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ORIGINAL ARTICLE

Breakfast quality and cardiometabolic risk profiles in an upper middle-aged German population

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BACKGROUND/OBJECTIVES: Little is known about relation of overall breakfast quality with cardiometabolic risk factors. Therefore, this study aimed to explore sex-specific associations between breakfast quality and cardiometabolic risk profiles in a sample of an upper middle-aged German population.

SUBJECTS/METHODS: Cardiometabolic profiles of 339 men and 329 women were cross-sectionally assessed using an overall biomarker score (BScore), glycated hemoglobin ($HbA1_c$), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), blood pressure, body mass index (BMI) and waist circumference (WC). Overall breakfast quality was assessed by using (i) an a-priori defined breakfast quality score (BQS) and (ii) data-driven breakfast patterns based on principal component analysis (PCA). Multiple linear regression models for association of breakfast quality with all outcomes were adjusted for all potential confounders including overall diet quality.

RESULTS: After adjustment for all potential confounders the BQS was inversely associated with the BScore (regression beta with 95% Confidence Interval: − 0.29 (052 − 0.06)) and HbA1c (−0.12 (−0.21, − 0.04)) in men; whereas no such associations were observed in women. Four breakfast (B) patterns were identified: B-processed-food pattern, B-cereal pattern, B-high fat pattern and B-dairy & cereal pattern. The B-processed-food pattern was positively associated with HbA1c (0.09(0.01, 0.18)), BMI (0.16 (0.06, 0.26)), and WC (0.17 (0.8, 0.26)) in men, and BMI (0.13 (0.1, 0.25)) and WC (0.11(0.01.0.22)) in women. The B-cereal pattern was inversely associated with BScore (−0.23 (−0.45, − 0.01)) and BMI (-0.11 (−0.20, − 0.01)) in men and WC(−0.16 (−0.27, − 0.05)) in women. The B-dairy & cereal pattern was also inversely associated with BScore (−0.26 (−0.48, − 0.04)) in men but not in women.

CONCLUSIONS: The overall breakfast quality was cross-sectionally associated with a healthier cardiometabolic profile, especially in upper-middle age men, independent of overall dietary quality. Such analyses should be supplemented by studies investigating the circadian sequence of food intake and metabolic consequences including hard disease endpoints.

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INTRODUCTION

Breakfast is considered an important component of a healthy eating pattern.[1] Studies have shown that regular breakfast consumption contributed to better overall diet quality[2] and lowered risk of obesity as well as cardiometabolic diseases. This reduction in risk was associated with improved energy balance and lower metabolic imbalances.[3,4] On the other hand, breakfast skipping was found to be associated with increased risk of overweight and obesity,[5] type 2 diabetes[6] and coronary heart diseases.[7] Nevertheless, it is unclear whether the breakfast consumption *per se* or the breakfast quality is associated with the observed influence on cardiometabolic health factors.[8]

Thus, there is a need to concentrate on the quality of breakfast to address the issue of adiposity and cardiometabolic disorders,[9] as underscored in several observational studies[10,11] and clinical trials.[12,13] This is important as composition of breakfast has important implications with regard to metabolic health.[8] For example, a breakfast high in cereals and fiber and low in refined carbohydrates has been reported to increase feelings of satiation, improve insulin sensitivity[13] and regulate appetite.[14] Therefore, the consumption of healthy breakfast must be distinguished from mere breakfast consumption for positive health outcomes.[12]

Moreover, the impact of breakfast quality needs to be distinguished from overall diet quality, when health outcomes are investigated. Existing studies on the health effects of breakfast have mostly investigated either a specific type of breakfast or breakfast component rather than the overall breakfast quality. Therefore, the aim of the current study was to investigate the sex-specific association of overall breakfast quality with cardiometabolic risk profiles in an upper-middle age German population enrolled in a sub-study of EPIC-Potsdam cohort.

MATERIALS AND METHODS

Study design and study population

This was a cross-sectional study designed within the European Prospective Investigation into Cancer and Nutrition (EPIC) Potsdam cohort for validation of used instruments. The study was conducted between August 2010 and December 2012. An age and sex stratified sample of 1447 individuals was randomly selected from 27548 participants of the EPIC-Potsdam cohort and invited for participation in the validation study. A total of 815 invitees agreed to participate in the EPIC-substudy. Written informed consent was obtained from all study participants and ethical approval from the Ethics Committee of the Medical Society of the federal state of Brandenburg. In the current study, participants aged 47–81 years

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with complete data available, that is, at least two 24-h dietary recalls, anthropometric measurements, objectively measured physical activity data and blood samples along with information on other covariates, were included in the analysis. More details regarding EPIC-Potsdam cohort and the validation study are available elsewhere.[15,16] Participants with missing exposure or covariates information were excluded (Supplementary Figure 1). After exclusion of all ineligible participants, the final analytical sample comprised of 664 participants including 339 men and 325 women.

Assessment of covariates

Data on age, sex, smoking status and educational level were recorded at the time of enrollment. All participants were examined by a study physician and disease history including medication use was recorded. Systolic and diastolic blood pressures were measured on right hand in sitting position by trained staff. Three consecutive measurements were taken, each two minutes apart. The last two measurements were averaged and used in the analysis. Physical activity was assessed with an accelerometer and heart rate monitoring device (Actiheart, CamNtech, Cambridge, UK), for seven days.[16] PAL in metabolic equivalents (MET) was obtained from the Actiheart software and used for adjustment.

