	< 0.01%	0.31	-0.06 [-0.53; 0.42]	0.81	< 0.01%	0.38
Yoghurt	-0.44 [-1.79; 0.92]	0.53	0.01%	0.02	-0.31 [-1.59; 0.96]	0.63	< 0.01%	0.04	0.17 [-1.17; 1.51]	0.81	0.01%	0.04
					Desserts/Sw	eets						
Cake/Pie	-0.44 [-1.10; 0.23]	0.20	0.03%	0.05	-0.51 [-0.86; -0.17]	3.38×10 ⁻⁰³	0.07%	0.19	-0.48 [-0.82; -0.14]	0.01	0.05%	0.11
*Candy	-0.40 [-1.06; 0.26]	0.23	0.02%	0.83	-0.50 [-1.17; 0.16]	0.13	0.02%	0.77	-0.49 [-1.15; 0.17]	0.15	0.02%	0.81
Chocolate	-0.04 [-1.08; 0.99]	0.93	0.03%	0.03	-0.24 [-1.26; 0.79]	0.65	0.05%	0.04	-0.53 [-1.04; -0.02]	0.04	0.04%	0.08
Muffins/Corn Bread	-1.19 [-2.52; 0.14]	0.08	0.05%	0.04	-1.26 [-2.69; 0.16]	0.08	0.07%	0.02	-1.04 [-1.75; -0.33]	4.13×10 ⁻⁰³	0.05%	0.05
					Fish/Seafoo	od						
Fish	0.52 [-0.26; 1.30]	0.19	0.01%	0.07	1.16 [0.32; 2.00]	0.01	0.06%	0.39	1.03 [0.23; 1.83]	0.01	0.05%	0.23
Shellfish	4.43 [1.56; 7.30]	2.49×10 ⁻⁰³	0.11%	0.46	4.61 [1.73; 7.49]	1.73×10 ⁻⁰³	0.13%	0.45	4.60 [1.72; 7.47]	1.73×10 ⁻⁰³	0.13%	0.48
					Fruit							
Citrus Fruit	-0.31 [-0.80; 0.19]	0.22	0.01%	0.21	-0.06 [-0.57; 0.45]	0.83	< 0.01%	0.17	0.05 [-0.46; 0.56]	0.85	< 0.01%	0.24
Non-Citrus Fruit	-0.22 [-0.41; -0.03]	0.02	0.03%	0.38	-0.10 [-0.32; 0.11]	0.35	< 0.01%	0.73	0.01 [-0.21; 0.23]	0.92	< 0.01%	0.42
**Apple/Pear	-0.32 [-0.81; 0.17]	0.20	0.02%	0.47	-0.06 [-0.59; 0.47]	0.82	< 0.01%	0.27	0.10 [-0.43; 0.63]	0.71	0.01%	0.50
**Banana	-0.52 [-1.15; 0.11]	0.11	0.04%	0.35	-0.34 [-0.99; 0.31]	0.30	0.01%	0.79	-0.09 [-0.76; 0.58]	0.79	< 0.01%	0.81
**Melon	-0.26 [-0.99; 0.46]	0.48	0.01%	0.27	-0.02 [-0.77; 0.74]	0.97	< 0.01%	0.46	0.08 [-0.67; 0.83]	0.83	< 0.01%	0.42
*Peach	-0.23 [-0.92; 0.46]	0.52	< 0.01%	0.91	0.07 [-0.64; 0.77]	0.85	< 0.01%	0.99	0.19 [-0.52; 0.90]	0.60	< 0.01%	0.99
					Grains							
Brown Bread	-0.51 [-0.78; -0.25]	1.66×10 ⁻⁰⁴	0.14%	0.31	-0.43 [-0.72; -0.14]	3.14×10 ⁻⁰³	0.09%	0.65	-0.37 [-0.66; -0.09]	0.01	0.06%	0.40

