Abating abdominal adiposity: Modifiable lifestyle risk factors for visceral and liver fat deposition

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Citation

Eekelen, E. van. (2020, April 21). *Abating abdominal adiposity: Modifiable lifestyle risk factors for visceral and liver fat deposition*. Retrieved from https://hdl.handle.net/1887/136535

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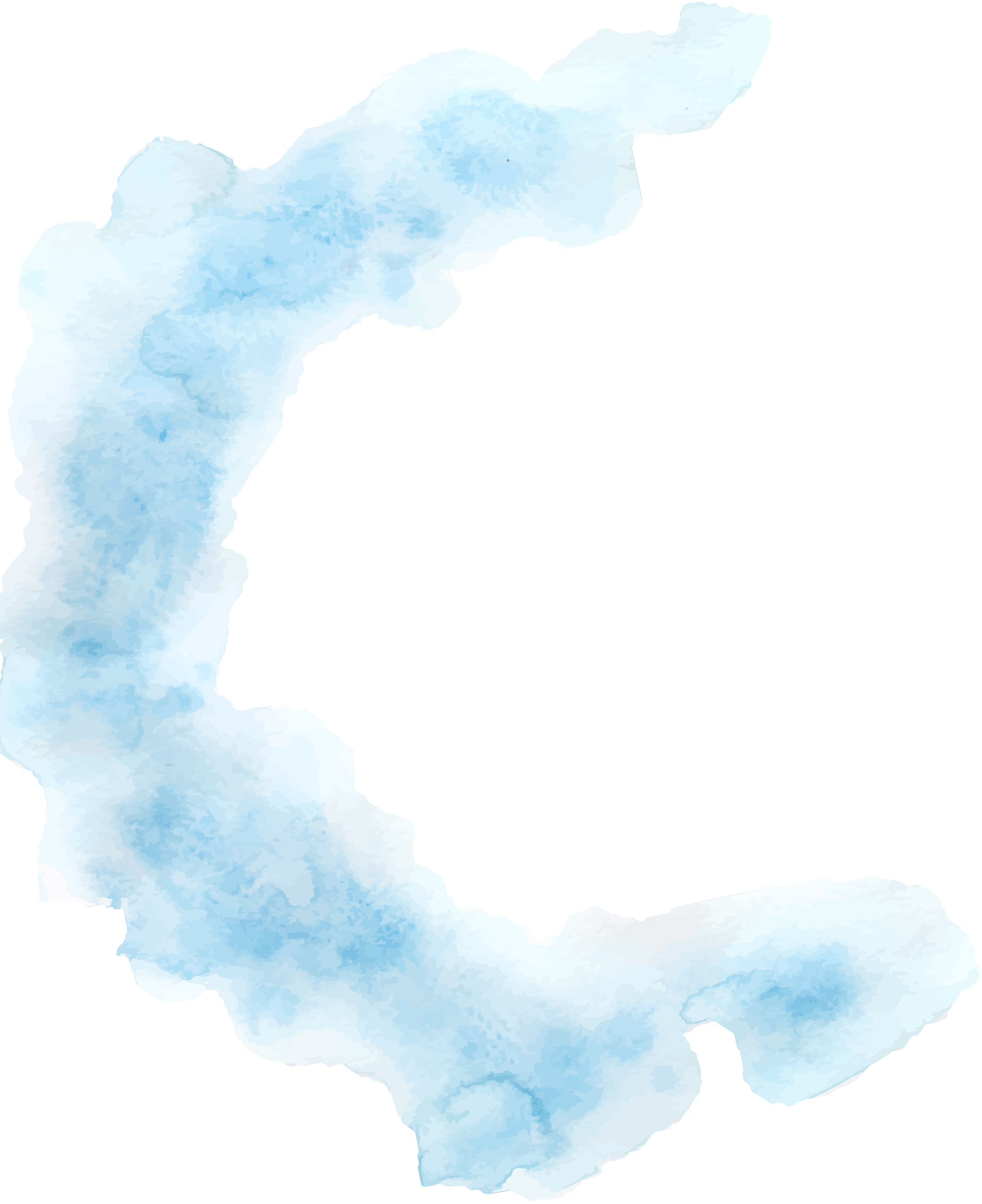
Title: Abating abdominal adiposity: Modifiable lifestyle risk factors for visceral and liver fat deposition
Issue date: 2020-04-21



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Sweet Snacks Are Positively and Fruits and Vegetables Are Negatively Associated with Visceral or Liver Fat Content in Middle-Aged Men and Women

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J Nutr 2019;149:304–313

ABSTRACT

Background

Visceral adipose tissue (VAT) and hepatic triglyceride content (HTGC) are major risk factors for cardiometabolic diseases.

Objective

We aimed to investigate the association of dietary intake of the main food groups with VAT and HTGC in middle-aged men and women.

Methods

We used data from the Netherlands Epidemiology of Obesity Study, a population-based study including 6,671 participants aged 45-65 years at baseline. In this cross-sectional analysis, VAT and HTGC were assessed by magnetic resonance imaging and spectroscopy, respectively, as the primary outcomes. Habitual intake of main food groups (dairy, meat, fish, fruits and vegetables, sweet snacks, and fats and oils) was estimated using a food frequency questionnaire. We examined associations of intake of different food groups with VAT and HTGC by linear regression analysis stratified by sex and adjusted for age, smoking, education, ethnicity, physical activity, basal metabolic rate, energy-restricted diet, menopausal state and total energy intake, stratified by sex.

Results

In women, a 100-g/d higher intake of dairy was associated with 2.0 cm^2 less VAT (95% CI: –3.4, –0.7 cm^2) and a 0.95-fold lower HTGC (95% CI: 0.90-, 0.99-fold). Moreover, a 100-g/d higher intake of fruit and vegetables was associated with 1.6 cm2 less VAT (95% CI: –2.9, –0.2 cm2) in women. Fruit and vegetables were negatively associated (0.95; 95% CI: 0.91, 1.00) with HTGC, and sweet snacks were positively associated (1.29; 95% CI: 1.03, 1.63). Patterns were weaker but similar in men. Fish intake was not associated with VAT or HTGC and plant-based fat and oil intake were only associated with VAT after adjustment for total body fat.

Conclusions

Despite some variation in the strength of the associations between men and women, dietary intake of sweet snacks was positively associated with HTGC, and fruit and vegetable intake were inversely associated with visceral fat and liver fat content. Prospective studies are needed to confirm these results.

