ABBREVIATIONS:

AHA: American Heart Association

BMI: Body Mass Index (kg/m²)

CI: Confidence Interval

CoN: Committee on Nutrition

DP: degree of polymerisation

EFSA: European Food Safety Authority

ESPGHAN: European Society for Paediatric Gastroenterology, Hepatology and Nutrition

HFCS: High-Fructose Corn Syrup

HDL: High-Density Lipoprotein

HOMA-IR: homeostasis model assessment, insulin resistance index

LDL: Low-Density Lipoprotein

NCD: Non-Communicable Diseases

NNS: Non-Nutritive Sweeteners

RCTs: Randomised Clinical Trials

SACN: The UK Scientific Advisory Committee on Nutrition

SEM: Standard Error of Mean

SSBs: Sugar Sweetened Beverages

T2D: Type 2 Diabetes Mellitus

US: United States

ABSTRACT

The consumption of sugars, particularly sugar-sweetened beverages (SSBs; beverages or drinks that contain added caloric sweeteners (i.e. sucrose, high-fructose corn syrup, fruit-juice concentrates), in European children and adolescents exceeds current recommendations. This is of concern because there is no nutritional requirement for free sugars, and infants have an innate preference for sweet taste, which may be modified and reinforced by pre- and postnatal exposures. Sugar containing beverages/free sugars increase the risk for overweight/obesity and dental caries, can result in poor nutrient supply and reduced dietary diversity and may be associated with increased risk of type 2 diabetes mellitus, cardiovascular risk, and other health effects. The term 'free sugars', includes all monosaccharides/disaccharides added to foods/beverages by the manufacturer/cook/consumer, plus sugars naturally present in honey/syrups/unsweetened fruit juices and fruit juice concentrates. Sugar naturally present in intact fruits and lactose in amounts naturally present in human milk or infant formula, cow/goat milk and unsweetened milk products is not free sugar. Intakes of free sugars should be reduced and minimised with a desirable goal of <5% energy intake in children and adolescents aged ≥ 2-18 years. Intakes should probably be even lower in infants and toddlers < 2 years. Healthy approaches to beverage and dietary consumption should be established in infancy, with the aim of preventing negative health effects in later childhood and adulthood. Sugar should preferably be consumed as part of a main meal and in a natural form as human milk, milk, unsweetened dairy products and fresh fruits, rather than as SSBs, fruit juices, smoothies and/or sweetened milk products. Free sugars in liquid form should be replaced by water or unsweetened milk drinks. National Authorities should adopt policies aimed at reducing the intake of free sugars in infants, children and adolescents. This may include education, improved labelling, restriction of advertising, introducing standards for kindergarten and school meals, and fiscal measures, depending on local circumstances.

Key words: sugar, free sugars, recommendations, sugars-containing beverages, sugar sweetened beverages, sweet taste, overweight, obesity, caries, paediatric

INTRODUCTION

Sugars are found naturally in fruits, vegetables, some grains, human milk, milk, and milk products (naturally-occurring sugar), but are also added to foods during processing, preparation, or at the table (1) (Tables 1 and 2). The added sugars sweeten the flavour of foods and beverages, improve their palatability, and are used to preserve food and to confer functional attributes, such as viscosity, texture, body, and color (browning capacity).

A healthy, well-balanced diet contains naturally-occurring sugars as integral components of whole foods (i.e. within whole fruits, vegetables, milk and dairy products, and some grains). Added sugars provide sensory effects to foods and promote enjoyment but although they may be required in some clinical situations, they are not a necessary component of the diet in healthy children. By providing calories without other essential nutrients (2), they can displace nutrient-dense foods and contribute to poor health outcomes, which is of special concern in children. Excessive consumption of sugars has been linked with several metabolic abnormalities and adverse health conditions (3).

The aim of this paper is to review: 1) the terminology, classification and definitions of sugars and sugar containing beverages; 2) current recommendations for intake of sugars and beverages; 3) intakes of sugars, sugars-sweetened foods/beverages in children/adolescents; 4) evidence on the development of sweet taste and preference for sweet foods;5) evidence on the health effects of sugar and sugar containing beverages in infants, children and adolescents; 6) what sugars should be replaced by; and 7) provide recommendations and practical points on the intake of free sugars in the paediatric population, with a focus on establishing healthy dietary practices and preventing health problems. The paper focuses on the general paediatric population.

METHODS

A systematic search of the literature was performed to identify publications relevant to the aims of the position paper. We searched PubMed, EMBASE and the Cochrane Central Register of Controlled Trials CENTRAL for randomized controlled trials (RCT), cohort studies, cross sectional studies, clinical trials, epidemiological studies, systematic reviews, meta-analyses and consensus statements/guidelines

published in English up to March 2015. Case-control studies and qualitative studies/research were not included. Reference lists of included studies and other relevant articles were also searched. For the literature search to identify studies relevant to the development of sweet taste or flavour preference and associations with sugars intake we used the search strategy in Appendix 1. Systematic reviews published after March 2015, up to September 2016, were also eligible but no formal search was undertaken after March 2015. Due to the heterogeneous nature of the literature, a narrative summary of the selected papers is provided in the text.

To identify studies on intake of sugars and health outcomes in infants, children, and adolescents a systematic search of the literature as described above was conducted up to February 2016 using defined search criteria (Appendix 2). Systematic reviews published after February 2016 up to September 2016 were also eligible (for example, a systematic review by the AHA (4)), but no formal search was undertaken after February 2016. Studies were included if the participants were infants, toddlers, children and adolescents; studies involving adults were included only if they also included children and adolescents. Due to the large body of literature, including several systematic reviews and meta-analyses, we presented the evidence relevant to the paediatric population from the largest, most comprehensive reviews conducted by the WHO (5, 6) and UK SACN (7), and discussed relevant individual studies published since the cut-off of the literature searches for those reviews. We gave the priority to RCTs over observational studies.

TERMINOLOGY, CLASSIFICATION AND DEFINITIONS OF TYPES OF SUGARS AND SUGARS-CONTAINING BEVERAGES IN THE DIET

Sugar is a ubiquitous term, but is not easy to define and measure. The term "total sugars" refers to the combination of naturally-occurring sugars and free sugars (of which added sugars are a sub-group). "Sugar-containing" means foods and beverages that contain sugar. Previous analytical methods measured only the total sugars in foods. Nutrient databases and nutrition labels include values for total sugars (2). Recently, a precise step-by-step method that enables systematic calculation of free sugars content of foods and beverages was developed within the University of Toronto's Food Label

Information Program Canada. A comprehensive assessment of total sugars and free sugars levels of 15,342 products was obtained. Free sugar accounted for 64% of total sugar content (8).

Various definitions of sugars are used in different contexts, for example in chemical classification (table 1), current dietary recommendations (table 2), research studies, regulations and food labelling.

Sugars: Chemical classification and relative sweetness

The term 'sugars' describes mono- and di-saccharides. The three principal monosaccharides - hexoses (six-carbon sugars) - are glucose, fructose and galactose, which are the building blocks of naturally occurring di- oligo- and poly-saccharides. Carbohydrates are a major source of energy in the diet and include a range of compounds containing carbon, hydrogen and oxygen. Carbohydrates are divided into three groups: a) mono-and di-saccharides (degree of polymerisation, (DP) 1-2; i.e. sugars, (Table 1), b) oligosaccharides (DP 3-9; e.g. maltodextrins) and c) polysaccharides (DP ≥10) (7).

Sweetness is a gustatory response evoked by sugars and sweeteners. The initiation of a taste response involves the interaction of a stimulant molecule with a receptor located at the taste-cell plasmamembrane. Sweetness is defined relative to sucrose which has a sweetness value of 1.00 (or 100%). The relative sweetness of sugars differs. Fructose is the sweetest (relative sweetness: 1.17), followed by sucrose (1.00), glucose (0.74), maltose (0.33), galactose (0.32) and lactose (0.16) (9).

Definitions for sugars used in dietary recommendations and research studies

The updated WHO definition of "free sugars" is: "monosaccharides and disaccharides added to foods and beverages by the manufacturer, cook or consumer (i.e. added sugars), plus sugars naturally present in honey, syrups, fruit juices and fruit juice concentrates (i.e. non milk extrinsic sugars) (5). This term describes sugars that may have physiological consequences different from intrinsic sugars incorporated within intact plant cell walls or lactose naturally present in milk. The UK Scientific Advisory Committee on Nutrition (SACN) also adopted the definition "free sugars" (7).

The European Food Safety Authority (EFSA) defines sugars as "total sugars", including both indigenous sugars naturally present in foods (i.e. "naturally-occurring sugars") such as fruit, vegetables, cereals and

lactose in milk products, and added sugars. The term 'added sugars' refers to sucrose, fructose, glucose, starch hydrolysates (glucose syrup, high-fructose syrup, isoglucose) and other isolated sugar preparations used as such, or added during food preparation and manufacturing (10).

The United States (US) dietary reference intakes define 'added sugars' as sugars and syrups that are added to foods during processing and preparation. Added sugars do not include naturally occurring sugars such as lactose in milk, and fructose in fruits (11).

The different terminology used in dietary recommendations is challenging. The EFSA and US definitions of "added sugars" (10), (11) do not include sugars present in unsweetened fruit and vegetable juice and fruit juice concentrate, all of which are, however, captured in the definition of free sugars (5). The US definition of "added sugars" further excludes sugars found in jellies, jams, preserves, and fruit spreads, while the EFSA definition also does not include honey; all of these are included in the definition of free sugars (5). In the US, there is now a mandatory requirement to include "added sugars," in grams under "Total Sugars" and as % Daily Value on labels (12).

In research studies, exact definitions of sugars are often omitted, making it very difficult to determine what was under investigation. In epidemiologic studies, sugars consumption is often underestimated (13, 14). Recently Nash *et al.* validated an expensive dual-isotope model based on red blood cell carbon (delta¹³C) and nitrogen (delta¹⁵N) isotope ratios that explained a large percentage of the variation in self-reported sugars intake. Red blood cell, plasma, and hair isotope ratios predict sugars intake and provide data that will allow comparison of studies using different sample types (15). This is a useful technique, but it is currently too expensive for use in epidemiological studies. In epidemiologic studies, it is often easier to assess intake of sugar sweetened beverages (SSBs) as these can be counted in food frequency instruments (2).

Definitions for sugars used in regulations and food labelling

The terminology used in regulations and on food labels differs from that used in dietary recommendations. In Europe, there is no mandatory labelling of added or free sugars and only "total sugar" has to be declared (10), (16).

Of specific relevance to infants, the WHO (5) and SACN (7) definitions of "free sugars" do not mention human milk and infant formulas. The compositional requirements of infant formulas and follow on formulas require a total glycaemic carbohydrate content of 9-14 g/100 kcal, with a minimum 4.5 g/100 kcal of lactose. For infant formulas, lactose is the preferred sugar, while sucrose, glucose and fructose are not permitted (17), (18), (19). Glucose and sucrose may, however, be added to infant formulae manufactured from protein hydrolysates to mask the bitter taste. For follow-on formulas, the addition of sucrose and fructose may be considered acceptable, because most infants will be exposed to these sugars in complementary foods. If honey is used (for follow on formulas only), it has to be treated in order to destroy spores of *Clostridium botulinum* (17).

