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ORIGINAL CONTRIBUTION

Impact of substituting added sugar in carbonated soft drinks by intense sweeteners in young adults in the Netherlands: example of a benefit–risk approach

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Abstract
Purpose Substituting added sugar in carbonated soft drinks with intense sweeteners may have potential beneficial, but also adverse health effects. This study assessed the benefits and risks associated with substituting added sugar in carbonated soft drinks with intense sweeteners in young adults in the Netherlands.
Methods A tiered approach was used analogous to the risk assessment paradigm, consisting of benefit and hazard identification, exposure assessment and finally benefit and risk characterization and comparison. Two extreme scenarios were compared in which all carbonated soft drinks were sweetened with either intense sweeteners or added sugar. National food consumption survey data were used, and intake of added sugar and intense sweeteners was calculated using the food composition table or analytical data for sweetener content.
Results Reduction in dental caries and body weight were identified as benefits of substituting sugar. The mean difference in total energy intake between the scenarios was 542 kJ per day in men and 357 kJ per day in women, under the assumption that no compensation takes place. In the 100% sweetener scenario, the average BMI decreased 1.7 kg/m^2 in men and 1.3 kg/m^2 in women when compared to the 100% sugar scenario. Risks are negligible, as the intake of intense sweeteners remains below the ADI in the substitution scenario.
Conclusions Substitution of added sugar by intense sweeteners in carbonated soft drinks has beneficial effects on BMI and the reduction in dental caries, and does not seem to have adverse health effects in young adults, given the available knowledge and assumptions made.

Keywords Benefit–risk assessment · Intense sweeteners · Added sugar · Carbonated soft drinks

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Introduction

Sugar-sweetened beverages have been linked to the obesity epidemic [38]. Their intake is not completely compensated for [8, 9], as liquid calories have less satiating effects than solid foods.

Thus, soft drink consumption may facilitate passive over-consumption, leading to higher energy intakes and ultimately weight gain [38].

Considering the increasing prevalence of overweight and obesity, consumption of artificially sweetened instead of sugar-sweetened soft drinks may be beneficial by reducing energy intake. On the other hand, health risks due to a high intake of artificial sweeteners cannot be ruled out a priori.

Previous European studies have assessed the intake of intense sweeteners from soft drinks and simulated worst-case scenarios, substituting sugar-sweetened beverages with intense sweetened beverages [2, 27, 32]. For example, in Italy the intake of artificial sweeteners in adolescents did not exceed the acceptable daily intake (ADI) in worst-case scenarios in subjects with a high intake of artificially sweetened soft drinks and table-top sweeteners [2]. These studies focused on risk assessment, while leaving the beneficial health effects of reducing added sugar intake aside.

In Norway, a benefit–risk assessment was performed examining the replacement of added sugar by intense sweeteners in beverages. In their substitution scenario, all sugar-containing beverages were replaced with beverages containing intense sweeteners [26]. A substantial reduction in total added sugar intake was estimated, particularly in adolescents, and no exceeding of the ADIs from increased intense sweetener intake was observed, except for acesulfame-K in young children. The aforementioned papers did not quantify the benefits or risks, though.

So far, no consensus has been reached on the general principles of a quantitative benefit–risk assessment. The Dutch National Institute for Public Health and the Environment (RIVM) in corporation with the Dutch Food Safety Authority developed a tiered approach for benefit–risk analyses, following the classical risk assessment paradigm [20]. A comparable tiered approach is developed in the European Benefit-Risk Analysis of Foods (BRAFO) project (www.brafo.eu) and also the European Food Safety Authority (EFSA) considers a similar method [13]. The RIVM developed a decision tree incorporating several stopping criteria, guiding whether the available information is sufficient to answer the benefit–risk question. In this study, we aim to assess the potential benefits and risks associated with substituting added sugar in carbonated soft drinks by intense sweeteners (acesulfame-K, aspartame, cyclamate and saccharin) in young adults aged 19–30 in the Netherlands. Consequently, we examine whether the developed decision tree is a usable tool to perform a benefit–risk assessment.

Benefit–risk assessment following the tiered approach

The benefit–risk assessment was performed using the structured methodology following the tiered approach of Fransen et al. [20]. In short, the methodology distinguishes the following steps to perform a benefit–risk assessment after the benefit–risk question has been defined: (1) benefit and hazard identification; (2) exposure assessment; (3) comparison of intake with guidelines; (4) benefit and risk characterization; and (5) integration into a common measure. The decision tree includes several decision moments, which enables informed choices when to continue or discontinue with the benefit–risk assessment. In the present paper, the methods and results for each tier are presented together, as the outcome of each tier will influence the continuation of the decision tree.

