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Prospective association of added sugars with frailty in older adults

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Abbreviations

Body mass index (BMI)
Confidence interval (CI)
Mediterranean Diet Adherence Score (MEDAS)
Odds ratio (OR)
ABSTRACT

BACKGROUND: Sugar-sweetened beverages and added sugars (monosaccharides and disaccharides) in the diet are associated with obesity, diabetes, and cardiovascular disease which, in turn, are risk factors for decline in physical function among older adults.

OBJECTIVE: To examine the association of added sugars in the diet with incidence of frailty in older people.

METHODS: Data were taken from 1973 Spanish adults ≥60 years old from the Seniors-ENRICA cohort. In 2008-2010 (baseline), added sugars consumption (including those in fruit juices) was obtained with a validated diet history. Study participants were followed-up to 2012-2013 to assess frailty using Fried’s criteria. Statistical analyses were performed with logistic regression adjusted for age, sex, education, smoking status, body mass index, energy intake, self-reported comorbidities, Mediterranean Diet Adherence Score (excluding sweetened drinks and pastries), TV watching time, and leisure-time physical activity.

RESULTS: Compared with participants consuming <15 g/day of added sugars (lowest tertile), those consuming ≥36 g/day (highest tertile) were more likely to develop frailty (odds ratio 2.27; 95% confidence interval 1.34, 3.90; p trend=0.003). Frailty components “low physical activity” and “unintentional weight loss” increased dose-dependently with added sugars. Association with frailty was strongest for sugars added during food production. Intake of sugars naturally appearing in foods was not associated with frailty.

CONCLUSIONS: Added sugars consumption in the diet of older people was associated with frailty, mainly when present in processed foods. Frailty components that were most associated with added sugars were low levels of physical activity and unintentional weight loss. These findings suggest that strategies to increase diet healthiness should consider reducing consumption of processed foods with added sugars.
INTRODUCTION

Evidence has accumulated indicating that consuming sugar-sweetened beverages contributes to worsening of cardiometabolic risk markers(1) and weight gain(2), and increases the risk of diabetes(3), coronary heart disease(4), and other chronic diseases(5,6), which hinder healthy ageing. Unhealthy effects of sugar sweetening have been studied beyond beverages, showing that the amount of added sugars intake in the whole diet is associated with cardiovascular mortality in US adults(7). Dietary sugars raise triglycerides, total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol concentrations, and blood pressure even within isocaloric replacement and absence of weight gain(8).

Many older people suffer a progressive loss of strength, agility, and mobility over time, which leads to disability. The frailty syndrome(9,10), characterized by increased vulnerability to even minor stressors, forecasts this process and is associated with greater risk of falls, institutionalization, and death(11). Cardiovascular risk factors are associated with prevalent(12) and incident(13) frailty, which implies that either they are in the frailty causal pathway or they share common lifestyle and socioeconomic causal factors(14). In particular, diet is well known to influence the risk of frailty and disability in older adults(15–22).

However, the specific role of added sugars in this process has not been addressed. Thus, we hypothesized that higher added sugars in the diet is associated with development of frailty in older people.

METHODS

Study design and participants

Data were taken from the Seniors-ENRICA cohort, whose methods have been reported elsewhere(23). In brief, the cohort was derived from the ENRICA study, a survey conducted in 2008-2010 among individuals representative of the non-institutionalized adult population
of Spain. The study participants aged 60 years or older (n=3289) were targeted to be followed-up as the Seniors-ENRICA cohort. At baseline, information on socio-demographic variables, lifestyle, health status and morbidity was collected through a phone interview; also, food consumption was obtained, and physical examination was performed by trained staff at the home of the participants. A wave of data collection was performed in 2012 to update the information of the cohort. In total, 675 participants were lost during follow-up and 95 deaths were identified. Among survivors (n=2519), we excluded participants with dementia or Alzheimer disease at baseline (n=9), with frailty at baseline (n=52), and with missing data on diet (n=12), questionnaires or function tests (n=473). Thus, the analytical sample comprised 1973 participants (Supplemental Figure 1). Informed written consent was obtained from all participants, and the study was approved by the Clinical Research Ethics Committee of La Paz University Hospital in Madrid.

