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Prospective study of changes in sugar-sweetened beverages consumption and incidence of metabolic syndrome and its components

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Keywords: sugar-sweetened beverages; metabolic syndrome; cohort; prospective;

Acronyms: MS: metabolic syndrome**;** SSB: sugared-sweetened beverages**;** IDF: International Diabetes Federation**;** AHA/NHLBI: America Heart Association/ National Heart, Lung, and Blood Institute**;** aOR: adjusted odds ratio**;** CI: confidence interval**;** SUN: Seguimiento Universidad de Navarra. Follow-up University of Navarra**;** Q6: questionnaire after 6 years of follow-up**;** Q0: baseline questionnaire**;** BMI: body mass index**;** FFQ: food frequency questionnaire**;**TG: triglycerides

Abstract:

Background and aims: The incidence of the metabolic syndrome (MS) is increasing and lifestyle behaviours may play a role in its development. Our aim was to assess prospectively the association between changes in sugar-sweetened beverages (SSB) consumption and the incidence of the MS and its components in a Spanish cohort of university graduates.

Methods and results: We included 8,157 participants initially free of MS and followed-up during ≥ 6 years. SSB consumption was collected through a food frequency questionnaire previously validated in Spain. Change in SSB consumption was calculated as the difference between SSB consumption at 6-year follow-up and the baseline consumption. The MS was defined according to the International Diabetes Federation and the American Heart Association/ National Heart, Lung, and Blood Institute new definition of MS that had harmonized previous definitions. Logistic regression models were used to adjust for potential confounders. We observed 361 incident cases of MS. Participants in the highest quintile of increase in SSB consumption presented a significantly higher risk of developing MS (adjusted odds ratio (aOR):2.2; 95% confidence interval (CI):1.4-3.4; p for trend 0.006). Similarly, they presented a significantly higher risk of developing high blood pressure (aOR:1.7; 95% CI:1.4-2.0), central obesity (aOR:1.9; 95% CI: 1.6-2.2); hypertriglyceridemia (aOR:1.6; 95% CI:1.1-2.2) or impaired fasting glucose (aOR:1.4; 95% CI:1.1-1.9).

Conclusions: An increase in SSB consumption was associated with higher risk of developing the MS and other metabolic disorders after 6 years of follow-up.

Introduction:

The prevalence of MS in developed countries affects around 25% of the population [1] and its incidence has increased over the last years. However, there is an heterogeneous distribution of MS across the different regions [2,3] that may be associated with lifestyles habits.

Food habits are an important factor determining MS, but not only food is a source of nutrients in the diet. Drinks can be a major source of carbohydrates and some of them contain sugar, other sweeteners, alcohol or caffeine [4].

Several reports indicated an increasing consumption of SSB among children and adults over the past 3 decades [5] and have linked the rising consumption of SSB to an increase in obesity and diabetes mellitus among children and adolescents [6] and to the development of hypertension and cardiovascular disease [7] in adults.

Furthermore, SSB consumption have been linked to an increase in serum triglycerides levels [8] and a decrease in serum HDL-cholesterol [9].

Regarding the MS, only three prospective studies have shown a link between SSB consumption and the risk of developing the complete MS [10-12]. All of them were summarized in a meta-analysis [13]. However, none of these studies have been conducted in the context of a Mediterranean dietary pattern where the average consumption of SSB is very low in comparison with the United States or North European countries. Additionally, all previous studies only assessed baseline consumption but not changes in SSB consumption during follow-up.

The aim of our study was to assess the association between changes in SSB consumption and the incidence of MS and its components in a cohort of Spanish university graduates.

Methods:

Study Population

The SUN (Seguimiento Universidad de Navarra) Project is a dynamic prospective cohort conducted in Spain with permanently open recruitment and whose participants are university graduates who are contacted and followed-up using mailed or web-based questionnaires. A description of the study methods has been previously published [14,15]. Briefly, beginning in December 1999, all graduates of the University of Navarra, registered nurses from some Spanish provinces, and university graduates from other colleges and associations received a mailed questionnaire and a letter of invitation to participate in the SUN Project. A response to the initial questionnaire was considered as informed consent to participate in the study. The project protocol was approved by the Institutional Review Board of the University of Navarra.

