

Results of the WHO public consultation on the scope of the guideline on non-sugar sweetener intake

Comments were received from the following individuals and organizations

Government agencies

Jacinta Holdway	Australian Government Department of Health
Rusidah Selemat	Nutrition Division, Ministry of Health, Malaysia

Nongovernmental and consumer organizations and associations

Asha Mettla	L V Prasad Eye Institute, India
Robert Rankin	Calorie Control Council, USA

Private sector (including industry organizations and associations)

Angelika De Bree	Unilever, Netherlands
Vasiliki Pyrogianni	International Sweeteners Association, Belgium
Anne Roulin	Nestlé, Switzerland
Laurence Rycken	International Dairy Federation, Belgium

Academic/research

Salmeh Bahmanpour	Shiraz University of Medical Sciences, Iran
Jennie Brand-Miller	University of Sydney, Australia
Ifeoma Uzoamaka Onoja	University of Nigeria Teaching Hospital, Nigeria
Barry Popkin	University of North Carolina at Chapel Hill, USA
Pankaj Shah	SRMC & RI, SRU, India

Full comments for non-sugar sweeteners

(alphabetical by contributor)

1. Salmeh Bahmanpour

Shiraz University of Medical Sciences, Iran (Islamic Republic of)

Comments

Populations

If NSS -containing foods habitually added to usual intake will lead to excessive energy intake?

Does NNS intake had effect on the glycemic responses and plasma lipid levels in adults with diabetes?

To examine the safety and to monitor long-term metabolic outcomes in human,

To monitor effects on appetite in human with DM,

To determine amounts consumed in human.

Interventions

No comments provided.

Comparators

No comments provided.

Outcomes

No comments provided.

Additional Comments

No comments provided.

2. Jennie Brand-Miller

University of Sydney, Australia

Comments

Populations

General population, people with diabetes and chronic disease

Interventions

Lower added sugars intake by replacement of usual sugars with low digestibility sugars eg sorbitol, maltitol, polydextrose etc

Palatinose (slowly but fully absorbed) may be helpful

Comparators

Usual added sugar intake

Outcomes

Risk factors for chronic disease (fasting glucose, 2 h post-load glucose, postprandial glycaemia, serum cholesterol fractions, inflammatory markers such as CRP) but also changes in microbiota, gastro-intestinal symptoms).

Additional Comments

I am concerned that the food industry and consumer response to reduce added sugars will be higher intake of low digestibility sugars that cause increase the risk of diarrhoea and potentially gastrintestinal inflammatory syndromes

I am concerned that the WHO recommendation to reduce added sugars intake to 5% Energy may have unintended consequences. If consumers substitute 5%E in the form of added sugar with %E in the form of starch (mostly high glycaemic index) and/or low digestibility sugars, this will cause an increased risk of diabetes, CVD and gastrointestinal conditions.

3. Angelika De Bree

Unilever, Netherlands

Comments

Populations

We recommend including subjects with diabetes as a sensitive population for markers of glycaemic control.

Interventions

It is not explicitly stated, but recommended that sugar alcohols are excluded from the assessment. If included, they should be examined completely separately from the intense sweeteners listed, because of significant differences in the levels and metabolism.

The subgroup analyses should be hypothesis-led. It is not clear what hypothesis would underpin analyses based on 'natural' vs 'artificial'. Similarly it is not clear what differential exposure is tested by 'sweetness' since in practice the amounts used of different sweeteners are adjusted to deliver a similar taste intensity in packets or products as eaten by consumers.

It is unclear what is meant by 'adjusted for sugars intake', or whether this is appropriate, since the putative beneficial effects of non-sugars are largely attributable to the replacement of free sugars in the diet (rather than a benefit per se). Clarity is needed on the rationale (ie what is tested by this).

Comparators

No comments provided.

Outcomes

No comments provided.

Additional Comments

If observational or cohort studies are included, it is essential that the results (or the absence) of analyses that assess potential reverse causality are highlighted and considered in interpretation (Drewnowski A, Rehm CD. Nutr Diabetes 2016;6(3):e202).

We note that several of the studies on body weight include markers of glycemia as additional outcomes.

Additional comments (covering all topics)

Many thanks for this opportunity to input into the consultation.