**Diet and added sugar**

A validated(24) computer-based diet history was used to collect the participant’s habitual consumption of 880 different foods. Taking into account weekly frequency of consumption of each food, this diet history provides an estimate in daily grams of foods that represents the average intake during the preceding year.

Carbohydrates present in diet can be chemically classified as simple, also known as sugars (monosaccharides and disaccharides), which have a marked sweet taste, and complex, which have a higher degree of polymerization. Sugars are naturally present in fruits, vegetables, and milk but they are also added to foods, mainly to sweeten them. Foods with sugars have higher glycemic indexes and produce stronger endocrine responses for glucose regulation.

Standard food composition tables allowed calculating the amount of sugars that each food contributed to participants’ diet. Those amounts were summed for foods belonging to the following groups: table sugar, honey and syrup; special breads; baked goods and cookies;
pastries; breakfast cereals; flavored milks; whole yogurt and fermented milk; dairy desserts; sweetened cheeses; cooked and canned fruits and vegetables; jam and jelly; candy; chocolate; soft drinks; and fruits juices and nectars. All sugars in these food groups were deemed added sugars, which correspond to the concept of “free sugars” elaborated by the World Health Organization because they include sugars in fruits juices (25). The variable total sugars included sugars from all foods with sugars in their composition, disregarding whether these were added or not. We considered that the amount of sugars naturally appearing in food (also known as intrinsic sugars) was the difference between total sugars and added sugars calculated as described above.

Frailty assessment

Frailty was defined as the presence of three of the following five Fried criteria (26): 1) Exhaustion, identified with an affirmative response to any of the two following questions from the Center for Epidemiologic Studies Depression Scale (27): “I feel that anything I do is a big effort” or “I feel that I cannot keep on doing things” at least 3-4 days a week; 2) Low physical activity, identified when self-reported walking was ≤ 2.5 h/week in men and ≤ 2 h/week in women (28); 3) Slow gait speed, considered as the lowest cohort-specific quintile in a 2.44 meters walking speed test which was performed as part of the Short Physical Performance Battery, adjusted for sex and height (29); 4) Unintentional weight loss, when ≥ 4.5 kg of body weight was lost in the preceding year; 5) Muscle weakness, when grip strength, measured with a Jamar dynamometer (highest of two consecutive measurements in the dominant hand) and adjusted for sex and body mass index (BMI), was in the cohort-specific lowest quintile (30).

Other variables

At baseline, we collected age, sex, education, smoking status, measured weight and height, self-reported physician-diagnosed diseases, time spent watching TV, and leisure-time
physical activity (using the EPIC cohort questionnaire). The Mediterranean Diet Adherence
Score (MEDAS) was used to assess accordance with the Mediterranean dietary pattern (31).
Because of the score overlap with intake of some sources of added sugar, we calculated a
modified MEDAS excluding sweetened drinks and pastries to be able to adjust for adherence
to a healthy diet. The new score has a range 0-12 and higher values indicate greater adherence
to the Mediterranean pattern. BMI was calculated as weight in kilograms divided by height
squared in meters.