After baseline assessment, participants received follow-up questionnaires every two years that contained a wide variety of questions on diet, lifestyle, risk factors and medical conditions.

For our MS study, a subsample of the cohort was selected. To warrant a minimum follow-up of 6 years, we included only those participants who had completed questionnaires up to 6 years of follow-up.14716 SUN participants responded to the baseline questionnaire before September 2004. Among them, 3,728 participants were excluded because they have one or more criteria for the MS. 1139 with extreme caloric intake (<800kcal/d for men, <500 kcal/d for women, >4000 kcal/d for men, or >3500 kcal/d for women) were also excluded. Among the remaining, 1,136 participants answered some follow-up questionnaire but not the 6-year or 8-year follow-up questionnaire and 556 did not answered any follow-up questionnaires. Therefore, 8,157 participants were included in the final analyses (Figure 1).

Definition and components of the MS

We defined MS according to the International Diabetes Federation (IDF) and American Heart Association/National Heart, Lung, and Blood Institute new definition of MS that has harmonized previous definitions [16]. According to this definition, the diagnosis of MS needs the presence of 3 of any of this 5 components: elevated waist circumference according to the population and country specific definition (in our study:≥94 cm in males and ≥80 cm in females), elevated triglycerides (≥150 mg/dL) or presence of drug treatment for elevated triglycerides, reduced HDL-cholesterol (<40 mg/dL in males and <50 mg/dL in females) or presence of drug treatment for reduced HDL-cholesterol, elevated blood pressure (systolic ≥130 and/or diastolic ≥85 mm Hg) or presence of drug treatment for hypertension and elevated fasting glucose ≥100 mg/dL or drug treatment of elevated glucose.

In the 6-year and 8-year follow-up questionnaires, self-reported data about these specific MS criteria were collected. A measure tape was sent to all participants with these questionnaires including an explanation about how to measure their own waist. The validation of the self-reported data of the criteria needed to classify participants into MS was assessed in a two different subsamples of the cohort finding significant intraclass correlation coefficients between 0.5 to 0.9 ($p<0.001$) depending on the MS criteria [17] and a proportion of confirmed MS of 91.2% (95%CI: 80.7-97.1) and non-confirmed MS of 92.2% (95%CI: 85.1-96.4) [18].

Incident cases of MS were defined as those participants who did not have MS at baseline and reported criteria of MS in either the 6 or 8-year follow-up questionnaire.

Assessment of dietary and non-dietary exposures.

Dietary habits at baseline were assessed using a semi-quantitative food-frequency questionnaire (FFQ) with 136 items, previously validated in Spain and recently re-evaluated [19]. We defined a Mediterranean dietary pattern "a priori" using the score proposed by Trichopoulou [20]. The baseline questionnaire also included different questions related to lifestyle, sociodemographic variables (sex, age and years of university education) anthropometric data, health-related habits (e.g., smoking status, alcohol consumption, and physical activity), and medical history information (medication use, cholesterol level and blood pressure). The reproducibility and validity of the self-reported anthropometrics [21], physical activity questionnaire [22], and the diagnosis of hypertension [23] were assessed in sub-samples of the cohort.

Assessment of SSB consumption

The change in SSB consumption was calculated as the difference between SSB drink consumption in the 6-year follow up (Q6) questionnaire and the baseline consumption (Q0). This difference in consumption was classified in quintiles of change (quintile 1 for those participants who decreased the most their consumption and quintile 5 for those participants who increased the most their consumption), considering the first quintile as the reference category.

Statistical analysis

The cumulative incidence of MS was computed for each quintile of change in SSB consumption. To avoid the confounding effect of other variables simultaneously associated with the outcome and the main exposure, we used non-conditional logistic regression models.