Benefit and hazard identification

Methods

First, an extensive computerized literature search, for both the beneficial and hazardous health effects of added sugar and intense sweeteners, was done. Pubmed was searched until October 2008 using the following terms: added sugar, sugar-sweetened beverages, sugar-sweetened soft drinks, soda, intense sweetener, artificial sweetener, aspartame, acesulfame-K, cyclamate, cyclohexylamine and saccharin. The search was limited to papers written in English or Dutch. Furthermore, for added sugar, the search was restricted to meta-analyses and systematic reviews of epidemiological studies. Studies published after the most recent reviews were used complementary to the meta-analyses and reviews. For intense sweeteners, studies were selected examining associations between individual intense sweeteners and health effects in humans. Due to the insufficient number of human studies, animal studies were screened for other potential health hazards as well as the toxicological databases of World Health Organisation (WHO)/Joint Expert Committee on Food Additives (JECFA) and EFSA/EU Scientific Committee on Foods where derived ADIs are described [6, 14, 63].

The selected studies were classified according to the WHO criteria for strength of evidence [62], as ‘convincing’, ‘probable’, ‘possible’ or ‘insufficient’. To meet the inclusion criteria for a benefit–risk assessment, health effects regarded as having sufficient evidence should be classified as ‘convincing’ or ‘probable’. Health effects can be rated as ‘convincing’ when the evidence is substantiated by multiple randomized controlled trials or prospective cohort studies of sufficient size, duration and quality showing consistent effects and ‘probable’ when the evidence is fairly consistent, but there are some shortcomings in the available evidence [62].

The strength of evidence of the risks is based on animal experiments and therefore ranks no higher than ‘possible’ according to the WHO criteria. However, as risks are a general concept in toxicological risk assessment, the risks were included as well.

Results

An overview of health effects related to added sugar and intense sweetener intake can be found in Table 1.

Added sugar The intake of added sugar, and particularly the frequency of intake, is convincingly related to development of dental caries [62] and is probably related to development of overweight and obesity, especially when present in sugar-sweetened soft drinks [23, 38, 58, 60]. Several other diseases such as diabetes type 2, cancer, micronutrient deficiencies, osteoporosis and behavioural problems have been linked to added sugar intake, but recent reviews emphasize the inconsistency, lack of multiple studies and methodological problems affecting the strength of those associations [4, 10, 28, 39, 44, 47, 55].

Table 1 Identification of beneficial and hazardous health effects for the substitution of added sugars with intense sweeteners in carbonated soft drinks

Health effect of:	Level of evidence[a]	Target population	Summary of results	References
Reducing added sugar				
Beneficial				
Dental caries	Convincing	Total population	Results of several trials and longitudinal studies have shown a consistent association between mono- and disaccharides intake, intake frequency and dental caries	[62]
Overweight/obesity	Probable	Total population	Several longitudinal and intervention studies have examined the association between added sugar consumption and overweight. The majority of the studies show a positive association between sugar intake and overweight and obesity, especially in sugar-sweetened beverages. However, not all studies do show a consistent association It is hypothesized that added sugars in carbonated soft drinks facilitate passive over-consumption	[5, 12, 19, 30, 34, 38, 52, 54, 60]
Micronutrient deficiency	Insufficient[d]	Children/elderly	Longitudinal and cross sectional studies showed that an increased intake of sugar sweetened beverages is related to lower milk and calcium consumption, lower intakes of fruits and dietary fibre consumption, and a lower consumption of a variety of macronutrients. It is hypothesized that sugar-sweetened beverages intake is related to poorer dietary habits, although they may also stimulate people's appetite for other non-nutritious foods	[11, 34, 59]
Cancer	Insufficient	Total population	Sugar-sweetened beverages have been related to pancreatic cancer, as they may contribute to high glycemic load, which is a risk factor for pancreatic cancer. However, results from epidemiological studies are inconsistent	[3, 28, 31, 50]
Type II diabetes	Insufficient	Total population	A few epidemiological studies show that the intake of sugar-sweetened beverages is associated with an increased risk for development of type 2 diabetes in women. The pathway is by raising blood glucose levels and thereby causing insulin resistance	[52]
Osteoporosis			Several prospective studies have examined the association between soft drink consumption and impaired bone mineral content. However, results are conflicting. The pathway is not exactly known. It is hypothesized that beverages may replace milk in diets, have low pH values, contain phosphoric acid and caffeine, but also that soft drink consumption reflect an unhealthy lifestyle	[33, 57, 59, 61]
Behavioural problems	Insufficient	Total population/ children	Double-blind randomized controlled trials did not adversely influence behaviour. A recent study showed an association between sugar-sweetened beverage intake and mental health problems in adolescents	[35, 65]
Increasing intense sweetener				
Beneficial				
Weight loss	Possible	Total population	Some intervention studies show that consumption of artificially sweetened beverages resulted in lower energy intakes compared to sugar sweetened beverages. However, these are short-term effects and long-term effects should be established	[8, 43, 56, 60]