Statistical analyses
Participants were classified in tertiles of the amount of added sugars in their diet. Cut-off
values used for classification were 14.952 and 35.795 g/day but, for the sake of readability, in
the text and tables they appear rounded as 15 and 36 g/day. Inter-tertile odds ratios (OR) and
their 95% confidence interval (CI) were calculated with logistic regression using the first
tertile as reference. Trend significance was calculated using tertile ordinals. Regression
models were built with four levels of adjustment: model 1 was adjusted for age, sex, and
education; model 2 was additionally adjusted for smoking status, BMI, energy intake, and
self-reported comorbidities (listed in Table 1); model 3 was additionally adjusted for the
modified MEDAS score; and model 4 was additionally adjusted for time spent watching TV
and leisure-time physical activity. Models 3 and 4 were segregated to explore whether added
sugars have an intrinsic effect or they are a proxy for unhealthy diet (as captured by MEDAS)
or unhealthy physical activity habits. Frail participants at baseline were excluded for the
analytic sample and only robust participants at baseline were considered for the specific
analysis estimating association of added sugars with incidence of each frailty trait. In order to
understand better whether the association is with the whole syndrome or with a particular
trait, sensitivity analyses were performed with modified definitions of frailty, requiring 3
criteria, but excluding those frailty criteria that show more intense association with added
sugars.
Subanalyses were performed with the same methods using as predictors the amount of added sugars from particular food groups: from table sugar, honey, and syrups; from foods that add sugars during food production (all other foods containing non-naturally-present sugars); from pastries and cookies; and from sweetened beverages. In these cases, we compared participants that did not consume these foods with those surpassing the median consumption among those that consumed. We also analyzed tertiles of sugars naturally appearing in foods. Lastly, we performed a stratified analysis by diabetes and by BMI (non-obese vs. obese), and also interaction models for these variables. Regression analyses were performed on R version 3.0.2.

RESULTS

Among the 1973 participants (mean age 68.5 years, 49.0% men), at baseline, higher added sugars intake was associated with lower age, higher energy intake, lower adherence to the Mediterranean diet, and lower frequency of diabetes (Table 1). During follow-up, 140 individuals developed frailty (Table 2).

In adjusted analyses (model 2), those participants consuming ≥36 g/day of added sugars (highest tertile) showed significantly increased odds for frailty (OR 2.48; 95% CI: 1.49, 4.19) when compared with those consuming <15 g/day (lowest tertile). After additionally adjusting for adherence to the Mediterranean diet and for physical activity (model 4), OR decreased but only by a small amount, to 2.27 (95% CI 1.34, 3.90). Interestingly, the latter additional adjustment for physical activity (model 4) did not materially change the estimates compared with the previous adjustment for MEDAS (model 3). Lastly, there was a statistically significant dose-response trend (Table 2). The specific frailty components that were associated with added sugars consumption in the fully adjusted model (model 4) were low physical activity (OR 1.50; 95% CI: 1.00, 2.26) and unintentional weight loss (OR 1.93; 95% CI: 1.10, 3.49), also with a statistically significant dose-response trend (Table 2).
association of added sugars with frailty was robust to criteria used to define the latter as excluding each one of these two above-mentioned criteria or both from the frailty definition did not substantially change the association magnitude or its statistical significance (data not shown).

Among this cohort of older people, one-third of added sugars was taken from table sugar (or honey or syrups). The remaining two-thirds were sugars added during food processing, including, among others, pastries and cookies (15% of the total) and sugar-sweetened beverages (6%). When considering specific sources of added sugars, those coming from foods that add sugars during food production (any food with added sugars except the table sugar group) showed the strongest association although most of these specific-source analyses did not reach statistical significance (Figure 1). Increased intake of added sugars seems to associate with frailty more strongly among obese participants (Figure 1).

Interestingly, the intake of sugars naturally appearing in foods was not statistically associated with worse outcomes. On the contrary, it showed an association with frailty in a protective direction (OR 0.53; 95% CI 0.32, 0.88); however, after considering adherence to the Mediterranean diet, the OR was still in the protective direction, but statistical significance was lost (OR 0.66; 95% CI 0.38, 1.13) (Table 3).

When tertiles of grams of foods containing added sugars were analyzed, we found deleterious associations for frailty with similar intensity to those found when considering only the grams of sugars contributed by those foods (Table 3).

**DISCUSSION**

After 3 years of follow-up, in this cohort of community-dwelling older people from Spain, a higher amount of added sugars consumed in the diet was associated with increased risk of frailty. This association was only partially explained by the co-occurrence of worse adherence
to Mediterranean diet and lower physical activity. Among the foods with added sugars, those with sugars added during production were more associated with frailty. Interestingly, the association could be asserted by simply accounting the amount of food containing added sugars consumed, disregarding their particular sugars contribution. In contrast, this adverse association was not seen for sugars naturally present in foods. Although some frailty components were more strongly associated to added sugars than others, the association with the frailty syndrome was robust to excluding them from its definition, reinforcing that our findings apply to frailty, and not only to particular traits.