We also assessed the association between quintiles of change of SSB consumption and each criteria for the MS. Linear trend tests were calculated using the median change of SSB consumption of each quintile and introducing this new variable as a continuous one in the models.

We evaluated effect modification through likelihood ratio tests for the product-term introduced in fully-adjusted models.

As secondary analyses we assessed the association between changes in artificially SSB consumption, as well as baseline SSB consumption and the incidence of the MS.

P values were based on two-tailed test and p values less than 0.05 were considered statistically significant.

As sensitivity analyses, we estimated the full-adjusted odds ratios for the fifth quintile of change in SSB after modifying several assumptions: a) using ATP-III criteria for MS, b) using IDF criteria for MS, c) adopting different limits for allowable total energy intake, d) excluding participants with diabetes, cancer or cardiovascular disease at baseline. In the same line, we calculated the hazard ratio for the fifth quintile of change in SSB using Cox regression models instead of ORs calculated by non-conditional logistic regression.

Results

The baseline characteristics of patients lost to follow-up did not substantially differ from those who completed the follow-up (data not shown). The characteristics of participants according to their quintiles of change in SSB consumption are presented in Table 1. Those participants who increased their SSB consumption the most were more likely to be men and presented a lower adherence to the Mediterranean dietary pattern.

Incidence of MS

During a median follow-up of 6 years, we identified 361 incident cases of MS among 8,157 participants initially free of MS.

Table 2 shows the incidence of MS according to quintiles of change in SSB consumption. After adjusting for age and sex, participants in the highest quintile of increase in SSB presented a significant greater risk of developing MS (OR: 2.2; 95%CI: 1.4-3.4; p for trend 0.003) compared with those in the lowest quintile. This association persisted (OR: 2.2; 95%CI: 1.4-3.4; p for trend 0.006) even after adjustment for potential confounding factors (baseline BMI, smoking, physical activity, alcohol intake, total energy intake, baseline SSB consumption and adherence to the Mediterranean dietary pattern). When we repeated the analyses using servings (1 can=330 ml) of change, those participants who increased their consumption of SSB during follow-up in more than one serving per week increased their risk of developing MS in 101% (adjusted OR: 2.01; 95%CI: 1.14-3.55) in comparison with those participants who decreased in one serving per week or more their consumption. We did not observe any significant interaction between changes in SSB drinks consumption and sex (p: 0.45) or age (p: 0.86).

In the SUN cohort the consumption of SD was very low. Only 405 participants included in the analyses (4.9%) consumed one or more servings per day at baseline. When we evaluated as a secondary analysis the baseline SSB consumption as exposure instead of evaluating change in consumption, we did not find any significant association for incidence of MS (data not shown). The consumption of non-sugared SD was even lower among the SUN participants. 75% of them never consumed non-sugared SD, and only 2.8% consumed one or more servings per day. Similarly, we did not find any association between baseline non-sugared SD consumption and incidence of MS.

As a sensitivity analysis we assessed the association between changes in SSB consumption between 6 years of follow-up and baseline (Q6-Q0) and the incidence of MS in the 8-year follow-up. We only identified 107 incident cases. We did not observe any significant association.

The association between an increase in the SSB consumption and the risk of MS was robust and remained statistically significant in all but one sensitivity analyses (Table 4). The only exception was the p for trend when we considered the definition of MS according to the ATP-III criteria, a more strict definition. By contrast, when we conducted Cox regression models the hazard ratio for the fifth quintile of change in SSB was 1.9 (95%CI: 1.2-3.0; p for trend: 0.032) in comparison with the first quintile of change in SSB, therefore the association remained statistically significant.