Interestingly, it is permitted to add free sugars to processed cereal-based foods and baby foods for infants and young children. It is stated: a) "if sucrose, fructose, glucose, glucose syrups or honey are added to 'processed cereal-based foods', i.e. simple cereals which are or have to be reconstituted with milk or other appropriate nutritious liquids or to rusks and biscuits which are to be used either directly or, after pulverisation, with the addition of water, milk; the amount of added carbohydrates from these sources shall not exceed 7.5 g/100 kcal" (20).

The health claims "no added sugar" and "naturally-occurring sugars" on foods for infants, children and adolescents are in accordance with "Regulation No 1924 on nutrition and health claims on foods" (21), but not with the WHO definition of "free sugars" and "naturally-occurring sugars" (= "intrinsic sugars") (5) (Table 2)). Labels on foods for infants, children and adolescents may therefore state "no added sugars" despite the fact that they contain "free sugars" which need to be limited in the diet. With the

current terminology in European regulations and food labelling, "free sugars" are "hidden" and consumers may not be aware that they are present in foods and beverages.

Sugars-containing beverages: Sugar Sweetened Beverages (SSBs) and fruit juices

SSBs, also called sugar or nutritively sweetened drinks/beverages, are beverages that contain added caloric sweeteners such as sucrose, high-fructose corn syrup (HFCS) and fruit-juice concentrates. They include the full spectrum of soft drinks, carbonated soft drinks, fruitades, fruit drinks, sports drinks, energy and vitamin water drinks, sweetened iced tea, cordial, squashes, fruit syrup, and sweetened lemonade (22). The HFCS that is commonly used in beverages contains 55% fructose and 45% glucose derived from corn, while sucrose consists of 50% fructose and 50% glucose (23), (24).

Fruit juices are not SSBs (23). Usually they have superior nutritional composition to SSBs, as they contain potassium, vitamins A and C and some are fortified with vitamin D and/or calcium, but they contain similar amounts of free sugars (5-17% of sucrose, glucose, fructose and/or sorbitol) and energy (23-71 kcal/100 ml) (24) to SSBs and have similar potential to promote weight gain in children (25, 26). Table 3 shows the main groups of SSBs and fruit juices with the ranges of energy and free sugars content (24). Smoothies are not included in the definition of SSBs, even though they contain free sugars. It is also important to note that sweetened milks (e. g. chocolate milks, chocolate soy drinks) are also not included in the definition of SSBs, although they contain 3.6-11.5 g of free sugars/100 ml and are commonly consumed by children and adolescents (24).

CURRENT RECOMMENDATIONS FOR INTAKE OF SUGARS AND BEVERAGES

The WHO recommends limiting the intake of free sugars to < 10% of total energy intake (strong recommendation) based on moderate quality evidence from observational studies of dental caries, and suggests that a reduction to <5% would have additional benefits in reducing the risk of dental caries (conditional recommendation) in children and adults (5). The UK SACN review recommends the average population intake of free sugars should be <5% of total dietary energy from 2 years upwards.

This figure was based on calculations of the mean reduction in free sugars intake needed to lower mean population energy intakes by 100kcal/day with the aim of addressing energy imbalance and leading to a moderate degree of weight loss in the majority of individuals, assuming a baseline of 10% sugars intake as per previous UK recommendations. They further recommend that the contribution of free sugars toward recommended total carbohydrate intake should, in people with a healthy body mass index (BMI) and in energy balance, be replaced by starches, sugars contained within the cellular structure of foods and lactose naturally present in milk and milk products. In overweight individuals, the reduction of free sugars should be part of decreasing energy intake. Finally, they recommend that the consumption of SSBs should be minimised in children and adults (7). Five % of daily energy for a 3-year old girl is equivalent to < 13 g of free sugars/day, (that is, < 3 teaspoons), which is present in an average 170 ml (81-260 ml) of fruit nectar for example (tables 3 and 4) (24). The American Heart Association (AHA) recommends that children consume ≤ 25 g (100 kcal or ~ 6 teaspoons) of added sugars/day and to avoid added sugars for children < 2 years of age. This recommendation is based on decreasing cardiovascular disease risk among children (excess weight gain and obesity, elevated blood pressure and uric acid levels, dyslipidemia, non-alcoholic fatty liver disease), insulin resistance and type 2 diabetes mellitus (T2D) and also to maintain diet quality (4). Several other scientific associations have called for reductions in consumption of SSBs for prevention of obesity and chronic diseases (27) (28), (29), (30), (31), (32).

The recommended fluid for thirst for infants after the introduction of solid foods is water. Infants should not be given sugars-containing drinks in bottles or training cups and children should be discouraged the habit of a child sleeping with a bottle (33). The recommended beverages for children and adolescents are water, mineral water or/and (fruit or herbal) tea without added sugars (34). It should be noted that existing recommendations focus on free or added sugars rather than on total sugars, as there is consistent evidence that free and added sugars are the major contributor to the weight gain, obesity, dental caries and other adverse health effects (see later). "Naturally occurring sugars" as integral components of whole foods (i.e. within whole fruits, vegetables, some grains and dairy products), that also contribute to the "total sugar intake," are of less concern as they are less likely to be overconsumed and contain a wide range of bioactive health-enhancing nutrients, fibre, antioxidants and phytochemicals that reduce

inflammation and improve endothelial function. Indeed, evidence in adults suggests that weight gain over a 4 year period is inversely associated with intake of naturally occurring sugars (35), whilst in another analysis, low intakes of fruits, vegetables, whole grains, or nuts and seeds or a high dietary intake of salt were reported to be individually responsible for 1.5% to more than 4% of the global disease burden" (36). It is also more practical to recommend a minimized intake of added/free sugars than to set a limit for total sugars.

INTAKES OF SUGARS, SUGARS-SWEETENED FOODS AND BEVERAGES IN CHILDREN AND ADOLESCENTS

Comparison of the intake of sugars and SSBs between countries is difficult, as studies use very different definitions for sugars-containing beverages. According to the ESPGHAN Position Paper on Complementary Feeding no sugars should be added to complementary foods and fruit juices or SSBs should be avoided (33). However, in a study in 5 European countries it was found that these liquids are frequently given to breastfed and particularly to formula fed infants during the first months of life. Infants given energy providing liquids showed lower intakes of infant formula and solids (37).

The current food environment is characterised by a cheap and abundant sugars supply (38). Added sugars contribute about 14% of daily energy intake in 2-9 years old children in Europe (39) and 2-18 years old in the USA (40). In Slovenian adolescents aged 15-16 years mean intake of free sugars constituted 16% of daily energy intake (130 g/day) in boys and 17% (110 g/day) in girls (41).

Consumption of SSBs has increased dramatically in recent decades among children and adults (42). In the UK, soft drinks provided almost a third of the intake of non-milk extrinsic sugars in children aged 11-18 years. Biscuits, buns, cakes, and puddings, confectionery and fruit juice were also significant contributors. There is a socio-economic gradient, with higher sugars intakes in lower income groups (7).

A study among adolescents aged 12-17 years from 9 European countries reported consumptions of 424 ml of sugars-containing beverages/day (228 ml SSBs, 63 ml sweetened tea and 133 ml fruit juice) (43). A German study reported a soft drink consumption of 480 ml/day in boys and 280 ml/day in girls aged 12-17 years (44). A Slovenian study reported SSBs (including sweetened tea and syrups) consumption of 683 and 715 ml/day in boys and girls aged 14-17 years; higher than the intake of milk and milk products (513 and 479 g/day in boys and girls) (45). Fruit juice consumption was 114 and 102 ml/day in boys and girls. SSBs contributed 9% and 10% of total energy intake in boys and girls, representing the primary source of free sugars in the diet of Slovenian adolescents (41, 45). In a cross-sectional survey of 200,000 adolescents aged 11-15 years from 43 countries and regions across Europe and North America, the prevalence of daily soft-drink consumption tended to increase between ages 11 and 15 years, especially in boys (46). There is a lack of studies in younger children.

THE DEVELOPMENT OF SWEET TASTE AND PREFERENCE FOR SWEET FOODS

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Innate and programmed preferences for tastes

Taste is simply defined as the sensation arising from the taste system, but flavour is considered a more inclusive term for the complex of sensory cues, including olfaction, taste and touch systems (47). An infant's experience with flavours begins early, in utero via amniotic fluid and later during breastfeeding, where flavours from the mother's diet are experienced (48, 49). Infants have innate preference for sweet, salty and umami tastes, and innate rejection of sour and bitter tastes (47, 50–52). Newborns prefer sugar solutions to water (47, 53) and sweeter solutions over less sweet solutions (47, 54) possibly due to the fact that ingestion of sweet sugars leads to endogenous opioid release (47, 55). This effect is used in neonatal practice for procedural pain relief in infants (56–58).

Individual sensitivity to and preference for sweet foods is determined not only by presence or absence of sugars on sweet taste receptors, but also by genetic sensitivity to taste including polymorphisms in the gene for sweet taste receptors TAS1R (59–61). Programming of preference for certain tastes and

palatable food is a complex process involving systems that regulate appetite and food preferences at a central level (altered development of systems regulating motivation, reward and perception of taste). There are also other influences; for example prenatal exposure to cocaine is associated with greater preference for sweet taste in newborns (62). In rats, a similar effect has been shown with morphine (63). Epigenetic changes may also contribute to the programming effect, however, the precise mechanisms still remain poorly understood (64–68).

Innate preference for energy-dense foods

Along with preference for sweet taste, we are also predisposed to prefer energy-dense foods, thus "healthy" foods given as complex carbohydrates and vegetables which are not sweet, salty and energy dense are initially rejected by children (47). Especially in young children, sweet taste by itself is probably not the main regulator of food intake. Young children show so-called "caloric compensation", adjustment of food intake based not primarily on sweetness, but on energy content of a previous preload meal given up to 1 hour prior to eating a self-selected meal. This mechanism seems not to be present in older children (9-10 years old) and in adults (69). Preference for energy dense foods was advantageous in the past when food resources were scarce. In today's obesogenic environment, this can contribute to development of overweight and obesity (47).

Postnatal taste and flavour learning

Children's food choices and preferences are influenced not only by genetic predisposition to certain tastes, but also by food availability and by cultural and parental influences, and they track through childhood and into adulthood (49, 70–73). Acceptance of basic taste in weaning may be different among breast-fed and formula-fed infants (49, 74, 75). Formula-fed infants are exposed to a constant flavour, a predominantly sweet taste. Human milk also has a sweet taste, but additionally exposes the infant to varying flavours and aromas, depending on the nutrition of the mother. Facial responses to various taste solutions at 3 months of age before weaning did not show any difference between breastfed and formula-fed infants and were consistent with inborn preference for sweet and salty tastes (49). However, in an observational study, breast-fed infants had a greater acceptance of new foods and flavours at 2-8 months

of age vs. formula-fed infants (70). Breastfeeding was also associated with greater diversity in foods and lower intake of juice at 9 months of age and healthier meat and vegetable dietary pattern at 2-8 years of age (70, 76). Longer exclusive breastfeeding was associated with higher vegetable intake at age of 5 years and longer breastfeeding duration has consistently been related to higher fruits and vegetables intake in young children (77, 78). In a recent study by Perrine et al. in 1,355 children, frequency of consumption of water, fruits and vegetables was positively associated, while the intake of SSBs was inversely associated, with any breastfeeding duration be it partial or exclusive (79). However, these are observational studies and it is not possible to determine whether these associations are causal.

