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ORIGINAL CONTRIBUTION

Association and substitution analyses of dietary sugars, starch and fiber for indices of body fat and cardiometabolic risk– a NoHoW sub-study

Karen A. Della Corte[1] · Dennis Della Corte[2] · David Camacho[1,2] · Graham Horgan[3] · Antonio L. Palmeira[4,5] · James Stubbs[6] · Berit L. Heitmann[7]

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Abstract

Purpose To examine the associations and substitutions of dietary sugars [extrinsic (free) or intrinsic (non-free)] as well as dietary starch and fiber intakes for indices of body fat and cardiometabolic health.

Methods Dietary intake was assessed at multiple times using multi-day 24-hour recalls over 18-months for indices of body fat (body fat %, waist circumference, BMI, and weight change) ($n=1066$) and at baseline and 12 months for cardiometabolic outcomes (LDL, HDL, HbA1c) ($n=736$). Bayesian modeling was applied to analyze the probabilistic impact of dietary carbohydrate components using credible intervals for association and substitution analyses with repeated measures random effects modeling.

Results A higher starch intake significantly associated with higher body fat %, BMI and waist circumference (WC) (all CrI > 0). Conversely, intrinsic sugar and fiber intakes were significantly linked to lower body fat indices, while free sugar showed no association. A 20 g substitution of free sugars with intrinsic sugars significantly associated with lower body fat (CrI: -4.2; -1.0%), BMI (CrI: -1.8; -0.4) and WC (CrI: -4.2; -1.0 cm), while substituting intrinsic sugars with starch resulted in significantly higher body fat, BMI, WC and weight change. Replacing starch with fiber associated with higher HDL-C (CrI: -0.0; 0.3) and lower LDL-C (CrI: -0.6; 0.1). Replacing free sugars with starch associated with a higher HbA1c level (CrI: 0.0;0.2).

Conclusion These results underscore the importance of distinguishing between intrinsic versus extrinsic sugars and highlight the potential benefits of increasing intrinsic sugars and fiber while reducing starch for better body fat management and cardiometabolic health.

Keywords Dietary sugar · Dietary starch, dietary fiber · Body fat · Cardiometabolic risk

✉ Karen A. Della Corte
karen_dellacorte@byu.edu

✉ Berit L. Heitmann
Berit.Lilienthal.Heitmann@regionh.dk

[1] Department of Nutrition, Dietetics, and Food Science, Brigham Young University, Provo, UT, USA

[2] Data Science, College of Computational, Mathematical, and Physical Sciences, Brigham Young University, Provo, UT, USA

[3] Biomathematics and Statistics Scotland, Aberdeen, UK

[4] University Lusófona de Humanidades e Tecnologias, Lisbon, Portugal

[5] Faculty of Human Kinetics, Technical University of Lisbon, Lisbon, Portugal

[6] Rowett Research Institute, Greenburn Road, Bucksburn, Aberdeen AB21 9SB, UK

[7] Department of Public Health, Section for General Practice, University of Copenhagen, Copenhagen, Denmark

Abbreviations

BMI	Body mass index
CrI	Credible Interval
HbA1c	Glycated hemoglobin A1c
NoHoW	Navigating to a Healthy Weight
HDL	High density lipoprotein
LDL	Low density lipoprotein
WHO	World Health Organization

Introduction

Dietary sugars are often considered significant contributors to the development of cardiometabolic diseases, but inconsistencies remain [1–4]. International dietary guidelines from the World Health Organization (WHO) suggest a free sugar intake of < 10% of total energy intake (E%), ideally less than 5% energy [5], however do not directly link sugar intake to increased risk of chronic disease. This is partially due to inconsistent findings arising from differences in types, amounts, sources, and forms of sugar as well as inadequate study design.

Observational studies have shown that both starch and added sugar contribute to increased weight gain over time [6]. A meta-analysis of cohort studies showed an overall association between higher sugar consumption and higher weight, but not in the subgroup of studies that adjusted for overall energy consumption [7]. In *ad libitum* and excess energy settings, added sugars appear to promote weight gain but not when exchanged for starches or other carbohydrates [8–10], suggesting that changes in body fatness are mediated via changes in energy intakes for both sugars and starch [5]. Studies comparing isocaloric substitution of fructose for glucose or sucrose have reported conflicting results [11–13]. Meta-analyses on the substitution of fructose or sucrose with other sources of carbohydrates reported a reduction in LDL cholesterol [14] and an improvement in long-term glycemic control [15]. In yet other studies, the isocaloric exchange of carbohydrates with fructose promoted the development of hepatic insulin resistance [13] and had no adverse effects on blood lipids [16].

The health effects of sugars can vary significantly based on the overall nutritional profile of sugar-containing foods and the form in which they are consumed. Sugars may be categorised as free/extrinsic sugars (all monosaccharides and disaccharides added to foods, plus sugars naturally present in honey, syrups, and unsweetened fruit juices) or non-free/intrinsic sugars (all sugars excluded from the definition for free sugars, mostly naturally occurring in fruit, vegetables, and dairy products) [17, 18]. Intrinsic or naturally-occurring sugars are often accompanied by essential nutrients that provide health benefits and help mitigate the potential negative effects of sugar. Free/extrinsic sugars, on the other hand, are often found in nutrient-poor foods that provide empty calories without essential nutrients. Further investigation is needed to evaluate the impact of replacing extrinsic with intrinsic sugars or other carbohydrates as these substitutions are likely to be the norm among persons in energy balance.

Bayesian inference and causal modeling are gaining popularity in the statistical analysis of nutritional data [19]. Bayesian analysis diverges from frequentist methods by focusing on the inspection and summarization of posterior distributions of fitted parameters rather than hypothesis testing. In this NoHoW sub-study, we aimed to investigate the substitution of dietary sugar sources (both intrinsic and extrinsic) with each other and other carbohyrate types such as starch and fiber on indices of body fat (body fat, waist circumference and BMI) and cardiometabolic outcomes (HbA1c, LDL, HDL) during an 18-month weight loss maintenance trial using Bayesian inference and causal modeling.