Incidence of individual components of MS

Table 3 shows the incidence of MS criteria during follow-up according to quintiles of change in SSB consumption. Increases in SSB consumption during follow-up were associated with higher risk of developing high blood pressure, central obesity, hypertriglyceridemia, and impaired fasting glucose. After adjusting for potential confounders, participants in the highest quintile of increase in SSB consumption presented a significant higher risk of developing the blood pressure criteria (OR: 1.7; 95%CI: 1.4-2.0; p for trend<0.001), the waist circumference criteria (OR: 1.9; 95%CI: 1.6-2.2; p for trend<0.001), the TG criteria (OR: 1.6; 95%CI: 1.1-2.2; p for trend: 0.021) and fasting glucose criteria (OR: 1.4; 95%CI: 1.1-1.9; p for trend: 0.028) in comparison with those who decreased their consumption.

As secondary analyses, when we assessed the association between baseline quintiles of SSB consumption and incidence of each criteria of the MS, we found that a higher

baseline consumption of SSB was significantly associated with a higher risk of developing the waist circumference criteria during follow-up (adjusted OR: 1.18; 95%CI: 1.01-1.37). We did not find any significant association for other criteria.

Discussion

In this prospective study of young-middle-aged (mean age: 36 years old) free-living Mediterranean university graduates, a small increase in SSB consumption during follow up was associated with higher risk of developing MS and with higher risk of developing four of its five components: high blood pressure, central obesity, hypertriglyceridemia, or impaired fasting glucose.

Among 8,157 participants included in this study, we observed 361 incident cases of MS. This incidence of MS was lower than those described in the general Spanish population[7] as it is to be expected in a cohort of young-middle aged adults, with a low baseline BMI and a high educational level.

Our study is partially consistent with previous results found in three prospective cohorts [10-12] that found that SSB consumption was a risk factor for developing MS. However, we did not find a direct association between baseline SSB consumption and higher risk of developing MS but only for changes in consumption during follow up. There are some differences between those studies and our cohort that may explain these results. First, in the SUN Project we recruited Spanish university graduates, in the Framingham Offspring Study the participants were white Americans [10], in the MESA study the participants were Caucasian, African American, Hispanic, and Chinese [11] and in the ARIC study the cohort was formed by white and black American [12]. Second, our cohort is younger than the other cohorts. Third, in the SUN cohort the incidence of MS was 4.4% during 6 years of follow-up, but it was 18.7% after 4-year

follow-up in the Framingham Offspring Study, 12.8% in the MESA study after 5-year follow-up, and 39.8% after 9-year follow-up in the ARIC study. Finally, the distribution of baseline SSB consumption was very different too, and while in the SUN cohort only 1.1% of participants consumed two or more servings of SSB per day, in the Framingham Offspring Study this percentage was 13.8%, in the MESA study 13.6% of participants and in the ARIC study a 33% of participants consumed a median of 1 serving per day.

Heidemann, et al. [24] found that a dietary pattern high in refined grains, processed meat, high-sugar beverages, beer, sweets and cakes, snacks and butter was associated with higher prevalence of abdominal obesity, hypertension, hypertriglyceridemia, and MS in a cross-sectional study of a nationally representative sample of German adults. Interestingly, our results are in accordance with recent results from the CARDIA cohort [25] reporting that baseline SSB consumption was associated with several components of the MS but not with the incidence of the MS as a whole.

In spite of the consumption of SSB was low among our participants, we found that a relatively small increase in SSB consumption (more than one serving –330 ml- per week) was associated with a significantly higher risk of developing MS and its conditions in comparison with participants who decreased their consumption more than one serving per week. In fact, changes from repeated measurements of dietary habits controlling for baseline exposure are useful in assessing the effects of changes in dietary intakes over time on the development of chronic diseases such as MS in a cohort study [26]. This is a methodological strength of our assessment.

There are different mechanisms that can explain the higher risk of MS associated with greater SSB consumption. Larger consumption of added sweeteners such as high fructose corn syrup can lead to weight gain, insulin resistance [27], a lowering of HDL-

cholesterol [9], and an increase in triglyceride levels [8]. Consumption of liquids is associated with a lesser degree of dietary compensation (the adjustment in energy intake made in subsequent meals in response to food intake) [28].