INTRODUCTION

Obesity, in particular abdominal obesity, is increasingly prevalent worldwide and is a major risk factor for type 2 diabetes and cardiovascular diseases (1, 2). The excess cardiometabolic risk associated with abdominal obesity is hypothesized to be due to the accumulation of fat in non-adipose tissue (2). Visceral adipose tissue (VAT) and hepatic triglyceride content (HTGC) have been associated with a cluster of metabolic risk factors, insulin resistance, coronary artery disease and cardiovascular disease in general (3-6). Furthermore, visceral adipose tissue is thought to possibly contribute to the excess cardiometabolic risk due to a high free fatty acid (FFA) release and a high rate of cytokine secretion (2). In addition, high concentrations of free fatty acids and insulin resistance are related to fat deposition in the liver (7) and are strongly related to type 2 diabetes and cardiovascular disease (8, 9).

Due to the many health-related consequences, both visceral fat and liver fat might be a key targets in the prevention or treatment of cardiometabolic disease and its consequences. In addition to physical activity, diet is a key modifiable lifestyle risk factor for obesity and chronic diseases (10-12). A recent systematic review has shown that dietary patterns recognized as healthy and intake of medium-chain triacylglycerols (MCTG) display an inverse association with visceral and subcutaneous fat. For visceral fat only, inverse associations were also shown with dietary fiber, calcium and phytochemicals (13). Interestingly, an overfeeding study of saturated and polyunsaturated fat showed distinct effects on visceral and liver fat (11). Most previous studies have assessed the role of nutrients in fat deposition (14-18), although higher energy intake during childhood has been suggested to be associated with greater NAFLD risk irrespective of the macronutrients this energy intake comes from (19). However, it is increasingly recognized that studying foods and food groups rather than single nutrients may be important in relation to health outcomes, as foods are not merely the sum of their nutrients (20-23). Within a food item, there may be unknown effects of other nutrients, or interactions between the separate nutrients, and the food matrix may play a role (22-24). Countries throughout Europe as well as the United States now have published dietary guidelines based on whole food products and groups rather than single nutrients (25). While evidence on major food groups (e.g. dairy, meat, fruit and vegetables) in relation to body weight (26) and clinical cardiometabolic outcomes including CHD (27) and diabetes (28) is increasing, knowledge of the relationships between food groups and ectopic fat deposition is scarce. We therefore aimed to investigate the associations between dietary intake of the main food groups and visceral fat and liver fat content in a population-based cohort of middle-aged men and women.

SUBJECTS AND METHODS

Study design and study population

The Netherlands Epidemiology of Obesity (NEO) study is a population-based prospective cohort study in 6,671 individuals aged 45 to 65 years, with an oversampling of persons with a BMI of 27 kg/m^2 or higher. Detailed information about the study design and data collection has been described elsewhere (29). Men and women aged between 45 and 65 years with a self-reported BMI of 27 kg/m^2 or higher living in the greater area of Leiden (in the west of The Netherlands) were eligible to participate in the NEO study. In addition, all inhabitants aged between 45 and 65 years from one municipality (Leiderdorp) were invited irrespective of their BMI, allowing a reference distribution of BMI.

Participants visited the NEO study center of the Leiden University Medical Center (LUMC) after an overnight fast. Prior to the NEO study visit, participants completed a questionnaire about demographic and clinical information, as well as a food frequency questionnaire. At the study center, the participants completed a screening form asking about anything that might create a health risk or interfere with magnetic resonance imaging (MRI) (most notably metallic devices, claustrophobia, or a body circumference of more than 1.70 m). Of the participants who were eligible for MRI, approximately 35% were randomly selected to undergo direct assessment of abdominal fat.

The present study is a cross-sectional analysis of the baseline measurements of the participants with a measurement of visceral adipose tissue. We excluded participants with self-reported diabetes prior to the study visit, participants with missing data on dietary intake, participants with implausibly high or low total energy intake (<600 kcal/day or >5,000 kcal/day) or participants with missing data on potential confounding factors. For the analyses on hepatic triglyceride content, we additionally excluded participants without assessment of hepatic triglyceride content and those who consumed more than four units of alcoholic beverages per day.

The study was approved by the medical ethics committee of the Leiden University Medical Center and all participants gave written informed consent.

Data collection

On the questionnaire, participants reported ethnicity by self-identification in eight categories which we grouped into white (reference) and other ethnicity. Tobacco smoking was categorized as current, former, or never smoking (reference). The highest level of education was reported in 10 categories according to the Dutch education system and grouped into high (including higher vocational school, university, and postgraduate education) versus low education (reference). Participants reported their medical history of diabetes and cardiovascular diseases. Body weight and percent body fat were assessed by the Tanita bio impedance balance (TBF-310, Tanita International Division, UK) without shoes, and one kilogram was subtracted from the body weight. BMI was calculated by dividing the weight in kilograms by the height in meters squared. The menopausal state was categorized as pre-, or postmenopausal according to information on ovariectomy, hysterectomy and the self-reported state of menopause in the questionnaire. The basal metabolic rate was calculated based on age, sex, height and weight according to the Mifflin-St Jeor equation. Participants reported the frequency and duration of their physical activity during leisure time, which was expressed in hours per week of metabolic equivalents (MET h/week) (30).

Dietary intake of food groups

Habitual dietary intake of all participants was estimated using a self-administered, semiquantitative 125-item food frequency questionnaire (FFQ) (31, 32). In this FFQ, participants were asked about the frequency of intake of foods during the past month (times per day, week, month, never). Additionally, the serving size was estimated (spoons of potatoes, pieces of fruit). In a random subsample of 110 men and 119 women, the relative validity of the FFQ against two 24-h dietary recalls was assessed regarding total fatty acids, saturated fatty acids (SFAs), monounsaturated fatty acids (MUFAs), and polyunsaturated fatty acids (PUFAs). The correlation coefficients corrected for within-person variation for total fatty acids, SFAs, MUFAs and PUFAs were approximately 0.5 (33). Intake of nutrients and total energy was calculated using the Dutch Food Composition Table (NEVO-2011).

Based on the FFQ, products were categorized into food groups on the basis of similar source, nutrient characteristics or hypothesized biological effects (28). Hereby, we followed the categorization of food groups of the Netherlands Nutrition Center (34) as much as possible based on the distinctive capabilities of the FFQ used. Food groups were categorized into dairy (including milk, cheese, yogurt and butter), meat, fruits and vegetables, sweet snacks (chocolate, cake, pie, candy bars and candy), fish and plant-based fats and oils (margarine, cooking oils). Additionally, subdivisions were made: dairy was also subdivided into cheese, milk, butter and yogurt; fruit and vegetables were studied separately; fats and oils were divided into margarine and oils; and sweet snacks were divided into cake and candy. The caloric intake of products within these food groups was summed and converted into percent of total energy intake (En%) by dividing the caloric intake of the food groups by the total caloric intake per day.