Dietary intake assessment

Dietary intake was assessed using a total of three 24-h recalls per participant on non-consecutive days (Monday to Sunday). The 24-h recall was meal structured and the meals including breakfast were subject defined. The first 24-h recall was interviewer-administered and recorded at the study center, while the other two recalls were recorded telephonically on randomly selected days. Intakes from 24-h recalls were averaged and segregated into breakfast and whole day dietary intake, and collapsed into 39 food groups as done previously.[17] However, as many of the food groups in breakfast had zero or very low mean intake; out of 39 food groups, sixteen food groups with mean intake above 5 g/breakfast were retained for breakfast pattern analysis (Supplementary Table 1).

Serum biomarkers

Blood samples were collected at the time of enrollment in the study using monovette tubes with anticoagulants and centrifuged for serum fractioning. Serum fractions were stored at − 80 °C until analysis. Triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C), as well as low-density lipoprotein cholesterol (LDL-C) were measured with ADVIA 1650 chemistry system (Siemens Medical Solutions, Erlangen, Germany). C-reactive protein was measured by high-sensitivity ELISA (Immun Diagnostic, Bensheim, Germany). Glycated hemoglobin ($HbA1_c$) was measured using Dako $HbA1_c$ test (DAKO Diagnostics, Cambridgeshire, United Kingdom).

Exposure variable (breakfast and overall dietary quality)

Breakfast quality was assessed using two approaches: a-priori by using a modified alternate Healthy Eating Index-2010 and a-posteriori by applying principal component analysis (PCA) to derive breakfast dietary patterns based on 24-h dietary recall data.

The a-priori approach was based on Alternate Healthy Eating Index-2010[18] and consisted of eight components (Table 1). Data on sodium, trans-fatty acid and Eicosapentaenoic acid (EPA) were not available and, therefore, were not included in the score. Alcohol was not included in the score due to low intakes in the morning. Similarly, an a-priori Daily Intake Quality Score (DQS) was constructed (with the same variables) and used as a covariate to adjust the breakfast information for the overall diet quality. For scoring, most components of the BQS and DQS (Table 1) were divided into tertiles. However, 'vegetables' as well as 'nuts & seeds' at breakfast and 'nuts & seeds' in 24-hours (whole day), which were consumed by less than one-third of the participants, were divided into consumers and non-consumers. All non-consumers were treated as a separate category and consumers were divided into two groups (based on median consumption level). Tertiles of food groups having potential favorable effects on cardiometabolic profiles were coded 0 to 2, while tertiles of food groups with potentially unfavorable effects were inversely coded (2 to 0; Table 1). For each participant, the score points from the individual components were summed up from the breakfast and whole day intakes. The a-priori scores ranged from 0 to 16, with higher score reflecting a better overall diet quality.

The a-posteriori approach was addressed by PCA. PCA was applied to a variance-covariance matrix of food group intake to give more weight to food groups with greater variability in intake. Food groups were initially log-transformed to prevent beverages from dominating the extracted components. Varimax rotation was applied to maintain uncorrelated factors and improve interpretability. Component loadings were used to assess the contribution of each food group to the extracted patterns. Four PCA patters were retained using scree plots (See Supplementary Figure 2) and interpretability using factor loadings (Eigenvalues) $\geqslant 0.20$. Selected patterns were named according to characteristics of food groups loading highest in the respective principal components. In linear regression analysis, the identified principal components were used as independent (exposure) variables to evaluate associations with cardiometabolic risk factors modeled as dependent variables.

Outcome assessment (Cardiometabolic risk profile)

As cardiometabolic abnormalities reflected by metabolic changes could be a manifestation of a cluster of underlying disorders, a composite multi-biomarker score was constructed. The biomarker score (BScore) was constructed by adding standardized values of HDL-C, LDL-C, HbA1c, C-reactive protein and TG. Standardized HDL-C values were reversed (i.e. lower values contributed to higher biomarker score) before addition to the score as higher HDL-C values are beneficial as opposed to the other components of the biomarker score. A higher BScore represented a higher cardiometabolic risk. Other cardiometabolic outcomes included HbA1c; HDL-C, LDL-C, TG, BMI, WC, systolic and diastolic blood pressures. Trained staff conducted anthropometric assessment in the study center as per protocol.[19] Weight and height were measured in light underwear without shoes. WC was measured at mid-point between lower rib and the ilium crest.

Table 1. Components and scoring criteria of a-priori Breakfast Quality Score (BQS) and a-priori Daily Intake Quality Score (DQS) constructed in the study

Original aHEI components (18)	*Components of BQS and DQS*	*Lowest Score (0 point each)*	*Highest Score (2 points each)*
Vegetables	Vegetables[a]	No intake	Above median
Fruit,	Fruit,	Lowest tertile	Highest tertile
Whole grains	Whole grains	Lowest tertile	Highest tertile
Sugar-sweetened beverages and fruit juice	Sugar-sweetened beverages and fruit juice	Highest tertile	Lowest tertile
Nuts and legumes	Nuts and legumes (incl. peanut butter)[a]	No intake	Above median
Red/processed meat	Red/processed meat	Highest tertile	Lowest tertile
trans fat	(Not included)	–	–
Long-chain (n-3) fats (EPA + DHA)	Long-chain (n-3) fats (DHA)[b]	Lowest tertile	Highest tertile
PUFA[c]	PUFA	Lowest tertile	Highest tertile
Alcohol	(Not included)	–	–
Sodium	(Not included)	–	–

[a]Over half of the participants of this food group were non-consumers; therefore, all non-consumers were treated as a separate category and assigned a score of '0' and consumers were divided into two groups based on median consumption level. Those below median were assigned a score of '1' and above median were assigned score of '2'. [b]DHA (Docosahexaenoid acid). [c]PUFA (Polyunsaturated fatty acid).