To our knowledge, this is the first attempt to study specifically the association of added sugars in the diet with frailty among older people. We previously reported that total carbohydrates or total sugars in the diet were not associated with incident frailty. In the current study, we observed that naturally present sugars tended to be associated in a protective way regarding frailty while added sugars were associated with increased risk, which may explain a null net association of total sugars present in the diet.

The effect of carbohydrates on physical function has received limited attention and research has focused only within the context of particular diseases: among older diabetic patients, exposure to higher glycemic levels, ascertained with glycosylated hemoglobin, was associated with worse physical function measured through the Short Physical Performance Battery, although it was mostly explained by diabetes mellitus comorbidities. Besides physical function, most other studies on carbohydrates have focused on cognitive decline; for instance, Hosking et al. showed that a dietary pattern that included high-sugar predicted a decline in several cognitive parameters.

The mechanisms of an adverse health effect of sugar-sweetened beverages, and by extension of added sugars in the diet, include an increased energy intake that is followed by greater BMI. It is hypothesized that sugars in liquids do not suppress solid foods intake enough to
maintain energy balance (36), although this insufficient inhibition could also occur for any high intake of sugars, regardless of whether they are ingested in liquid or solid form, or could be attributed to the different endocrine response to fructose (37). Fructose is one of the components of sucrose, the most common sugar consumed. Because fructose is sweeter than glucose or sucrose itself, the latter is usually partially broken down into its components, and it is used in food preparation in the forms of inverted sugar or high-fructose corn syrup. Weight gain does not explain all the effects associated with added sugars; in fact, fructose undergoes a different liver metabolism than glucose, favoring hepatic lipid synthesis and increasing post-prandial circulating triglycerides (37) and atherosclerotic lipids (38). Other effects attributed to fructose are increasing uric acid levels (39) and hepatic ATP depletion (40). Sugars have a high glycemic index, which can stress and wear the insulin axis for glucose control. All these mechanisms have been proposed to link sugar-sweetened beverages consumed in large quantities with increased obesity, diabetes mellitus, cardiovascular risk factors, coronary heart disease, other chronic diseases, and cardiovascular mortality.

It is possible that some of these mechanisms could contribute to the physical decline associated with added sugars intake, including the increase in frailty, whose mechanisms are still being elicited. Sarcopenia, which includes a loss of muscle mass and weakness, is one of the mechanisms associated with frailty. In addition, insulin resistance and low-grade inflammation, favored by added sugars intake, impair muscle glucose handling and intracellular energy production and reduce protein synthesis, disbalancing muscles towards a proteolytic state, and thus, compromising efficient muscle contraction (41,42). Insulin resistance may also produce macro- and micro-vascular complications and favors cognitive impairment in the elderly, mechanisms that also contribute to frailty (43,44). With respect to obesity, our estimates were adjusted for baseline BMI and total energy intake, and one of the frailty components associated with added sugars intake was unintentional weight loss, so there must be some other mechanisms that go beyond weight differences associated with diet.
Higher carbohydrate intake and, in particular, higher added sugars intake is associated with worse diet quality (45). Older people may find it difficult to include enough proteins in their diet, to prevent sarcopenia, while maintaining a low caloric content adequate to the reduced need of energy in the old age. Diets with added sugars may thus draw them further away from this goal. Also, micronutrient dilution has been described to occur among older people with diets high on added sugars (46, 47). Micronutrient deficiencies relate to functional decline of older people (48), vitamin D deficiency (49) and lower anti-oxidant vitamins C and E (50). Micronutrient deficiencies associate with frailty, and lower vitamin B with impaired mobility (51), which point towards another possible explanation of the association that we describe.