Despite the innate preference for sweet tastes, children are also typically phobic to new foods, especially to sour fruits, vegetables and protein foods. Food neophobia is highly heritable, as shown in twin studies (80). Sweet taste is preferred, but only in familiar food contexts and is influenced by the increase in the availability of sweet products associated with urbanisation (59, 81). Sweet and fat taste preferences vary across geographical regions even in Europe and are related to weight status in European children. However, sweet preference is not always related to consumption of sweet food (82). Acceptance of novel foods in infants can be enhanced by exposure to variety of flavours (83). A positive correlation was observed between sensitivity to bitter taste and sweet taste perception (59) and between salty and sweet taste preferences (84). Children have the ability to learn preferences for foods made available to them, thus innate preference for sweet taste can be partly modified by experience with food even in early infancy (47, 85, 86).

Are interventions to modify taste preferences effective?

Observational studies show inconclusive results in the association between feeding experience during fetal development and early infancy and later taste preferences (52), (87), (88). Exposure to palatable foods high in fat and sugars before birth via maternal intake or in early infancy may lead to overall increase in food intake and increased preference for palatable foods after weaning (64).

Mother's choices of drinks for their young children are also influenced by various social, environmental and behavioural factors, such as child age, child preference and temperament, grandparents' influence and sweetened drinks given as a reward (89). Caution is required when trying to introduce strategies in order to encourage children to consume nonpreferred foods. These feeding practices may lead to children disliking rather than accepting these foods and restriction of energy dense, sweet, salty and fatty foods may promote their liking for and intake of those foods (47, 90). It seems that the best opportunity for promoting patterns of preference consistent with healthier diets may be to focus on the very young (47). In 7-16 year old children, sensory preferences did not change within 12 months in a long-term outpatient obesity lifestyle intervention programme based on behaviour and exercise therapy as well as a nutritional course including session on taste training (91).

Intervention studies trying to show effects of repeated exposure to specific foods on food preference have some methodological pitfalls. Novel whole food products (consisting of many taste combinations) are often used for testing which does not allow discrimination between individual taste dimensions. Using novel foods also makes it difficult to distinguish the effect of reduction in food neophobia from an increase in preference for the specific taste (92). . (92). Attempts have been made to develop reliable methods to test taste sensitivity and aversion even in young children (93, 94). Liem et al. have shown that exposure to sweet orangeade in 9 years old children (age range 6-11 years) for 8 days increases preference for sweet orangeade, but not in adults. It is not clear whether this effect is stable over time and if it is possible to extrapolate it to other sugars rich food (92).

In a recent systematic review by Nehring et al. (published after the cut-off date of the literature search), the hypothesis that foetuses and infants exposed to sweet, salty, sour, bitter, umami, or specific tastes show greater acceptance of that same taste later in life was explored (52). The authors identified 20 studies (15 intervention and 5 observational), of which 10 studies in 13 subgroups examined the effect of exposure to sweet tastes. All were conducted in infants below 1 year of age. Of these, 6 showed a statistically significant increase in intake, while 7 showed no difference. Subgroups not finding an effect

had smaller sample sizes. Based on intervention studies alone, the authors concluded that it is not clear whether exposure to sweet taste affects the later intake of sweet-flavoured foods.

Persistence of learned preferences

Infants routinely fed sweetened water by their mothers show a greater preference for sweetened water at 6 months (47, 85), 2 years (92, 95), 6 years (96) and 6-10 years of age (97). A prospective study among 166 girls from US reported that soda (carbonated SSB or artificially sweetened beverages) drinkers at age 5 years continued to have higher mean consumption of sodas at 7-15 years of age (98). These mostly observational studies suggest that SSB intake during infancy and early childhood might influence SSB intake in later childhood and continue through adolescence, but they do not allow causal inferences.

Children prefer higher concentrations of sucrose in water than do adults (84). They are less well able to discriminate between different sucrose concentrations than adolescents, and adolescents in turn have higher optimal preferred sucrose concentrations than adults. The age effects are similar for sucrose in water and sucrose in lemonade (99). Children at 8-9 years of age have a much higher density of taste pores and thus greater sensitivity to sucrose than adults (100). Eating habits with preferences for fatty and sweet food are likely to persist at least during early childhood. The Bogalusa Heart study has shown in a prospective manner that persistence of eating behaviours appears to begin as early as age 2 years, and consistency of intake levels of several nutrients including total sugars and sucrose lasts until at least 4 years of age (72). The preference for sweet taste seems to decline with age (101).

INTAKE OF SUGARS, SUGARS-SWEETENED FOODS/BEVERAGES AND HEALTH OUTCOMES IN CHILDREN/ADOLESCENTS

The WHO commissioned a systematic review and meta-analysis on the association of sugars intake and body weight (5, 6) as well as dental caries (see below) (5, 102) in children and adults. The systematic review on the association between sugars intake and body weight in children and adults included 30 randomised clinical trials (RCTs; 5 in children) and 38 prospective cohort studies (21 in

children) (5, 6) The UK SACN also performed a systematic review and meta-analysis and reviewed the relationships between carbohydrates, including sugars, sugars-sweetened foods and SSBs, and health, including body weight and dental caries in children, adolescents and adults (7). The two reviews employed different inclusion criteria for studies; the WHO considered a wider evidence base including studies of shorter duration, non-randomised trials, population and cross-sectional studies (5, 6) compared to SACN (7). A summary of the two reviews focusing on outcomes in the paediatric age group, and their conclusions and recommendations is provided in Table 6 in Appendix 3, and the main conclusions are described in the following sections along with data published since these reviews.

Intake of sugars/ SSBs and body weight or adiposity in children and adolescents

Effect of a higher intake of SSBs and/or sugars

The WHO meta-analysis of 5 prospective cohort studies in children revealed that after 1-year follow-up a higher consumption of SSBs was associated with a 55% higher risk of becoming overweight/obese vs. those with the lowest intake. Among free living people consuming *ad libitum* diets, intake of free sugars or SSBs is associated with body weight (5, 6). SACN reviewed evidence from prospective cohort studies and RCTs on the relationships between all types of carbohydrates in diet, including sugars, sugars-sweetened foods and SSBs, and health in children, adolescents and adults. They highlighted several associations between sugars intake and body weight, BMI, body fatness as a part of other health parameters.

A recent longitudinal study examined the association between SSB intake during infancy and obesity at age 6 years in 1,189 US children. The odds for obesity were 71% higher for any SSB intake and 92% higher for SSB introduction before age 6 months compared to children who had no SSB intake during infancy. The odds of obesity at 6 years among children who consumed \geq 3 SSBs/week (1 SSB = 230 ml; 106 kcal) between 10 and 12 months was twice that of children who were not fed SSBs (103). A cross-sectional study assessed the effects of SSBs on obesity prevalence in 2295 2-4 year olds. High intakes of SSBs were linked to increases in obesity prevalence. Compared to \geq 2 SSB/day, no SSB intake was associated with a 28% reduction in obesity prevalence (104).

A recent longitudinal, multicentre study investigated associations between SSB consumption in childhood and adolescence with subsequent changes in body fatness in early adulthood at 6- and 12-year follow-up. They enrolled 283 Danish children aged 9 years and collected data at 9, 15 and 21 years. Subjects who consumed more than one serving of SSB/day at age 15 years had larger increases in BMI and waist circumference (WC) than non-consumers over the subsequent 6 years. Subjects who increased their SSB consumption from age 9-15 years also had larger increases in BMI and WC from 15-21 years than those with no change in consumption. (105).

Effect of reduced intake of SSBs and/or sugars

The WHO meta-analysis of 5 RCTs in children that reduced SSBs and sugar-sweetened foods showed no change in body weight measured by standardized BMI or BMI z-score. Evidence was found to be less consistent in children than in adults due to low compliance with dietary advice. Nutrition education alone as an intervention to reduce free sugars intake had a limited effect (6). However, the meta-analysis did not include two more recent studies which (106, 107) overcame the limitations of previous trials, and a case-control study (108).

The double-blind placebo-controlled trial by De Ruyter *et al.* randomised 641 normal-weight Dutch children aged 5-11 years to an 18-month intervention (250 ml sugars-free, sucralose-sweetened beverage/day; 0 g sucrose (=0 kcal/serving)) versus a control group (250 ml SSBs, 26 g sucrose (=104 kcal/serving)). Compliance was measured by urinary sucralose. After 18 months, children receiving the non-calorically sweetened beverage had lower BMI z-score, skinfold thickness, waist to hip ratio, and less fat mass compared to children receiving SSBs. A reduction of 104 kcal from SSBs/day (~5% of daily energy at the diet 2,000 kcal/day) was associated with 1.01 kg lower weight gain over 1.5 years in normal weight children. The results were similar for dropouts. This study had good retention rates, was sufficiently powered and provided evidence that masked replacement of SSBs with non-caloric beverages reduces weight gain and fat accumulation in normal-weight children (106).

Ebbeling *et al.* randomly assigned 224 overweight and obese US adolescents who regularly consumed SSBs or 100% fruit juice (1.7 serving/day at baseline in both groups) to intervention (home delivery of water or non-caloric beverages for one year in place of SSBs) or a control group with the usual consumption. After 1-year of active intervention, the intervention group consumed significantly fewer SSBs (mean ± SEM 0.2±0.4 vs. 0.9±1.1 servings/day in control group; 1 serving=355ml), gained less weight (mean difference ± SEM -1.9±0.9 kg; p=0.04) and had a smaller increase in BMI (mean difference ± SEM -0.57±0.28 kg/m²; p=0.045) vs. control group. Both groups were followed up for an additional year without any intervention. At 2-years the consumption of SSBs was lower in the intervention group (mean ± SEM 0.4±0.5 vs. 0.8±0.8 servings/day in control group), but there was no significant difference in weight or BMI between the groups (107). These RCTs provide some evidence that decreasing consumption of SSBs, as a part of active intervention, may reduce childhood obesity (106, 107). They suggest an inadequate energy compensation (degree of voluntary reduction in intake of other foods/drinks) for energy delivered as sugars. Both studies were included by SACN after their initial systematic review and contributed to upgrading their recommendation (7).

A cluster RCT of a school-based education programme in 644 English children aged 7-11 years (overweight: 19% girls, 21% boys; obese: 10% girls, 11% boys in the study group and similar in the control group) produced a reduction in carbonated beverages, included non-calorically-sweetened and SSBs, consumed. This was associated with a reduction in the number of overweight and obese children after the 1-year intervention (included in WHO (5, 6) and SACN reviews (7)), (109), but not 2-years after the educational programme was discontinued (110). This results supports a benefit of reducing SSB consumption as part of an active intervention programme on childhood obesity, but points to the need for continuing intervention to promote a healthy food environment and healthy behaviours in children in order to maintain the effect (107, 110).

A RCT investigated the effect of decreasing SSBs consumption on body weight in US adolescents (13-18 years). Environmental intervention for 25 weeks almost completely eliminated SSBs consumption. The beneficial effect of reducing SSBs consumption on body weight increased with increasing baseline body weight. Decreasing SSBs consumption had a beneficial effect on body weight only in children in the upper tertile of BMI (included in WHO (5, 6)) (111).