Statistical analysis

Basic characteristics of all participants were described stratified by sex. Intakes of the three 24-hour recalls were averaged to estimate mean daily and breakfast consumption. Continuous variables including age, weight, BMI, hypertension, and serum biomarkers were described by arithmetic mean and respective standard deviation while categorical variables including smoking status, educational level and medication use were described by frequencies and percentages. Alpha (α) level of 0.05 was used for all statistical tests.

A priori (BQS and DQS) and PCA patterns scores were used as continuous exposure variables. Association between the exposure variables and cardiometabolic risk factors were initially investigated using Pearson partial correlations (r), adjusted for age, education, physical activity and alcohol intake). Multivariable analysis using multiple linear regressions was performed for outcome variables that were associated with breakfast quality scores in initial analysis. Three regression models were developed. Model 1 was adjusted only for age; Model II included model I+smoking status, physical activity, education, energy and alcohol consumption; and Model III included Model II+overall diet quality, HDL-C, LDL-C, C-reactive protein, HbA1c, systolic blood pressure and medication for treatment of diabetes, lipidemia or hypertension. Covariates of Model III were modified according to the respective outcomes in order to avoid over-adjustment. Breakfast and daily intake quality scores and PCA patterns were mutually adjusted in their respective models to get insight in whether the associations of breakfast quality are independent of overall diet quality.

Sensitivity analyses were conducted to evaluate whether association of breakfast quality with cardiometabolic profiles was affected by removing participants consuming anti-diabetic drugs. We also reanalyzed association of the breakfast quality with BScore and HbA1c in a subgroup of the participants (*n*: men = 311, women = 294) on whom data on fasting state was also collected. Moreover additional analyses were conducted to evaluate association of the overall breakfast quality with the metabolic syndrome (MetS). For this purpose, MetS was defined according to International Diabetes Federation criteria,[20] as the presence of obesity defined by a WC $\geqslant$ 95 cm among men and $\geqslant$ 80 cm in women and the presence of two risk factors among the following: (i) TG $\geqslant$ 1.7 mmol/l, (ii) HDL-C $<$ 0.9 mmol/l among men and $<$ 1.29 mmol/l in women (iii) systolic blood pressure $\geqslant$ 130 mm Hg or diastolic blood pressure $\geqslant$ 85 mm Hg or previous history of hypertension and (iv) hyperglycemia ($\geqslant$ 5.6 mmol/l) or previous history of diabetes. In the current study, most of the participants did not provide fasting blood samples; therefore, abnormal glucose metabolism was defined by HbA1c $\geqslant$ 5.7% that corresponds to fasting plasma glucose levels of 100 mg/dl, according to the guidelines of the American Diabetes Association.[21]

All statistical analyses were performed using SAS (Version 9.4, Enterprise Guide 6.1, SAS Institute Inc., Cary, NC, USA).

RESULTS

General characteristics

Mean age, among men, was 67 ± 8 years, mean BMI was 27.6 ± 4.0 and mean PAL was 1.6. Moreover, approximately one-fourth, of men, had basic education/vocational training; two thirds were current or former smokers and over 90% were consuming treatment drugs for hypertension, diabetes or dyslipidemia. Mean age, among women, was 64.8 ± 8.7 years, mean BMI was 27.2 ± 4.5 and mean PAL was 1.6 ± 0.2. Moreover, over one-third of the women had basic education/vocational training, 38.4% were current or former smokers and 75% were consuming treatment drugs for hypertension, diabetes or dyslipidemia (Table 2).

Table 2. Background characteristics of study participants, stratified by sex, in the study

Characteristics (unit)	*Men (n = 339)*[a]		*Women (n = 325)*	
	Mean/ Frequency	*Standard deviation/ Percentages*	*Mean/ Frequency*	*Standard deviation/ Percentages*
Age (years)	67	8	64.8	8.7
Energy intake at breakfast (kcal)	524.2	213.2	384.2	153.3
Daily energy intake (kcal)	2349.8	595	1759.6	409.6
Alcohol consumption (g/day)	17.6	19.8	8	9.9
BMI (kg/m^2)	27.6	4	27.2	4.5
PAL (Met[b])	1.6	0.2	1.6	0.2
Educational Status (frequency and percentage)				
No vocational training	97	28.6	117	36
Technical college	50	14.8	95	29.2
University	192	56.6	113	34.8
Smoking Status (frequency and percentage)				
Non smoker	110	32.5	200	61.5
Current smoker	193	56.9	92	28.3
Former smoker	36	10.6	33	10.1
Treatment Drugs (frequency and percentage)				
Antihypertensive	191	56.3	147	45.4
Antidiabetic	47	13.9	14	4.3
Antilipid	98	28.9	75	23.1

[a]Continuous variables are presented as mean ± standard deviation and categorical variables as frequencies (percentage). [b]TEE (total energy expenditure), REE (resting energy expenditure).

Breakfast and daily food consumption

All study participants were breakfast consumers. Intakes of 16 breakfast food groups showed that men had comparatively higher intakes of bread and processed meat. No major differences were observed for other food groups. Compared with breakfast amounts, the intakes of daily amounts of the 39 food groups showed higher consumption of potatoes, bread, red and processed meat, juices and soft drinks, and beer among men and higher intakes of fruits and wine among women (Supplementary Table 2).