4. Jacinta Holdway

Australian Government Department of Health, Australia

Comments

Populations

No comments provided.

Interventions

No comments provided.

Comparators

No comments provided.

Outcomes

Australia recommends changing 'dental erosion' to 'dental health' to capture all adverse (or beneficial) dental outcomes in addition to caries, which is already listed separately e.g. tooth loss, tooth wear, delayed tooth eruption (in children).

Additional Comments

No comments provided.

Additional comments (covering all topics)

Australia considers the PICOs developed by WHO to be very comprehensive. We are supportive of the GRADE approach being implemented.

5. Asha Mettla

L V Prasad EyeInstitute, India

Comments

Populations

No comments provided.

Interventions

Glycemic index for no-sugar sweeteners and role of non sugar sweeteners on the glycemic control

Comparators

No comments provided.

Outcomes

No comments provided

Additional Comments

No comments provided.

6. Ifeoma Uzoamaka Onoja

University of Nigeria Teaching Hospital, Nigeria

Comments

Populations

adults and children

Interventions

high vs low intake non sugar sweeteners.

Comparators

Placebo

Outcomes

cancer ,sweet preference,dental caries ,overweight/ obesity.

Additional Comments

No comments provided.

Additional comments (covering all topics)

High intake of carbohydrates, non sugar sweeteners could lead to chronic diseases both in children and in adults, whereas intake of high dietary fibre that is within the recommended level protects against some diseases.

The use of polyunsaturated fatty acids equally of great importance in maintaining adequate health.

7. Barry Popkin

University of North Carolina at Chapel Hill, USA

Comments

Populations

Two group preschoolers and children adolescents and adults

Interventions

yes-no to low calorie sweeteners

Comparators

water and caloric sweeteners in beverages, no solid food studies

ignore mouse world: mice are 100 times as receptive and reactive to sweeteners per gram of body weight as humans. the model does not work.

Outcomes

energy intake food choice, weight gain, cardiometabolic

Additional Comments

Non-sugar or low calorie sweeteners(LCS)

There is enormous pressure from those who fear any type of processing to focus on water vs all other beverages with low calorie or calorie sweeteners. i want to speak to science of public health and not the environment where the data is thin but politics rein heavy.

At this time I do not feel from my research and that of other scholars globally we have evidence that should allow us to put limits on low calorie non-sugar sweeteners. However research on sweetness preference for children, adolescents and young adults is lacking. One new RCT by Ludwig with young adults will come out within a year and essentially show the same murky message i am echoing. that young adults like older adults with a healthy diet will benefit from low calorie sweeteners.

This is a major research and policy issue. Currently the global food supply contains far more calorie sweeteners than most scholars understand as we have shown by going through the ingredients lists on the approximate 1.5 million US barcoded foods between 2000-2014. And then the ingredients of the posted ingredients on the nutrition facts panels often have caloric sweeteners¹. Over 70% of the calories consumed in the US contain caloric sweeteners and this same relationship will be seen globally when scholars begin to replicate the US research. With the new WHO sugar guidelines and with the focus on either positive or negative front-of-the-package food profiles focusing on added sugar, we expect to see a vast increase in foods and beverages with low calorie sweeteners in the coming decades.

First we must ignore animal research in this area. For gram of body weight mice have about 100

times the sweetness preference and reactivity as do humans. Much of the literature on mice provides extremely misleading evidence.

The role of low calorie sweeteners (LCS) sweeteners as they affect weight gain and diabetes risk has been studied very often in a careless manner. While careful reviews and random controlled trials (RCT's) have not shown any adverse relationship of LCS on energy intake or increased consumption of sweet foods 2,3, several longitudinal cohort studies implicate LCS as a cause of increased weight and diabetes and other adverse cardiometabolic outcomes 4-6. But these studies ignored a major issue, namely the potential for "affect modification" by an existing unhealthy diet. In fact, two analyses of earlier studies (Harvard cohorts and CARDIA cohort) with the same cohort data showed that the impact of diet beverage consumption on cardiometabolic health outcomes were reversed from a negative impact of increased LCS beverage intake to a positive reduced risk or no risk effect when diet was considered carefully. The revised studies considering the role of diet found that consumers of LCS beverages with an unhealthy western diet had a higher risk, while those consumers of LCS with a prudent healthier diet had a significantly lower risk 7,8.