White Bread	0.24 [0.00; 0.49]	0.05	0.06%	0.64	0.16 [-0.10; 0.43]	0.22	0.03%	0.89	0.11 [-0.15; 0.36]	0.40	0.02%	0.90
Cold Cereal	-0.68 [-1.48; 0.12]	0.10	0.06%	0.02	-0.70 [-1.54; 0.15]	0.11	0.06%	0.01	-0.52 [-1.26; 0.22]	0.17	0.04%	0.04
*Cooked Cereal	-0.42 [-1.95; 1.12]	0.59	< 0.01%	0.01	-0.21 [-1.92; 1.49]	0.81	0.01%	2.09×10-03	0.05 [-1.60; 1.70]	0.96	0.01%	4.18×10 ⁻⁰³
Pasta	-0.29 [-1.42; 0.84]	0.61	< 0.01%	0.95	-0.13 [-1.27; 1.00]	0.82	< 0.01%	0.91	-0.14 [-1.27; 0.99]	0.81	< 0.01%	0.89
*Rice	0.18 [-0.73; 1.10]	0.69	0.01%	0.96	0.42 [-0.51; 1.34]	0.38	0.03%	0.96	0.60 [-0.34; 1.53]	0.21	0.04%	0.96
					Legumes/Nu	ts						
Legumes	0.17 [-1.68; 2.03]	0.86	0.01%	0.04	0.44 [-1.51; 2.40]	0.66	0.02%	0.03	0.74 [-1.22; 2.70]	0.46	0.04%	0.03
**Nuts	-0.17 [-0.96; 0.63]	0.68	0.01%	0.20	-0.18 [-0.99; 0.64]	0.67	< 0.01%	0.27	0.01 [-0.82; 0.84]	0.98	< 0.01%	0.36
*Peanuts	-0.59 [-1.21; 0.02]	0.06	0.06%	0.20	-0.45 [-1.08; 0.17]	0.16	0.03%	0.29	-0.30 [-0.94; 0.33]	0.35	0.01%	0.45
					Meat							
*Bacon	0.90 [-0.49; 2.29]	0.21	0.02%	0.38	0.53 [-0.87; 1.94]	0.45	0.01%	0.20	0.05 [-1.39; 1.50]	0.94	< 0.01%	0.15
Beef/Pork/Lamb	0.50 [-0.10; 1.10]	0.10	0.04%	0.52	0.39 [-0.23; 1.00]	0.22	0.02%	0.53	0.14 [-0.50; 0.78]	0.68	< 0.01%	0.78
**Hamburger	1.53 [-0.11; 3.16]	0.07	0.03%	0.25	1.18 [-0.48; 2.83]	0.16	0.01%	0.19	0.54 [-1.16; 2.24]	0.54	< 0.01%	0.12
**Hotdog	1.00 [-1.47; 3.46]	0.43	0.01%	0.32	0.57 [-1.91; 3.04]	0.66	< 0.01%	0.59	-0.33 [-2.86; 2.20]	0.80	< 0.01%	0.59
Organ Meats	-1.10 [-6.83; 4.63]	0.71	< 0.01%	0.23	-1.56 [-7.28; 4.16]	0.59	< 0.01%	0.23	-2.43 [-8.16; 3.31]	0.41	< 0.01%	0.20
*Sausage/Lunch Meat	0.68 [-0.31; 1.67]	0.18	0.04%	0.47	0.42 [-0.58; 1.42]	0.41	0.02%	0.73	0.08 [-0.95; 1.11]	0.87	< 0.01%	0.73
Poultry	0.61 [-0.02; 1.24]	0.06	0.05%	0.38	0.94 [0.28; 1.60]	0.01	0.11%	0.78	0.93 [0.29; 1.57]	4.40×10 ⁻⁰³	0.10%	0.72
					Vegetables							
*Cabbage/ Cauliflower	0.40 [-0.45; 1.26]	0.35	0.02%	0.78	0.94 [0.05; 1.84]	0.04	0.06%	0.90	1.06 [0.17; 1.94]	0.02	0.06%	0.95
*Broccoli	0.08 [-0.67; 0.82]	0.84	< 0.01%	0.32	0.49 [-0.30; 1.27]	0.23	0.02%	0.94	0.65 [-0.13; 1.43]	0.10	0.03%	0.72