Behavioural modifications

Additionally to the reviews by WHO (5, 6) and SACN (7), a systematic review and meta-analysis of studies in children, adolescents and adults by Malik *et. al* concluded that SSB consumption promotes weight gain. Sensitivity analyses of RCTs in children showed more pronounced benefits in preventing weight gain in SSB substitution trials than in school-based educational programs and among overweight compared to normal-weight children (112). Kaiser *et. al* performed a meta-analysis of studies in children and adults that added SSBs to diets and reported dose-dependent increases in weight. A meta-analysis of studies attempting to reduce SSB consumption in children and adolescents showed an equivocal effect on BMI in all subjects, whilst there was greater weight loss/less weight gain in subjects who were overweight at baseline. Thus the effect of SSBs may be more pronounced in obese children (113). These RCTs are trials of behavioural modifications and the findings are affected by intervention intensity and limited by adherence (114).

Intake of sugars/SSBs and oral health or dental caries

Sucrose is the most cariogenic sugar (33). It can form glucans that enable bacterial adhesion to teeth and limit diffusion of acid and buffers in the plaque (115, 116). Dental diseases are the most prevalent non-communicable diseases (NCD) worldwide (5, 117, 118). Their treatment consumes 5-10% of health-care costs in industrialized countries (5, 117, 119). SSBs intake is associated with increased risk of dental caries due to sugars and acidity that results in enamel erosion (120–122). Also the frequency of SSBs and sugars-containing foods consumption as well as oral hygiene play a role. In some studies, results are adjusted for tooth brushing frequency.

The WHO systematic review included studies if they reported an intervention to alter sugars intake, provided information on dental caries and lasted at least one year. Observational studies were included if they reported absolute or partial change in sugars intake and information on dental caries. Studies that reported solely on the frequency of sugars intake were excluded. The majority of studies were conducted in children (1 nonrandomized intervention study, 50 observational studies). 84% of studies in children and 100% studies in adults reported at least one positive association between sugars and caries. For the systematic review on dental caries, in most studies, dental caries was diagnosed at the level of cavitation (an advanced stage). It was concluded that there is a moderate level of evidence that the incidence of caries is lower when free-sugars intake is < 10% of energy. Using the <5% free-sugars cut-off, a significant decrease in dental caries was observed in 18,447 Japanese children around the second world war, when consumption of free sugars fell from 15 kg/person/year (i.e. 5-10% of energy) to <10 kg/person/year (i.e. <5% of energy intake), but the evidence was of very low quality, as it came from the ecological studies, which precludes linking exposure data to outcomes along with any assessment of causality (5, 102).

The SACN systematic review on dental caries included cohort studies and trials conducted in children and adolescents. The cohort studies that adjusted results for tooth brushing frequency were given more weight. Consumption of larger amounts of total sugars, sugars-containing foods/beverages as well as greater frequency of consumption of sugars-containing foods/beverages, but not the frequency of consumption of total sugars, was associated with a greater risk of dental caries in deciduous and permanent dentitions. The review concluded that there is consistent evidence, from prospective cohort studies, that the consumption of sugars is associated with increased risk of dental caries (7).

In a recent longitudinal study of 1,274 U.S. children frequent SSBs intake between 10 and 12 months was associated with a significantly greater likelihood of having dental caries at age 6 years; children with an average frequency intake of $SSBs \ge 3$ times/week had 83% higher odds for having dental caries by age 6 compared to children who were never fed SSBs, after adjusting for covariates including sweet

foods intake. Infancy may be an important time for mothers to establish healthy beverage habits for their children (123) as well as good dental hygiene practice with regular tooth-brushing.

Intake of sugars/SSBs and type 2 diabetes mellitus (T2D) and cardiometabolic risk

There are no relevant studies focusing on the intake of SSBs in children and adolescents and later T2D. However, in adults, the SACN review concluded that there is consistent evidence from prospective cohort studies that the intake of SSBs is associated with an increased risk of T2D, and that the effect may be biologically relevant (7). Two meta-analyses of prospective studies in adults showed an association between SSBs consumption and incidence of T2D (23, 124). Another meta-analysis of 10 large prospective studies in adults showed significant relative risk reduction of T2D by adherence to a healthy dietary pattern including decreased consumption of SSBs (125). The econometric analysis of Basu *et al.* ascertained that sugars meets the Bradford Hill criteria for causation for diabetes, including dose, duration, directionality, and precedence (126).

There are several RCTs in adults using diets differing in the proportion of sugars in relation to blood pressure (127–131). In a cross sectional study in adolescents, consumption of fructose and added sugars from SSBs was associated with higher blood pressure (132). The SACN concluded that there was not enough evidence on the effect of sugars intake on cardiovascular diseases to draw conclusions (7), however a number of studies published since this review suggest possible associations between sugars consumption and cardiovascular risk factors. A prospective cohort study suggested a significant relationship between added sugars consumption in adults and increased risk for cardiovascular disease mortality (133). A systematic review and meta-analysis in adults on the association between sugars intake and blood pressure and lipids concluded that dietary sugars influence diastolic blood pressure and serum lipids. In trials that lasted ≥ 8 weeks, higher consumption of sugars was associated with higher blood pressure independent of the effect of sugars on body weight (134). A possible effect of sugars on blood pressure is also suggested by some reviews in children, adolescents and adults (135, 136).

Two studies showed a relationship between sugars consumption and markers of cardiovascular disease in adolescents (137, 138). In a study of 559 14-18 year old adolescents living in the southern US higher total fructose consumption (free fructose + 50% of free sucrose) was positively associated with multiple markers of increased risk for cardiovascular disease and T2D. The relationships were independent of likely potentially confounding factors including physical activity, socioeconomic status, energy intake, and fibre consumption and were modified by visceral obesity (137). Whether fructose has specific metabolic effects is still controversial (139).

In a cross-sectional study of 2,157 US adolescents aged 12-18 years consumption of added sugars was positively associated with multiple measures known to increase cardiovascular disease risk. Added sugars intake was negatively correlated with mean HDL-cholesterol levels, while positively with LDL-cholesterol and triglycerides levels. Among overweight and obese adolescents, added sugars were positively correlated with the insulin resistance index (138).

A recent scientific statement from the AHA reviewed cardiovascular disease risk outcomes associated with added sugars including excess weight gain/obesity, elevated blood pressure and uric acid levels, dyslipidemia, and non-alcoholic fatty liver disease in children (risk factors). They cite several epidemiological and clinical trials studies where "excessive fructose intake resulted in increased blood pressure in children and young adults" and concluded that added sugars are a source of excess fructose, while the reduction of fructose from added sugars is likely to decrease uric acid, possibly improving blood pressure in children (4).

Other possible health effects of sugars-containing beverages

Malabsorption of sugars from fruit juice, especially when consumed in excessive amounts or even in non-excessive amounts (i.e. 240 ml of apple juice) in susceptible infants and children, can result in chronic diarrhoea, flatulence, bloating, and abdominal pain, and growth faltering in children (140, 141),

(142), (143) as well as in adults (144). Withdrawal of apple juice from the diets of susceptible children was curative in all cases (140).

SSBs and fruit juices given to infants may displace human milk or infant formula which may adversely affect nutrient supply and decrease dietary quality (7). Consumption of SSBs in children and adolescents is also associated with inadequate intake of calcium, iron, and vitamin A (145, 146).

Metabolic and satiety responses to fluid vs. solid forms of sugars

The form (liquid or solid) of dietary intake is related to energy balance. In a 6-year longitudinal study of 359 Danish children aged 8-10 years, liquid sucrose consumption was more strongly associated with changes in WC and BMI z-scores compared to solid sucrose consumption (147). Lee *et al* used data from a 10-year study of 2,021 US girls aged 9-10 years at baseline to determine if the association with adiposity varies by the form (liquid vs. solid) of sugars consumed. Before total energy adjustment, each additional teaspoon of liquid or solid added sugar was significantly associated with an increase in WC and BMI z-score. After adjustment for total energy intake, the association remained statistically significant only between liquid added sugars and WC among all subjects and between solid added sugars and WC among overweight/obese subjects only. There was no significant association with naturally occurring sugars. These findings suggest a positive association between added sugars intake (liquid and solid) and BMI that is mediated by total energy intake and an association with WC that is independent of it (148).

Studies in adults suggest whole foods are more satiating than liquid foods and that people do not compensate well for calories consumed as liquids by eating less food (130, 149, 150). A whole food decreases food intake at subsequent meals, while fibre added to a drink is not effective (2). Study participants consumed fewer calories at lunch after consuming apples compared to equal calories as apple sauce, apple juice, or apple juice with added fibre (151). Whole carrots were associated with lower calorie intake compared to carrot juice or a carrot juice cocktail that contained all the nutrients in

carrots (152). In lean and obese adults, liquid foods elicited a weaker compensatory dietary response than solid foods (watermelon juice vs. watermelon). Energy intake was 12.4% higher on the days the liquid forms of the high-carbohydrate foods were ingested, due to weaker satiety effect (153). Fruit juices have no nutritional advantages over whole fruits and, as they lack fibre, they are consumed more quickly than whole fruits (25).

WHAT SHOULD SUGARS BE REPLACED WITH IN PRODUCTS, OR IN THE DIET?

Effect of replacing sugars-containing beverages with water or milk

A randomized, controlled cluster trial conducted by Mucklebauer *et al.* in 32 elementary schools in 8 year old German children tested an education programme with environmental interventions (provision of drinking water in 17 schools; 15 control schools) and showed a modest reduction in the amount of SSBs consumed, which was associated with a 31% lower adjusted risk of overweight and obesity (154). A systematic review from six electronic databases from inception to November 2013 included 6 cohort studies and 4 RCTs in children and adults and showed a potential beneficial effect on long-term body weight management when SSBs are replaced by water, tea, coffee (in adults) or, in some studies, low-calorie artificially sweetened beverages. The optimal beverage alternative to SSBs may vary according to age group and/or disease outcome (155).

A study examined the association between different types of beverage intake and substitution of SSBs by water, milk, or 100% fruit juice in relation to 6-y change in body fatness. A cohort of 358 children aged 9 years who participated in the Danish part of the European Youth Heart Study was followed for development of body fatness over 6 years. SSB intake was associated with long-term changes in body fatness in children. Replacing SSBs with water or milk, but not 100% fruit juice, was inversely associated with body fatness development (156).

Secondary analysis of a nationally representative cross-sectional study of 3,098 US children and adolescents (aged 2-19 years) found that each additional 235 ml serving of SSB corresponds to 106 kcal/day higher total energy intake. Replacing SSBs with water was associated with a significant decrease in total energy intake; each 1% of replacement was associated with 6.6 kcal lower daily energy

intake and this reduction was not negated by compensatory increase in other food or beverages. The authors calculated that replacing all SSBs with water would result in an average net reduction of 235 kcal/day (157).

A secondary analysis of data from a 1.5-year RCT designed to prevent overweight among Danish children (aged 2–6 years) showed that every 100 g/day increase in sugary drink intake was associated with 0.10 kg and 0.06 unit increases in body weight and BMI z-score. Substitution of 100 g sugar containing beverages/day with 100 g milk/day was inversely associated with Δ weight and Δ BMI z-score. Sugary drink consumption was associated with body weight gain among young children with high predisposition for overweight (158).