Four breakfast and daily intake patterns were identified as best solutions reflecting meal and daily intakes from the PCAs. Among breakfast (B) patterns PC1 loaded highly on processed meat, cheese, fruiting vegetables, margarine, and negatively on sugar and confectionary, and was named as 'B-processed-food pattern'; PC2 loaded highly on tea and breakfast cereals and termed 'B-cereal pattern'; breakfast pattern PC3 loaded highly on sugar & confectionary, eggs, butter, and bread and was named 'B-high-fat pattern'; PC4 loaded highly on milk and dairy products and cereals and named 'B-dairy & cereal pattern' (Table 3). Among the daily intake (D) patterns, PC1 loaded highly on wine, leafy vegetables, nuts and seeds, vegetable oils, soft drinks (negatively), fish and tea and was named 'D-prudent pattern'; PC2 loaded high on pasta & rice and was named 'D-pasta & rice pattern'; PC3 loaded highly on soups, root vegetables, cakes and cookies, other vegetables, cereals and red meat and named 'D-mixed pattern'; and PC4 loaded highly on wine, cabbage, red meat, and sauces and named 'D-meat pattern' (Table 4).

In both men and women, BQS was positively correlated ($P < 0.05$) with higher DQS, B-high fat diet pattern, B-dairy and cereal pattern and D-prudent pattern score. Moreover, B- cereal pattern was positively correlated with D-prudent intake pattern. Further details are provided in Supplementary Tables 3 and 4.

Association of breakfast quality with cardiometabolic risk profiles

In men, the partial correlations (adjusted for age, smoking status and alcohol intake) between a-priori breakfast quality (BQS) and cardiometabolic risk profiles showed that BQS was negatively correlated ($P < 0.05$) with BScore and HbA1c, and positively correlated with HDL-C. Furthermore, the a-posteriori B-processed-food pattern was positively correlated with the BScore, HbA1c, triglyceride, diastolic blood pressure, BMI and WC, whereas the B-cereal pattern was negatively correlated with BScore, HbA1c,

Table 3. Factor-loading matrix for the four breakfast patterns derived from three 24-hours recalls, in the study[a,b]

Food Groups	*Processed food pattern*	*Cereal pattern*	*High fat diet pattern*	*Dairy & cereal pattern*
Processed meat	**0.76**	−0.03	0.05	−0.03
Cheese	**0.69**	−0.03	0.06	−0.14
Fruiting vegetables	**0.54**	0.1	0	0.04
Margarine	**0.36**	−0.06	−0.09	−0.05
Sugar & confectionary	**−0.34**	−0.07	**0.33**	−0.11
Tea	−0.03	**0.85**	0.16	−0.1
Cakes & cookies	−0.07	−0.1	−0.02	−0.07
Coffee	0.05	**−0.84**	**0.22**	−0.09
Eggs	**0.21**	0	**0.89**	0.16
Butter	−0.16	0.01	**0.49**	−0.1
Bread	**0.32**	−0.02	**0.33**	**−0.2**
Milk & dairy products	−0.07	−0.15	−0.04	**0.93**
Breakfast cereals	−0.09	**0.23**	−0.07	**0.54**
Fruits	0.01	0.07	−0.02	0.16
Other non-alcoholic drinks	0.04	0.06	−0.05	0.02
Fruit & vegetable juice	0.05	0.03	0.08	0.03

[a]Breakfast intake was extracted from 24-hours recalls. [b]Loadings with an absolute value of 0.2 or higher are bold printed.

BMI and positively correlated with HDL-C. Moreover, in men, the B-dairy and cereal pattern was positively correlated with HDL-C. No correlations were observed between BQS and LDL-C, blood pressure, BMI and WC (Supplementary Table 5).

In women, the BQS was inversely correlated with BScore. Among the breakfast patterns, the B-processed-food pattern was positively and B-cereal pattern was negatively correlated with WC. Moreover, B-dairy and cereal pattern was inversely correlated with systolic and diastolic blood pressure. In women, both BQS and the breakfast patterns were not correlated with HDL-C, LDL-C and BMI (Supplementary Table 6).

Higher scores of both BQS and TQS were positively correlated with energy intake at breakfast. Pearson partial correlations between BQS and energy intake during breakfast was 0.30 (P-value < 0.001) among men and 0.39 (P-value < 0.001) among women.

Further analysis of BQS components and cardiometabolic risk factors showed that among the BQS components breakfast cereals were negatively (r: −0.12) and red & processed meat was positively correlated ($P < 0.05$) with $HbA1_c$ (r: −0.24) and Biomarker score (r: 0.14).

Fully adjusted (Model III) multivariable analysis of breakfast quality scores was conducted for BScore, HBA1C, BMI and WC (Figures 1, 2, 3, 4), blood pressure and HDL-C. The models showed that, in men, BQS was inversely associated with BScore and HbA1c. No associations were observed for DQS with cardiometabolic risk factors. Furthermore, in men, B-processed-food pattern was positively associated with HbA1c, BMI and WC; B-cereal pattern was inversely associated with BScore and BMI; and B-dairy & cereal pattern was inversely associated with BScore. No associations were observed for blood pressure (both systolic and diastolic) and HDL-C. Results for women (Figures 1–4) revealed that BQS was not associated with cardiometabolic risk factors. However, B-processed-food pattern was positively associated with BMI and WC; whereas B-cereal pattern was inversely associated with WC, in women. The D-prudent intake pattern was inversely associated with BScore in men and WC and BScore in women. No associations were observed for other daily intake patterns with BMI, WC or HbA1c. Breakfast quality scores were not associated with blood pressure (systolic and diastolic) and other biomarkers.