*Carrot	-0.24 [-0.77; 0.29]	0.37	0.01%	0.16	-0.12 [-0.68; 0.43]	0.66	< 0.01%	0.79	0.06 [-0.50; 0.62]	0.83	0.01%	0.78
**Corn	-0.48 [-1.90; 0.94]	0.51	< 0.01%	0.34	-0.25 [-1.68; 1.17]	0.73	< 0.01%	0.22	-0.35 [-1.78; 1.07]	0.63	< 0.01%	0.29
**Lettuce	-0.08 [-0.52; 0.35]	0.71	< 0.01%	0.73	-0.10 [-0.56; 0.37]	0.68	< 0.01%	0.25	0.04 [-0.41; 0.50]	0.85	< 0.01%	0.38
**Peas	-0.30 [-1.58; 0.98]	0.65	< 0.01%	0.57	-0.01 [-1.31; 1.29]	0.99	< 0.01%	0.23	0.01 [-1.28; 1.30]	0.99	< 0.01%	0.34
Potato	0.74 [0.11; 1.38]	0.02	0.09%	0.64	0.72 [0.08; 1.36]	0.03	0.07%	0.84	0.58 [-0.06; 1.22]	0.08	0.05%	0.80
Spinach	0.38 [-0.37; 1.13]	0.32	0.02%	0.27	0.61 [-0.18; 1.40]	0.13	0.06%	0.31	0.81 [0.03; 1.59]	0.04	0.07%	0.28
**String Beans	-0.51 [-1.48; 0.45]	0.30	0.03%	0.90	-0.08 [-1.08; 0.92]	0.87	0.01%	0.87	-0.03 [-1.02; 0.96]	0.95	< 0.01%	0.95
Tomato	0.31 [-0.20; 0.83]	0.24	0.02%	0.33	0.44 [-0.10; 0.98]	0.11	0.05%	0.62	0.63 [0.09; 1.17]	0.02	0.08%	0.43
Winter Squash	-0.20 [-1.53; 1.14]	0.77	< 0.01%	0.48	0.21 [-1.16; 1.58]	0.77	0.01%	0.20	0.49 [-0.87; 1.86]	0.48	0.02%	0.30
Other Food Items												
**Creamer	-0.10 [-0.66; 0.46]	0.73	< 0.01%	0.47	-0.13 [-0.69; 0.43]	0.65	< 0.01%	0.47	-0.15 [-0.71; 0.41]	0.60	0.01%	0.46
Margarine	-0.36 [-0.59; -0.12]	3.26×10 ⁻⁰³	0.09%	0.61	-0.35 [-0.59; -0.11]	4.21×10 ⁻⁰³	0.09%	0.56	-0.36 [-0.60; -0.12]	3.08×10 ⁻⁰³	0.10%	0.57
*Mayonnaise/ Dressing	-0.05 [-1.04; 0.95]	0.93	< 0.01%	0.04	-0.06 [-0.56; 0.43]	0.80	< 0.01%	0.07	0.00 [-0.49; 0.49]	0.99	< 0.01%	0.06
Eggs	-0.56 [-1.91; 0.79]	0.41	0.01%	0.03	-0.34 [-1.03; 0.36]	0.34	0.01%	0.05	-0.89 [-2.48; 0.70]	0.27	0.02%	0.01
**Fried Food	0.74 [-0.10; 1.57]	0.08	0.07%	0.17	0.51 [-0.34; 1.35]	0.24	0.04%	0.18	0.33 [-0.53; 1.19]	0.46	0.02%	0.22
Chips/Popcorn	0.36 [-0.28; 1.01]	0.27	0.01%	0.15	0.31 [-0.34; 0.96]	0.35	0.01%	0.36	0.20 [-0.45; 0.86]	0.54	< 0.01%	0.42
*Condiments	0.88 [0.15; 1.61]	0.02	0.07%	0.32	0.81 [0.08; 1.55]	0.03	0.08%	0.32	0.85 [0.12; 1.58]	0.02	0.08%	0.44
*Table Sugar	1.03 [-0.09; 2.14]	0.07	0.11%	0.01	0.27 [0.06; 0.48]	0.01	0.07%	0.20	0.19 [0.00; 0.39]	0.05	0.08%	0.13

..g the change in serum ur.