Visceral adipose tissue and hepatic triglyceride content assessment by imaging techniques

Imaging was performed on a 1.5 Tesla MR system (Philips Medical Systems, Best, The Netherlands). Visceral adipose tissue was quantified by a turbo spin echo imaging protocol using MRI. At the level of the fifth lumbar vertebra, three transverse images each with a slice thickness of 10 mm were obtained during a breath-hold. Visceral fat area was converted from the number of pixels to centimeters squared using in-house-developed software (MASS, Medis, Leiden, The Netherlands) and the average of the three slices was used in the analyses (29).

Hepatic triglyceride content was quantified by proton spectroscopy (^{1}H-MRS) of the liver (35). An 8 ml voxel was positioned in the right lobe of the liver, avoiding gross vascular structures and adipose tissue depots. Sixty-four averages were collected with water suppression. Spectra were obtained with an echo time of 26 ms and a repetition time of 3,000 ms. Data points (1,024) were collected using a 1,000 Hz spectral line. Without changing any parameters, spectra without water suppression, with a repetition time of 10 s and four averages were obtained as an internal reference. ^{1}H-MRS data were fitted using Java-based magnetic resonance user interface software (jMRUI version 2.2, Leuven, Belgium), as described previously (36). Hepatic triglyceride content relative to water was calculated as the sum of the signal amplitudes of methyl and methylene divided by the signal amplitude of water and then multiplied by 100.

Statistical analysis

In the NEO study, there is an oversampling of persons with a BMI of 27 kg/m^2 or higher. To correctly represent associations in the general population (37), adjustments for the oversampling of individuals with a BMI ≥ 27 kg/m^2 were made by weighting individuals toward the BMI distribution of participants from the Leiderdorp municipality (38), which was similar to that of the general Dutch population (39). All results were based on the weighted analyses, and consequently, the results apply to a population-based study without oversampling of individuals with a BMI ≥ 27 kg/m^2. As a result of the weighted analyses, percentages and proportions are given instead of numbers of participants. Other characteristics are expressed as percentages or means (standard deviations). We tested for interactions with sex and performed all analyses for the total population and for men and women separately due to major differences in body fat distribution between men and women and previously observed gender differences in the relation between food group scores and abdominal obesity (40). Linearity of the main food groups was checked by adding a quadratic term to the main multivariable adjusted model and visual inspection of scatter plots.

We performed linear regression analyses with multiple models to examine the associations between dietary intake of the food groups with visceral fat and liver fat content. First, we examined the crude associations of dietary intake of 100 grams/day of each food group with visceral fat and liver fat content. Second, we adjusted the models for age, smoking, education, ethnicity, physical activity, basal metabolic rate, menopausal state, total energy intake and adherence to an energy restricted diet and liver fat models were also adjusted for alcohol intake. Third, we additionally adjusted the models for total body fat, to examine whether the associations were specific for visceral fat and liver fat instead of merely reflecting associations with overall adiposity. Fourth, to examine whether associations were specific for the food groups and not merely reflecting a healthy diet, we additionally adjusted all models for the food group fruit and vegetables, and the food group fruit and vegetables model for the food sweet snacks. As secondary analyses, we subdivided several food groups into a finer categorization: dairy into milk, cheese, yogurt and butter; sweet snacks into cake and candy; plant-based fat and oils into margarine and oils; and fruit and vegetables into fruit and vegetables separately. We performed subgroup analyses and stratified the multivariable model 2 (not including total body fat and markers of a healthy diet) by and menopausal state (pre- and postmenopausal). This stratification was done because for example visceral fat may differ greatly between pre- and postmenopausal women (41). We additionally stratified the same multivariable models of hepatic triglyceride content by the rs738409 single nucleotide polymorphism in the PNPLA3 gene to examine whether associations would be different in carriers of the risk allele that is associated with high liver fat content (42). Due to a skewed distribution of hepatic triglyceride content, we used the natural logarithm of this variable in the analyses. For interpretation of the results, we back transformed the regression coefficients of hepatic triglyceride content toward a ratio with 95% confidence interval, which can be interpreted as a ratio in hepatic triglyceride content associated with dietary intake of 100 grams/day of the food groups (for example 1.2, can be interpreted as a 1.2-fold higher hepatic triglyceride content, which in a person with a hepatic triglyceride content of 5% would reflect an increase to 6%). The regression coefficients of visceral adipose tissue represent an absolute difference in visceral adipose tissue in cm^2 per 100 grams/day of the food groups.

As a means of sensitivity analysis, we additionally performed two types of isocaloric substitution analyses in which dairy was specifically replaced by the other food groups: one per 100 grams per day and one per 10% of the energy (En%) derived from the food groups.

In these substitution models, we included all the food groups under study (meat, fruits and vegetables, sweet snacks, fish, and plant-based fats and oils), except dairy, the food group to be substituted, in addition to all other food consumed that was not categorized in one of the food groups, and all confounding factors. Finally, we performed a sensitivity analysis including a variable in our fully adjusted model that divides energy intake by basal metabolic rate, to adjust for potential under- and overreporting.

We performed all analyses using STATA statistical software (Statacorp, College Station, Texas, USA), version 14.

RESULTS

In total, 6,671 participants were included in the NEO study between September 2008 and October 2012, of whom 2,580 underwent an MRI of the abdomen. For 11 of those participants, the quality of the MRI images was insufficient for quantification of abdominal visceral adipose tissue. MRI was performed in random subsample of those without contraindications. As a result, those who underwent the MRI have a slightly lower BMI (26.0 kg/m^2 versus 26.6 kg/m^2) and slightly less often a medical history of cardiovascular disease (4.1% versus 6.8%).

After exclusion of participants with a medical history of diabetes (n=161), extreme energy intake (<600 kcal/day or >5,000 kcal/day (n=19)), an incomplete FFQ (n=16) or missing data on smoking (n=2), education (n=22), ethnicity (n=3), energy-restricted diet (n=4) and physical activity (n=38), 2,304 participants were included in the analyses on visceral adipose tissue. Participants included in the analyses did not substantially differ from those excluded due to missing data regarding total body fat (30.7% for those without missing data versus 30.6% for those with missing data), visceral fat (87.6 cm2 versus 88.2 cm2), nor regarding dietary intake of the food groups. Liver fat was slightly lower in the participants with missing data (4.3% compared to 5.6%).