Methods

Study population

The present analysis is an ancillary study based on data collected on participants from the Navigating to a Healthy Weight (NoHoW) trial, an 18-month randomized controlled trial for which the aim was to test the efficacy of an evidence-based digital toolkit, targeting self-regulation, motivation, and emotion regulation on weight loss maintenance among British, Danish, and Portuguese adults. Before enrolment, participants were ≥ 18 years and had achieved a verified weight loss of ≥ 5% and had a BMI of ≥ 25 kg/m^2 prior to losing weight. Participants were enrolled between March 2017 and March 2018. A detailed description of the NoHoW trial can be found elsewhere [20]. The present study analyzed the data from an observational point of view by pooling all participants from the three study centres, irrespective of original randomization. This study is reported according to the Strengthening of the Reporting of Observational Studies in Epidemiology (STROBE) checklist.

Dietary assessment

During the 18-month follow-up period, the diet was assessed within seven days of all four clinical investigation dates (CID) (at baseline, 6, 12 and 18 months) using 24-hour-web-based dietary recalls (INTAKE 24 [21]) on at least four consecutive days, including at least one weekend day. The sugar category of free sugars were labeled as non-milk extrinsic sugars and were defined as all monosaccharides

and disaccharides added to foods by the manufacturer, cook or consumer, plus sugars naturally present in honey, syrups and unsweetened fruit juices. Under this definition, lactose naturally present in milk and milk products and the sugars contained within the cellular structure of foods were considered to be intrinsic sugar and were excluded.

Outcome assessments

The anthropometric variables of body fat percentage, waist circumference and BMI were measured at baseline, 6, 12, and 18 months. For cardiometabolic risk outcomes, LDL (mmol/L), HDL (mmol/L), and HbA1c (%) were assessed at baseline and 12 months. Thus, these cardimetabolic disease risk outcomes were analyzed separately. Excluded were those with missing data for the main carbohydrate predictors or outcomes ($n=128$ for cardiometabolic risk; $n=46$ for indices of body fat) as well as those who reported implausible energy intakes (<600 or >3500 kcal for women ($n=25$), <800 or >4200 kcal/day for men ($n=16$)) [6]. Finally, those without baseline values ($n=680$), or who did not return for follow-up ($n=441$), i.e., those who had baseline measurements only were excluded. This resulted in a total population of 1066 participants in the indices of body fat group (266, 385, 415 participants had exactly 1, 2, or 3 follow ups, respectively) and 736 participants in the indices of cardiometabolic risk group for final analysis (each had one 12 month follow up). For indices of cardiometabolic risk, these participants represented the countries of Denmark ($n=274$), Portugal ($n=188$), and the UK ($n=274$) and for indices of body fat group of Denmark ($n=369$), Portugal ($n=290$), and the UK ($n=407$).

Body weight (±0.1 kg) was measured using a Seca 704 s instrument (SECA, Germany) in participants wearing light clothing. Multifrequency whole bioimpedance spectroscopy was measured by ImpediMed (SFB7, Queensland, Australia), which measures impedance over a spectrum of frequencies for the estimation of body fat percentage. Fasted capillary blood samples were collected to determine HbA1c (mmol/mol, %) and full lipid profiles, including low-density lipoprotein, high-density lipoprotein (HDL) and low-density lipoprotein assayed using a benchtop analyser (Alere Afinion AS100 Analyser, Alere, Stockport, UK) [21].

Bayesian modeling

Bayesian inference offers several advantages, such as informed priors that encode theoretical knowledge, optimal conditioning of models on data via Bayes' Theorem, accurate error propagation, and the intuitive interpretation of results through posterior distributions [22]. All potential confounding factors were selected a priori based on previous research, biological plausibility, and availability of variables. To help isolate the causal impact of the dietary predictors and to identify confounding variables, theoretical considerations were mapped out using directed acyclic graphs (DAGs) as recommended for epidemiological studies (see Figure S1) [23, 24]. In the construction of models, the covariates of age, sex, participant effect, and study center were included in model 1; model 2 further included saturated fat, protein, fiber, and alcohol intake; and model 3 further included remaining energy intake. For blood-based outcomes, body fat percentage was included in models 2 and 3. We use 89% credible intervals throughout the analysis, as this is common in Bayesian analyses as a balance between interpretability and informativeness, further it avoids the readers viewing them as significance tests [22].

For association analyses, general linear models (GLM) were fitted using Markov Chain Monte Carlo, where the posterior distribution of the model parameters was approximated by a multivariable normal distribution. Posterior distributions for the β estimates of the primary predictors were obtained. Instead of the traditional use of p-values, statistical significance was assessed by evaluating whether the 89% credible intervals of the posterior distributions excluded zero and was indicated with symbols. The exclusion of zero within these intervals indicated that the predictor's effect was credibly different from zero, analogous to rejecting the null hypothesis in a frequentist t-test. To evaluate the effects of intake on outcome, intake amounts needed to be converted to kilocalories, logarithmically transformed, standardized to z-scores using population means and standard deviations, and then multiplied by the ß estimates. For more details on **Bayesian modeling see SI**. Bayesian models were fitted with *R* and the *rethinking* package leveriging STAN. Results were summarized and figures created with *Python* and *matplotlib*.

To account for changes in diet over time, dietary variables were averaged per participant, and the participant effect was included in a hierarchical repeated measures random effect model. This approach captures the variability due to changes in diet measured over time by modeling individual participant variability. Adjusting for total energy intake may lead to multicollinearity in some analyses owing to the highly correlated nature of dietary variables. Thus in model 3 we adjusted for remaining total energy intake of dietary variables not included in the model, as recommended by Tomova et al. [25]. Remaining energy was calculated as the total energy subtract all energy contribution from included dietary covariates and predictor variables. Both intakes and outcomes were analyzed as continuous variables. Outcomes were predicted in original units (the original measured units of the outcomes, without transformation or scaling).