Individuals with greater intake of SSB have also a dietary pattern characterized by lower consumption of fiber and dairy products, and a more sedentary lifestyle [24]. Nonetheless, in the present study, we adjusted for total energy intake, smoking, physical activity, alcohol intake and adherence to a Mediterranean dietary pattern in multivariable analyses and still we observed a significant association between changes in SSB consumption and the risk of developing MS and its component criteria. It is conceivable, though, that because of the observational nature of our study, we cannot completely rule out residual confounding caused by lifestyle factors not adjusted for in the present analyses.

Our participants are not representative of the general Spanish population. We restricted our cohort to highly educated participants to obtain a good quality of self-reported information, to improve the retention rate and to prevent confounding by educational level, and therefore, by socio-economic status [29].

Inherent to the nutritional epidemiology methods, we have to point out the possibility of some degree of misclassification in the dietary assessment. However, we have used a FFQ previously validated in Spain [20]. In addition, we would expect this misclassification to be non-differential and, therefore, it may drive the association toward the null value.

Our study has important strengths such as the repeated measurement of the dietary exposure, the large number of participants, the long follow-up period, the previously published validation studies assessing the validity of our methods, the ability to control

for an important number of potential confounders, and the good quality of the self-reported data of our highly-educated volunteers.

In summary, even a relatively small increase in SSB consumption was associated with higher risk of developing MS and metabolic disorders in a cohort of young-middle-aged Spanish university graduates. However, since the incidence of MS was low, further studies should be conducted to confirm these findings.

Acknowledgements

The authors thank the collaboration of the participants in the SUN Study.

We thank to other members of the SUN Group: Alonso A, Balaguer A, Benito S, de Irala J, de la Fuente-Arrillaga C, Delgado-Rodriguez M, Guillén-Grima F, Krafka J, López del Burgo C, Llorca J, Marti A, Martinez JA, Nuñez-Cordoba JM, Pimenta AM, Sanchez D, Sánchez-Villegas A, Serrano-Martinez M, Toledo E, Vazquez Z.

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Table 1. Baseline characteristics of participants according to quintiles (Q) of change in Sugar-Sweetened Beverages (SSB) Consumption.

	Q 1	*Q 2*	*Q 3*	*Q 4*	*Q 5*
N	1890	1334	1796	1626	1511
Change in SSB (ml/day)	≤-28.57	-28.58 to <0	0	>0 to 33.81	>33.81
Age (years)	31.4 (8.4)	34.9 (9.7)	41.2 (11.5)	36.7 (10.1)	34.5 (10.1)
Women (%)	65.6	71.4	74.0	64.1	51.4
Alcohol consumption (g/d)	6.4 (8.2)	4.9 (7.7)	5.7 (9.5)	5.1 (6.9)	6.8 (8.9)
Baseline SSB consumption (ml/d)	109.6 (119.8)	26.53 (35.1)	0 (NA)	13.5 (9.9)	58.6 (80.6)
Baseline BMI (kg/m^2)	22.5 (2.8)	22.5 (2.7)	22.7 (2.7)	22.6 (2.7)	23.0 (2.9)
Leisure-time physical activity (METs-h/week)	19.7 (2.7)	19.0 (20.4)	20.4 (21.4)	20.8 (23.4)	20.3 (23.8)
Total energy intake (kcal/day)	2472.3 (604.6)	2367.8 (575.9)	2222.1 (606.8)	2331.2 (585.1)	2464.1 (633.6)
Mediterranean diet adherence[a]	3.8 (1.7)	4.0 (1.8)	4.4 (1.8)	4.0 (1.8)	1.7 (1.7)
Current smokers (%)	30.7	23.1	18.9	20.0	27.2
Former smokers (%)	19.6	24.4	33.8	26.1	23.6
Snacking between meals (%)	43.9	35.1	29.5	31.0	36.0
Television watching (h/week)	5.6 (4.3)	5.8 (4.3)	6.0 (4.4)	5.9 (4.4)	5.9 (4.4)

Continuous variables are expressed as means and (standard deviations). Categorical variables are expressed as percentages.