Table 1 continued

Health effect of:	Level of evidence[a]	Target population	Summary of results	References
Hazardous[b,c]				
Aspartame: Adverse effects on neurotransmitters and development of foetus during reproduction and gestation	Insufficient	Total population	Adverse effects on brain neurotransmitter levels and on pup development during reproduction and gestation have been observed in animal studies when very high doses of aspartame were given Consumption of aspartame has also been linked to other health effects, such as cancer, onset of headaches, migraine, hyperactivity and epilepsy, but the evidence is inconclusive The ADI was established at 40 mg/kg bw	[21, 22, 36, 37]
Cyclamate: Testicular atrophy	Insufficient	Fertile men	The intake of extreme high doses of *cyclamate* in rats showed that *cyclohexylamine* (the metabolite of cyclamate) induced testicular atrophy, which has influences on the testes' weight and the sperm production Only one study examined the effect of cyclohexylamine and fertility in men, but could not observe any effect Although cyclamate intake has been linked with bladder cancer, several studies could not confirm these findings. The ADI was established at 7 mg/kg bw	[46, 49, 53]
Saccharin: Undesired weight loss	Insufficient	Total population	The intake of saccharin in animals leads to undesired weight loss Two meta-analyses of case–control studies on the association between saccharin use and bladder cancer could not observe any association The ADI was established at 5 mg/kg bw	[18, 41, 64]

[a] The level of evidence is based on WHO/WCRF criteria for strength of evidence ("convincing", "probable", "possible" and "insufficient")

[b] The effects are based on lowest observed adverse effect level (LOAEL). It is possible that other effects occur at higher doses. An intake below ADI does not induce adverse health effects

[c] Acesulfame-K is not included in the present table; the hazardous health effects at exceeding ADI are unknown for acesulfame-K

[d] This association is classified as insufficient. An association between added sugar consumption causing higher energy intakes and micronutrient deficiencies for subjects with a low energy intake, such as children and elderly, is probable. However, in the present study, substitution of added sugar with intense sweeteners in carbonated soft drinks is not likely to reduce micronutrient deficiencies and therefore not relevant in the present benefit–risk assessment

Intense sweeteners All intense sweeteners provide a sweet taste without any or just a few calories and are therefore used to substitute added sugar in carbonated soft drinks.

Aspartame Human data on health effects of aspartame is scarce and inconsistent [37, 45]. In animals, adverse effects of aspartame after very high doses on brain neurotransmitter levels and on pup development during reproduction and gestation have been observed [37]. Based on these observations, the ADI was established at 40 mg/kg bw per day [15, 17].

Cyclamate Cyclamate is an intense sweetener that is metabolized into cyclohexylamine in the gastrointestinal tract, which is the toxicological component. Based on the formation of cyclohexylamine, the ADI was established at 7 mg/kg bw per day [49]. Studies in rats showed that cyclohexylamine produces testicular toxicity [7]. However, these observations were not confirmed in a human case–control study [53].

Acesulfame-K Animal studies do not show any potential carcinogenic or toxicological effect [48]. The no-observed effect level of acesulfame-K was 900 mg/kg bw in dogs, so the ADI was established at 9 mg/kg bw per day [48].

Saccharin Saccharin is a non-genotoxic bladder carcinogen in animal studies, but the effects are specific for rats and not for humans [29]. Several human studies have confirmed this observation as two meta-analyses failed to show any association between saccharin intake and bladder cancer [18, 41]. In animal studies, extreme high doses of saccharin lead to undesired weight loss. Based on these observations, the ADI was established at 5 mg/kg bw [64].