A 16-week intervention trial in 8-10 year old Chilean children showed that replacing SSBs with milk may have beneficial effects on lean body mass and growth, with no changes in percentage body fat (159).

A systematic review of studies in adults showed that drinking water vs. SSBs or fruit juices before a meal was associated with a lower energy intake. In short-term feeding trials in adults drinking SSBs or fruit juices before a meal was associated with 7.8% or 14.4% higher total energy intake compared to drinking water (160). Findings suggest a role of water in reducing energy intake and obesity prevention.

Effect of replacing sugars with non-nutritive sweeteners (NNS)

NNS (or non-caloric sweeteners) are low in calories or have no calories and include artificial sweeteners (aspartame, acesulfame-K, saccharin, sucralose, neotame, advantame), very low-calorie sweeteners (stevia, a natural low-calorie sweetener and sugar alcohols) and non-caloric sweeteners (161).

A recent systematic review on early exposure of pregnant women, infants, or children below 12 years of age, to NNS and long-term metabolic health concluded that the effect of NNS exposure on metabolic health in children is uncertain, with conflicting evidence regarding the effects on BMI gain and fat accumulation. No studies have investigated this association among pregnant women and infants. Further

research is required to understand the long-term metabolic impact of NNS exposure during gestation, infancy, and childhood and to inform evidence-based recommendations for NNS use in this sensitive population (162).

A recent secondary, explorative analysis of a double-blind RCT (106) which showed that replacement of 250 ml SSBs/day by a sugar-free drink for 18 months significantly reduced weight gain in German chidren, aimed to estimate the extent of spontaneous compensation for changes in the intake of liquid kilocalories (i.e. liquid sugars, SSBs kcal) (163). Spontaneous compensation was more pronounced in children with a low BMI. Relative to the SSBs, consumption of the sugar-free beverage for 18 months reduced the BMI z-score in lower vs. higher BMI group by 0.05 vs. 0.21 SD units, and body weight gain by 0.62 vs. 1.53 kg. A physiologically-based model of growth and energy balance to estimate the degree to which children had compensated for the covertly removed sugars kilocalories by increasing their intake of other foods predicted that children with a lower BMI had compensated for 65%, whereas children with a higher BMI compensated only 13%. The authors postulated that in children with higher BMI, the sensing of kilocalories might be compromised (163).

It has been suggested that artificial sweeteners may be associated with increased risk of the same chronic diseases linked to sugars consumption and that they can interfere with basic learning processes that serve to anticipate the normal consequences of consuming sugars, leading to overeating, diminished release of hormones such as glucagon-like peptide-1, and impaired blood glucose regulation. It is also possible that they may alter gut microbiota, which could contribute to impaired glucose regulation, and that use of artificial sweeteners may be particularly problematic in children since exposure to hyper-sweetened foods and beverages at young ages may have effects on sweet preferences that persist into adulthood. (164) For children, the long-term effects of consuming artificially-sweetened beverages are unknown, so it has been proposed that it is best for children to avoid them (161) and that a focus on reducing sweetener intake (caloric or non-caloric) is a better strategy for combating overweight and obesity than use of artificial sweeteners (164). However the AHA and the American Diabetes Association concluded that there are insufficient data to determine conclusively whether the use of NNS to displace caloric

sweeteners in beverages and foods reduces added sugars or carbohydrate intakes, or benefits appetite, energy balance, body weight, or cardiometabolic risk factors (165). The American Academy of Pediatrics and AHA also noted that data on NNSs are scarce in terms of the long-term benefits for weight management in children and adolescents or the consequences of the long-term consumption. They concluded that a recommendation for or against the routine use of NNSs in the diets of children cannot be made at this time (166), (4).

Effect of replacing sugars with starch

A study in children (27 Latino, 16 African-American; aged 8-18 years) with obesity and metabolic syndrome investigated whether isocaloric replacement of sugars (disaccharides that consist of glucose and fructose) with starch (polymeric carbohydrate that consist of glucose units) would improve metabolic parameters. Children consumed a diet restricted in added sugars (reduced from 28% to ≤10% energy, and substituted with starch; fructose was reduced to ≤ 4% energy)), while the % of energy from protein, fat, and carbohydrate remained unchanged. After 10 days, reductions in diastolic blood pressure, lactate, triglyceride, and LDL-cholesterol were noted; glucose tolerance and hyperinsulinemia improved significantly, while weight and fat-free mass reduced. In a sub-group of children (n=10) who did not lose weight over the 10 days hyperinsulinemia improved significantly as well. Intervening in children and adjusting for effects of energy, weight gain, and adiposity, the isocaloric fructose restriction improved metabolic parameters in children with obesity and metabolic syndrome irrespective of weight change. The health detriments of sugars, specifically fructose, were independent of its caloric value or effects on weight(167).

SUMMARY AND CONCLUSIONS:

Regarding the terminology, classification and definitions of sugars and sugar containing beverages

- Existing studies use different definitions of sugars, so comparisons between studies are difficult.
- Smoothies and sweetened milks/milk products, including condensed milk, contain free sugars
 (above the level naturally present in milk or yogurt) but are not classified as SSBs. However they

are commonly consumed by children and represent an important source of free sugars in liquid form.

Regarding current recommendations and intakes of sugars, sugars-sweetened foods/beverages in children/adolescents

- There is no nutritional requirement for free sugars in infants, children and adolescents.
- Current average intake levels of sugars, particularly SSBs, among European children and adolescents far exceed recommended levels. Data are scarce for younger children.

Regarding the development of sweet taste and preference for sweet foods

- The preference for sweet taste is innate, has a strong genetic component and decreases with age. It may be modified or reinforced by pre- and postnatal exposures. Preference for sweet taste is driven by an interplay of many factors that involve feeding behaviour (reward system), food choices (senses and emotions) and taste (genetic and programming effects).
- Breastfeeding may be associated with greater acceptability of new foods and flavours.

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 Observational studies, show that SSB intake during infancy and early childhood is associated with SSB intake in childhood and adolescence, but cannot demonstrate that this is casual.

Regarding the evidence on health effects of sugars/sugar containing beverages in infants, children and adolescents

- A higher than recommended intake of sugars, particularly SSBs in children and adolescents, is associated with increased incidence of dental caries and adiposity.
- A higher than recommended intake of added sugars among adolescents may be positively
 associated with multiple measures known to increase cardiovascular disease risk. Data in
 adolescents reflect interventional studies in adults suggesting that higher fructose consumption

(from added sugars) is also associated with multiple factors that increase risk for cardiovascular disease and T2D.

Sugars-containing beverages do not promote satiety compared to the equivalent amount of sugars
in solid form and therefore induce excessive energy intakes.

Regarding what sugars should be replaced by

- Reducing the intake of SSBs by replacing them with water in children and adolescents is associated with reduced weight and adiposity.
- Replacing free sugars with NNS may reduce energy intake in the short-term, but their effectiveness
 and safety as a long-term weight management strategy remains to be evaluated. There is a lack of
 research in children on the effects of NNSs.

Based on these conclusions, the ESPGHAN Committee on Nutrition recommends:

- The WHO definition of 'free sugars' should be used uniformly in dietary recommendations, studies, regulations and foods labelling. "Free sugars' include monosaccharides and disaccharides added to foods and beverages by the manufacturer, cook or consumer, and sugars naturally present in honey, syrups, unsweetened fruit juices and fruit juice concentrates. This term describes sugars that may have physiological consequences different from intrinsic sugars incorporated within intact plant cell walls or lactose naturally present in milk.
- Smoothies and sweetened milk drinks/products (i.e. milk products containing a higher
 concentration of sugars than unprocessed human, cow or goat milk, such as chocolate milks,
 condensed milks, fruit yogurts) are not specifically mentioned in the WHO definition, however
 they are an important source of free sugars and their intake should be limited.
- Sugars naturally present in intact fruits (fresh, frozen or dried) and lactose in amounts naturally
 present in human milk or infant formula as well as in cow/goat milk and unsweetened milk
 products (e.g. natural yogurt) are not free sugars.

- Intakes of free sugars should be reduced and minimised with a desirable upper limit of < 5% energy intake in children and adolescents aged ≥ 2-18 years. This represents: 15-28 g of free sugars (3.5-7 teaspoons) for girls; 16-37 g (4-9 teaspoons) for boys, according to age (Table 4). Intakes should be even lower in infants and toddlers < 2 years.
- Sugar containing beverages and foods (SSBs, fruit juices, fruit-based smoothies and sweetened
 milk drinks/products) should be replaced by water or, in the latter case, with unsweetened milk
 drinks/products with lactose up to the amount naturally present in milk and unsweetened milk
 products.
- In Europe, the term "free sugars" should be included on food composition labels, expressed both in grams (under "Total Sugars") and as % daily energy intake. A more practical way of informing consumers might be to add the number of teaspoons of "total sugars" and "free sugars" (1 tea spoon = 4 g sugars) on front-of-pack labels. However, further research testing consumer preferences and understanding is required.

Practical points:

- National Authorities should adopt policies aimed at reducing the intake of free sugars in infants, children and adolescents. Depending on local circumstances, this may include education, improved labelling, restriction of advertising, introducing standards for kindergarten and school meals that include limits on free sugars, and fiscal measures such as taxation for SSBs and sugar rich foods and/or incentivising the purchase of healthy food...
- Sugars should preferably be consumed:
 - a. In its natural form such as human milk, milk, unsweetened dairy products, fresh fruits (Table 5, left column), rather than as SSBs, fruit juices, smoothies, and/or or sweetened milk drinks/products
 - b. As a part of a main meal, not as snacks.

- It is especially important to avoid or limit free sugars in infants and obese/overweight children/adolescents.
- Parents should be educated about the importance of regular tooth-brushing with fluoride toothpaste
 from the time the first tooth erupts

SUGGESTED FUTURE RESEARCH DIRECTIONS

- Better understanding of how infants and toddlers develop their food preferences and self-regulatory
 mechanisms, especially for sweet foods, to enable the development of evidence-based guidance for
 caregivers on how to feed infants and toddlers to favourably influence children's intake patterns.
- Systematic calculation of free sugars content in infant formulas, infant/toddlers/children/adolescent's foods and beverages should be promoted. This would allow: 1.) the incorporation of "free sugars" for all foods and beverages to food composition tables and nutritional software programmes, 2) more precise studies evaluating intake and health effects of free sugars 3) better information for the menu planners in kindergartens and schools, and 4) better information for the consumers.
- Long-term RCTs of dietary sugars consumption are difficult, because there are no biomarkers for dietary total sugars and/or free sugars for measure of compliance. The development of cheap and easy to use dietary biomarkers of total sugars and free sugars intake that would be suitable for use in large-scale studies are needed. They would enable objectively assess dietary consumption without the bias of self-reported dietary intake.
- The hypothesis that the effect of SSBs may depend on baseline BMI should be further studied in randomised double blind studies.

• The interaction between free sugars intake in infants, children, adolescents and the microbiome.