One pressing issue is the impact of LCS beverage intake on sweetness preference. Only one RCT to date has tested this effect. Participants from the Choose Healthy Options Consciously Everyday (CHOICE) RCT (a 6-month 3-arm study) were included in the analysis (water arm n=106 (94% women); LCS beverage arm n=104 (82% women)). For energy, macronutrient and food/beverage intake, we investigated the main effect of time, treatment and the treatment by time interaction using mixed models. Overall, the macronutrient composition changed in both groups without significant differences between groups over time. Both groups reduced absolute intake of total daily energy, carbohydrates, fat, protein, saturated fat, total sugar, added sugar and other carbohydrates. The LCS beverage group decreased energy from all beverages more than the water group only at month 3 ($P<0.05$). While the water group reduced more grains at month 3 and increased more fruit and vegetables at month 6 ($P<0.05$), the LCS beverage group decreased more in desserts than the WA group at month 6 ($P<0.05$).

More research on sweetness preference is needed.

1. Popkin BM, Hawkes C. Sweetening of the global diet, particularly beverages: patterns, trends, and policy responses. *The Lancet Diabetes & Endocrinology*. 2016;4(2):174-186.
2. Mattes RD, Popkin BM. Nonnutritive sweetener consumption in humans: effects on appetite and food intake and their putative mechanisms. *The American Journal of Clinical Nutrition*. Jan 2009;89(1):1-14.
3. Piernas C, Tate, Deborah, Wang, Xiaoshan, Popkin, Barry Does diet beverage intake affect dietary consumption patterns? Results from the Choose Healthy Options Consciously Everyday

(CHOICE) randomized clinical trial. American Journal of Clinical Nutrition. 2013;97:1-8.

4. Dhingra R, Sullivan L, Jacques PF, et al. Soft drink consumption and risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community. Circulation. Jul 31 2007;116(5):480-488.
5. Lutsey PL, Steffen LM, Stevens J. Dietary Intake and the Development of the Metabolic Syndrome: The Atherosclerosis Risk in Communities Study. Circulation. February 12, 2008 2008;117(6):754-761.
6. de Koning L, Malik VS, Rimm EB, Willett WC, Hu FB. Sugar-sweetened and artificially sweetened beverage consumption and risk of type 2 diabetes in men. The American Journal of Clinical Nutrition. May 1, 2011 2011;93(6):1321-1327.
7. Duffey KJ, Steffen L, Van Horn L, Jacobs D, Jr., Popkin B. Dietary patterns matter: Diet beverages and cardio-metabolic risks in the longitudinal CARDIA Study. American Journal of clinical nutrition. 2011.
8. de Koning L, Malik VS, Kellogg MD, Rimm EB, Willett WC, Hu FB. Sweetened Beverage Consumption, Incident Coronary Heart Disease and Biomarkers of Risk in Men. Circulation. March 12, 2012 2012:1735-1741.

I fear that WHO must focus on the health side. We have far too many countries where the only alternative to sugary beverages is bottled water or bottled low calorie sweeteners beverages. there is a huge gap in knowledge so i prefer for preschoolers and young children to have water only in schools and all facilities buyt taxing and banning low calorie sweeteners without adequate science and enough RCT's and other studies to suggest they provide benefits is dangerous for WHO and the globe.

I should add from a practical side i am working on taxes with at least 5-6 countries and none feel the evidence is there yet to ban and tax diet beverages so WHO must have really careful solid evidence that reviews all the literature and not just selectively pick the literature to address this topic.

8. Vasiliki Pyrogianni

International Sweeteners Association, Belgium

Comments

Populations

No comments provided.

Interventions

With regard to proposed grouping of low calorie sweeteners into 'artificial' and 'natural', the International Sweeteners Association (ISA) believes that this type of grouping has no scientific basis. The term 'artificial sweetener' is not a recognised scientific term nor is it a term found in the regulatory approval of these ingredients. Low/no calorie sweeteners include both synthetic/man-made sweeteners, as well as plant-derived sweeteners such as steviol glycosides.

Comparators

The International Sweeteners Association (ISA) believes that more clarity is required with regards to the suggested comparators in PICO format document, and specifically about which ingredients will be grouped under the term 'other type of sweeteners'.