..analysis beta value, p-values in itan.

.:—partial R² value (R²n) converted to a percen.

.et model was used in the meta-analysis. * – indicates no.

.sing data. β – inverse-variance weighted meta-analysis beta value, reflecting the change in serum urate level (μmol/L) per one extra serve per week of the food item. 95% CI – 95% confidence intervals of the beta value. P_{β} – p-value for meta-analysis beta value, p-values in italics were nominally significant ($P_{\beta} < 0.05$; $P_{\beta} > 7.69 \times 10^{-04}$), p-values in italics and bold were diet-wide significant ($P_{\beta} < 7.69 \times 10^{-04}$). R^2 – partial R^2 value (R_B^2) converted to a percentage ($R^2 * 100$). P_Q – p-value for the heterogeneity Q-statistic generated during the meta-analysis, if $P_Q < 0.05$ a random-effect model was used in the meta-analysis. * – indicates not all data-sets were included in the analysis, the number of asterisks represents the number of data-sets missing data.

FIGURE LEGENDS

Figure S1. Exclusion criteria for each data-set.

Demographic and medical exclusion criteria are in normal font, dietary data exclusion criteria are in italics. The cohort sizes before and after exclusion are shown in bold font. Study-specific criteria were exclusion of related family members in the ARIC and NHANES III cohorts and exclusion of CHS individuals who were also part of the ARIC, Systolic Hypertension in the Elderly (SHEP), or NHANES III studies. CHS interviewers did not assess the reliability of participant's answers nor acquire data on gout status.

Figure S2. Distribution of the 'Healthy-Eating' score in the ARIC (A), CARDIA (B), CHS (C), FHS (D), and NHANES III (E) cohorts.

Solid blue line –smoothed density curve of the 'Healthy-Eating' score distribution. Dashed red line – smoothed density curve for a random approximation of the normal distribution for data of the same length, mean, and standard deviation.

Figure S3. Distribution of the DASH diet score in the ARIC (A), CARDIA (B), CHS (C), FHS (D), and NHANES III (E) cohorts.

Solid blue line –smoothed density curve of the DASH diet score distribution. Dashed red line – smoothed density curve for a random approximation of the normal distribution for data of the same length, mean, and standard deviation.

Figure S4. Power curves.

Figure S5. Correlogram of consumption of 65 food items (serves/week).

Correlations were calculated using a Pearson's product-moment correlation test in the full cohort. Blue indicates a positive correlation, orange a negative correlation. X – non-significant correlation p-value ($P_{\text{Cor}} \ge 2.4 \times 10^{-5}$; Bonferroni multiple-testing correction of 0.05 divided by 2,080 correlations), no mark indicates a significant correlation ($P_{\text{Cor}} < 2.4 \times 10^{-5}$).

Figure S1. Exclusion criteria for each data set.

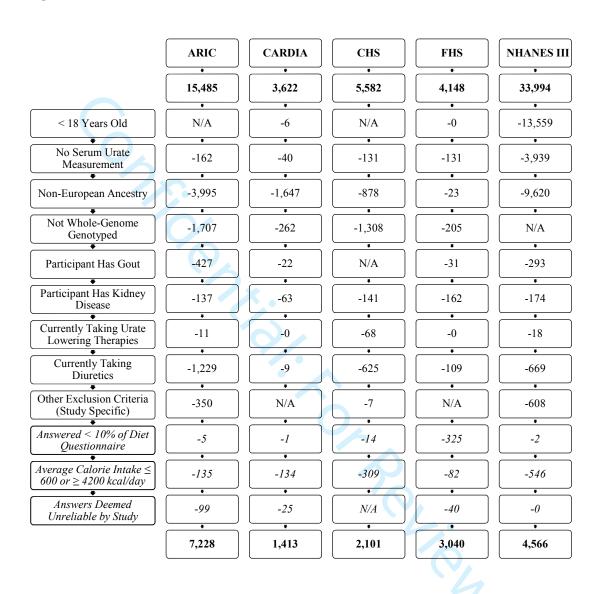
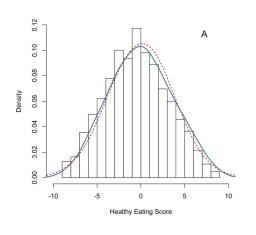
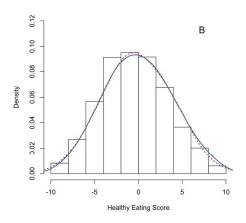
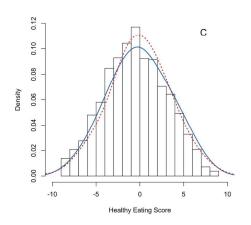
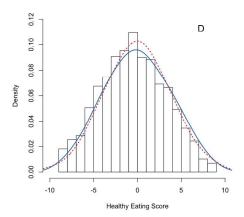