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References

- 1. Hess J, Latulippe ME, Ayoob K, Slavin J: The confusing world of dietary sugars: definitions, intakes, food sources and international dietary recommendations. *Food Funct* 2012; 3:477–86.
- 2. Slavin J: Beverages and body weight: challenges in the evidence-based review process of the Carbohydrate Subcommittee from the 2010 Dietary Guidelines Advisory Committee. *Nutr Rev* 2012; 70 Suppl 2:S111-20.
- 3. Johnson RK, Appel LJ, Brands M, et al.: Dietary sugars intake and cardiovascular health: a scientific statement from the American Heart Association. *Circulation* 2009; 120:1011–20.
- 4. Vos MB, Kaar JL, Welsh JA, et al.: Added Sugars and Cardiovascular Disease Risk in Children. A Scientific Statement From the American Heart Association. *Circulation* 2016; 134:00–00.
- 5. World Health Organization: *Guideline: Sugars Intake for Adults and Children*. Geneva, Switzerland: WHO; 2015.
- 6. Te Morenga L, Mallard S, Mann J: Dietary sugars and body weight: systematic review and metaanalyses of randomised controlled trials and cohort studies. *BMJ* 2013; 346:e7492.
- 7. SACN, Scientific Advisory Committee on Nutrition: *Carbohydrates and Health*. London: TSO, Ireland; 2015(August).
- 8. Bernstein JT, Schermel A, Mills CM, L'Abbé MR: Total and Free Sugar Content of Canadian Prepackaged Foods and Beverages. *Nutrients* 2016; 8.
- 9. Joesten MD, Hogg JL, Castellion ME: Oxidation-reduction reactions. In *World Chem Essentials*. 4th edition. Belmont, California: Thomson Brooks/Cole; 2007:203–220.
- 10. EFSA: Review of labelling reference intake values. Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to the review of labelling reference intake values for selected nutritional elements. *EFSA J* 2009; 1008:1–14.
- 11. Institute of Medicine: *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids.* Washington DC: National Academies Press; 2005.

- 12. U.S. Food and Drug Administration: Changes to the Nutrition Facts Label. Silver Spring; 2016.Web
- http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/LabelingNutrition/ucm385663.htm. Published March 8, 2016. Acessed Jun 30, 2017
- 13. Rangan A, Allman-Farinelli M, Donohoe E, Gill T: Misreporting of energy intake in the 2007 Australian Children's Survey: differences in the reporting of food types between plausible, under- and over-reporters of energy intake. *J Hum Nutr Diet* 2014; 27:450–8.
- 14. Kobe H, Kržišnik C, Mis NF: Under- and Over-Reporting of Energy Intake in Slovenian Adolescents. *J Nutr Educ Behav* 2012; 6:574–83.
- 15. Nash SH, Kristal AR, Hopkins SE, Boyer BB, Brien DMOÕ: Stable Isotope Models of Sugar Intake Using Hair, Red Blood Cells, and Plasma, but Not Fasting Plasma Glucose, Predict Sugar Intake in a Yup Õ ik Study Population. *J Nutr* 2014; 144:75–80.
- 16. The European Parliment and the Council of the European Union: Regulation (EU) No 1169/2011 of the European Parliament and of the Council on the provision of food information to consumers, amending Regulations (EC) No 1924/2006 and (EC) No 1925/2006 of the European Parliament and of the Council, *Off J Eur Union* 2011; 25 October:18–63.
- 17. EFSA Panel on Dietetic Products Nutrition and Allergies NDA: Scientific Opinion on the essential composition of infant and follow-on formulae. *EFSA J* 2014; 12:3760.
- 18. Codex Alimentarius.: Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants. CODEX STAN 72 1981. 1981.
- 19. Koletzko B, Baker S, Cleghorn G, et al.: Global standard for the composition of infant formula: recommendations of an ESPGHAN coordinated international expert group. *J Pediatr Gastroenterol Nutr* 2005; 41:584–99.
- 20. The Commission of the European Communities: Commission directive 2006/125/EC of 5 December 2006 on processed cereal-based foods and baby foods for infants and young children. *Off J Eur Union*

- 21. European Parliament and Council of the European Union: Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December on nutrition and health claims made on foods. *Off J Eur Communities* 2000; L 269(13.12.2014):1–31.
- 22. Hu FB, Malik VS: Sugar-sweetened beverages and risk of obesity and type 2 diabetes: Epidemiologic evidence. *Physiol Behav* 2010; 100:47–54.
- 23. Malik VS, Popkin BM, Bray GA, Després J-P, Willett WC, Hu FB: Sugar-Sweetened Beverages and Risk of Metabolic Syndrome and Type 2 Diabetes. A meta analysis. *Diabetes Care* 2010; 33:2477–2483.
- 24. Open platform for clinical nutrition (OPEN). 2016. Web site. http://www.opkp.si/sl_SI/fooddiary/diary. Published 2010. Accessed Jun 30th, 2017
- 25. Village EG: The Use and Misuse of Fruit Juice in Pediatrics. *Pediatrics* 2001; 107:1210–1213.
- 26. Faith MS, Dennison BA, Edmunds LS, Stratton HH: Fruit juice intake predicts increased adiposity gain in children from low-income families: weight status-by-environment interaction. *Pediatrics* 2006; 118:2066–75.
- 27. Agostoni C, Braegger C, Decsi T, et al.: Role of dietary factors and food habits in the development of childhood obesity: a commentary by the ESPGHAN Committee on Nutrition. *J Pediatr Gastroenterol Nutr* 2011; 52:662–9.
- 28. Barlow SE: Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. *Pediatrics* 2007; 120 Suppl:S164-92.
- 29. Gidding SS, Dennison BA, Birch LL, et al.: Dietary recommendations for children and adolescents: a guide for practitioners. *Pediatrics* 2006; 117:544–59.
- 30. Institute of Medicine of the National Academie: *Local Government Actions to Prevent Childhood Obesity*. Washington DC; 2009.
- 31. US Department of Health and Human Services and US Department of Agriculture: Dietary

- Guidelines for Americans. 6th ed. Washington, DC: US Government Printing Office; 2010.
- 32. WHO: Set of Recommendations on the Marketing of Foods and Non-Alcoholic Beverages to Children. Geneva; 2010.
- 33. Fewtrell M, Bronsky J, Campoy C, et al.: Complementary Feeding: A Position Paper by the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) Committee on Nutrition. *J Pediatr Gastroenterol Nutr* 2017; 64:119–132.
- 34. Kersting M, Alexy U, Clausen K: Using the concept of Food Based Dietary Guidelines to Develop an Optimized Mixed Diet (OMD) for German children and adolescents. *J Pediatr Gastroenterol Nutr* 2005; 40:301–8.
- 35. Mozaffarian D, Hao T, Rimm EB, Willett WC, Hu FB: Changes in diet and lifestyle and long-term weight gain in women and men. *N Engl J Med* 2011; 364:2392–404.
- 36. Lim S, Vos T, Flaxman A, Danaei G, Shibuya K, Adair-Rohani H: A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380:2224–2260.
- 37. Schiess S a, Grote V, Scaglioni S, et al.: Intake of energy providing liquids during the first year of life in five European countries. *Clin Nutr* 2010; 29:726–32.
- 38. Popkin BM, Nielsen SJ: The sweetening of the world's diet. *Obes Res* 2003; 11:1325–32.
- 39. Svensson A, Larsson C, Eiben G, et al.: European children's sugar intake on weekdays versus weekends: the IDEFICS study. *Eur J Clin Nutr* 2014; 68:822–8.
- 40. Poti JM, Slining MM, Popkin BM: Solid fat and added sugar intake among U.S. children: The role of stores, schools, and fast food, 1994-2010. *Am J Prev Med* 2013; 45:551–9.
- 41. Fidler Mis N, Kobe H, Štimec M: Dietary Intake of Macro- and Micronutrients in Slovenian Adolescents: Comparison with Reference Values. *Ann Nutr Metab* 2012; 61:305–313.
- 42. Popkin BM, Ph D, Chaloupka FJ, et al.: The Public Health and Economic Benefits of Taxing Sugar-Sweetened Beverages. *N Engl J Med* 2009; 361:1599–605.

- 43. Duffey KJ, Huybrechts I, Mouratidou T, et al.: Beverage consumption among European adolescents in the HELENA Study. *Eur J Clin Nutr* 2012; 66:244–52.
- 44. Kohler S, Kleiser C, Richter A, et al.: The Fluid intake of adolescents in Germany. Results collected in EsKiMo. *Ernährung -wiss und Prax* 2007; 1(10):444–450.
- 45. Kobe H, Štimec M, Ribič CH, Fidler Mis N: Food intake in Slovenian adolescents and adherence to the Optimized Mixed Diet: a nationally representative study. *Public Health Nutr* 2012; 15:600–8.
- 46. Currie C, Zanotti C, Morgan A, Currie D, All E: Social Determinants of Health and Well-Being among Young People. Behaviour in School-Aged Children (HBSC) Study: International Report from the 2009/2010 Survey. 2012.
- 47. Birch LL: Development of food preferences. Annu Rev Nutr 1999; 19:41-62.
- 48. Mennella J a, Jagnow CP, Beauchamp GK: Prenatal and postnatal flavor learning by human infants. *Pediatrics* 2001; 107:E88.
- 49. Alves JGB, Russo PC, Alves GV: Facial responses to basic tastes in breastfeeding and formula-feeding infants. *Breastfeed Med* 2013; 8:235–236.
- 50. Anliker J a., Bartoshuk L, Ferris a. M, Hooks LD: Children's food preferences and genetic sensitivity to the bitter taste of 6-n-propylthiouracil (PROP). *Am J Clin Nutr* 1991; 54:316–320.
- 51. Ramirez I: Why do sugars taste good? Neurosci Biobehav Rev 1990; 14:125–134.
- 52. Nehring I, Kostka T, von Kries R, Rehfuess EA: Impacts of in utero and early infant taste experiences on later taste acceptance: a systematic review. *J Nutr* 2015; 145:1271–1279.
- 53. Maller O, Turner RE: Taste in acceptance of sugars by human infants. *J Comp Physiol Psychol* 1973; 84:496–501.
- 54. Nisbett RE, Gurwitz SB: Weight, sex, and the eating behavior of human newborns. *J Comp Physiol Psychol* 1970; 73:245–253.
- 55. Blass EM, Fitzgerald E: Milk-induced analgesia and comforting in 10-day-old rats: opioid

- mediation. Pharmacol Biochem Behav 1988; 29:9-13.
- 56. Gibbins S, Stevens B: Mechanisms of sucrose and non-nutritive sucking in procedural pain management in infants. *Pain Res Manag* 2001; 6:21–28.
- 57. Stevens B, Yamada J, Lee GY, Ohlsson A: Sucrose for analgesia in newborn infants undergoing painful procedures. *Cochrane database Syst Rev* 2013; 1:CD001069.
- 58. Harrison D, Beggs S, Stevens B: Sucrose for Procedural Pain Management in Infants. *Pediatrics* 2012; 130:918–925.
- 59. Furquim TRD, Poli-Frederico RC, Maciel SM, Gonini-Júnior A, Walter LRF: Sensitivity to bitter and sweet taste perception in schoolchildren and their relation to dental caries. *Oral Heal {&} Prev Dent* 2010; 8:253–259.
- 60. Drewnowski a., Henderson S a., Barratt-Fornell a.: Genetic taste markers and food preferences. Drug Metab Dispos 2001; 29(4 II):535–538.
- 61. Max M, Shanker YG, Huang L, et al.: Tas1r3, encoding a new candidate taste receptor, is allelic to the sweet responsiveness locus Sac. *Nat Genet* 2001; 28:58–63.
- 62. Maone TR, Mattes RD, Beauchamp GK: Cocaine-exposed newborns show an exaggerated sucking response to sucrose. *Physiol* {&} *Behav* 1992; 51:487–491.
- 63. Gagin R, Cohen E, Shavit Y: Prenatal exposure to morphine alters analgesic responses and preference for sweet solutions in adult rats. *Pharmacol Biochem Behav* 1996; 55:629–634.
- 64. Muhlhausler BS, Ong ZY: The fetal origins of obesity: early origins of altered food intake. *Endocr Metab immune Disord drug targets* 2011; 11:189–197.
- 65. Bayol S a, Farrington SJ, Stickland NC: A maternal "junk food" diet in pregnancy and lactation promotes an exacerbated taste for "junk food" and a greater propensity for obesity in rat offspring. *Br J Nutr* 2007; 98:843–851.
- 66. Mennella JA, Beauchamp GK: Flavor experiences during formula feeding are related to preferences during childhood. *Early Hum Dev* 2002; 68:71–82.