Outcomes

With regard to the selected critical outcomes for adults and children, the International Sweeteners Association (ISA) would like to submit a list of published scientific references to be taken into consideration by the WHO Department of Nutrition for Health and Development (NHD), and the Nutrition Guidance Expert Advisory Group (NUGAG) Subgroup on Diet and Health, in the systematic review and development of the guidelines for non-sugar sweeteners.

Adults:

Overweight/ Obesity

The balance of scientific evidence indicates that use of low calorie sweeteners such as aspartame, acesulfame-K, cyclamate, saccharin, sucralose and steviol glycosides in place of sugar, in both children and adults, leads to reduced energy intake and body weight. Furthermore, the effects of low calorie sweetened beverages on body weight also appear neutral relative to water, or even beneficial in some contexts. (Rogers et al, 2016)

List of evidence in support of this outcome (in alphabetical order):

1. Bellisle F, Drewnowski A. Intense sweeteners, energy intake and the control of body weight. Eur J Clin Nutr 2007; 61: 691–700
2. Blackburn GL, Kanders BS, Lavin PT, Keller SD, Whatley J. The effect of aspartame as part of a multidisciplinary weight-control program on short-and long-term control of body weight. Am J Clin

Nutr 1997; 65: 409–418.

3. de la Hunty A, Gibson S, Ashwell M. A review of the effectiveness of aspartame in helping with weight control. *Nutr Bull* 2006; 31: 115–128
4. Drewnowski A, Massien C, Louis-Sylvestre J, Fricker J, Chapelot D, Apfelbaum M. The effects of aspartame versus sucrose on motivational ratings, taste preferences, and energy intakes in obese and lean women. *Int J Obes Relat Metab Disord* 1994; 18: 570–578.
5. Fitch C, Keim KS, Academy of Nutrition and Dietetics. Position of the Academy of Nutrition and Dietetics: use of nutritive and nonnutritive sweeteners. *J Acad Nutr Diet* 2012; 112: 739–58
6. Gardner C, Wylie-Rosett J, Gidding SS, Steffen LM, Johnson RK, Reader D, Lichtenstein AH. Nonnutritive sweeteners: current use and health perspectives: a scientific statement from the American Heart Association and the American Diabetes Association. *Circulation* 2012; 126:509–519
7. Gibson S, Drewnowski J, Hill A, Raben B, Tuorila H and Windstrom E. Consensus statement on benefits of low calorie sweeteners. *Nutrition Bulletin* 2014; 39(4): 386-389
8. Kanders BS, Lavin PT, Kowalchuk MB, Greenberg I, Blackburn GL. An evaluation of the effect of aspartame on weight loss. *Appetite* 1988; 11: 73–84
9. Maersk M, Belza A, Holst JJ, Fenger-Grøn M, Pedersen SB, Astrup A et al. Satiety scores and satiety hormone response after sucrose-sweetened soft drink compared with isocaloric semi-skimmed milk and with non-caloric soft drink: a controlled trial. *Eur J Clin Nutr* 2012; 66: 523–529
10. Maersk M, Belza A, Stødkilde-Jørgensen H, Ringgaard S, Chabanova E, Thomsen H et al. Sucrose-sweetened beverages increase fat storage in the liver, muscle, and visceral fat depot: a 6-mo randomized intervention study. *Am J Clin Nutr* 2012; 95: 283–289
11. Mattes RD, Popkin BM. Nonnutritive sweetener consumption in humans: effects on appetite and food intake and their putative mechanisms. *Am J Clin Nutr* 2009; 89: 1–14
12. Miller P, Perez V. Low-calorie sweeteners and body weight and composition: a meta-analysis of randomized controlled trials and prospective cohorts (391.1). *FASEB J* 2014; 28: 391
13. Munsters MJ, Saris WH. The effect of sugar-sweetened beverage intake on energy intake in an ad libitum 6-month low-fat high-carbohydrate diet. *Ann Nutr Metab* 2010; 57: 116–123
14. Pereira MA, Odegaard AO. Artificially sweetened beverages—do they influence cardiometabolic risk? *Curr Atheroscler Rep* 2013; 15: 375
15. Peters JC, Wyatt HR, Foster GD, Pan Z, Wojtanowski AC, Vander Veur SS et al. The effects of water and non-nutritive sweetened beverages on weight loss during a 12-week weight loss treatment program. *Obesity* 2014; 22: 1415–1421
16. Peters JC, Beck J, Cardel M, et al. The effects of water and non-nutritive sweetened beverages on weight loss and weight maintenance: A randomized clinical trial. *Obesity* (Silver Spring)