Concluding, added sugar intake is convincingly related to dental caries. Moreover, the intake of sugar-containing carbonated soft drinks is probably associated with overweight and obesity. Other health effects in humans related to added sugar intake do not fulfil the inclusion criteria, because the strength of evidence is rated less than probable. They are not further considered in this benefit–risk assessment. The beneficial effect of intense sweeteners is actually the removal of the energy provided by added sugars in carbonated soft drinks. The identified hazards may turn into a risk when the intake of intense sweeteners exceeds the ADI. As no adverse effects in humans are known, these effects must be deduced from the effects observed in animals.

In conclusion in this tier, both beneficial and adverse health effects of have been identified. Therefore, the benefit–risk assessment proceeds with an exposure assessment.

Exposure assessment

Methods

To assess the exposure of added sugar and intense sweeteners in Dutch young adults, two hypothetical and extreme scenarios were defined:

1) All consumed carbonated soft drinks are fully sweetened with added sugar (100% sugar scenario)
2) All consumed carbonated soft drinks are fully sweetened with intense sweeteners (100% sweetener scenario)

The difference between the scenarios shows the maximally attainable health effect when all carbonated soft drinks are sweetened with either added sugar or intense sweeteners. In practice, a certain proportion of the carbonated soft drinks contains added sugar and a certain proportion contains intense sweeteners, so the health effect obtained by implementing either of the two scenarios is less than the difference between the two extreme scenarios.

Data from the Dutch National Food Consumption Survey on young adults aged 19–30 (DNFCS-Young adults), containing information on 352 men and 398 women, were used to assess the intake of carbonated soft drinks in the Netherlands. Two independent 24-h dietary recalls were obtained by a trained dietician [25]. For the analysis, carbonated soft drinks were selected using codes for soft drinks from the Dutch Food Composition Database (NEVO, www.rivm.nl/nevo_en) and verified manually to distinguish carbonated from non-carbonated soft drinks. The final selection of carbonated soft drinks included: all different types of cola, orange soda, up soda, bitter lemon, tonic water, ice tea and whey-based carbonated soft drink.

Based on average nutrient information from the food composition database, two main levels of added sugar content in carbonated soft drinks could be distinguished. The sugar content of 9.7 g/100 ml was assigned to cola, orange soda, up soda, bitter lemon and whey-based carbonated soft drink, and the sugar content of 7.7 g/100 ml was assigned to ice tea and tonic water.

Analysed data from the years 2006 and 2008 of the Dutch Food Safety Authority was used to assign the type and level of intense sweeteners in carbonated soft drinks. If no analysed data was available for a specific carbonated soft drink, the level of intense sweeteners of similar carbonated soft drinks were averaged and assigned to the carbonated soft drink concerned.

We assigned the relevant amount of added sugar or intense sweeteners to each carbonated soft drink consumed in the 100% sugar or 100% sweeteners scenario, respectively. Then, we calculated the actual hypothetical daily intake of added sugar and intense sweeteners from carbonated soft drinks as the average of the observed consumption of carbonated soft drinks over the 2 recall days. The mean energy intake in the 100% sugar scenario was calculated by adding the additional energy from carbonated soft drinks in the hypothetical situation that all carbonated soft drinks are sweetened with added sugar to the total energy calculated in the national food consumption survey. The mean energy intake in the 100% sweetener scenario was calculated by subtracting the reduced energy from carbonated soft drinks in the situation that all carbonated soft drinks are sweetened with intense sweeteners from the total energy intake calculated in the national food consumption survey. We used the total sample, including non-consumers, representative for the population of young adults in the Netherlands. We did not translate the actual 2-day average intake to the habitual intake.

For each individual, the intake of added sugar from carbonated soft drinks was calculated as percentage of total energy intake (en%) from the 100% added sugar scenario and the intake of intense sweeteners from carbonated soft drinks was divided by individual's body weight and expressed as mg/kg body weight (mg/kg bw).