For the analyses with hepatic triglyceride content as an outcome, we excluded 424 participants without hepatic triglyceride content measurement. Due to the limited time available per subject it was not possible to check the spectra during the measurement and repeat the measurement when technical failures were present. As a consequence, ^{1}H-MRS of the liver could not be completed in 424 participants, for whom the majority were due to technical failures. However, the failure rate of the MR spectroscopy was not related to age (56 years for participants with hepatic triglyceride content measurement versus 55 years for participants without hepatic triglyceride content measurement), sex (47% male versus 46%), BMI (26.0 kg/m^2 versus 25.8 kg/m^2), visceral adipose tissue (90.1 cm^2 versus 87 cm^2), total body fat (30.7% versus 30.9%) or any of the food groups. Lastly, participants who drank more than 4 units of alcohol per day (n=165) were excluded for the analyses of hepatic triglyceride content.

The baseline characteristics of the study population participants are shown in **Table 1**. Whereas women had more total body fat, men had more visceral adipose tissue and hepatic triglyceride content.

Table 1. Baseline characteristics of of participants of the Netherlands Epidemiology of Obesity study, men and women between 45 and 65 years of age with direct assessment of abdominal fat depots and who were not using glucose-lowering therapy[1]

	Total population	**Men (46.4%)**	**Women (53.6%)**
Demographic variables			
Age (year)	55 (6)	56 (6)	55 (6)
Ethnicity (% white)	96	96	95
Education level (% high)[2]	47	51	43
Tobacco smoking (% current)	15	16	13
Menopausal state (% post)			58
Physical activity in leisure time (MET h/wk)	38.3 (33.1)	40.0 (38.8)	36.9 (28.1)
Dietary variables			
Dairy intake (g/d)	322 (196)	341 (223)	306 (172)
Meat intake (g/d)	83 (46)	96 (50)	72 (38)
Fish intake (g/d)	18 (17)	19 (19)	16 (15)
Fruit and vegetable intake (g/d)	326 (163)	304 (169)	345 (154)
Sweet snack intake (g/d)	82 (57)	89 (59)	75 (54)
Fat and oil intake (g/d)	35 (22)	41 (26)	29 (17)
Energy restricted diet (%)	10	6	14
Basal metabolic rate (MJ/d)	6.3 (1.1)	7.3 (0.7)	5.5 (0.6)
Body fat measures			
BMI (kg/m^2)	25.8 (3.9)	26.5 (3.5)	25.2 (4.0)
Total body fat (%)	30.7 (8.3)	24.5 (5.7)	36.1 (6.1)
Visceral adipose tissue (cm^2)	87.6 (54.2)	113.0 (58.7)	65.5 (39.8)
Hepatic triglyceride content (%)[3]	5.6 (7.7)	6.8 (8.2)	4.5 (7.2)
Fatty liver (HTGC>5.56%) (%)	28.2	37.5	20.2
Waist circumference (cm)	90.9 (12.6)	97.3 (10.4)	85.3 (11.3)
CVD risk factors			
CVD (%)	3.8	3.9	3.7
Lipid lowering medication (%)	7	11	4
Total serum cholesterol (mmol/L)	5.75 (1.04)	5.63 (1.04)	5.86 (1.03)
Fasting serum triglycerides (mmol/L)	1.23 (0.82)	1.43 (0.97)	1.06 (0.64)
HDL serum cholesterol (mmol/L)	1.58 (0.46)	1.35 (0.36)	1.79 (0.43)

[1] Values are means ± SDs. Results are based on analyses weighted toward the BMI distribution of the general population (n=2,304). BMI, body mass index; CVD, cardiovascular disease; HDL, high-density lipoproteins; MET, metabolic equivalent of task.

[2] Low education: none, primary school, or lower vocational education as highest level of education.

[3] Mean HTGC only calculated in persons with HTGC measurement (n=1880)

Dietary intake of the main food groups in relation to visceral adipose tissue

We assessed the reproducibility of the dietary intake of the food groups in 100 participants who completed the FFQ twice with approximately three months in between. The individual measurement intraclass correlation coefficients of the food group dairy were 0.80, of fruit and vegetables 0.56, meat 0.83, sweet snacks 0.59, fish 0.64 and fats and oils 0.65. The individual intraclass correlation coefficient for total energy intake was 0.68.

In the total population, after adjustment for confounding factors, total body fat and a marker for an (un)healthy lifestyle, dietary intake of fruit and vegetables was associated with 1.2 cm^2 (95% CI -2.4, 0.0) less visceral adipose tissue (**Table 2**). Intake of plant-based fats and oils was also associated with 13.9 cm^2 less visceral adipose tissue (-23.7, -4.1). Dietary intake of dairy, fish, meat and sweet snacks was not associated with visceral adipose tissue (Table 2).

Tests for an interaction between the food groups and sex were nonsignificant, but we a priori decided to perform the analyses separately for men and women because of the large differences in body fat distribution. All associations were attenuated in the stratified analyses, although in women intake of dairy remained associated with visceral adipose tissue (-1.2 cm^2, -2.5, 0.0) (Table 2)

After a finer categorization of the food groups, yogurt seemed to drive the negative association between dairy and visceral adipose tissue in women (**Table 4**). Dietary intake of dairy, meat, and fruit and vegetables was more strongly associated with visceral adipose tissue in postmenopausal women than in premenopausal women (P-values for interactions: 0.56, 0.09 and 0.21) **(Supplemental table 1)**. The results remained similar after substituting dairy with other food groups (**Supplemental table 3**) and when including participants with diabetes (**Supplemental table 5**). The results did not differ when adjusting for potential under- or overreporting (data not shown).

Dietary intake of main food groups in relation to hepatic triglyceride content

In the total population of 1,715 participants with hepatic triglyceride content measurements, after adjustment for confounding factors, total body fat and a marker for an (un)healthy lifestyle, dietary intake of sweet snacks were associated with a 1.19-fold (95% CI 1.04, 1.37) higher hepatic triglyceride content (**Table 3**). The intake of dairy, fruit and vegetables, fish, meat, and fats and oils was not associated with hepatic triglyceride content (Table 3). In men and women separately, the associations were attenuated (Table 3).