2016; 24(2): 297-304

17. Piernas C, Tate DF, Wang X, Popkin BM. Does diet-beverage intake affect dietary consumption patterns? Results from the Choose Healthy Options Consciously Everyday (CHOICE) randomized clinical trial. *Am J Clin Nutr* 2013; 97: 604–611
18. Raben A, Vasilaras TH, Müller AC, 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: 721–729
19. Raben A, Richelsen B. Artificial sweeteners: a place in the field of functional foods? Focus on obesity and related metabolic disorders. *Curr Opin Clin Nutr Metab Care* 2012; 15: 597–604
20. Rogers PJ, Hogenkamp PS, de Graaf K, et al. Does low-energy sweetener consumption affect energy intake and body weight? A systematic review, including meta-analyses, of the evidence from human and animal studies. *Int J Obes* 2016; 40(3): 381-94
21. Steinert RE, Frey F, Topfer A, Drewe J, Beglinger C. Effects of carbohydrate sugars and artificial sweeteners on appetite and the secretion of gastrointestinal satiety peptides. *Br J Nutr*. 2011 May;105(9):1320-8
22. Tate DF, Turner-McGrievy G, Lyons E, Stevens J, Erickson K, Polzien K et al. Replacing caloric beverages with water or diet beverages for weight loss in adults: main results of the Choose Healthy Options Consciously Everyday (CHOICE) randomized clinical trial. *Am J Clin Nutr* 2012; 95: 555–563
23. Tordoff MG, Alleva AM. Effect of drinking soda sweetened with aspartame or high-fructose corn syrup on food intake and body weight. *Am J Clin Nutr* 1990; 51: 963–969

Dental caries

The beneficial role of low calorie sweeteners in dental health is well documented for both children and adults. Reviewing the scientific data in 2011, EFSA's Panel on Dietetic Products Nutrition and Allergies concluded that there is sufficient scientific information to support the claims that intense sweeteners, as all sugar replacers, maintain tooth mineralisation by decreasing tooth demineralisation if consumed instead of sugars (EFSA, 2011). Based on this scientific opinion, the European Commission authorised the health claim that the consumption of foods containing low calorie sweeteners instead of sugar contributes to the maintenance of tooth mineralisation (Commission Regulation (EU) No 432/2012).

Furthermore, the regular use of chewing gum containing non-cariogenic sweeteners has a role to play in preventing dental caries because of its non-cariogenic nature and its salivary stimulatory effect (FDI Policy Statement, 2008).

List of evidence in support of this outcome (in alphabetical order):

1. Commission Regulation (EU) No 432/2012 of 16 May 2012 establishing a list of permitted

health claims made on foods, other than those referring to the reduction of disease risk and to children's development and health.