Substitution analyses

The substitution analyses were performed by using covariates from model 2, the substitute variable in question, and total energy intake, as recommended by established substitution modeling methods [26]. In a Bayesian framework, substitution effects were assessed by first deriving posterior distributions for the predictor and substitute variables from a specified model. The changes in these variables were then standardized, and the posterior samples were used to estimate the expected change in the outcome. This approach yielded a distribution of potential outcomes, offering a probabilistic assessment of the substitution effects instead of a singular point estimate. Here, posterior distributions from fitted models that included continuous changes in the same multivariable model of simultaneously-tested dietary intakes were sampled 10,000 times to simulate the effect of substituting 20 g of intake variables (5 g for fiber). The posterior distributions of beta coefficients were sampled and multiplied by the mean intake ± the substitution amount to estimate the effect on the outcome. The distribution of differences for each predictor and substitute yielded a distribution visualized as a histogram. Values at 0, less than zero, or greater than zero indicated no change, decrease, or increaser in the outcome due to the substitution, respectively. This approach compares to the established ß coefficient analysis in frequentist substitutions [6], but visualizes expected population effects and credible intervals more clearly through distributions.

Table 1 Baseline characterstics of NoHoW (navigating to a healthy weight) study participants

	Indices of body fat outcome group (up to 18-months follow-up)		Cardiometabolic risk outcome group (12-months follow-up)	
Characteristic	*n*	Mean ± SD	*n*	Mean ± SD
Age (years)	1066	45.2 ± 11.7	736	46.6 ± 11.8
Sex (% male)	1066	25.9	736	24.7
Dietary Factors				
Energy (kcal)	1066	1782 ± 621	736	1704 ± 561
Fat (g)	1066	69.1 ± 32.5	736	65.9 ± 30.4
Saturated fat (g)	1066	19.5 ± 11.8	736	18.4 ± 10.9
Protein (g)	1066	87.8 ± 33.5	736	82.9 ± 29.7
Carbohydrate (g)	1066	187.7 ± 76.0	736	180.9 ± 70.7
Fiber (g)	1066	8.8 ± 6.7	736	8.6 ± 6.7
Intrinsic sugars (g)	1066	26.1 ± 26.0	736	24.9 ± 25.3
Free sugars (g)	1066	24.6 ± 24.9	736	24.1 ± 25.3
Starch (g)	1066	76.3 ± 49.1	736	74.8 ± 49.2
Total sugars (g)	1066	52.3 ± 42.0	736	50.6 ± 41.8
Alcohol (g)	1066	8.8 ± 16.0	736	8.3 ± 14.7
Cholesterol (mg)	1066	286 ± 183	736	265 ± 164
Anthropometric Outcomes				
BMI (kg/m^2)	1066	29.5 ± 5.2	736	29.4 ± 5.1
Body fat (kg)	1066	32.5 ± 12.0	736	32.3 ± 12.0
Body fat (%)	1066	38.0 ± 8.9	736	38.0 ± 8.8
Waist circumference (cm)	1066	93.7 ± 13.9	736	93.1 ± 13.3
Cardiometabolic Outcomes				
HbA1c (%)			736	5.2 ± 0.4
HDL (mmol/L)			736	1.7 ± 0.4
LDL (mmol/L)			736	2.7 ± 0.9

Data are baseline means ± standard deviations. BMI: body mass index; HbA1c: glycated hemoglobin A1c; HDL: high-density lipoprotein; LDL: low-density lipoprotein

Sensitivity analysis

Sensitivity analyses were conducted on model 3 to assess the robustness of the main findings. Specifically, we analyzed the impact of excluding individual covariates on the posterior distributions of the regression coefficients for free and intrinsic sugars intakes with body fat, LDL cholesterol, and HbA1c (see **Table S2**). A second sensitivity analysis excluded dropout participants whose last investigation visit was at 6 months ($n = 193$ dropouts for indices of body fat group, see **Tabel S3**).

Results

Table 1 shows the baseline characteristics of 1066 participants (736 participants for the indices of cardiometabolic risk group) with a mean age of 46.2 years and a BMI of 29.5 kg/m^2. For the indices of body fat group, the mean free sugars intake and intrinsic sugars was 24.6 and 26.1 g/day, respectively. Mean fiber intake was relatively low at 8.8 g/day. The mean baseline levels of HDL, LDL, TG, and HbA1c were in optimal ranges for the cardiometabolic risk outcome group. Table S4 reports these characteristics at the last available CID. Table S5, Figure S2, and Figure S3 reports that nutrient intake decreased slightly over time, unspecific to any given nutrient.

Indices of body fat

A higher intake of starch was significantly associated with a higher body fat, BMI and waist circumference (see Fig. 1; Table 2), while free sugar intake had no association. In contrast, the intake of intrinsic sugars was linked to a significantly lower body fat %, BMI, and weight change. Specifically, intake of 26.1 g of intrinsic sugars resulted in a 0.3%, 0.2, and 0.2 kg lower body fat %, BMI, and change in weight, respectively (Model 3). Similarly, dietary fiber intakes were significantly inversely associated with body fat