Table 4. Factor-loading matrix for the four daily intake patterns derived from three 24-h recalls, in the study[a,b]

Food Groups	*Prudent diet pattern*	*Pasta & rice pattern*	*Mixed diet pattern*	*Meat pattern*
Wine	**0.8**	0.19	0.16	**0.29**
Leafy vegetables	**0.38**	−0.03	−0.08	−0.04
Nuts & seeds	**0.24**	0.08	0.12	0.02
Vegetable oils	**0.24**	0.06	0	0.04
Fruiting vegetables	0.18	−0.06	−0.07	−0.01
Other fruits	0.14	−0.06	0.06	0.01
Soft drinks	**−0.22**	0.08	0.1	0.13
Pasta & rice	−0.07	**0.72**	0.09	0.18
Offals	0	−0.11	−0.04	0
Margarine	**−0.21**	**−0.27**	0.04	0.07
Potatoes	0.01	**−0.62**	0.11	0.03
Soups	−0.18	0.19	**0.87**	−0.06
Root vegetables	0.16	−0.18	**0.38**	−0.11
Cakes & cookies	0.01	−0.09	**0.25**	0.02
Other vegetables	0	−0.01	**0.22**	0.03
Breakfast cereals	0.15	0.12	**0.21**	−0.01
Legumes	−0.06	0.06	0.19	−0.03
Cabbage	0.06	**−0.4**	0.18	**0.61**
Poultry	0.07	0.13	−0.01	**0.53**
Red meat	−0.13	**−0.33**	**0.27**	**0.35**
Sauces	0.18	−0.05	−0.02	**0.23**
Fish	**0.44**	−0.16	0.18	**−0.52**
Beer	0.06	−0.06	−0.03	0.01
Spirits	0.01	0.04	0.12	0.02
Bread	−0.05	−0.09	−0.01	0.01
Butter	0.07	0	0.03	−0.01
Other alcoholic beverages	0.1	0.13	0.13	0.03
Processed meat	−0.13	−0.09	0.11	0.06
Milk & dairy products	−0.05	0.03	0.11	−0.14
Other non-alcoholic drinks	0.02	−0.05	−0.06	0.03
Tea	**0.26**	0.1	0.04	0.15
Other fats	0	−0.09	0	0.08
Coffee	0.03	0.04	−0.05	−0.02
Fruit & vegetable juice	0.12	−0.03	0.06	−0.08
Eggs	−0.01	−0.07	−0.07	0.07
Fruits	0.04	−0.05	0.05	−0.11
Cheese	0.1	0.05	−0.02	0.06
Sugar & confectionary	0	0.01	0.06	−0.05
Miscellaneous	0.09	0.08	0.08	−0.02

[a]Breakfast intake was extracted from 24-h recalls. [b]Loadings with an absolute value of 0.2 or higher are bold printed.

Sensitivity analysis

In sensitivity analyses (Supplementary Figures 3), exclusion of diabetic participants (men = 47 and women = 13), did not change the primary findings for HbA1c and BScore in relation to BQS and cereals dominated dietary pattern. Similarly, adjustment of the fasting state for triglyceride did not change results for both biomarker score (Beta with 95% Confidence Interval: −0.26 (−0.51, −0.01) and hba1c (−0.16 (−0.26, −0.05)) in the sensitivity analysis.

Additional analysis for metabolic syndrome (MetS) showed that the B-processed-food pattern was positively and the B-cereal pattern was inversely associated with (MetS) in men. No associations were observed for women.

DISCUSSION

In this population-based study with separate analyses of men and women regarding the cardio-metabolic health effects of breakfast, we could confirm the overall impression that breakfast is an important meal associated with cardiometabolic risk factors. After

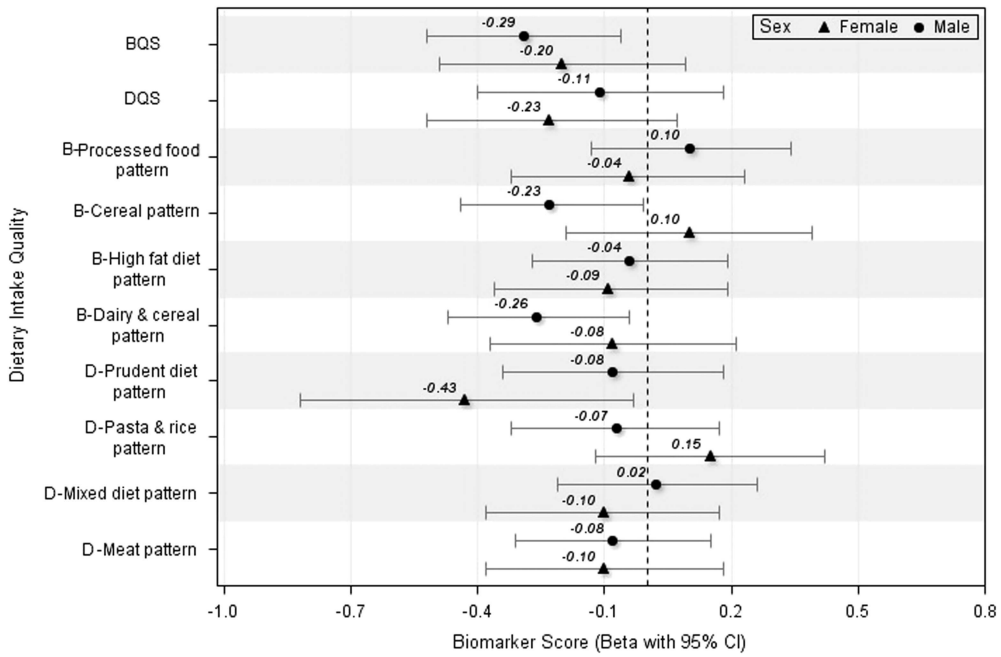

Figure 1. Betas with 95% Confidence Intervals (CI) of Biomarker Score according to the a-priori breakfast and daily intake quality scores (BQS and DQS) and principal component analysis derived breakfast and daily intake patterns. Models were adjusted for age, education, smoking, physical activity, alcohol intake, total energy, blood pressure and medication. The Prefixes 'B' and 'D' represent breakfast and daily intakes patterns, respectively.