Figure S2. Distribution of the 'Healthy-Eating' score in the ARIC (A), CARDIA (B), CHS (C), FHS (D), and NHANES III (E) cohorts.









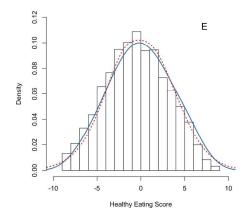
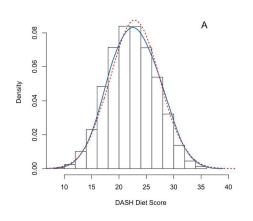
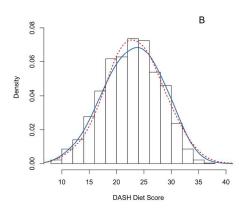
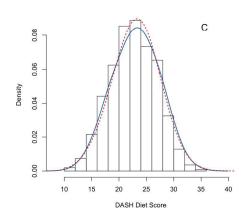


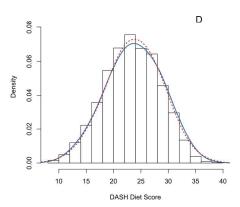


Figure S3. Distribution of the DASH diet score in the ARIC (A), CARDIA (B), CHS (C), FHS (D), and NHANES III (E) cohorts.









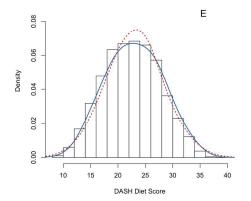




Figure S4. Power curves.

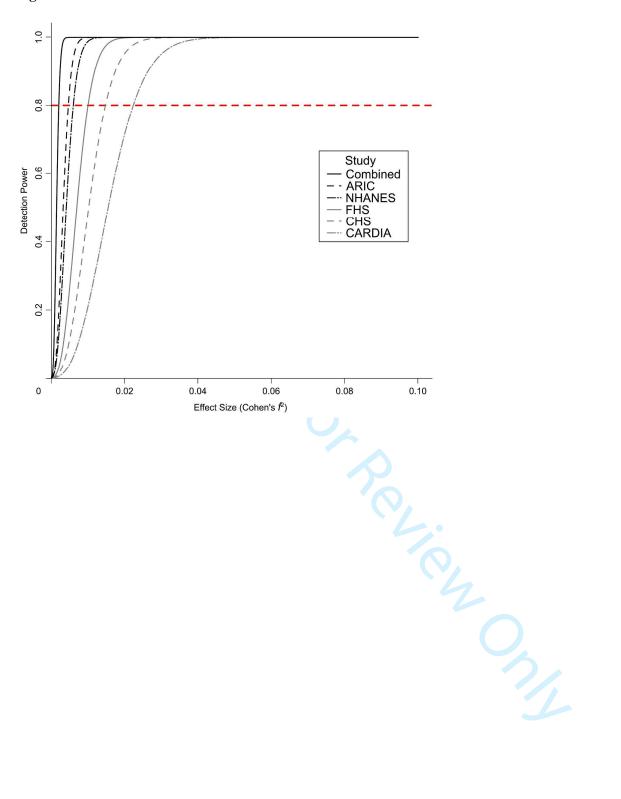


Figure S5. Correlogram of consumption of 65 food items (serves/week).