- 67. Mennella JA: Flavour programming during breast-feeding. Adv Exp Med Biol 2009; 2:113–120.
- 68. Mennella J a, Johnson a, Beauchamp GK: Garlic ingestion by pregnant women alters the odor of amniotic fluid. *Chem Senses* 1995; 20:207–209.
- 69. Birch LL, Fisher JO: Food intake regulation in children. Fat and sugar substitutes and intake. *Ann N Y Acad Sci* 1997; 819:194–220.
- 70. Grieger JA, Scott J, Cobiac L: Dietary patterns and breast-feeding in Australian children. *Public Health Nutr* 2011; 14:1939–1947.
- 71. Larsen JK, Hermans RCJ, Sleddens EFC, Engels RCME, Fisher JO, Kremers SPJ: How parental dietary behavior and food parenting practices affect children's dietary behavior. Interacting sources of influence? *Appetite* 2015; 89:246–257.
- 72. Nicklas TA, Webber LS, Berenson GS: Studies of consistency of dietary intake during the first four years of life in a prospective analysis: Bogalusa Heart Study. *J Am Coll Nutr* 1991; 10:234–241.
- 73. Nicklaus S: Development of food variety in children. *Appetite* 2009; 52:253–255.
- 74. Hausner H, Nicklaus S, Issanchou S, Mølgaard C, Møller P: Breastfeeding facilitates acceptance of a novel dietary flavour compound. *Clin Nutr* 2010; 29:141–148.
- 75. Rosenstein D, Oster H: Differential facial responses to four basic tastes in newborns. *Child Dev* 1988; 59:1555–1568.
- 76. Conn JA, Davies MJ, Walker RB, Moore VM: Food and nutrient intakes of 9-month-old infants in Adelaide, Australia. *Public Health Nutr* 2009; 12:2448–2456.
- 77. Möller LM, de Hoog MLA, van Eijsden M, Gemke RJBJ, Vrijkotte TGM: Infant nutrition in relation to eating behaviour and fruit and vegetable intake at age 5 years. *Br J Nutr* 2013; 109:564–571.
- 78. de Lauzon-Guillain B, Jones L, Oliveira A, et al.: The influence of early feeding practices on fruit and vegetable intake among preschool children in 4 European birth cohorts. *Am J Clin Nutr* 2013; 98:804–812.

- 79. Perrine CG, Galuska DA, Thompson FE, Scanlon KS: Breastfeeding Duration Is Associated With Child Diet at 6 Years. *Pediatrics* 2014; 134(Supplement):S50--S55.
- 80. Cooke LJ, Wardle J: Genetic and environmental influences on children's food. *Am J Clin Nutr* 2007; 86:428–433.
- 81. Jamel HA, Sheiham A, Cowell CR, Watt RG: Taste preference for sweetness in urban and rural populations in Iraq. *J Dent Res* 1996; 75:1879–1884.
- 82. Lanfer A, Knof K, Barba G, et al.: Taste preferences in association with dietary habits and weight status in European children: results from the IDEFICS study. *Int J Obes* 2012; 36:27–34.
- 83. Gerrish CJ, Mennella J a.: Flavor variety enhances food acceptance in formula-fed infants. *Am J Clin Nutr* 2001; 73:1080–1085.
- 84. Mennella JA, Finkbeiner S, Lipchock S V, Hwang L-D, Reed DR: Preferences for salty and sweet tastes are elevated and related to each other during childhood. *PLoS One* 2014; 9:e92201.
- 85. Beauchamp GK, Moran M: Dietary experience and sweet taste preference in human infants. *Appetite* 1982; 3:139–152.
- 86. Sullivan S a., Birch LL: Pass the sugar, pass the salt: Experience dictates preference. *Dev Psychol* 1990; 26:546–551.
- 87. Birch LL, Gunder L, Grimm-Thomas K, Laing DG: Infants' consumption of a new food enhances acceptance of similar foods. *Appetite* 1998; 30:283–295.
- 88. Mennella JA, Griffin CE, Beauchamp GK: Flavor programming during infancy. *Pediatrics* 2004; 113:840–845.
- 89. Hoare A, Virgo-Milton M, Boak R, et al.: A qualitative study of the factors that influence mothers when choosing drinks for their young children. *BMC Res Notes* 2014; 7:430.
- 90. Fisher JO, Birch LL: Restricting access to palatable foods affects children's behavioral response, food selection, and intake. *Am J Clin Nutr* 1999; 69:1264–1272.

- 91. Alexy U, Schaefer A, Sailer O, et al.: Sensory preferences and discrimination ability of children in relation to their body weight status. *J Sens Stud* 2011; 26(October 2004):409–412.
- 92. Liem DG, de Graaf C: Sweet and sour preferences in young children and adults: role of repeated exposure. *Physiol* {&} *Behav* 2004; 83:421–429.
- 93. Knof K, Lanfer A, Bildstein MO, Buchecker K, Hilz H: Development of a method to measure sensory perception in children at the European level. *Int J Obes* 2011; 35:S131--S136.
- 94. Visser J, Kroeze JH, Kamps W a, Bijleveld CM: Testing taste sensitivity and aversion in very young children: development of a procedure. *Appetite* 2000; 34:169–176.
- 95. Beauchamp GK, Moran M: Acceptance of sweet and salty tastes in 2-year-old children. *Appetite* 1984; 5:291–305.
- 96. Park S, Pan L, Sherry B, Li R: The association of sugar-sweetened beverage intake during infancy with sugar-sweetened beverage intake at 6 years of age. *Pediatrics* 2014; 134(September):S56–S62.
- 97. Pepino MY, Mennella JA: Factors contributing to individual differences in sucrose preference. *Chem Senses* 2005; 30 Suppl 1:i319-20.
- 98. Fiorito LM, Marini M, Mitchell DC, Smiciklas-Wright H, Birch LL: Girls' early sweetened carbonated beverage intake predicts different patterns of beverage and nutrient intake across childhood and adolescence. *J Am Diet Assoc* 2010; 110:543–50.
- 99. De Graaf C, Zandstra EH: Sweetness intensity and pleasantness in children, adolescents, and adults. *Physiol Behav* 1999; 67:513–520.
- 100. Segovia C, Hutchinson I, Laing DG, Jinks AL: A quantitative study of fungiform papillae and taste pore density in adults and children. *Dev Brain Res* 2002; 138:135–146.
- 101. Desor JA, Beauchamp GK: Longitudinal changes in sweet preferences in humans. In *Physiol Behav. Volume 39*; 1987:639–641.
- 102. Moynihan PJ, Kelly SAM: Effect on caries of restricting sugars intake: Systematic review to inform WHO guidelines. *J Dent Res* 2014; 93:8–18.

- 103. Pan L, Li R, Park S, Galuska DA, Sherry B, Freedman DS: A Longitudinal Analysis of Sugar-Sweetened Beverage Intake in Infancy and Obesity at 6 Years. *Pediatrics* 2014; 134(Supplement):S29–S35.
- 104. Davis JN, Koleilat M, Shearrer GE, Whaley SE: Association of infant feeding and dietary intake on obesity prevalence in low-income toddlers. *Obesity (Silver Spring)* 2014; 22:1103–11.
- 105. Zheng M, Rangan A, Olsen NJ, et al.: Sugar-sweetened beverages consumption in relation to changes in body fatness over 6 and 12 years among 9-year-old children: the European Youth Heart Study. *Eur J Clin Nutr* 2014; 68:77–83.
- 106. de Ruyter JC, Olthof MR, Seidell JC, Katan MB: A trial of sugar-free or sugar-sweetened beverages and body weight in children. *N Engl J Med* 2012; 367:1397–406.
- 107. Ebbeling CB, Feldman HA, Chomitz VR, et al.: A Randomized Trial of Sugar-Sweetened Beverages and Adolescent Body Weight. *N Engl J Med* 2012; 367:1407–1416.
- 108. Martin-Calvo N, Martínez-González M-A, Bes-Rastrollo M, Gea A, Ochoa MC, Marti A: Sugar-sweetened carbonated beverage consumption and childhood/adolescent obesity: a case-control study. *Public Health Nutr* 2014; 17:1–9.
- 109. James J, Thomas P, Cavan D, Kerr D: Preventing childhood obesity by reducing consumption of carbonated drinks: cluster randomised controlled trial. *BMJ* 2004; 328:1237.
- 110. James J, Thomas P, Kerr D: Preventing childhood obesity: two year follow-up results from the Christchurch obesity prevention programme in schools (CHOPPS). *BMJ* 2007; 335:762.
- 111. Ebbeling CB, Feldman H a, Osganian SK, Chomitz VR, Ellenbogen SJ, Ludwig DS: Effects of decreasing sugar-sweetened beverage consumption on body weight in adolescents: a randomized, controlled pilot study. *Pediatrics* 2006; 117:673–80.
- 112. Malik VS, Pan A, Willett WC, Hu FB: Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. *Am J Clin Nutr* 2013; 98:1084–102.
- 113. Kaiser KA, Shikany JM, Keating KD, Allison DB: Will reducing sugar-sweetened beverage

- consumption reduce obesity? Evidence supporting conjecture is strong, but evidence when testing effect is weak. *Obes Rev* 2013; 14:620–33.
- 114. Malik VS, Willett WC, Hu FB: Nutritively sweetened beverages and obesity. *JAMA* 2009; 301:2210; author reply 2210-1.
- 115. Bowen WH, Pearson SK, Rosalen PL, Miguel JC, Shih AY: Assessing the cariogenic potential of some infant formulas, milk and sugar solutions. *J Am Dent Assoc* 1997; 128:865–71.
- 116. Anderson A: Sugars and health risk assessment to risk management. *Public Health Nutr* 2014; 17:2148–2150.
- 117. World Health Organization: *The World Oral Health Report* 2003. *Continuous Improvement of Oral Health in the 21st Century-the Approach of the WHO Global Oral Health Programme*. Geneva; 2003.
- 118. Marcenes W, Kassebaum NJ, Bernabe E, et al.: Global Burden of Oral Conditions in 1990-2010: A Systematic Analysis. *J Dent Res* 2013; 92:592–597.
- 119. Petersen PE, Bourgeois D, Ogawa H, Estupinan-Day S, Ndiaye C: The global burden of oral diseases and risks to oral health. *Bull World Health Organ* 2005; 83:661–9.
- 120. Warren JJ, Weber-Gasparoni K, Marshall TA, et al.: A longitudinal study of dental caries risk among very young low SES children. *Community Dent Oral Epidemiol* 2009; 37:116–22.
- 121. Ismail AI, Sohn W, Lim S, Willem JM: Predictors of dental caries progression in primary teeth. *J Dent Res* 2009; 88:270–5.
- 122. Jamel HA, Sheiham A, Watt RG, Cowell CR: Sweet preference, consumption of sweet tea and dental caries; studies in urban and rural Iraqi populations. *Int Dent J* 1997; 47:213–7.
- 123. Park S, Lin M, Onufrak S, Li R: Association of Sugar-Sweetened Beverage Intake during Infancy with Dental Caries in 6-year-olds. *Clin Nutr Res* 2015; 4:9–17.
- 124. Greenwood DC, Threapleton DE, Evans CEL, et al.: Association between sugar-sweetened and artificially sweetened soft drinks and type 2 diabetes: systematic review and dose-response meta-analysis of prospective studies. *Br J Nutr* 2014; 112:725–34.