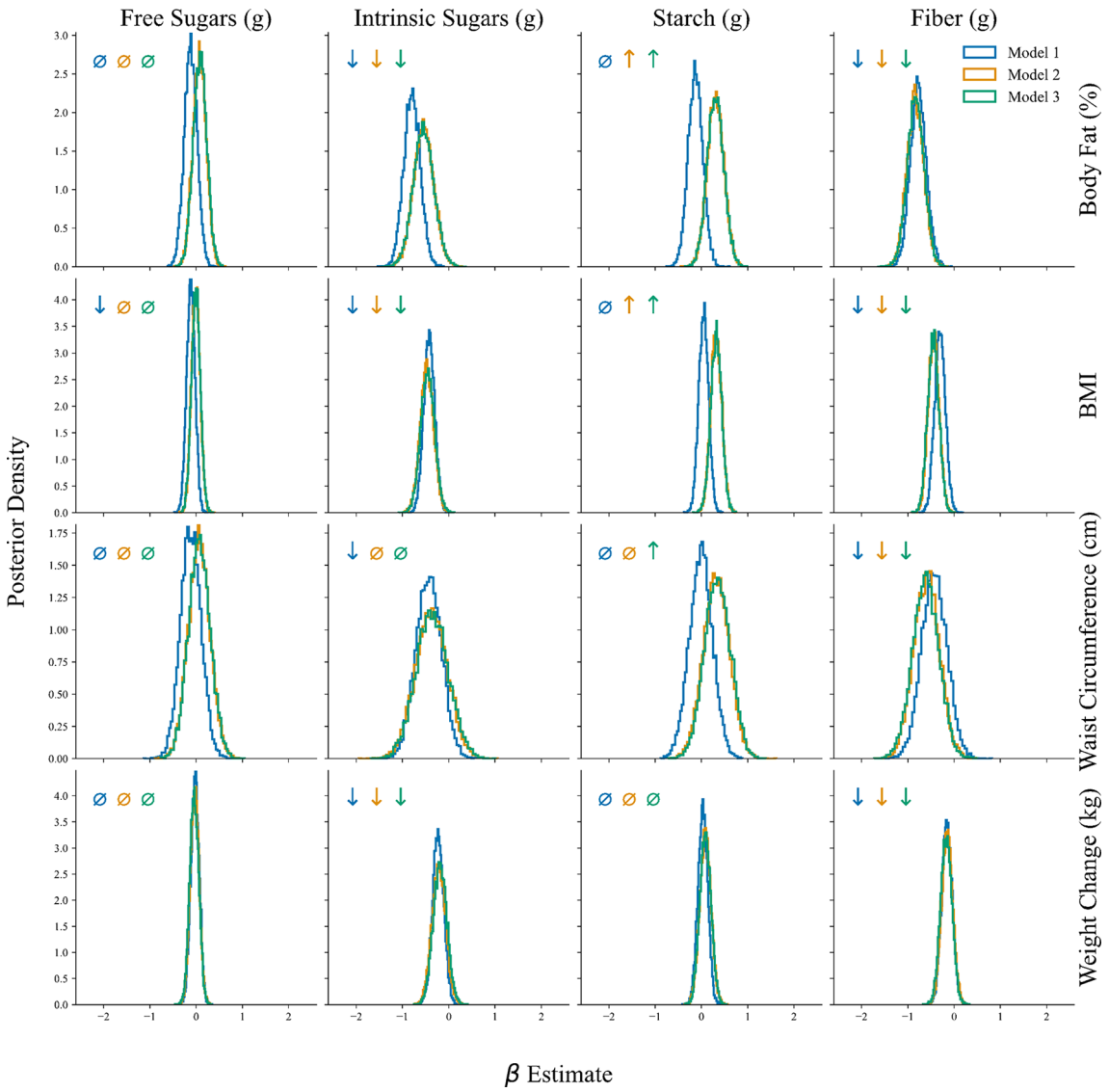

Fig. 1 Associations of free sugars, intrinsic sugars, starch and fiber with indices of body fat Posterior distributions of ß estimates for body fat percentage, BMI (body mass index), waist circumference, and weight change measurements due to free sugars, intrinsic sugars, starch and fiber intakes ($n = 1066$). Model 1 adjusted for age, sex, participant effect, intervention center, Model 2 additionally adjusted for protein, alcohol, saturated fat, fiber, and Model 3 additionally adjusted for remaining energy intake. Arrows (↑, ↓) indicate significant associations (89% of posterior credible interval did not include zero). ⌀ indicates non-significant associations

%, BMI, waist circumference and weight change (all 89% CrI < 0).

Markers of cardiometabolic risk

A higher intake of dietary starch was significantly associated with a lower HDL at 12 months (models 2 & 3 89% CrI < 0; see Fig. 2). Both dietary fiber and free sugar intakes were associated with significantly lower LDL in all three models. Free sugar intake was inversely associated with HbA1c (models 2 & 3), with intrinsic sugars and fiber showing inverse trends.

Substitution analyses

Figure 3 reports the effects of substituting 20 g of free sugars, intrinsic sugar, and starch, or 5 g of fiber with each other for indices of body fat (see Table S3). A 20 g substitution of free sugars with intrinsic sugars was associated with significantly lower body fat % (CrI: -4.2; -1.0) and BMI (CrI: -3.0; -0.8). For dietary fiber substitutions, replacing 20 g of free sugars with 5 g of fiber was associated with significantly lower indices of body fat (body fat % (CrI: -3.4; -1.3), BMI (CrI: -1.8; -0.4), waist circumference (CrI: -3.3; 0.1) and the 20 g replacement of dietary starch with 5 g of dietary fiber

Table 2 Associations of free sugars, intrinsic sugars, starch and fiber intakes with indices of body fat ($n = 1066$)

	Free Sugar		Intrinsic Sugar		Starch		Fiber	
		ø, ↑, ↓		ø, ↑, ↓		ø, ↑, ↓		ø, ↑, ↓
Intake (g/d)^	24.0 (5.9, 34.5)		24.2 (6.7, 34.9)		78.5 (36.9, 110.2)		78.5 (36.9, 110.2)	
Body Fat (%)								
Model 1	-0.1	ø -0.3; 0.1	-0.8	↓ -1.1; -0.5	-0.1	ø -0.4; 0.1	-0.8	↓ -1.0; -0.5
Model 2	0.1	ø -0.2; 0.3	-0.5	↓ -0.9; -0.2	0.3	↑ 0.0; 0.6	-0.8	↓ -1.1; -0.6
Model 3	0.1	ø -0.2; 0.3	-0.5	↓ -0.9; -0.2	0.3	↑ 0.0; 0.6	-0.8	↓ -1.1; -0.5
BMI								
Model 1	-0.1	↓ -0.3; 0.0	-0.4	↓ -0.6; -0.2	0.0	ø -0.1; 0.2	-0.3	↓ -0.5; -0.1
Model 2	0.0	ø -0.2; 0.1	-0.5	↓ -0.7; -0.2	0.3	↑ 0.1; 0.5	-0.4	↓ -0.6; -0.2
Model 3	0.0	ø -0.2; 0.1	-0.5	↓ -0.7; -0.2	0.3	↑ 0.1; 0.5	-0.4	↓ -0.6; -0.3
Waist Circumference (cm)								
Model 1	-0.1	ø -0.5; 0.2	-0.4	↓ -0.9; 0.0	0.0	ø -0.4; 0.4	-0.4	↓ -0.9; 0.0
Model 2	0.1	ø -0.3; 0.4	-0.4	ø -0.9; 0.2	0.3	ø -0.1; 0.8	-0.6	↓ -1.0; -0.1
Model 3	0.1	ø -0.3; 0.5	-0.4	ø -0.9; 0.2	0.3	↑ -0.1; 0.8	-0.6	↓ -1.1; -0.2
Weight Change (kg)								
Model 1	0.0	ø -0.2; 0.1	-0.2	↓ -0.4; -0.0	0.0	ø -0.1; 0.2	-0.2	↓ -0.3; 0.0
Model 2	0.0	ø -0.2; 0.1	-0.2	↓ -0.5; 0.0	0.1	ø -0.1; 0.3	-0.1	↓ -0.3; 0.0
Model 3	0.0	ø -0.2; 0.1	-0.2	↓ -0.4; 0.0	0.1	ø -0.1; 0.3	-0.2	↓ -0.4; 0.0