Table 2. Difference in VAT (cm^2) with 95% confidence intervals per 100 g/day consumption of the food groups in of participants of the Netherlands Epidemiology of Obesity study, men and women between 45 and 65 years of age with direct assessment of abdominal fat depots and who were not using glucose-lowering therapy[1]

	Crude	**Multivariable**	**Multivariable + TBF**	**Multivariable + TBF + healthy diet**
Food groups	Difference in VAT (cm^2) with 95% CI	Difference in VAT (cm^2) with 95% CI	Difference in VAT (cm^2) with 95% CI	Difference in VAT (cm^2) with 95% CI
Dairy				
Total	0.1 (-1.3; 1.6)	-1.4 (-2.5; -0.3)*	-0.6 (-1.6; 0.4)	-0.6 (-1.6; 0.4)
Men	-0.6 (-2.6; 1.3)	-0.8 (-2.5; 0.9)	0.0 (-1.4; 1.5)	0.0 (-1.4; 1.5)
Women	-1.3 (-2.7; 0.2)	-2.0 (-3.4; -0.7)*	-1.3 (-2.5; 0.0)	-1.2 (-2.5; 0.0)
Meat				
Total	26.1 (20.2; 31.9)*	5.4 (0.1; 10.6)*	1.5 (-3.1; 6.0)	1.0 (-3.5; 5.6)
Men	10.9 (2.3; 19.4)*	3.9 (-4.3; 12.1)	-1.1 (-7.8; 5.6)	-1.4 (-8.0; 5.3)
Women	15.7 (8.7; 22.7)*	6.6 (0.7; 12.6)*	3.4 (-2.0; 8.7)	2.8 (-2.6; 8.2)
Fish				
Total	30.5 (13.4; 47.5)*	6.1 (-5.8; 18.1)	3.7 (-6.8; 14.2)	6.2 (-4.7; 17.1)
Men	14.6 (-8.3; 37.5)	5.2 (-14.3; 24.8)	1.9 (-15.2; 18.9)	3.0 (-14.6; 20.6)
Women	25.4 (6.8; 44.0)*	6.7 (-6.1; 19.5)	5.4 (-5.7; 16.6)	9.1 (-2.6; 20.9)
Fruit and vegetables				
Total	-3.1 (-4.8; -1.4)	-1.7 (-3.0; -0.4)*	-1.2 (-2.4; -0.0)*	-1.2 (-2.4; 0.0)
Men	-2.3 (-4.8; 0.2)	-1.8 (-4.2; 0.5)	-1.0 (-3.2; 1.2)	-0.8 (-3.1; 1.4)
Women	-0.4 (-2.1; 1.4)	-1.6 (-2.9; -0.2)*	-1.1 (-2.3; 0.1)	-1.2 (-2.4; 0.1)
Sweet snacks				
Total	4.3 (-0.7; 9.2)	-0.3 (-4.7; 4.2)	0.9 (-3.1; 5.0)	0.2 (-3.9; 4.4)
Men	-1.6 (-9.1; 5.8)	-0.6 (-8.1; 7.0)	4.0 (-2.3; 10.3)	3.7 (-2.6; 10.0)
Women	-0.0 (-5.0; 5.0)	0.4 (-4.8; 5.6)	0.6 (-4.5; 5.6)	-0.4 (-5.7; 5.0)
Fat and oils				
Total	33.5 (21.2; 45.9)	-8.2 (-20.2; 3.8)	-12.5 (-22.2; -2.7)*	-13.9 (-23.7; -4.1)*
Men	3.7 (-12.5; 19.8)	-13.1 (-30.9; 4.6)	-18.3 (-31.3; -5.3)*	-19.8 (-33.1; -6.4)*
Women	6.8 (-9.0; 22.6)	-1.2 (-14.4; 11.9)	-7.3 (-19.9; 5.3)	-8.3 (-20.9; 4.3)

[1] Multivariable: adjusted for age, total energy intake, smoking, education, ethnicity, physical activity in leisure time, basal metabolic rate, menopause and energy restricted diet. Results are based on analysis weighted toward the body mass index distribution of the general population (n=2,304, 1191 men and 1113 women). CI, confidence interval; TBF, total body fat; VAT, visceral adipose tissue.

*p-value<0.05

After the finer categorization, vegetables were more strongly associated with hepatic triglyceride content than fruit, and yogurt was most strongly associated with liver fat of all the dairy components (**Table 5**). The association between sweet snacks and hepatic triglyceride content was stronger in premenopausal women than in postmenopausal women (P-value for interaction 0.59) **(Supplemental table 2)**.

Substituting dairy with other food groups showed similar results as the multivariable analyses (**Supplemental table 4**), as did the analyses including participants with diabetes (**Supplemental table 6**). The results did not differ when adjusting for potential under- or overreporting (data not shown).

Table 3. Relative difference in HTGC with 95% confidence intervals per 100 g/day consumption of the food groups in of participants of the Netherlands Epidemiology of Obesity study, men and women between 45 and 65 years of age with direct assessment of abdominal fat depots and who were not using glucose-lowering therapy[1]

	Crude	**Multivariable**	**Multivariable + TBF**	**Multivariable + TBF + healthy diet**
Food groups	Relative difference in HTGC with 95% CI	Relative difference in HTGC with 95% CI	Relative difference in HTGC with 95% CI	Relative difference in HTGC with 95% CI
Dairy				
Total	0.98 (0.95; 1.02)	0.97 (0.93; 1.00)*	0.97 (0.94; 1.01)	0.97 (0.94; 1.01)
Men	0.98 (0.94; 1.03)	0.98 (0.94; 1.03)	0.99 (0.94; 1.03)	0.99 (0.94; 1.03)
Women	0.96 (0.91; 1.02)	0.95 (0.90; 0.99)*	0.96 (0.92; 1.01)	0.96 (0.92; 1.01)
Meat				
Total	1.48 (1.28; 1.71)*	1.14 (0.98; 1.33)	1.06 (0.92; 1.22)	1.05 (0.91; 1.20)
Men	1.16 (0.95; 1.41)	1.06 (0.86; 1.29)	0.97 (0.83; 1.15)	0.97 (0.82; 1.14)
Women	1.45 (1.16; 1.80)*	1.21 (0.97; 1.52)	1.10 (0.89; 1.36)	1.07 (0.87; 1.32)
Fish				
Total	1.18 (0.78; 1.80)	0.82 (0.57; 1.19)	0.79 (0.58; 1.08)	0.85 (0.61; 1.16)
Men	1.03 (0.63; 1.70)	0.96 (0.57; 1.63)	0.93 (0.59; 1.47)	0.96 (0.61; 1.50)
Women	1.08 (0.61; 1.90)	0.71 (0.45; 1.14)	0.69 (0.46; 1.04)	0.76 (0.48; 1.19)
Fruit and vegetables				
Total	0.95 (0.91; 0.99)	0.96 (0.92; 0.99)*	0.97 (0.93; 1.00)*	0.97 (0.94; 1.01)
Men	0.95 (0.90; 1.01)	0.97 (0.92; 1.02)	0.98 (0.94; 1.02)	0.99 (0.94; 1.03)
Women	0.98 (0.93; 1.03)	0.95 (0.91; 1.00)	0.96 (0.92; 1.00)	0.97 (0.93; 1.02)
Sweet snacks				
Total	1.17 (1.03; 1.33)*	1.22 (1.05; 1.42)*	1.21 (1.06; 1.39)*	1.19 (1.04; 1.37)*
Men	1.06 (0.91; 1.22)	1.13 (0.94; 1.35)	1.17 (1.01; 1.35)*	1.16 (0.99; 1.35)
Women	1.17 (0.95; 1.44)	1.29 (1.03; 1.63)*	1.26 (1.01; 1.57)*	1.23 (0.97; 1.54)
Fats and oils				
Total	1.84 (0.39; 2.44)	1.20 (0.88; 1.64)	1.16 (0.88; 1.53)	1.12 (0.85; 1.48)
Men	1.30 (0.91; 1.86)	1.26 (0.84; 1.88)	1.22 (0.86; 1.74)	1.20 (0.84; 1.71)
Women	1.42 (0.87; 2.30)	1.21 (0.75; 1.94)	1.08 (0.68; 1.70)	1.04 (0.66; 1.65)