Results

Table 2 presents the distribution of intake of added sugar and intense sweeteners from carbonated soft drinks (100% sugar scenario and 100% intense sweeteners scenario) and total energy intake. In the DNFCS-Young adults, 54% of the women and 70% of the men consumed carbonated soft drinks. In the 100% sugar scenario, the 95th percentile of

Table 2 Distribution of sweeteners and added sugar intake from carbonated soft drinks in two scenarios and based on 2 days of actual consumption data in young adults (DNFCS-Young Adults)

Intake (average of 2 days)	Gender	Percentiles[a]						PNG[b]/ADI
		p5	p25	p50	p75	p95	p99	
Scenario 1: 100% sugar—All of the carbonated soft drinks sweetened with added sugars								
Added sugar (g)	Women	0	0	8.4	29.3	95.6	135	
	Men	0	0	21.1	49.1	102	181	
Added sugar (en%)	Women	0	0	1.7	6.1	18.3	27.9	10
	Men	0	0	2.8	7.0	16.1	27.1	
Total energy intake (kJ)	Women	5,062	6,791	8,295	9,714	12,207	14,123	
	Men	7,432	9,541	11,257	13,758	17,556	20,276	
Scenario 2: 100% intense sweeteners—All of the carbonated soft drinks sweetened with intense sweeteners								
Cyclamate (mg/kg bw)	Women	0	0	0	0.73	2.03	4.01	7
	Men	0	0	0.37	1.06	2.57	3.62	
Saccharin (mg/kg bw)	Women	0	0	0	0.02	0.17	0.32	5
	Men	0	0	0	0.04	0.18	0.36	
Aspartame (mg/kg bw)	Women	0	0	0.16	0.66	2.03	4.01	40
	Men	0	0	0.39	0.93	2.24	3.60	
Acesulfame-K (mg/kg bw)	Women	0	0.0066	0.20	0.79	2.45	4.33	9
	Men	0	0.019	0.45	1.05	2.65	4.18	
Total energy intake (kJ)	Women	4,580	6,519	7,896	9,253	11,624	13,915	
	Men	6,810	8,994	10,792	13,391	16,748	19,977	

[a] Distribution among percentiles calculated separately for each exposure

[b] Population nutrient intake goal added sugars WHO [62]

actual intake of added sugar is 16.1 en% and 18.3 en% for men and women, respectively. In the 100% sweetener scenario, the 95th percentile for actual cyclamate intake for men and women is 2.57 mg/kg bw per day and 2.03 mg/kg bw per day, respectively. The 95th percentile for actual intake of saccharin is 0.18 mg/kg bw per day in men and 0.17 mg/kg bw per day in women and for aspartame 2.24 mg/kg bw per day and 2.03 mg/kg bw per day in men and women. Finally, the 95th percentile for actual intake for acesulfame-K is 2.65 mg/kg bw and 2.45 mg/kg bw per day in men and women, respectively.

The mean total energy intake in the 100% sugar scenario is 11,800 kJ for men and 8,327 kJ for women for the total population, including non-consumers. In the 100% intense sweeteners scenario, the total energy intake is 11,258 kJ for men and 7,970 kJ for women. Thus, the mean difference in daily total energy intake between the two scenarios is 542 kJ for men and 357 kJ for women.

In this tier, there is exposure to added sugar and intense sweeteners in carbonated soft drinks in young Dutch adults and we will thus proceed to the next tier in the benefit–risk approach. We have maximized the exposure by means of two extreme scenarios and will compare the intakes with reference values.

Comparison of intake with guidelines

Methods

The intake of added sugar in the 100% sugar scenario was compared with the population nutrient goal for added sugar of the WHO [62]. The intake of intense sweeteners in the 100% sweetener scenario was compared with the ADIs established by WHO/JECFA/SCF committees [15, 48, 49, 64]. These levels are presented in Table 2.

Results

In the 100% sugar scenario, a substantial proportion of the Dutch young adults exceeds the population nutrient goal of the WHO for added sugar, which is 10 en% for the total diet. In this hypothetical situation, approximately 15% of men and women exceed this solely by their intake of carbonated soft drinks sweetened by sugar only. In contrast, the intake of all intense sweeteners remains below the ADI in the 100% sweetener scenario, as shown in Table 2. In the 100% sweetener scenario, the 99th percentile for cyclamate is closest to the corresponding ADI but does not even reach 60%. Intake of cyclamate may exceed the ADI when background exposure is considered. In the present study, background exposure could not be calculated. Husoy et al. [26] estimated the Norwegian intake for cyclamate from foods other than beverages at 2.9 mg/kg bw (95th percentile). The intake of cyclamate could be very close to the ADI if this estimation is used to estimate the background exposure. It should be mentioned that the background exposure in the Netherlands is probably even higher, as the beverage category in the study from Norway also included non-carbonated beverages. However, we consider it unlikely that the ADI will be exceeded, as we must then assume that the consumers in the 99th percentile of intense sweetened carbonated soft drinks are the same consumers as the consumers in the 95th percentile of other intense sweetened products.