NA: Not applicable

[a]Score proposed by Trichopoulou[20]

Q1-Q5: quintiles of change in SSB consumption

Table 2. Odds Ratios (OR) (95% CI) of incident MS according to Quintiles (Q) of change in Sugar-Sweetened Beverages (SSB) Consumption. The SUN Project 1999-2011.

	Q1	*Q2*	*Q3*	*Q4*	*Q5*	p for trend
n	1890	1334	1796	1626	1511	
Changes (servings[a]/wk; median)	-1.35	-0.3	0	+0.4	+2.4	
Changes (ml/day)	≤-28.57	-28.58 to <0	0	>0 to 33.81	>33.81	
MS incidence	33 (1.7%)	59 (4.4%)	105 (5.8%)	83 (5.1%)	81 (5.4%)	
Crude OR	1 (Ref.)	2.6 (1.7-4.0)	3.5 (2.3-5.2)	3.0 (2.0-4.6)	3.2 (2.1-4.8)	<0.001
Age-sex adjusted OR	1 (Ref.)	2.2 (1.4-3.5)	1.9 (1.3-3.0)	2.2 (1.4-3.3)	2.2 (1.4-3.4)	0.003
Multivariate[b] adjusted OR	1 (Ref.)	2.2 (1.4-3.6)	1.9 (1.2-3.0)	2.2 (1.4-3.5)	2.2 (1.4-3.4)	0.006

[a]1 serving: 330 ml

[b]Adjusted for age, sex, baseline BMI, smoking, physical activity, alcohol intake, basal soft drink intake, total energy intake and adherence to the Mediterranean dietary pattern (Score proposed by Trichopoulou[20]).

Q1-Q5: quintiles of change in SSB consumption.

Table 3. Odds Ratios (OR) (95% CI) of incident MS criteria according to Quintiles (Q) of change in Sugar-Sweetened Beverages (SSB) Consumption. The SUN Project 1999-2011.

	Q1	*Q2*	*Q3*	*Q4*	*Q5*	p for trend
N	1890	1334	1796	1626	1511	
Changes (servings[a]/wk; median)	-1.35	-0.3	0	+0.4	+2.4	
Changes (ml/day)	≤-28.57	-28.58 to <0	0	0 to 33.81	>33.81	
Blood pressure criteria						
Incident cases	227	235	363	311	328	
Crude OR	1 (Ref.)	1.6 (1.3-1.9)	1.9 (1.5-2.2)	1.7 (1.4-2.1)	2 (1.7-2.4)	<0.001
Age-sex adjusted OR	1 (Ref.)	1.3 (1.1-1.7)	1.2 (0.9-1.4)	1.3 (1.1-1.5)	1.6 (1.3-1.9)	<0.001
Multivariate[b] adjusted OR	1 (Ref.)	1.5 (1.2-1.9)	1.3 (1.1-1.6)	1.4 (1.2-1.8)	1.7 (1.4-2.0)	<0.001
Waist criteria						
Incident cases	688	550	749	771	770	
Crude OR	1 (Ref.)	1.2 (1.1-1.4)	1.2 (1.1-1.4)	1.6 (1.4-1.8)	1.8 (1.6-2.1)	<0.001
Age-sex adjusted OR	1 (Ref.)	1.1 (0.9-1.2)	0.8 (0.7-1.0)	1.3 (1.1-1.5)	1.6 (1.4-1.9)	<0.001
Multivariate[b] adjusted OR	1 (Ref.)	1.2 (1.0-1.5)	1.0 (0.8-1.2)	1.7 (1.4-2.0)	1.9 (1.6-2.2)	<0.001

Table 3 (cont.). Odds Ratios (OR) (95% CI) of incident MS criteria according to Quintiles (Q) of change in Sugar-Sweetened Beverages (SSB) Consumption. The SUN Project 1999-2011.