Higher consumption of foods with added sugars could be a marker of poor lifestyle and dietary patterns, which are associated with physical decline and frailty (16, 17). We observed that the association does not concentrate plainly on sugars quantity, but on sugars ingested from foods assumed to have them as an addition. Furthermore, also the amount of those foods consumed was associated with frailty. Our results were adjusted for a modified MEDAS score and remained practically unchanged, indicating that in the case that the association is due to a potential harmful dietary pattern, it is not captured as a lack of Mediterranean diet adherence. Because the association with table sugar was not the same as that with sugars added during food production, we could conjecture that a dietary pattern with predominantly processed foods might be the underlying problem captured by the added sugars variable. Based on this evidence, targeting an improvement in diet healthiness might be more beneficial than exclusively focusing on sugars (52).

This study’s strengths include a prospective design, a detailed measurement of food consumption with a validated diet history, and a relatively large sample size. Trained staff within a re-training schedule collected both exposure and outcome data with high precision, and nutrient intake is based on Spanish tables of food composition. However, there are some
limitations as well. We assumed that all sugars in the composition of foods that have added
sugars were from external addition. There are no means for discriminating which amount of
sugars was present naturally and which was added. Nonetheless, this would have as a
consequence a dilution of the effect and weaker association magnitudes, but we still found
relatively strong associations. In our analyses, we adjusted for the main confounders;
however, we cannot rule out some residual confounding. Finally, given that mean age of the
participants at baseline is 68.5 years, caution should be applied in case of trying to extrapolate
these results to the very old. Those excluded for missingness in clinical or functional variables
ate the same amount of added sugars although they were more likely to be women, with lower
education, less energy intake, more TV watching time, and higher prevalence of osteo-
muscular disease. This might decrease generalizability but because missingness is not
associated with the exposure variable but only with adjustment variables it is likely to have
only a minor effect on internal validity.

The amount of added sugars present in the diet of older people was associated with the risk of
frailty. Frailty components that were most associated with added sugars were low levels of
physical activity and unintentional weight loss. This was not explained by a lack of adherence
to the Mediterranean diet or by worse physical activity habits, but it could be related to
dietary patterns that include higher amounts of processed foods.
ACKNOWLEDGMENTS

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The authors have no potential conflicts of interest.

All authors designed the research. ML and ELG performed the statistical analyses; All authors contributed to results interpretation; ML, FRA, and ELG drafted the manuscript; ELG and FRA supervised the conduct of research. ML had primary responsibility for final content. All authors reviewed the manuscript for important intellectual content, read and approved the final manuscript.
REFERENCES

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Table 1. Characteristics of the study participants across tertiles of daily intake of added sugars