The conclusion in this tier, where the intake is compared with the guideline, is that substitution of added sugar by intense sweeteners in carbonated soft drinks does not have any adverse health effects. According to Fransen et al. [20], the benefit–risk assessment can be stopped now, because there are clearly potential benefits and no potential health risks. However, the magnitude of the positive health effects is worthwhile knowing in case different options need to be prioritized. Therefore, we continue with a benefit characterization.

Benefit characterization of reduced added sugar intake

Methods

The benefit characterization includes the determination of a quantitative relationship (dose–response function) between the exposure and the health effect, often expressed as the probability to develop a particular disease. Here it is expressed as an increasing probability of obesity with increasing intake of added sugar.

The beneficial health effects of substituting added sugar by intense sweeteners are the prevention of dental caries and the prevention of weight gain. The available population-based studies do no provide the information that can be used to determine a dose–response function for dental caries. The effect of added sugar on caries is mostly related to the frequency of sugar intake instead of to the level of sugar intake, and this frequency cannot be estimated in the present study [16, 62]. So, we focus on the benefit of weight reduction. The dose–response function expresses the increase in weight due to the increased intake of sugar, expressed in energy percentage.

To calculate the change in body mass index (BMI), we used the population of young adults from the DNFCS-Young adults and presumed they were representative for Dutch young adults with regard to their carbonated soft drink consumption and BMI. Weight, height and carbonated soft drink consumption are known for subjects involved in the survey and as a result also their energy intake in both scenarios due to carbonated soft drink consumption is known. Presumably, the difference in energy intake results in a change in weight and hence BMI. Body weight and energy intake are related through the basic metabolic rate according to the so-called Schofield equation [51]. We assume that if the energy intake is greater than energy expenditure, which is assumed to be a multiple of the basic metabolic rate, the body converts the additional energy to extra body mass. This will cause an increased basic metabolic rate and overall energy expenditure. Over time the body will find a new equilibrium weight in which the energy intake corresponds to the energy expenditure. The opposite applies too: if the energy intake is less than the energy expenditure, the body will convert its fat into energy until the energy expenditure and energy intake match. So, if the energy intake is changed through the substitution of sugar by intense sweeteners or vice versa, we assume that at some point in time body weight has changed to a new equilibrium. At that time, energy intake equals energy expenditure. This equilibrium is described by the relationship between body mass and basic metabolic rate. For the age group 19 to 30 years, we assume a physical activity level of 1.5 and we use the equations and parameter values as presented by McNeill [40] to describe the relationship between energy intake via a multiple of the basic metabolic rate and weight. As a result, we deduce the following relationship between change in energy intake and weight change of each individual in DNFCS-Young:

$$\Delta BW = \frac{\Delta E}{94.5} \quad \text{for men}$$

and

$$\Delta BW = \frac{\Delta E}{93} \quad \text{for women}$$

where ΔBW is the change in body weight (kg) compared with that persons weight in DNFCS-Young adults, and ΔE the change in energy intake (kJ)between the scenarios and DNFCS-Young adults. For the purpose of this study, we assume that no energy compensation takes place in the 100% sweetener scenario.

For each subject in DNFCS-Young adults, the change in energy intake is related to a change in actual body weight in both the 100% sweetener scenario and the 100% sugar scenario, according to the abovementioned equation. This will cause a change in BMI in each individual and as a result the BMI distribution in the population will change.

Results

The maximum effect of the substitution of added sugar by intense sweeteners in carbonated soft drinks is shown, assuming that people do not compensate the energy difference in the scenarios. For example, if we look at a man from participating in the DNFCS-Young adults (actual weight: 80 kg, height: 182 cm and a BMI of 24.2 kg/m^2) whose actual energy intake from sugars in carbonated soft drinks is 559 kJ. If the sugar in his actual carbonated soft drink consumption is replaced by intense sweeteners (100% sweetener scenario), this man will loose 5.9 kg and his BMI becomes 22.3 kg/m^2. In the 100% sugar scenario, the energy intake from sugars in carbonated soft drinks increases with 702 kJ. This means he increases his weight by 7.4 kg and his BMI in the 100% sugar scenario becomes 26.4 kg/m^2.