Values are means (89% CrIs) of ß estimate posterior distributions unless otherwise indicated. Transformations of variables for analysis: z-scores of logs of intakes in kcal. Model 1 adjusted for age, sex, participant effect, intervention center; Model 2 additionally adjusted for protein, alcohol, saturated fat, and fiber; Model 3 additionally adjusted for remaining energy. ^ Values are unadjusted medians (25th, 75th percentiles) in grams per day. Arrows (↑, ↓) indicate significant associations (89% credible interval did not include zero), i.e., significant increases or decreases in the outcome observed in 89% of the samples. ø indicates non-significant findings (credible intervals included zero)

also associated with significant decreases in body fat, BMI and waist circumference.

The substitution of 20 g of free sugars with 20 g of starch intake was associated with a significantly higher body fat % (CrI: -0.3; 2.5) and BMI (CrI: 0.5; 2.4). The substitution of intrinsic sugars with starch was associated with all four indices of body fat: a significantly higher body fat % (CrI: 1.4; 4.9), BMI (CrI: 1.8; 4.1), waist circumference (CrI: -0.3; 5.3 cm) and change in weight (CrI: -0.2; 2.2).

For the cardiometabolic outcomes, the 20 g substitution of starch with 5 g of fiber intake was associated with a significantly higher HDL (CrI: -0.0; 0.3) and a significantly lower LDL (CrI: -0.6; 0.1) (Fig. 4, Table S3). For the outcome long-term glycemia, a 20 g substitution of free sugars with starch was associated with a significant increase in HbA1c (CrI: 0.0; 0.2), with a similar trend indicated for a starch-with-fiber substitution.

Discussion

In this 18-month longitudinal study of overweight individuals, a higher intake of starch was associated with an increase in indices of body fat. Conversely, higher intakes of intrinsic sugars and dietary fiber were inversely linked to all four measures of body fat, while free sugar intake showed no association. The substitution of free sugars with intrinsic sugar was associated with significantly lower body fat, while replacing intrinsic sugar with starch and free sugar intake was associated with higher body fat. Substituting free sugar with starch intake was associated with significantly higher BMI and body fat percentage. For cardiometabolic risk outcomes, starch intake was inversely associated with HDL, and replacing starch with fiber showed a significant association with higher HDL. For HbA1c, replacing free sugar with starch led to significant increases. These findings may provide important insights into the differing impacts of