<table>
<thead>
<tr>
<th>Added sugars (g)</th>
<th>Tertile 1</th>
<th>Tertile 2</th>
<th>Tertile 3</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>1973</td>
<td>659</td>
<td>656</td>
<td>658</td>
</tr>
<tr>
<td>Men</td>
<td>49.0 [966]</td>
<td>48.0 [316]</td>
<td>47.3 [310]</td>
<td>51.7 [340]</td>
</tr>
<tr>
<td>Age, y</td>
<td>68.5 (6.3)</td>
<td>68.8 (6.3)</td>
<td>68.7 (6.4)</td>
<td>68.1 (6.3)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary or less</td>
<td>52.8 [1041]</td>
<td>52.5 [346]</td>
<td>53.2 [349]</td>
<td>52.6 [346]</td>
</tr>
<tr>
<td>Secondary</td>
<td>25.0 [494]</td>
<td>23.7 [156]</td>
<td>26.5 [174]</td>
<td>24.9 [164]</td>
</tr>
<tr>
<td>University</td>
<td>22.2 [438]</td>
<td>23.8 [157]</td>
<td>20.3 [133]</td>
<td>22.5 [148]</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.4 (4.3)</td>
<td>28.6 (4.5)</td>
<td>28.3 (4.4)</td>
<td>28.3 (3.9)</td>
</tr>
<tr>
<td>Energy intake, kcal/d</td>
<td>2037.8 (570.3)</td>
<td>1814.1</td>
<td>2005.0 (493.7)</td>
<td>2294.5 (568.1)</td>
</tr>
<tr>
<td>Time spent watching TV, h/wk</td>
<td>17.7 (10.9)</td>
<td>17.8 (11.0)</td>
<td>17.8 (10.4)</td>
<td>17.5 (11.1)</td>
</tr>
<tr>
<td>Leisure-time physical activity, MET-h/wk</td>
<td>22.0 (15.3)</td>
<td>22.5 (15.4)</td>
<td>22.3 (15.8)</td>
<td>21.4 (14.6)</td>
</tr>
<tr>
<td>Modified MEDAS</td>
<td>5.7 (1.6)</td>
<td>6.0 (1.6)</td>
<td>5.8 (1.6)</td>
<td>5.3 (1.7)</td>
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<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>11.4 [225]</td>
<td>11.4 [75]</td>
<td>11.0 [72]</td>
<td>11.9 [78]</td>
</tr>
<tr>
<td>Former smoker</td>
<td>30.9 [610]</td>
<td>32.8 [216]</td>
<td>27.1 [178]</td>
<td>32.8 [216]</td>
</tr>
<tr>
<td>Never smoker</td>
<td>57.7 [1138]</td>
<td>55.8 [368]</td>
<td>61.9 [406]</td>
<td>55.3 [364]</td>
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<td>Comorbidities</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>15.0 [295]</td>
<td>22.5 [148]</td>
<td>11.6 [76]</td>
<td>10.8 [71]</td>
</tr>
<tr>
<td>Bronchitis or asthma</td>
<td>7.1 [140]</td>
<td>8.2 [54]</td>
<td>5.8 [38]</td>
<td>7.3 [48]</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>5.0 [99]</td>
<td>6.1 [40]</td>
<td>4.0 [26]</td>
<td>5.0 [33]</td>
</tr>
<tr>
<td>Osteo-muscular disease</td>
<td>47.0 [928]</td>
<td>49.3 [325]</td>
<td>47.0 [308]</td>
<td>44.8 [295]</td>
</tr>
<tr>
<td>Depression</td>
<td>7.3 [145]</td>
<td>6.5 [43]</td>
<td>7.6 [50]</td>
<td>7.9 [52]</td>
</tr>
</tbody>
</table>

Data are shown as percentage [number] or mean (standard deviation). P-trend values were calculated from linear and logistic regressions using tertile ordinal as predictor variable.

BMI, Body Mass Index, MET, metabolic equivalent, Modified MEDAS, MEditerranean Diet Adherence Score excluding sweetened drinks and pastries.
Table 2. Odds ratios (95% Confidence Interval) for the association of daily intake of added sugars with frailty and its components

<table>
<thead>
<tr>
<th>Added sugars (g)</th>
<th>Tertile 1 (Ref)</th>
<th>Tertile 2</th>
<th>Tertile 3</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frailty, n/N</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>1.00</td>
<td>1.64</td>
<td>1.75</td>
<td>0.019</td>
</tr>
<tr>
<td></td>
<td>(1.04,2.61)</td>
<td>(1.11,2.81)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td>1.00</td>
<td>2.19</td>
<td>2.48</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>(1.35,3.60)</td>
<td>(1.49,4.19)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 3</td>
<td>1.00</td>
<td>2.12</td>
<td>2.29</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>(1.30,3.49)</td>
<td>(1.37,3.90)</td>
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<td></td>
</tr>
<tr>
<td>Model 4</td>
<td>1.00</td>
<td>2.10</td>
<td>2.27</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>(1.28,3.50)</td>
<td>(1.34,3.90)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>1.00</td>
<td>1.11</td>
<td>1.07</td>
<td>0.770</td>
</tr>
<tr>
<td></td>
<td>(0.72,1.73)</td>
<td>(0.66,1.73)</td>
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<td>1.10</td>
<td>1.04</td>
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<td>(0.64,1.70)</td>
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<tr>
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<td>1.13</td>
<td>1.50</td>
<td>0.047</td>
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<td>(0.76,1.68)</td>
<td>(1.00,2.26)</td>
<td></td>
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<td>1.12</td>
<td>1.54</td>
<td>0.026</td>
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<td>(0.77,1.64)</td>
<td>(1.05,2.27)</td>
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<td>1.13</td>
<td>1.50</td>
<td>0.047</td>
</tr>
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<td>(0.76,1.68)</td>
<td>(1.00,2.26)</td>
<td></td>
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<td>1.10</td>
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<td>(0.73,1.66)</td>
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<td>Unintentional weight loss, n/N</td>
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<tr>
<td>Model 2</td>
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<td>1.54</td>
<td>1.93</td>
<td>0.024</td>
</tr>
<tr>
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<td>(0.89,2.70)</td>
<td>(1.10,3.46)</td>
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<td>1.05</td>
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<td></td>
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<td>(0.76,1.43)</td>
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<td>1.00</td>
<td>0.987</td>
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<tr>
<td></td>
<td>(0.83,1.49)</td>
<td>(0.72,1.38)</td>
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</table>