2. Das S, Das AK, Murphy RA, Punwani IC, Nasution MP, Kinghorn AD. Evaluation of the cariogenic potential of the intense natural sweeteners stevioside and rebaudioside A. *Caries Res* 1992; 26(5): 363-6
3. Deshpande A, Jadad AR. The impact of polyol-containing chewing gums on dental caries: a systematic review of original randomized controlled trials and observational studies. *J Amer Dent Assoc.* 2008; 139(12): 1602-614
4. Edgar WM. Sugar substitutes, chewing gum and dental caries: a review. *Br Dent J.* 1998; 184(1): 29-32
5. EFSA NDA (EFSA Panel on Dietetic Products Nutrition and Allergies). Scientific opinion on the substantiation of health claims related to intense sweeteners and contribution to the maintenance or achievement of a normal body weight (ID 1136, 1444, 4299), reduction of post-prandial glycaemic responses (ID 4298), maintenance of normal blood glucose concentrations (ID 1221, 4298), and maintenance of tooth mineralisation by decreasing tooth demineralisation (ID 1134, 1167, 1283) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. *EFSA 2011 Journal* 9: 2229.
6. FDI World Dental Federation Policy Statement: Sugar substitutes and their role in caries prevention. Adopted by the FDI General Assembly, 26 September 2008, Stockholm, Sweden. Available online here: <http://www.fdiworldental.org/media/11367/Sugar-substitutes-and-their-role-in-caries-prevention-2008.pdf>
7. Gibson S, Drewnowski J, Hill A, Raben B, Tuorila H and Windstrom E. Consensus statement on benefits of low calorie sweeteners. *Nutrition Bulletin* 2014; 39(4): 386-389
8. Grenby TH. Update on low calorie sweeteners to benefit dental health. *Int Dent J* 1991; 41(4): 217-24
9. Kinghorn AD, Kaneda N, Baek NI, Kennelly EJ, Soejarto DD. Noncariogenic intense natural sweeteners. *Med Res Rev* 1998; 18(5): 347-60
10. Mandel ID, Grotz VL. Dental considerations in sucralose use. *J Clin Dent.* 2002; 13(3): 116-8.
11. Matsukubo T and Takazoe I. Sucrose substitutes and their role in caries prevention. *International Dental Journal* 2006; 56(3): 119-30
12. Roberts MW and Wright JT. Food sugar substitutes: a brief review for dental clinicians. *J Clin Pediatr Dent* 2002; 27(1): 1-4
13. Roberts MW and Wright JT. Nonnutritive, Low Caloric Substitutes for Food Sugars: Clinical Implications for Addressing the Incidence of Dental Caries and Overweight/Obesity. *Int J Dent* 2012; 625701

14. Touger-Decker R, van Loveren C. Sugars and dental caries. *The American Journal of Clinical Nutrition*. 2003;78(4):881S–892S.

Pre-diabetes/ type 2 diabetes

A large body of evidence shows that low calorie sweeteners do not affect blood glucose levels and insulin secretion in people with diabetes and healthy individuals, both normal-weight or obese.

Therefore, low calorie sweeteners have a clear benefit for people with type 1 and type 2 diabetes, as well as pre-diabetic individuals, when used in place of sugar.

Reviewing the scientific evidence in 2011, EFSA's Panel on Dietetic Products Nutrition and Allergies concluded, "Consumption of foods containing low calorie sweeteners instead of sugar induces a lower blood glucose rise after their consumption compared to sugar-containing foods". Based on this scientific opinion, the European Commission authorised the above health claim with regard to the beneficial effect of low calorie sweeteners in postprandial glucose (Commission Regulation (EU) No 432/2012).

List of evidence in support of this outcome (in alphabetical order):

1. Anton SD, Martin CK, Han H, Coulon S, Cefalu WT, Geiselman P et al. Effects of stevia, aspartame, and sucrose on food intake, satiety, and postprandial glucose and insulin levels. *Appetite* 2010; 55: 37–43
2. Barriocanal LA, Palacios M, Benitez G, Benitez S, Jimenez JT, Jimenez N, et al. Apparent lack of pharmacological effect of steviol glycosides used as sweeteners in humans. A pilot study of repeated exposures in some normotensive and hypotensive individuals and in Type 1 and Type 2 diabetics. *Regulatory toxicology and pharmacology: RTP*. 2008; 51(1): 37–41
3. Baird IM, Shephard NW, Merritt RJ, Hildick-Smith G. Repeated dose study of sucralose in human subjects. *Food Chem Toxicol*. 2000; 38 Suppl 2:S123-9.
4. Brown AW et al. Short-term consumption of sucralose, a nonnutritive sweetener, is similar to water with regard to select markers of hunger signaling and short-term glucose homeostasis in women. *Nutr Res* 2011; 31(12): 882-8
5. Bryant CE, Wasse LK, Astbury N, Nandra G, McLaughlin JT. Non-nutritive sweeteners: no class effect on the glycaemic or appetite responses to ingested glucose. *European journal of clinical nutrition*. 2014; 68(5): 629–31
6. Commission Regulation (EU) No 432/2012 of 16 May 2012 establishing a list of permitted health claims made on foods, other than those referring to the reduction of disease risk and to children's development and health.
7. EFSA NDA (EFSA Panel on Dietetic Products Nutrition and Allergies). Scientific opinion on the substantiation of health claims related to intense sweeteners and contribution to the maintenance

or achievement of a normal body weight (ID 1136, 1444, 4299), reduction of post-prandial glycaemic responses (ID 4298), maintenance of normal blood glucose concentrations (ID 1221, 4298), and maintenance of tooth mineralisation by decreasing tooth demineralisation (ID 1134, 1167, 1283) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA 2011 Journal 9: 2229.