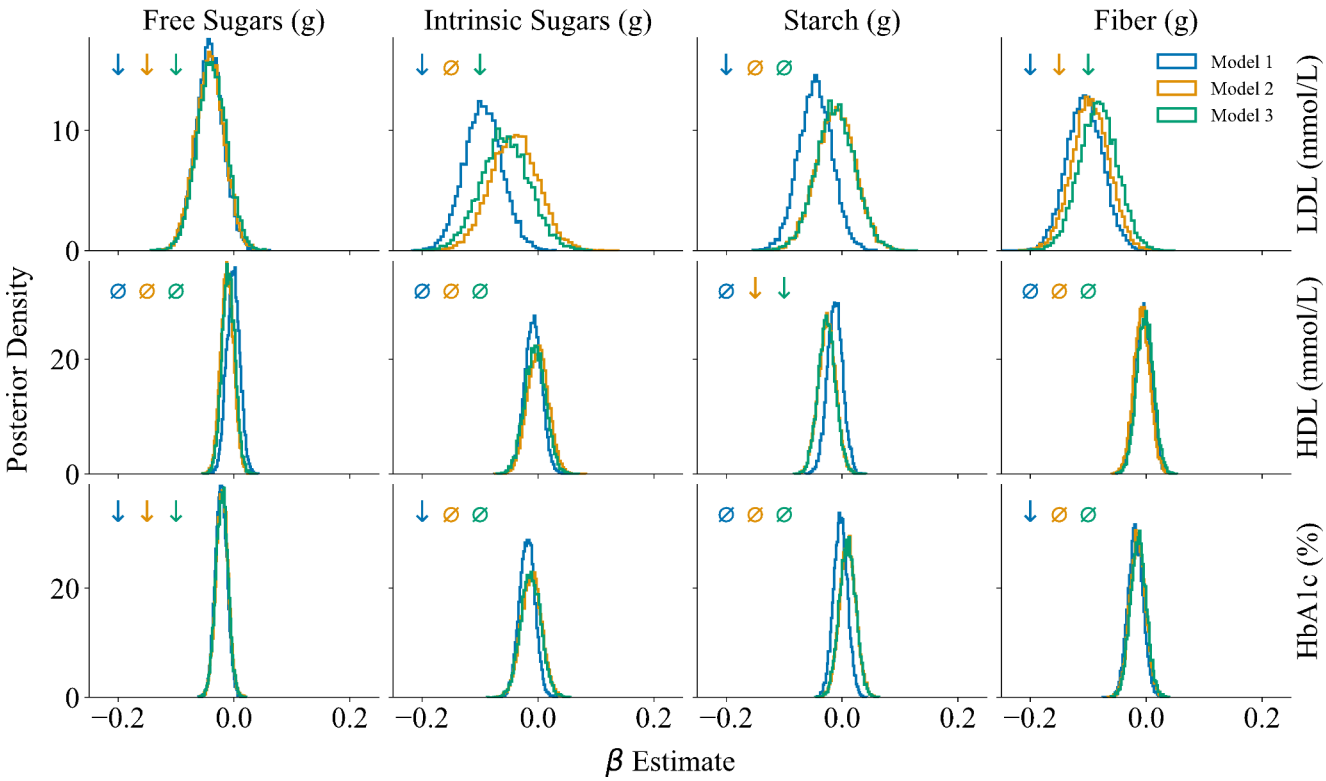

Fig. 2 Associations of free sugars, intrinsic sugars, starch and fiber with cardiometabolic health Plasma levels of low-density lipoprotein (LDL), high-density lipoprotein (HDL), and HbA1c (glycated hemoglobin) percentage of free sugars, intrinsic sugars, starch and fiber intakes for the cardiometabolic risk outcome group ($n = 736$). Data are posterior distributions of ß estimate of predictor for Model 1 (adjusted for age, sex, CID, intervention center), Model 2 (additionally adjusted for protein, alcohol, saturated fat, fiber), and Model 3 (additionally for remaining energy intake). Arrows (↑, ↓) indicate significant associations (89% of posterior credible interval did not include zero) i.e., significant increases or decreases in the outcome observed in 89% of the samples. ⌀ indicates non-significant findings (credible intervals included zero)

various carbohydrate sources on body fat indices and cardiometabolic risk factors.

The concept of free sugars primarily distinguishes between intrinsic sugars (those naturally integrated into the cellular structure of whole foods like fruit, vegetables, and dairy) and extrinsic sugars (all sugars added to foods and beverages by manufacturers, cooks, or consumers, as well as sugars naturally present in honey, syrups, and fruit juices). These distinctions underscore the importance of the source of sugars in dietary recommendations and health outcomes. The overall nutritional profiles of sugar-containing foods determine their health benefits. Intrinsic or naturally-occurring sugars are often accompanied by essential nutrients such as vitamins, minerals, fiber, and bioactive polyphenols. Free/extrinsic sugars, on the other hand, are often found in nutrient-poor foods that provide empty calories without essential nutrients. The beneficial associations of intrinsic sugars versus free sugars in our study may reflect these components in the food matrix or the type of sugar (glucose, fructose, sucrose, lactose) present.

Our findings align with previous studies showing that naturally occurring sugars in whole fruits do not carry the same health risks as free sugars, which can promote weight gain and adverse health outcomes by increasing overall caloric intake without satiety. A high intake of fruits that are naturally high in fructose is associated with good metabolic health [27]. For instance, fruit consumption is consistently associated with a lower risk of T2D, whereas fruit juice, with its higher glycemic load and lack of fiber, is linked to an increased risk [28, 29]. Interestingly, our findings also highlighted the differential impact of starch and free sugar intakes. Increased starch intake strongly related to higher body fat percentage, BMI, and waist circumference while an intake free sugar intakes was not related. Indeed, replacing free sugar with starch in the substitution models resulted in significant gains in body fat % and BMI. These results suggest that while starches can negatively impact body fat indices, free sugar consumed in lower amounts can be included as part of a healthy diet. Comparing sugars to other macronutrients, a cross-sectional analysis from the UK Biobank study reported that while sugar intake was associated with obesity in British adults, there were much stronger dose-response associations with starch, fat, and protein [7]. It was concluded by the Scientific Advisory Committee of