[1] Multivariable: adjusted for age, total energy intake, smoking, education, ethnicity, physical activity in leisure time, basal metabolic rate, menopause, alcohol consumption and energy restricted diet. Results are based on analysis weighted toward the body mass index distribution of the general population (n=1,715, 831 men and 884 women). CI, confidence interval; HTGC, hepatic triglyceride content; TBF, total body fat.
*p-value<0.05

Table 4. Difference in VAT (cm^2) with 95% confidence intervals per 100 g/day consumption of the food groups in of participants of the Netherlands Epidemiology of Obesity study, men and women between 45 and 65 years of age with direct assessment of abdominal fat depots and who were not using glucose-lowering therapy[1]

	Crude	**Multivariable**	**Multivariable + TBF**	**Multivariable + TBF + healthy diet**
Food groups	Difference in VAT (cm^2) with 95% CI	Difference in VAT (cm^2) with 95% CI	Difference in VAT (cm^2) with 95% CI	Difference in VAT (cm^2) with 95% CI
Cheese				
Total	6.9 (-4.2; 17.9)	-0.2 (-8.7; 8.3)	-0.1 (-7.7; 7.6)	-0.2 (-7.9; 7.5)
Men	16.8 (2.2; 31.4)*	7.8 (-5.8; 21.4)	0.4 (-10.7;11.6)	0.2 (-10.9; 11.4)
Women	-6.6 (-19.5; 6.3)	-8.6 (-19.0; 1.9)	-4.2 (-13.8; 5.4)	-4.3 (-13.9; 5.3)
Milk				
Total	1.5 (-0.2; 3.2)	-0.3 (-1.5; 0.8)	0.2 (-0.9; 1.2)	0.1 (-0.9; 1.2)
Men	0.19 (-2.1; 2.5)	-0.1 (-2.0; 1.8)	0.7 (-0.9; 2.4)	0.7 (-1.0; 2.3)
Women	-0.4 (-1.9; 1.1)	-0.6 (-1.7; 0.5)	-0.2 (-1.4;0.9)	-0.3 (-1.4; 0.8)
Yogurt				
Total	-8.8 (-13.1; -4.5)*	-7.4 (-11.0; -3.9)*	-5.2 (-7.8; -2.6)*	-5.0 (-7.6; -2.4)*
Men	-7.4 (-12.6; -2.2)*	-6.0 (-11.3; -0.6)*	-3.9 (-7.8; 0.0)	-3.7 (-7.6; 0.2)
Women	-5.9 (-10.0; -1.7)*	-9.2 (-12.3; -6.1)*	-6.6 (-9.4; -3.7)*	-6.3 (-9.1; -3.4)*
Cream butter				
Total	-3.5 (-48.0; 40.9)	-9.6 (-37.8; 18.5)	-6.8 (-33.8; 20.2)	-7.3 (-34.6; 20.0)
Men	-29.8 (-85.7; 26.1)	-43.8 (-97.2; 9.6)	-30.3 (-69.7; 9.0)	-27.8 (-67.0; 11.4)
Women	-7.4 (-52.4; 37.5)	13.0 (-23.5; 49.5)	10.4 (-27.3; 48.1)	10.8 (-27.0; 48.7)
Fruit				
Total	-5.2 (-7.7; -2.7)	-2.3 (-4.2; -0.4)	-1.2 (-2.9; 0.5)	-1.2 (-2.9; 0.5)
Men	-3.9 (-7.3; -0.4)*	-2.6 (-5.9; 0.8)	-0.6 (-3.5; 2.3)	-0.5 (-3.4; 2.3)
Women	-1.7 (-4.1; 0.8)	-1.9 (-3.9; 0.0)	-1.3 (-3.1; 0.5)	-1.3 (-3.1; 0.5)
Vegetables				
Total	-0.8 (-3.6; 2.1)	-1.2 (-3.3; 1.0)	-1.5 (-3.4; 0.4)	-1.5 (-3.4; 0.4)
Men	-0.4 (-5.0; 4.2)	-0.8 (-5.0; 3.5)	-2.1 (-5.9; 1.6)	-1.8 (-5.6; 1.9)
Women	1.5 (-1.3; 4.3)	-1.5 (-3.7; 0.7)	-1.3 (-3.2; 0.7)	-1.3 (-3.3; 0.8)
Cake				
Total	4.7 (-4.9; 14.3)	-1.8 (-9.9; 6.3)	-3.3 (-10.1; 3.5)	-3.8 (-10.6; 3.1)
Men	-2.1 (-16.5; 12.2)	0.1 (-13.7; 13.9)	-0.1 (-10.6; 10.5)	0.1 (-10.5; 10.7)
Women	3.6 (-6.8; 14.1)	-1.6 (-10.4; 7.2)	-2.2 (-10.3; 5.9)	-3.3 (-11.5; 4.8)
Candy				
Total	1.5 (-6.2; 9.2)	0.1 (-6.2; 6.5)	1.7 (-4.0; 7.4)	1.0 (-4.9; 6.9)
Men	-1.4 (-12.6; 9.9)	-2.4 (-14.1; 9.2)	1.9 (-7.6; 11.3)	1.6 (-7.9; 11.1)
Women	-0.4 (-7.2; 6.3)	2.4 (-4.2; 9.0)	2.7 (-3.8; 9.3)	1.8 (-4.9; 8.6)
Margarine				
Total	34.1 (20.0; 48.2)	-10.5 (-23.0; 2.0)	-14.2 (-24.3; -4.1)*	-16.6 (-26.8; -6.4)*
Men	-2.7 (-21.0; 15.6)	-18.3 (-36.3;-0.4)*	-19.2 (-32.6; -5.8)*	-21.1 (-34.9; -7.3)*
Women	11.1 (-7.1; 29.3)	2.1 (-11.7; 15.8)	-7.0 (-20.1; 6.0)	-9.4 (-22.5; 3.8)
Oils				
Total	27.1 (-4.3; 58.5)	10.0 (-15.4; 35.4)	2.1 (-20.1; 24.3)	5.6 (-17.2; 28.3)
Men	24.0 (-14.9; 63.0)	13.2 (-23.9;50.4)	-10.4 (-41.6; 20.9)	-8.2 (-40.0; 23.7)
Women	4.1 (-35.1; 43.4)	5.4 (-27.6; 38.4)	9.8 (-20.3; 39.9)	13.8 (-16.5; 44.2)