8. Ford HE, Peters V, Martin NM, Sleeth ML, Ghatei MA, Frost GS et al. Effects of oral ingestion of sucralose on gut hormone response and appetite in healthy normal weight subjects. *Eur J Clin Nutr* 2011; 65: 508–513
9. Fujita Y et al. Incretin release from gut is acutely enhanced by sugar but not by sweeteners in vivo. *Am J Physiol Endocrinol Metab*, 2009; 296(3): E473-9
10. Gregersen S, Jeppesen PB, Holst JJ, Hermansen K. Antihyperglycemic effects of stevioside in type 2 diabetic subjects. *Metabolism: clinical and experimental*. 2004; 53(1): 73–6
11. Grotz VL, Henry RR, McGill JB, Prince MJ, Shamoon H, Trout JR and Pi Sunyer FX. Lack of effect of sucralose on glucose homeostasis in subjects with type 2 diabetes. *Journal of the American Dietetic Association*, 2003; 103: 1607-1612
12. Gougeon R, Spidel M, Lee K and Field CJ, 2004. Canadian Diabetes Association National Nutrition Committee Technical Review: Non-nutritive intense sweeteners in diabetes management. *Canadian Journal of Diabetes*, 28, 385-399
13. Horwitz DL, McLane M, Kobe P. Response to single dose of aspartame or saccharin by NIDDM patients. *Diabetes care*. 1988; 11(3): 230–4
14. Ma J et al. Effect of the artificial sweetener, sucralose, on gastric emptying and incretin hormone release in healthy subjects. *Am J Physiol Gastrointest Liver Physiol*, 2009; 296(4):G735-9
15. Ma J, Chang J, Checklin HL, Young RL, Jones KL, Horowitz M, et al. Effect of the artificial sweetener, sucralose, on small intestinal glucose absorption in healthy human subjects. *The British journal of nutrition*. 2010; 104(6): 803–6
16. Maersk M, Belza A, Holst JJ, Fenger-Gron M, Pedersen SB, Astrup A, et al. Satiety scores and satiety hormone response after sucrose-sweetened soft drink compared with isocaloric semi-skimmed milk and with non-caloric soft drink: a controlled trial. *European journal of clinical nutrition*. 2012; 66(4): 523–9
17. Maki KC, Curry LL, Reeves MS, Toth PD, McKenney JM, Farmer MV, et al. Chronic consumption of rebaudioside A, a steviol glycoside, in men and women with type 2 diabetes mellitus. *Food and chemical toxicology: an international journal published for the British Industrial Biological Research Association*. 2008; 46 Suppl 7: S47–53
18. Mezitis NH, Maggio CA, Koch P, Quddoos A, Allison DB, Pi-Sunyer FX. Glycemic effect of a single high oral dose of the novel sweetener sucralose in patients with diabetes. *Diabetes care*. 1996;