- 125. Esposito K, Kastorini C-M, Panagiotakos DB, Giugliano D: Prevention of type 2 diabetes by dietary patterns: a systematic review of prospective studies and meta-analysis. *Metab Syndr Relat Disord* 2010; 8:471–6.
- 126. Basu S, Yoffe P, Hills N, Lustig RH: The Relationship of Sugar to Population-Level Diabetes Prevalence: An Econometric Analysis of Repeated Cross-Sectional Data. *PLoS One* 2013; 8:e57873.
- 127. Surwit RS, Feinglos MN, McCaskill CC, et al.: Metabolic and behavioral effects of a high-sucrose diet during weight loss. *Am J Clin Nutr* 1997; 65:908–15.
- 128. Vasilaras TH, Raben A, Astrup A: Twenty-four hour energy expenditure and substrate oxidation before and after 6 months' ad libitum intake of a diet rich in simple or complex carbohydrates or a habitual diet. *Int J Obes Relat Metab Disord* 2001; 25:954–65.
- 129. Poppitt SD, Keogh GF, Prentice AM, et al.: Long-term effects of ad libitum low-fat, high-carbohydrate diets on body weight and serum lipids in overweight subjects with metabolic syndrome. *Am J Clin Nutr* 2002; 75:11–20.
- 130. Raben A, Vasilaras TH, Møller a C, Astrup A: Sucrose compared with artificial sweeteners: different effects on ad libitum food intake and body weight after 10 wk of supplementation in overweight subjects. *Am J Clin Nutr* 2002; 76:721–9.
- 131. Black RNA, Spence M, McMahon RO, et al.: Effect of eucaloric high- and low-sucrose diets with identical macronutrient profile on insulin resistance and vascular risk: a randomized controlled trial. *Diabetes* 2006; 55:3566–72.
- 132. Nguyen S, Choi HK, Lustig RH, Hsu C: Sugar-sweetened beverages, serum uric acid, and blood pressure in adolescents. *J Pediatr* 2009; 154:807–13.
- 133. Yang Q, Zhang Z, Gregg EW, Flanders WD, Merritt R, Hu FB: Added sugar intake and cardiovascular diseases mortality among US adults. *JAMA Intern Med* 2014; 174:516–24.
- 134. Te Morenga L a, Howatson AJ, Jones RM, Mann J: Dietary sugars and cardiometabolic risk: systematic review and meta-analyses of randomized controlled trials of the effects on blood pressure

- and lipids. Am J Clin Nutr 2014; 100:65–79.
- 135. Malik VS, Popkin BM, Bray G a, Després J-P, Hu FB: Sugar-sweetened beverages, obesity, type 2 diabetes mellitus, and cardiovascular disease risk. *Circulation* 2010; 121:1356–64.
- 136. Malik VS, Hu FB: Sugar-sweetened beverages and health: where does the evidence stand? *Am J Clin Nutr* 2011; 94:1161–2.
- 137. Pollock NK, Bundy V, Kanto W, et al.: Greater Fructose Consumption Is Associated with Cardiometabolic Risk Markers and Visceral Adiposity in Adolescents 1 3. *J Nutr* 2012; 142:251–258.
- 138. Welsh J a, Sharma A, Cunningham S a, Vos MB: Consumption of added sugars and indicators of cardiovascular disease risk among US adolescents. *Circulation* 2011; 123:249–57.
- 139. Khan TA, Sievenpiper JL: Controversies about sugars: results from systematic reviews and metaanalyses on obesity, cardiometabolic disease and diabetes. *Eur J Nutr* 2016; 55:1–19.
- 140. Hyams JS, Leichtner AM: Apple juice. An unappreciated cause of chronic diarrhea. *Am J Dis Child* 1985; 139:503–5.
- 141. Hyams JS, Etienne NL, Leichtner AM, Theuer RC: Carbohydrate malabsorption following fruit juice ingestion in young children. *Pediatrics* 1988; 82:64–8.
- 142. Lifschitz CH: Carbohydrate absorption from fruit juices in infants. *Pediatrics* 2000; 105:e4.
- 143. Cole CR, Rising R, Lifshitz F: Consequences of incomplete carbohydrate absorption from fruit juice consumption in infants. *Arch Pediatr Adolesc Med* 1999; 153:1098–102.
- 144. Rumessen JJ, Gudmand-Høyer E: Functional bowel disease: malabsorption and abdominal distress after ingestion of fructose, sorbitol, and fructose-sorbitol mixtures. *Gastroenterology* 1988; 95:694–700.
- 145. Frary CD, Johnson RK, Wang MQ: Children and adolescents' choices of foods and beverages high in added sugars are associated with intakes of key nutrients and food groups. *J Adolesc Health* 2004; 34:56–63.
- 146. Ballew C, Kuester S, Gillespie C: Beverage choices affect adequacy of children's nutrient intakes.

Arch Pediatr Adolesc Med 2000; 154:1148-52.

- 147. Olsen NJ, Andersen LB, Wedderkopp N, Kristensen PL, Heitmann BL: Intake of liquid and solid sucrose in relation to changes in body fatness over 6 years among 8- to 10-year-old children: the European Youth Heart Study. *Obes Facts* 2012; 5:506–12.
- 148. Lee AK, Chowdhury R, Welsh JA: Sugars and adiposity: the long-term effects of consuming added and naturally occurring sugars in foods and in beverages. *Obes Sci Pract* 2015; 1:41–49.
- 149. Van Wymelbeke V, Béridot-Thérond M-E, de La Guéronnière V, Fantino M: Influence of repeated consumption of beverages containing sucrose or intense sweeteners on food intake. *Eur J Clin Nutr* 2004; 58:154–61.
- 150. DiMeglio DP, Mattes RD: Liquid versus solid carbohydrate: effects on food intake and body weight. *Int J Obes Relat Metab Disord* 2000; 24:794–800.
- 151. Flood-Obbagy JE, Rolls BJ: The effect of fruit in different forms on energy intake and satiety at a meal. *Appetite* 2009; 52:416–22.
- 152. Anne Moorhead S, Welch RW, Barbara M, et al.: The effects of the fibre content and physical structure of carrots on satiety and subsequent intakes when eaten as part of a mixed meal. *Br J Nutr* 2006; 96:587–95.
- 153. Mourao DM, Bressan J, Campbell WW, Mattes RD: Effects of food form on appetite and energy intake in lean and obese young adults. *Int J Obes (Lond)* 2007; 31:1688–95.
- 154. Muckelbauer R, Libuda L, Clausen K, Toschke AM, Reinehr T, Kersting M: Promotion and provision of drinking water in schools for overweight prevention: randomized, controlled cluster trial. *Pediatrics* 2009; 123:e661-7.
- 155. Zheng M, Allman-Farinelli M, Heitmann BL, Rangan A: Substitution of Sugar-Sweetened Beverages with Other Beverage Alternatives: A Review of Long-Term Health Outcomes. *J Acad Nutr Diet* 2015; 115:767–779.
- 156. Zheng M, Rangan A, Olsen NJ, et al.: Substituting sugar-sweetened beverages with water or milk

is inversely associated with body fatness development from childhood to adolescence. *Nutrition* 2015; 31:38–44.

- 157. Wang YC, Ludwig DS, Sonneville K, Gortmaker SL: Impact of change in sweetened caloric beverage consumption on energy intake among children and adolescents. *Arch Pediatr Adolesc Med* 2009; 163:336–43.
- 158. Zheng M, Rangan A, Allman-Farinelli M, Rohde JF, Olsen NJ, Heitmann BL: Replacing sugary drinks with milk is inversely associated with weight gain among young obesity-predisposed children. *Br J Nutr* 2015; 114:1448–1455.
- 159. Albala C, Ebbeling CB, Cifuentes M, Lera L, Bustos N, Ludwig DS: Effects of replacing the habitual consumption of sugar-sweetened beverages with milk in Chilean children. *Am J Clin Nutr* 2008; 88:605–11.
- 160. Daniels MC, Popkin BM: Impact of water intake on energy intake and weight status: a systematic review. *Nutr Rev* 2010; 68:505–21.
- 161. Artificial sweeteners [http://www.hsph.harvard.edu/nutritionsource/healthy-drinks/ artificial-sweeteners/]
- 162. Reid AE, Chauhan BF, Rabbani R, et al.: Early Exposure to Nonnutritive Sweeteners and Long-term Metabolic Health: A Systematic Review. *Pediatrics* 2016; 137:1–10.
- 163. Katan MB, de Ruyter JC, Kuijper LDJ, Chow CC, Hall KD, Olthof MR: Impact of Masked Replacement of Sugar-Sweetened with Sugar-Free Beverages on Body Weight Increases with Initial BMI: Secondary Analysis of Data from an 18 Month Double-Blind Trial in Children. *PLoS One* 2016; 11:e0159771.
- 164. Swithers SE: Artificial sweeteners are not the answer to childhood obesity. *Appetite* 2015; 93:85–90.
- 165. Gardner C, Wylie-Rosett J, Gidding SS, et al.: Nonnutritive sweeteners: current use and health perspectives: a scientific statement from the American Heart Association and the American Diabetes

Association. *Diabetes Care* 2012; 35:1798–808.

166. Council on School Health, Committee on Nutrition: Snacks, sweetened beverages, added sugars, and schools. *Pediatrics* 2015; 135:575–83.

167. Lustig RH, Mulligan K, Noworolski SM, et al.: Isocaloric fructose restriction and metabolic improvement in children with obesity and metabolic syndrome. *Obesity (Silver Spring)* 2015; 24:453–60.

168. Deutsche Gesellschaft für Ernährung (DGE), Österreichische Gesellschaft für Ernährung (ÖGE), Schweizerische Gesellschaft für Ernährung (SGE): *D-A-CH Referenzwerte Für Die Nährstoffzufuhr*. 2. Auflage. Bonn: DGE; 2015.