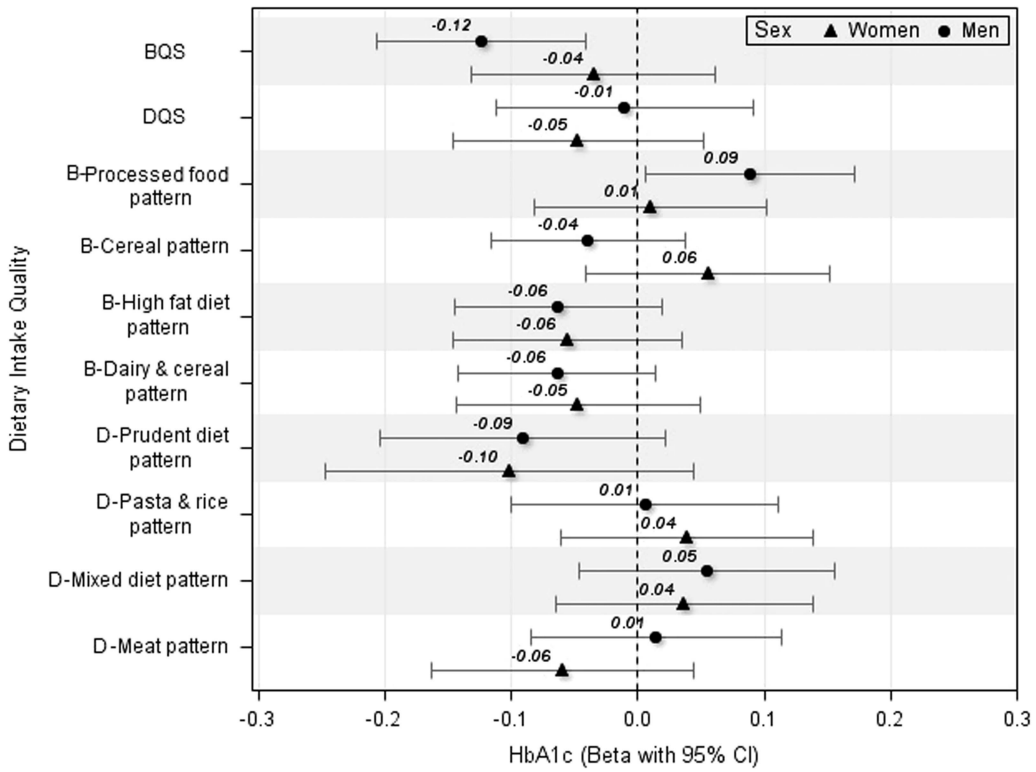

Figure 2. Betas with 95% Confidence Intervals (CI) of HbA1c according to the a-priori breakfast and daily intake (whole day) quality scores (BQS and DQS) and principal component analysis derived breakfast and daily intake patterns. Models were adjusted for age, education, smoking, physical activity, alcohol intake, total energy, blood pressure and medication. The Prefixes 'B' and 'D' represent breakfast and daily intakes patterns, respectively.

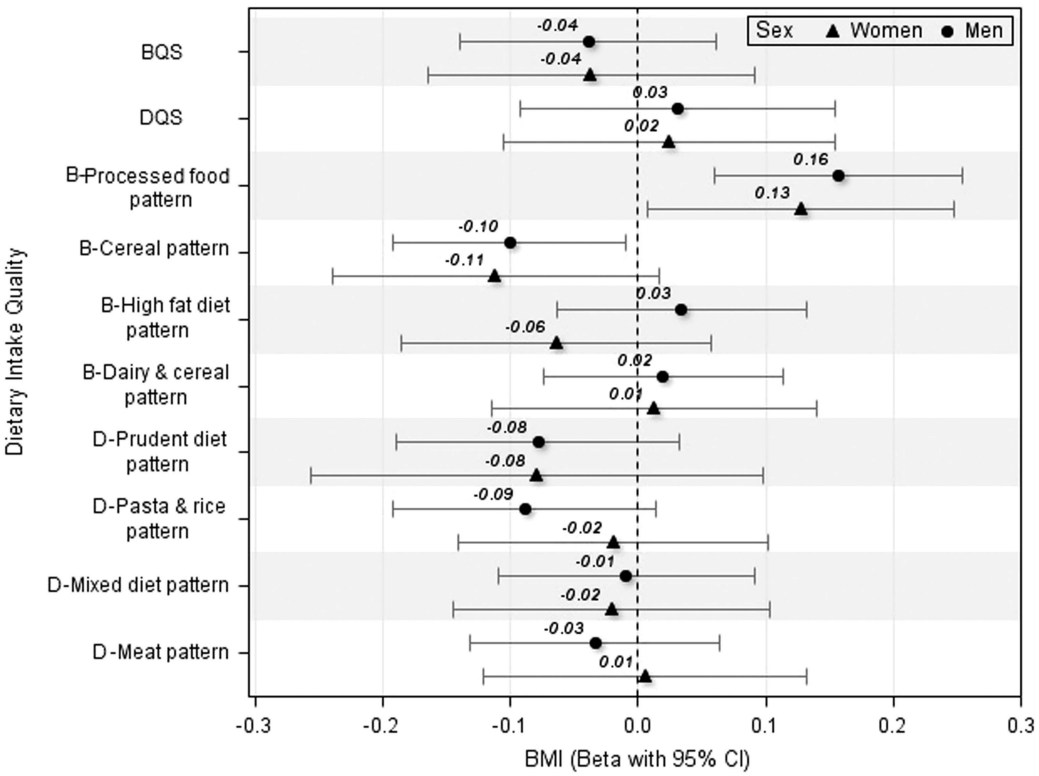

Figure 3. Betas with 95% Confidence Intervals (CI) of body mass index according to the a-priori breakfast and daily intake quality scores (BQS and DQS) and principal component analysis derived breakfast and daily intake patterns. Models were adjusted for age, education, smoking, physical activity, alcohol intake, and total energy. The Prefixes 'B' and 'D' represent breakfast and daily intakes patterns, respectively.