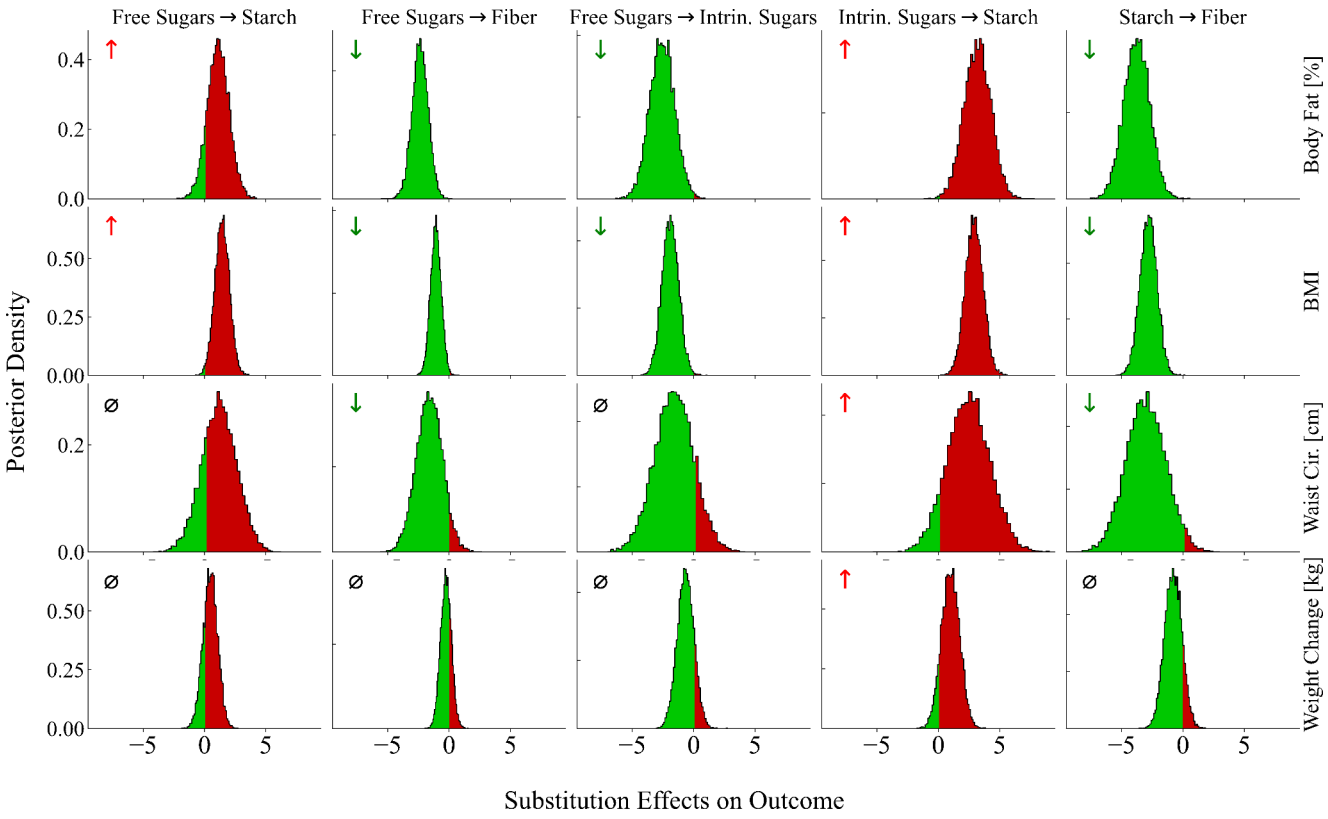

Fig. 3 Substitution analyses of carbohydrate components for indices of body fat Substitution analyses for indices of body fat. Histograms are posterior distributions of differences for each 20 g (5 g fiber) of each predictor decreased ◊ and substitute increased from the mean. Green indicates beneficial and red harmful substitution effects. Values less than zero indicate a decrease in the outcome, values greater than zero an increase in the outcome. Density indicates that distributions are proper posteriors, i.e. integrate to 1. Arrows (↑, ↓) indicate significant associations (89% of posterior credible interval did not include zero) i.e., significant increases or decreases in the outcome observed in 89% of the samples. ⌀ indicates non-significant findings, i.e., no change due to the substitution (credible intervals included zero). BMI: body mass index, Waist Cir.: Waist Circumference

Nutrition that the available body of evidence from prospective cohorts did not show a positive relationship between obesity and added/free sugar intakes in isocaloric exchange with other macronutrients [30]. Our findings suggest that the substitution of free sugar with intrinsic sugars may lead to significant decreases in body fat %, and BMI (see Fig. 3). Higher dietary fiber and intrinsic sugar intakes were linked to reductions in body fat in our study, emphasizing a possible protective role of higher-quality carbohydrates that protect against obesity-related outcomes.

Although anecdotally many health professionals assume that sugar intake increases risk markers for cardiometabolic disease, the results from the present study suggest that free sugars in moderate amounts may not have a direct detrimental impact on chronic disease risk markers. Free sugars intake was in fact related to a decrease in LDL and HbA1c in our study. Although free sugars, particularly in liquid forms like sugar-sweetened beverages (SSBs), have been linked to increased type 2 diabetes (T2D) risk [3, 31] and coronary heart disease [32], epidemiological evidence has shown that average amounts of comprehensive added sugars intake have either no relationship [1, 33–35], or even a beneficial association [2, 36, 37] with chronic disease risk. Indeed, foods that are sweetened with added sucrose have shown a protective association (whole-grain cereals, fruit, yogurt) with T2D [38]. This indicates that the amount and form or source in which sugars are consumed plays a crucial role in mediating health outcomes.

The impact dietary starch has on body fat and cardiometabolic outcomes can depend on its quality, or how rapidly digestible the starch is, often measured as the glycemic index (GI) of foods [39]. While GI was not measured in this study, fiber intake, another indicator of carbohydrate quality, was relatively low in the present population, suggesting that the type of starch consumed was of a lower quality or more refined. Numerous studies have shown that the hypolipidemic effect of whole foods are influenced by the fiber content [40, 41]. Dietary fiber in this study was inversely related to LDL cholesterol and the substitution of 20 g of starch for 5 g of fiber resulted in significant decreases in LDL and increases in HDL cholesterol. Considering dietary sugars, pooled analyses indicate that fructose only