n/N, number of cases/number at risk.

Odds ratios and 95% confidence interval were estimated with logistic regression models with different levels of adjustment. For frailty, participants without it were considered at risk while for frailty components, only robust participants were considered at risk.

Model 1 was adjusted for age, sex, and education;
Model 2 was additionally adjusted for smoking status, body mass index, energy intake, and comorbidities;
Model 3 was additionally adjusted for MEDAS score (excluding sweetened drinks and pastries);
Model 4 was additionally adjusted for time spent watching TV and leisure-time physical activity.

Trend was calculated with the tertile ordinal as a continuous variable.
Table 3. Additional analyses: Odds ratios (95% Confidence Interval) for the association with frailty of daily intake of sugars naturally appearing in foods, and of daily intake of foods (total amount) classified as having added sugars

<table>
<thead>
<tr>
<th>Naturally appearing sugars (g)</th>
<th>P-trend</th>
<th>Food containing added sugars (g)</th>
<th>P-trend</th>
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<tbody>
<tr>
<td>Tertile 1</td>
<td>Tertile 2</td>
<td>Tertile 3</td>
<td>Tertile 1</td>
</tr>
<tr>
<td>Frailty, n/N</td>
<td></td>
<td></td>
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<tr>
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<td>1.01</td>
<td>0.54</td>
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<tr>
<td>(Ref)</td>
<td>(0.67,1.52)</td>
<td>(0.33,0.86)</td>
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<td>0.53</td>
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<tr>
<td>(Ref)</td>
<td>(0.66,1.56)</td>
<td>(0.32,0.88)</td>
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<td>0.63</td>
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<td>(Ref)</td>
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<td>(0.36,1.06)</td>
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<td>1.10</td>
<td>0.66</td>
</tr>
<tr>
<td>(Ref)</td>
<td>(0.70,1.71)</td>
<td>(0.38,1.13)</td>
<td></td>
</tr>
</tbody>
</table>

n/N, number of cases/number at risk.
Odds ratios and 95% confidence interval were estimated with logistic regression models with different levels of adjustment.

Model 1 was adjusted for age, sex, and education;
Model 2 was additionally adjusted for smoking status, body mass index, energy intake, and comorbidities;
Model 3 was additionally adjusted for MEDAS score (excluding sweetened drinks and pastries);
Model 4 was additionally adjusted for time spent watching TV and leisure-time physical activity.

Trend was calculated with the tertile ordinal as a continuous variable.

Naturally appearing sugars were calculated as the difference between total sugars and added sugars.
Food containing added sugars summed grams of foods belonging to the food groups specified in the methods section as containing added sugars.
Figure legends

Figure 1. Odds ratios for frailty for participants in the highest vs. the lowest consumption group of added sugars from specific food sources and for participants in the highest vs. the lowest added sugars consumption group stratified by diabetes and by body mass index.

Models were adjusted for age, sex, education, smoking status, body mass index, energy intake, and comorbidities, except diabetes in the stratified analyses. The lines depict the 95% confidence interval. An interaction model for obesity showed that the association differed with statistical significance between obese and non-obese participants (p=0.028).