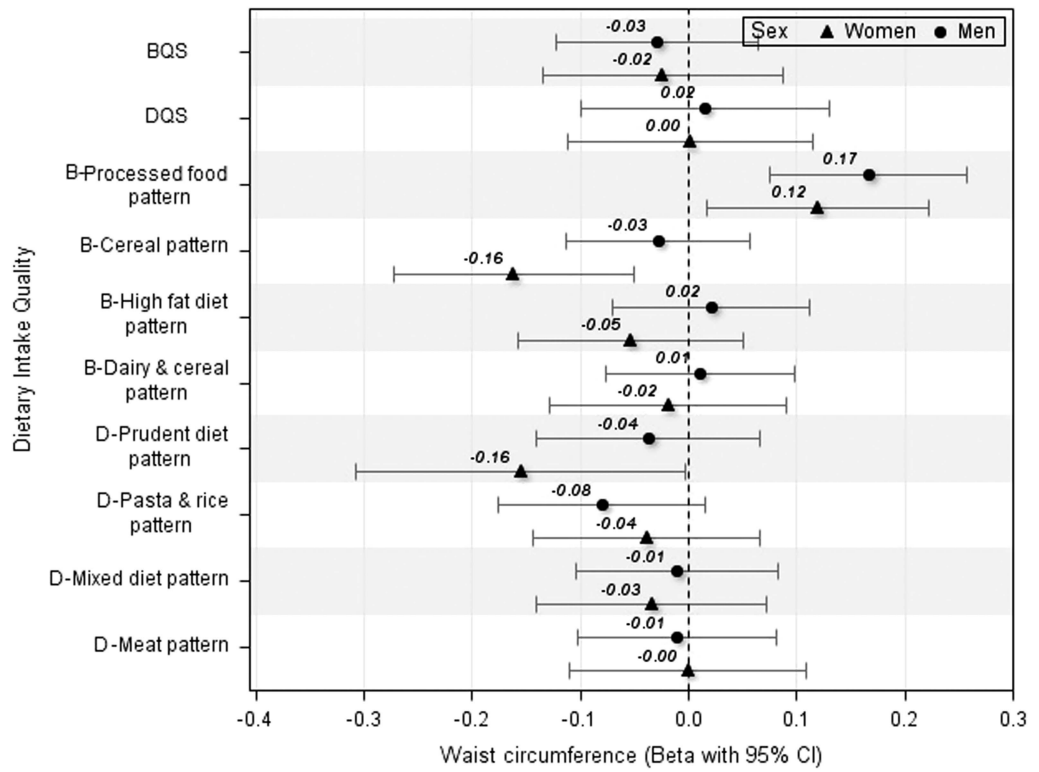

Figure 4. Betas with 95% Confidence Intervals (CI) of waist circumference according to the a-priori breakfast and daily intake quality scores (BQS and DQS) and principal component analysis derived breakfast and daily intake patterns. Models were adjusted for age, education, smoking, physical activity, alcohol intake, and total energy. The Prefixes 'B' and 'D' represent breakfast and daily intakes patterns, respectively.

adjustment for overall diet quality, associations between a priori, as well as a posteriori breakfast quality scores and cardio-metabolic parameters could be observed. In general, high quality breakfast seems to be beneficial regarding cardio-metabolic health.

Overall BQS was inversely associated with lower long-term hyper-glycaemia and metabolic syndrome markers (BScore) among men. These results were independent of the effect for overall diet quality score and did not change in the sensitivity analysis after excluding the prevalent diabetes cases. In the current study, overall breakfast quality was assessed using a priori diet quality score based on aHEI components, which was shown to be associated with lower risk of chronic diseases including type 2 diabetes, in men.[22] Our analysis of the components of the BQS revealed whole grain cereals were inversely and processed meat intake was positively associated with HbA1c and BScore ($P < 0.05$). Although we cannot draw any causal conclusion, nevertheless, these results showed the favorable effect of the BQS might be related to combination of healthy foods especially higher intakes of whole grain cereals and lower intake of processed meat.[23,24] A healthy breakfast especially high in fiber-rich cereals, as well as fruits and low in glycemic index is suggested to be causally linked to appetite control and lower blood glucose levels.[14] Data on overall breakfast quality and cardiometabolic risk factors are limited. However, other studies have reported lower BMI, better cardiometabolic risk profiles[25] and lower fasting glucose concentration[26] in individuals consuming whole grain cereals. Similarly red meat and processed red meat consumption has been associated with higher fasting glucose[27] and higher risk of MetS.[28]

Another important finding in this study was the positive association between processed-food breakfast pattern and HbA1c in men, and markers of adiposity among both sexes. The processed-food breakfast pattern loaded high on foods including processed meat, cheese and (mostly) white bread in our study. Although other studies assessing breakfast intake did not report similar patterns, a prospective cohort study among US upper-middle age adults, assessing usual intake patterns and risk of MetS, showed that a western-type pattern including these food beside others were associated with higher risk of MetS.[29] These results indicate a processed-food breakfast pattern similar to the western-type daily intake pattern,[30,31] may be a potential risk factor in development of obesity and metabolic syndrome.