In total in the 100% sweetener scenario, men lost on average 4.9 kg and women lost on average 2.2 kg compared to their actual weight and gained 0.8 kg in men and 1.6 kg in women compared to the actual weight in the 100% sugar scenario. Women have a higher intake of intense sweetened carbonated soft drinks which explains the difference in weight change between men and women. In the 100% sweetener scenario, the average BMI decreased with 1.7 kg/m^2 in men and 1.3 kg/m^2 in women compared with the 100% sugar scenario. The effects on the BMI distributions in the population are presented in

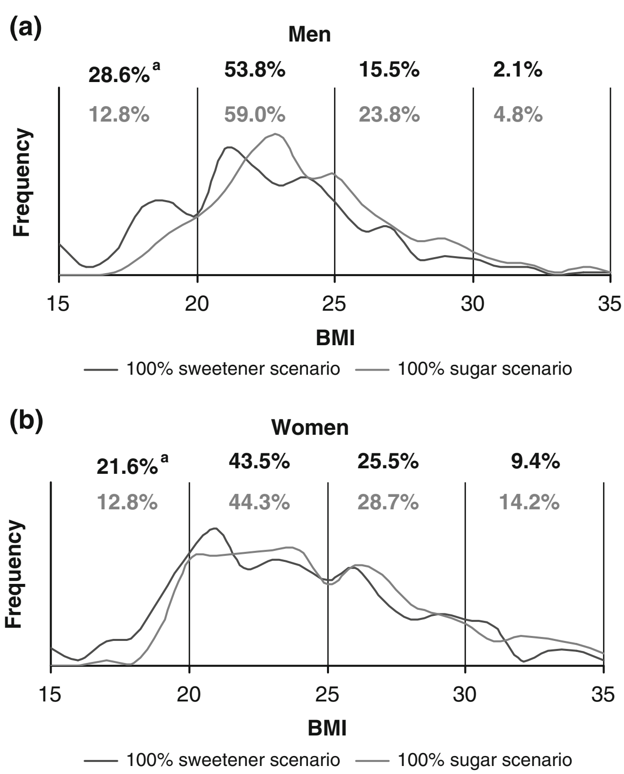

Fig. 1 **a** Benefit characterization of BMI distribution for men in the 100% sweetener and 100% sugar scenario. **b** Benefit characterization of BMI distribution for women in the 100% sweetener and 100% sugar scenario. [a]: *The numbers in the figures denote the fraction of the population with a BMI $<$ 20, 20 $\leq$ BMI $<$ 25, 25 $\leq$ BMI $<$ 30 and 30 $\geq$ BMI for both scenarios*

Fig. 1a, b. In women, the prevalence of obesity (BMI $\geq$ 30 kg/m^2) would decrease from 14% in the 100% sugar scenario to approximately 9% in the 100% sweetener scenario. In men, the prevalence of obesity would decrease from almost 5% in the 100% sugar scenario to 2% in the 100% sweetener scenario.

The conclusion is that the substitution of added sugar with intense sweeteners in carbonated soft drinks lowers BMI. In the presumed absence of risks, the net health benefits prevail.

Discussion

This study examined the health effects of substituting added sugars in carbonated soft drinks by intense sweeteners in Dutch young adults using data from the DNFCS-Young adults in combination with analytical data on sweetener content. If all added sugars in carbonated soft drinks were substituted with intense sweeteners, total energy intake of Dutch young adults would decrease, resulting in lower BMI levels. No adverse health effects are expected because none of the individual ADIs for intense sweeteners is exceeded through the extra intake of intense sweeteners. The restrictions in our benefit–risk question with respect to product group and population were made because exposure data are lacking for the total diet and consumption data for the total population are not recent.

In the present study, all subjects remained below ADI in the 100% sweetener scenario, and therefore no risks were involved. It should be mentioned that we examined the intake of intense sweeteners from a very specific category of beverages, and we did not consider background exposure. It cannot be excluded that absolutely no one will exceed the ADI when background exposure is taken into account, although we consider it to be unlikely. Other studies that have considered total exposure show that intense sweeteners do not exceed ADI in worst-case scenarios [2, 32]. However, some studies observed that subgroups of the population are vulnerable to exceed the ADI, such as young children and diabetics [26, 27]. Therefore, the conclusions of this study are restricted to healthy, young adults aged 19–30 years. A benefit–risk assessment of substituting sugar by intense sweeteners in young children may be more relevant in terms of health risks. However, for the present study, a specific category of beverages were examined that are not frequently consumed by young children.