[1] Multivariable: adjusted for age, total energy intake, smoking, education, ethnicity, physical activity in leisure time, basal metabolic rate, menopause and energy restricted diet. Results are based on analysis weighted toward the body mass index distribution of the general population (n=2304, 1191 men and 1113 women). CI, confidence interval; TBF, total body fat; VAT, visceral adipose tissue.
*p-value<0.05

Table 5. Relative difference in HTGC with 95% confidence intervals per 100 g/day consumption of the food groups groups in of participants of the Netherlands Epidemiology of Obesity study, men and women between 45 and 65 years of age with direct assessment of abdominal fat depots and who were not using glucose-lowering therapy[1]

	Crude	**Multivariable**	**Multivariable + TBF**	**Multivariable + TBF + healthy diet**
Food groups	Relative difference in HTGC with 95%CI	Relative difference in HTGC with 95%CI	Relative difference in HTGC with 95%CI	Relative difference in HTGC with 95%CI
Cheese				
Total	1.11 (0.85; 1.46)	1.01 (0.78; 1.32)	1.01 (0.80; 1.29)	1.00 (0.79; 1.28)
Men	1.34 (0.94; 1.89)	1.34 (0.96; 1.86)	1.10 (0.82; 1.48)	1.09 (0.81; 1.47)
Women	0.94 (0.64; 1.38)	0.82 (0.56; 1.20)	0.98 (0.67; 1.44)	0.97 (0.67; 1.43)
Milk				
Total	1.00 (0.95; 1.05)	0.97 (0.94; 1.01)	0.98 (0.95; 1.01)	0.98 (0.95; 1.01)
Men	0.99 (0.93; 1.05)	0.98 (0.93; 1.04)	0.99 (0.94; 1.04)	0.99 (0.94; 1.04)
Women	0.98 (0.92; 1.04)	0.97 (0.92; 1.02)	0.98 (0.93; 1.02)	0.97 (0.93; 1.02)
Yogurt				
Total	0.89 (0.81; 0.97)	0.89 (0.82; 0.98)*	0.91 (0.85; 0.99)	0.92 (0.85; 1.00)*
Men	0.91 (0.84; 0.99)*	0.94 (0.85; 1.04)	0.95 (0.87; 1.03)	0.95 (0.88; 1.03)
Women	0.88 (0.77; 1.02)	0.82 (0.72; 0.94)*	0.87 (0.76; 0.99)*	0.88 (0.78; 1.01)
Cream butter				
Total	0.58 (0.25; 1.34)	0.75 (0.38; 1.46)	0.79 (0.43; 1.47)	0.79 (0.43; 1.46)
Men	0.57 (0.13; 2.41)	0.90 (0.20; 4.11)	1.07 (0.26; 4.41)	1.09 (0.23; 5.08)
Women	0.50 (0.20; 1.22)	0.74 (0.34; 1.59)	0.72 (0.37; 1.39)	0.69 (0.35; 1.35)
Fruit				
Total	0.94 (0.89; 0.99)*	0.96 (0.92; 1.01)	0.98 (0.94; 1.03)	0.98 (0.94; 1.03)
Men	0.94 (0.89; 1.00)	0.96 (0.90; 1.02)	0.98 (0.93; 1.04)	0.99 (0.93; 1.04)
Women	0.98 (0.91; 1.06)	0.96 (0.89; 1.03)	0.98 (0.90; 1.05)	0.98 (0.91; 1.06)
Vegetables				
Total	0.94 (0.88; 1.01)	0.94 (0.88; 1.00)*	0.93 (0.88; 0.98)	0.94 (0.89; 1.00)*
Men	0.96 (0.85; 1.07)	0.98 (0.89; 1.07)	0.97 (0.89; 1.05)	0.98 (0.90; 1.07)
Women	0.96 (0.89; 1.05)	0.93 (0.85; 1.00)	0.92 (0.86; 0.99)*	0.93 (0.86; 1.00)
Cake				
Total	1.28 (1.00; 1.62)*	1.21 (0.96; 1.51)	1.11 (0.91; 1.37)	1.10 (0.89; 1.35)
Men	1.05 (0.78; 1.42)	1.09 (0.78; 1.53)	1.00 (0.76; 1.32)	1.00 (0.76; 1.33)
Women	1.38 (0.97; 1.96)	1.24 (0.91; 1.69)	1.19 (0.88; 1.60)	1.15 (0.85; 1.55)
Candy				
Total	1.18 (0.97; 1.43)	1.20 (0.98; 1.47)	1.23 (1.03; 1.46)*	1.20 (1.00; 1.44)
Men	1.12 (0.92; 1.37)	1.11 (0.88; 1.39)	1.20 (1.00; 1.45)*	1.19 (0.99; 1.44)
Women	1.21 (0.88; 1.67)	1.26 (0.93; 1.71)	1.21 (0.91; 1.61)	1.18 (0.87; 1.58)
Margarine				
Total	2.02 (1.47; 2.79)*	1.19 (0.85; 1.68)	1.15 (0.86; 1.53)	1.09 (0.81; 1.47)
Men	1.28 (0.84; 1.96)	1.15 (0.72; 1.82)	1.18 (0.80; 1.72)	1.14 (0.77; 1.69)
Women	1.64 (0.99; 2.71)	1.22 (0.75; 1.98)	1.03 (0.66; 1.61)	0.97 (0.61; 1.52)
Oils				
Total	1.18 (0.54; 2.53)	1.03 (0.49; 2.17)	0.88 (0.47; 1.65)	0.96 (0.51; 1.82)
Men	1.20 (0.46; 3.08)	1.26 (0.47; 3.41)	0.88 (0.39; 2.02)	0.92 (0.40; 2.11)
Women	0.98 (0.32; 3.01)	1.06 (0.37; 3.07)	1.10 (0.40; 2.99)	1.29 (0.47; 3.56)