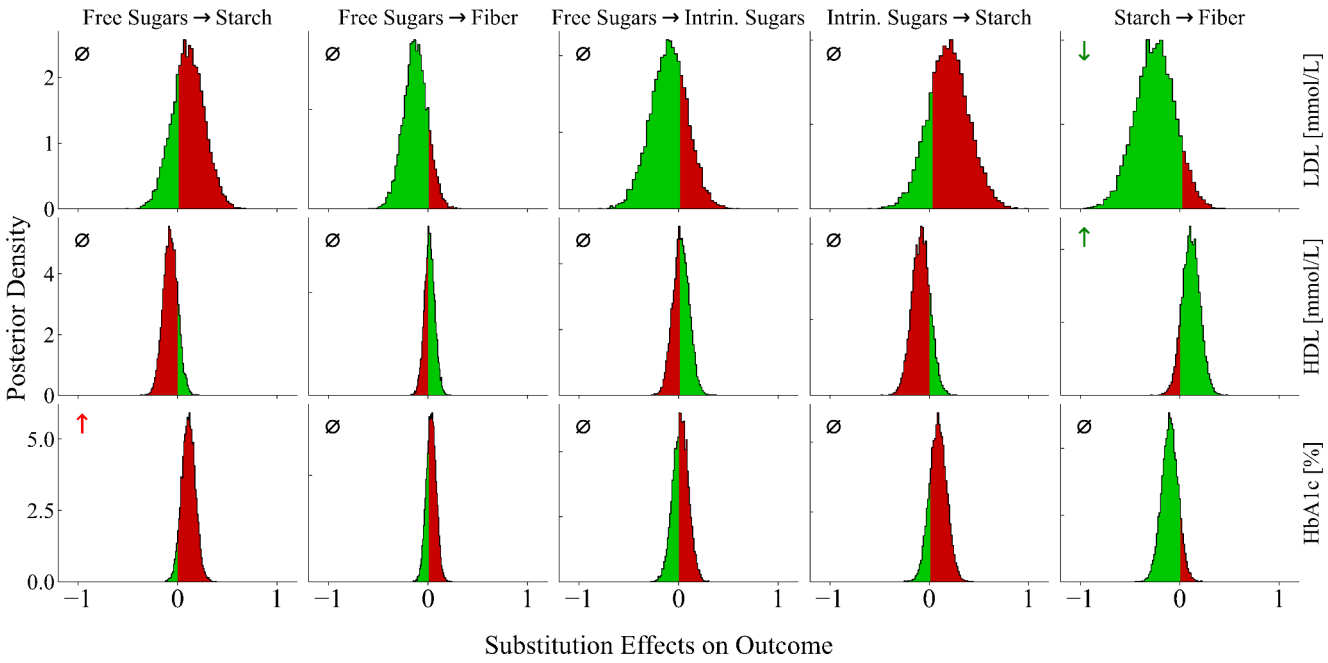

Fig. 4 Substitution analyses of carbohydrate components for indices of cardiometabolic health. Substitution analyses for blood lipids. Histograms are posterior distributions of differences for each 20 g (5 g fiber) of each predictor decreased ◊ and substitute increased from the mean. Green indicates beneficial and red harmful substitution effects. Values less than zero indicate a decrease in the outcome, values greater than zero an increase in the outcome. Density indicates that distributions are proper posteriors, i.e. integrate to 1. Arrows (↑, ↓) indicate significant associations (89% of posterior credible interval did not include zero) i.e., significant increases or decreases in the outcome observed in 89% of the samples. ⌀ indicates non-significant findings, i.e., no change due to the substitution (credible intervals included zero)

adversely affects lipid targets when it was added to diets in excess (+21–35% energy). When isocalorically exchanged for other carbohydrates, fructose had no adverse impact on blood lipids [16]. In our study, free sugar was protectively associated with LDL. On another note, when free sugar was substituted with starch intake, a significant increase in HbA1c was observed. This indicates that dietary starch may be more impactful on long-term glycemia than moderate intakes of free sugars [39].

There are notable strengths of the present study. First, we provide new evidence of the associations of intrinsic and extrinsic sugars compared with each other as well as dietary starch and fiber during a weight loss maintenance period, which is more likely to address an issue for overweight individuals. Secondly, we determined these associations in a free-living context and an *ab libitum* diet. Thirdly, because dietary and anthropometric markers were collected regularly over 18 months, we were able to leverage repeated and real-time data over the 18 months. This large dataset allowed for multiple outcome indices of both body fat and cardiometabolic health and it allowed for the adjustments of multiple confounders. In addition, we performed substitution analyses which go beyond basic associations to attempt the determination of causality in diet and health relations. Finally, the findings may be more generalizable because three different European countries, albeit relatively similar in terms of economy and food availability, were represented.

Several limitations should also be noted. Dietary sugar intakes were calculated from self-reported 24-hour recalls. Although these records estimate food intake more accurately than food-frequency questionnaires, misreporting can occur [42]. It is possible that sugar-rich foods were selectively underreported due to their perceived unhealthiness [43]. It should be noted in the interpretation of these results that because the reporting bias of sugar is higher, the relatively low intake of free sugars may limit the ability to observe an association with body fat and cardiometabolic risk. On the other hand, these findings confirm that sugar consumed in moderate amounts may not cause harm. Further, intrinsic sugar intake may be a proxy for a certain type of diet, including one which is rich in fruit, vegetables, legumes, berries, and dairy foods. It is important to note that our analyses did not account for the quality or specific food sources of starch, which could potentially influence its associations with body fat indices and cardiometabolic outcomes. For example, starchy foods that are minimally processed or have a lower glycemic index (e.g., legumes or whole grains) may have different health effects than refined or high-GI starches. This limitation precludes more granular insights into the observed associations and substitutions, underscoring the need for future research to incorporate detailed food

source data and measures of carbohydrate quality. Although we have tested and adjusted for dietary macronutrient composition, there are other dietary components (e.g., vitamins, minerals, and polyphenols) that we could not adjust for, hence residual and unmeasured confounders may exist. In addition, the starch category could not be divided into rapidly digestible starch, slowly digestible starch, and resistant starch. Further, intakes and outcomes were analyzed at the same timepoints, limiting the ability to infer causal relationships by temporal sequencing. Additionally, the analysis does not account for dietary changes occurring during the intervention trial prior to the baseline assessment, which could provide further context to the discussion. Finally, as the participants were generally overweight, our findings may not be relevant to individuals with normal weight.

In conclusion, this 18-month weight-loss maintenance study reveals that a higher intake of starch was linked to increases in body fat indices. Conversely, higher intakes of intrinsic sugars and dietary fiber were associated with lower body fat indices, while free sugar intake was not related. Substitution analyses confirm that replacing free sugars with intrinsic sugars may reduce body fat while replacing intrinsic sugars with free sugars and starch may increase it. Starch intake was also linked to lower HDL levels and replacing starch with fiber resulted in significantly higher HDL. For HbA1c, replacing free sugars with starch led to significant increases. These results underscore the importance of distinguishing between dietary sugar types (intrinsic versus extrinsic) for weight control and disease prevention and highlight the neutrality of free sugars consumed in moderate amounts. Our findings suggest potential benefits of decreasing dietary starch while increasing intrinsic sugars and fiber for better body fat management and cardiometabolic health.

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Author contributions KDC and BLH conceived the research project. KDC and DDC were responsible for the statistical analyses and DC assisted with them. KDC and BLH interpreted the data. KDC wrote the manuscript. GH prepared and provided the data. BLH, JS, and AP contributed to the implementation of the experimental trial.

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Declarations

Ethics approval and consent to participate The study complies with relevant EC legislation, international conventions and declarations relating to ethical research practices [44].

Competing interests All authors have no competing interests to declare that are relevant to the content of this article.

Conflict of interest The authors declare that they have no conflict of interest.

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