Our data also suggest an inverse association of the cereal pattern with adiposity among both sexes. The cereal pattern was also inversely associated with BScore, although, this association was stronger for the dairy and cereal pattern. These results are consistent with most of the earlier studies. Bazzano *et al* found that breakfast cereal was inversely associated with BMI and weight gain in US men.[5] A study by Cho *et al* reported a significantly lower BMI among US adults consuming ready-to-eat cereals, cooked cereals or quick bread but no other type of breakfast.[10] Similarly, Good *et al* reported lower BMI and WC among women consuming ready-to-eat breakfast cereals.[32] Moreover, Taskar *et al* reported that breakfast consumption especially ready-to-eat breakfast cereals were inversely associated with cardiometabolic risk profiles.[25] Likewise, in an Italian population, a breakfast quality score derived from standardized intakes of selected Italian breakfast foods including cereals was inversely associated with prevalence of metabolic syndrome.[33] However, in contrast to our results, McGill *et al* reported, in comparison to no breakfast or other type of breakfast, ready-to-eat breakfast was associated with lower BMI, and lower WC in young adults but not in age group 51–70 years.[34] The beneficial effect of breakfast cereals could be attributed to its nutrient content.[35] Breakfast cereals are low in saturated fat and high in dietary fiber, and often fortified with important nutrients.[25,36,37] In addition to the beneficial effect of cereals, dairy may also have some role in the observed association with biomarker score. Kim *et al* reported that higher intake of dairy product is associated with lower risk of MetS,[38] an observation similar to our study. Dairy products are rich sources of essential amino acids, calcium, vitamin D and magnesium, which might enhance insulin sensitivity.[39]

There are several potential explanations of the beneficial associations of a healthier breakfast. Results from clinical trials reveal that breakfast low in glycemic index suppress appetite and improve glucose tolerance during the whole day.[40,41] Moreover, Pal *et al* in a randomized cross-over trial demonstrated that fasting glucose and appetite can be suppressed by decreasing glycemic index of the breakfast meals.[42] These studies suggest that the positive associations of breakfast quality on body fat measures and metabolic syndrome could possibly be explained through mechanisms involving appetite control and satiety. In addition, fiber-rich breakfast foods, through slow absorption and digestion of starch from carbohydrates blunt post-prandial glycemic response, improve insulin sensitivity response to the next meal and prevent hypoglycemia between meals.[13,43,44] These metabolic changes may affect appetite and total energy intake that may prevent weight gain.[45,46] Moreover, foods rich in complex-carbohydrates may also affect release or activity of gut hormones that include cholecystokinin, which may affect satiety.[47] Similarly a lower as compared with higher intake of red and processed meat is associated with decreased risk of MetS and central obesity.[28] This association with processed meat may be attributed to its nitrate content beside other components, which are linked to lower insulin secretion[48] and poor glucose tolerance.[49] In addition, time of intake is also an important factor related to satiety. The morning meal is considered more satiating[50] and consumption of regular breakfast especially whole grain products has been attributed to lower risk of chronic diseases.[9]

We could also observe a positive association between higher breakfast quality and higher energy intake at breakfast. As high breakfast quality was also associated with lower BMI and waist circumference, this observation, alludes to the suggestions that circadian distribution of energy intake, that is, higher energy intake early in the day may have beneficial role in prevention of weight gain.[51] This is also in line with results of a recent cohort study, which reported that higher energy intake early in the day (lunch) was associated with lower risk of weight gain[52] However, the circadian distribution of energy intake and how much should be consumed during each occasion including at breakfast is still an open question for future research.

There are certain limitations of the current study that needs to be considered. We use three 24-h recalls and estimated average consumption of individuals that may not completely reflect the usual intakes. A better approach for estimation of usual intakes is application of modelling approaches like National Cancer Institute usual intake estimation method, which may derive reliable usual intake estimates. Nevertheless, such approaches require information on both multiple 24-h recall intakes as well as frequencies of intakes. Due to non-availability of frequencies information about foods consumed in breakfast, we were unable to use such approach. Nonetheless, use of multiple 24-recall reduced the day to day variation in our study. In addition, it was a cross-sectional study; therefore, neither can we establish causation nor rule out reverse causation in our study.

The strength of this study includes multiple 24-h recalls and the two breakfast quality assessment methods. Multiple 24-h recalls is an important strength as most of the earlier breakfast studies relied on single 24-h recalls. Moreover, the breakfast quality in this study was evaluated with both a-priori (BQS and DQS), using a modified Healthy Eating Index and a-posteriori, using PCA. Combinations of the two methods helped to identify the healthy components of the breakfast and also helped to explore contribution of food groups to the observed associations.

In conclusion, an overall breakfast quality, high in cereals, fruits and vegetables and low in red and processed meat may be helpful

to maintain a healthy cardiometabolic profile, especially in upper-middle age men and may be critical to lower the risk of obesity among both sexes. These findings allude to the importance of overall breakfast quality to maintain a healthy cardiometabolic risk profile. Such analyses should be supplemented by studies investigating the circadian sequence of food intake and metabolic consequences including hard disease endpoints.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

KI and HB conceived the idea and developed the analysis plan, KI conducted analysis and wrote the manuscript, SK provided support in statistical analysis, LS assisted in manuscript writing. All the authors provided inputs in data interpretation, critically reviewed the manuscript and approved the last version.

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