Fifteen per cent of the study population exceeded the population nutrient goal of added sugar, solely by their intake of carbonated soft drinks. This percentage seems quite reasonable as a Dutch report concluded that in the Dutch Food Consumption Survey of 1998 nearly 50% of the population aged 19 to 50 exceeded the population nutrient intake goal of 10%. Carbonated soft drinks were a main contributor to the intake of added sugar. [24].

Both scenarios represent hypothetical and extreme situations. First, the true consumption of carbonated soft drinks on a population level will consist of drinks sweetened with sugar, sweetened with intense sweeteners or with a combination of the two. Thus, the health gain in terms of BMI will be smaller compared with the current situation. Furthermore, it was assumed that no energy compensation takes place. In practice, energy intake in the 100% sweetener scenario is likely to be an underestimation of the actual total energy intake. Subjects will probably partly compensate for their loss in total energy intake after consumption of artificially sweetened beverages [8, 42]. Presumably, total energy intake in the 100% sweetener scenario is therefore higher than calculated. This implies that the potential health gain in terms of BMI reduction is lower than presented in this study. However, using extreme scenarios and calculating the accompanying benefits and risks provide a valuable estimate of the maximal effect of the substitution.

Substitution of added sugar with intense sweeteners may have other adverse effects, such as reduced shelf-life. Sugar functions as a preservative. Therefore, other preservatives are often added to beverages that contain intense sweeteners instead of sugar. Hence, increased use of artificially sweetened soft drinks will also increase intake of preservatives. Benzoic acid is a commonly used preservative in artificially sweetened carbonated soft drinks. A previous study has shown that the ADI of benzoic acid could be exceeded at very high intakes of artificially sweetened soft drinks [26]. The Dutch food composition table does not include levels of preservatives nor are levels of preservatives available at the Dutch Food Safety Authority, and thus an estimation of the intake of e.g. benzoic acid can not be made. However, given the results of benzoic acid intake in Norway, the possible adverse health effect of benzoic acid in the Netherlands should not be ignored.

An additional aim of the present study was to test the RIVM-tiered approach developed for performing a benefit–risk assessment [20]. This case study shows that a benefit–risk assessment requires a substantial amount and wide variety of information. Moreover, it showed that conducting a comprehensive benefit–risk assessment is not always necessary. The conclusions could already be drawn before all benefits and risks were quantified and properly integrated in a common health metric. This approach also revealed that some data and methodological limitations were present. First, the level of *added* sugar in food products is not available in the Dutch food composition table. Therefore, a benefit–risk assessment of replacing added sugar with intense sweeteners in all foods relies on additional data. As the level of mono- and disaccharides in carbonated soft drinks is largely comparable to the amount of added sugars and analytical data for intense sweeteners in beverages were available, a focus on carbonated soft drinks was feasible. However, as the assessment of background exposure of intense sweeteners could only be estimated with large uncertainties, the results apply only for the specific subgroup young adults.

Second, the study population does not represent the entire Dutch population. The latest food consumption survey among the total Dutch population was conducted in 1997/1998. It was decided not to use this data, as research demonstrated that the intake of carbonated soft drinks has increased over the past decades [1], and that survey data would thus not provide actual information. More recent data was available for young adults, which are important consumers of carbonated soft drinks, so they became the targeted (sub)population of this study.

Third, the selection of carbonated soft drinks was difficult, as no predefined category of carbonated soft drinks exists. In the present study, it was decided to include ice tea among the carbonated soft drinks, although it is known that only some ice teas are carbonated. However, the intake of ice tea in the present study was low. Also fruit juices were not included in the carbonated soft drink category.

Fourth, there is a lack of human data on the adverse health effects of intense sweeteners. Therefore, the effects need to be extrapolated from animal studies. This gives some additional uncertainty to the results. However, because the intake is low and remained below ADI, we were able to conclude that adverse health effects were absent.

Overall conclusion

Using two hypothetical and extreme scenarios, 100% added sugar and 100% intense sweeteners in carbonated soft drinks, we conclude that the substitution of added sugar by sweeteners in carbonated soft drinks shows benefits with respect to caries and BMI and does not confer risks. Our optional quantitative benefit assessment directed at BMI revealed a considerable maximum effect.

The tiered approach as developed by Fransen et al. [20] proved to be usable in this case study.

It is important to note that a benefit–risk assessment always depends on currently available scientific information. Should more information become available, for example data on benzoic acid content of drinks, new dose–response information or adjustments of the ADI, then this assessment may give different results. It should be regularly repeated to critically evaluate the previous results.

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Conflict of interest The Authors declare that they have no conflicts of interest.

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