[1] Multivariable: adjusted for age, total energy intake, smoking, education, ethnicity, physical activity in leisure time, basal metabolic rate, menopause, alcohol consumption and energy restricted diet. Results are based on analysis weighted toward the body mass index distribution of the general population (n=1,715, 831 men and 884 women). CI, confidence interval; HTGC, hepatic triglyceride content; TBF, total body fat.
*p-value>0.05

DISCUSSION

In this population-based study of participants aged 40 to 65 without contraindications for a MRI, we examined for the first time to what extent dietary intake of the main food groups was specifically associated with visceral fat and liver fat content, as assessed with MRI and ^{1}H-MRS. In the total population, dietary intake of fruit and vegetables and plant-based fats and oils was associated with less visceral fat, and intake of sweet snacks was associated with more liver fat. Although confidence intervals were wide, both in the total population and in men and women separately, a similar pattern of positive associations with intake of sweet snacks and inverse associations with intake of fats and oils, dairy, and fruit and vegetables could be observed.

The observed associations were largely explained by total body fat. On the one hand, the remaining observed associations may suffer from residual confounding due to imperfectly measured total body fat. On the other hand, the results of the associations of fruit and vegetables and plant-based fats and oils with visceral fat and that of sweet snacks with liver fat that remained in the total population after multivariate adjustment including total body fat and a marker for an (un)healthy diet, support the presence of specific associations of certain food groups with visceral and liver fat, and need to be confirmed in larger studies.

Although few studies have investigated the association between food groups and visceral adipose tissue and hepatic triglyceride content, our findings are in accordance with the current literature on food groups in relation to cardiometabolic diseases and the current food group-based dietary guidelines in the European region (25) and they support the dietary patterns of the DASH diet and Alternative Healthy Eating Index (AHEI) (43). Dietary intake of meat and sugar-sweetened beverages has been associated with an increased risk of type 2 diabetes (28, 44) and intake of dairy and fruits with a lower risk of type 2 diabetes (28, 45). In a recent meta-analysis, dietary intake of fish and fruit and vegetables has also been associated with a decreased risk of all-cause mortality, whereas red meat and processed meat were associated with an increased risk (46).

Dairy was negatively associated with visceral fat in women, and this association was mostly driven by yogurt, which supports previous results from the Women's Health Initiative Observational Study showing that high yogurt consumption significantly decreased diabetes risk (47). When butter was excluded from the dairy food group, the associations remained similar, indicating that butter intake did not contribute to the inverse association.

In our study, we did not observe an association between fish intake and liver fat or visceral fat. Although the point estimate for fish intake and visceral adipose tissue was positive, confidence intervals were very wide. It must be noted that we could not distinguish between fresh fish and fried fish on the basis of our food frequency questionnaire, and thus, this food group was relatively heterogeneous. However, a recent meta-analysis showed that fish intake was inversely associated with diabetes in Asian populations but positively associated with diabetes in Western populations, in which no distinction was made between fresh and fried fish (48).

In this study, meat was not associated with visceral or liver fat. However, our food frequency questionnaire did not make a distinction between poultry, red meat or processed meat. Associations with red meat and processed meat might potentially be stronger than those observed with total meat. Even though the exact mechanism remains unidentified, the dietary cholesterol, protein, heme-iron, advanced glycation products or preservatives such as sodium and nitrites/nitrates in meat have been hypothesized to be responsible for the positive association with visceral adipose tissue and diabetes (49). Regarding dairy, calcium, vitamin D, magnesium, fatty acids, protein and the effect on satiety are hypothesized to underlie the beneficial effect (45). However, dairy products are often differentially categorized across different studies (23), making it difficult to compare. Different dairy products, such as fermented dairy or low- and high-fat dairy, might be associated differently with cardiometabolic outcomes, but all are categorized as dairy. Other nutrients and dietary aspects have already been shown to be associated with measures of adiposity, such as dietary fiber with less visceral adipose tissue (50), high-glycemic index diets with higher waist circumference (51) and high protein (either animal or plant) and n-6 polyunsaturated fatty acids with less hepatic triglyceride content (52, 53). However, food groups instead of single nutrients in relation to visceral adipose tissue and hepatic triglyceride content have not yet been studied.

Strengths of this study include the direct assessment of visceral fat and hepatic triglyceride content by MRI and ^{1}H-MRS, respectively, in a relatively large sample size. Additionally, the extensive phenotypic measurements allowed adjustment for many potential confounding factors, and the large study population enabled us to investigate possible sex differences. A limitation of this study is that the FFQ was self-administered and therefore prone to measurement error. When assessing reproducibility in a random subsample, the ICCs of fruit and vegetables and sweet snacks were moderate to low, which could be due to seasonal variation, but might also indicate potential over- or underreporting. Furthermore, a limitation of studying food groups may be that they cover a broad range of food products and might comprise both relatively healthy and unhealthy products. As we could not distinguish between white meat, red meat and processed meat, this might have attenuated our associations due to regression dilution. Moreover, the observational cross-sectional design of this study precludes any causal inference, and residual confounding, for example due to unmeasured or insufficiently measured lifestyle factors, may still be present despite our efforts to minimize confounding as much as possible. Additionally, potential selection bias might have occurred due to missing data. However, the number of participants excluded due to missing data was limited (n=96) and the failure rate of liver fat measurement was not dependent on sex, age or body fat measurements, so we do not expect this factor to substantially alter our results. Lastly, our study population consisted primarily of white, middle-aged participants, and there might be differences in dietary habits (54) and visceral adipose tissue (55) and hepatic triglyceride content accumulation (56) between different ethnic populations. Therefore, our findings need to be confirmed in prospective studies and in other ethnic groups.

In conclusion, in this population-based study in middle-aged men and women without contra-indications of an MRI, dietary intake of plant-based fats and oils and fruits and vegetables was associated with less visceral adipose tissue. Intake of sweet snacks was associated with more liver fat. Larger prospective studies on the relation between a food group and ectopic fat accumulation are needed to confirm whether associations between dietary intake of certain food groups are specifically associated with visceral fat or liver fat. In addition, intervention studies are needed to establish to what extent dietary changes can specifically reduce ectopic fat accumulation and the risk of cardiometabolic disease.

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