	Q1	*Q2*	*Q3*	*Q4*	*Q5*	p for trend
HDL criteria						
Incident cases	86	68	89	97	74	
Crude OR	1 (Ref.)	1.1 (0.8-1.6)	1.1 (0.8-1.5)	1.3 (1.0-1.8)	1.1 (0.8-1.5)	0.6
Age-sex adjusted OR	1 (Ref.)	1.0 (0.7-1.5)	0.9 (0.7-1.3)	1.2 (0.9-1.7)	1.1 (0.8-1.5)	0.6
Multivariate[b] adjusted OR	1 (Ref.)	1.1 (0.8-1.6)	1.0 (0.7-1.5)	1.3 (1.0-1.9)	1.1 (0.8-1.5)	0.5
Triglycerides criteria						
Incident cases	68	75	109	91	98	
Crude OR	1 (Ref.)	1.6 (1.1-2.2)	1.7 (1.3-2.4)	1.6 (1.1-2.2)	1.9 (1.3-2.5)	0.001
Age-sex adjusted OR	1 (Ref.)	1.4 (1.0-2.0)	1.2 (0.9-1.7)	1.3 (0.9-1.8)	1.5 (1.1-2.1)	0.018
Multivariate[b] adjusted OR	1 (Ref.)	1.5 (1.1-2.2)	1.3 (0.9-1.9)	1.4 (1.0-1.9)	1.6 (1.1-2.2)	0.021
Fasting glucose criteria						
Incident cases	105	101	198	161	146	
Crude OR	1 (Ref.)	1.4 (1.1-1.8)	2.1 (1.6-2.7)	1.9 (1.4-2.4)	1.8 (1.4-2.4)	<0.001
Age-sex adjusted OR	1 (Ref.)	1.2 (0.9-1.6)	1.3 (1.0-1.7)	1.4 (1.1-1.8)	1.4 (1.1-1.8)	0.022
Multivariate[b] adjusted OR	1 (Ref.)	1.3 (0.9-1.7)	1.4 (1.0-1.9)	1.5 (1.1-2.0)	1.4 (1.1-19)	0.028

[a]1 serving: 330 ml

[b]Adjusted for age, sex, baseline BMI, smoking, physical activity, alcohol intake, basal soft drink intake, total energy intake and adherence to the Mediterranean dietary pattern (Score proposed by Trichopoulou[20]).

Q1-Q5: quintiles of change in SSB consumption.

Table 4. Sensitivity analyses. Multivariate-adjusted odds ratio (OR) and 95% confidence intervals (95%CI) of metabolic syndrome (MS) for the highest quintile of change (Q5) in Sugar-Sweetened Beverages (SSB) Consumption taking as the reference category the first quintile (Q1) of change in SSB under several assumptions. The SUN Project 1999-2011.

	n	MS (%)	OR (95% CI) [a]	p for trend
Using ATP-III criteria for MS	8157	214 (2.62%)	1.74 (1.00-3.02)	0.172
Using IDF criteria for MS	8157	338 (4.14%)	2.22 (1.36-3.58)	0.008
Energy limits: percentiles 5 to 95	8234	356 (4.00%)	2.35 (1.48-3.74)	0.008
Energy limits: percentiles 1 to 99	8906	338 (4.10%)	2.30 (1.47-3.60)	0.005
Excluding participants with diabetes, cancer, or cardiovascular disease at baseline.	7996	347 (4.34%)	2.12 (1.29-3.40)	0.010

[a]Adjusted for age, sex, baseline BMI, smoking, physical activity, alcohol intake, basal soft drink intake, total energy intake and adherence to the Mediterranean dietary pattern (Score proposed by Trichopoulou et al[20]).