19(9): 1004–5

19. Nehrling JK, Kobe P, McLane MP, Olson RE, Kamath S, Horwitz DL. Aspartame use by persons with diabetes. *Diabetes care*. 1985; 8(5): 415–7
 20. Okuno G, Kawakami F, Tako H, Kashiwara T, Shibamoto S, Yamazaki T, et al. Glucose tolerance, blood lipid, insulin and glucagon concentration after single or continuous administration of aspartame in diabetics. *Diabetes research and clinical practice*. 1986; 2(1): 23–7
 21. Olalde-Mendoza L, Moreno-Gonzalez YE. [Modification of fasting blood glucose in adults with diabetes mellitus type 2 after regular soda and diet soda intake in the State of Queretaro, Mexico]. *Archivos latinoamericanos de nutrición*. 2013; 63(2): 142–7
 22. Renwick AG, Molinary SV. Sweet-taste receptors, low-energy sweeteners, glucose absorption and insulin release. *Br J Nutr* 2010; 104: 1415–1420
 23. Reyna NY, Cano C, Bermudez VJ, Medina MT, Souki AJ, Ambard M, Nunez M, Ferrer MA and Inglett GE. Sweeteners and beta-glucans improve metabolic and anthropometrics variables in well controlled type 2 diabetic patients. *American Journal of Therapeutics*, 2003; 10: 438-443
 24. Romo-Romo A, Aguilar-Salinas CA, Brito-Cordova GX, et al. Effects of the non-nutritive sweeteners on glucose metabolism and appetite regulating hormones: Systematic review of observational prospective studies and clinical trials. *Plos One* 2016; 11(8): e0161264
 25. Steinert RE, Frey F, Topfer A, Drewe J, Beglinger C. Effects of carbohydrate sugars and artificial sweeteners on appetite and the secretion of gastrointestinal satiety peptides. *Br J Nutr*. 2011 May;105(9):1320-8.
 26. Stellingwerff T, Godin JP, Beaumont M, Tavenard A, Grathwohl D, van Bladeren PJ, Kapp AF, le Coutre J, Damak S. Effects of pre-exercise sucralose ingestion on carbohydrate oxidation during exercise. *Int J Sport Nutr Exerc Metab*. 2013 Dec; 23(6):584-92.
 27. Sylvetsky AC, Brown RJ, Blau JE, Walter M, Rother KI. Hormonal responses to non-nutritive sweeteners in water and diet soda. *Nutr Metab (Lond)* 2016: 71.
 28. Temizkan S, Deyneli O, Yasar M, Arpa M, Gunes M, Yazici D, et al. Sucralose enhances GLP-1 release and lowers blood glucose in the presence of carbohydrate in healthy subjects but not in patients with type 2 diabetes. *European journal of clinical nutrition*. 2015; 69(2): 162–6
 29. Wu T, Ahao BR, Bound MJ, Checklin HL, Bellon M, Little TJ, Young RL, Jones KL, Horowitz M, Rayner CK. Effects of different sweet preloads on incretin hormone secretion, gastric emptying, and postprandial glycemia in healthy humans. *Am J Clin Nutr*. 2012 Jan;95(1):78-83.
 30. Wu et al. Artificial Sweeteners Have No Effect on Gastric Emptying, Glucagon-Like Peptide-1, or Glycemia After Oral Glucose in Healthy Humans. *Diabetes Care*, 2013; 36(12): e202-e203
- Children:

Overweight/ Obesity

The balance of scientific evidence indicates that use of low calorie sweeteners in place of sugar, in children and adults, leads to reduced energy intake and body weight. (Rogers et al, 2016)

To date, results from randomised clinical trials (RCTs) in children and adolescents have been consistent with studies in adults, showing that the use of low calorie sweeteners and replacement of sugar-sweetened beverages with low calorie sweetened options reduce weight gain and fat accumulation, in both normal-weight and overweight/ obese children and adolescents. (Ebbeling et al 2006; Rodearmel et al, 2007; de Ruyter et al, 2012; Ebbeling et al 2012)

List of evidence in support of this outcome (in alphabetical order):

1. 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: 1397–1406
2. Ebbeling CB, Feldman HA, 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
3. Ebbeling CB, Feldman HA, Chomitz VR, Antonelli TA, Gortmaker SL, Osganian SK et al. A randomized trial of sugar-sweetened beverages and adolescent body weight. *N Engl J Med* 2012; 367: 1407–1416
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6. Rogers PJ, Hogenkamp PS, de Graaf K, et al. Does low-energy sweetener consumption affect energy intake and body weight? A systematic review, including meta-analyses, of the evidence from human and animal studies. *Int J Obes* 2016; 40(3): 381-94
7. Williams CL, Strobino BA, Brotanek J. Weight control among obese adolescents: a pilot study. *Int J Food Sci Nutr* 2007; 58: 217–230

Dental caries

The beneficial role of low calorie sweeteners in dental health is well documented for both children and adults. Reviewing the scientific data in 2011, EFSA's Panel on Dietetic Products Nutrition and Allergies concluded that there is sufficient scientific information to support the claims that intense sweeteners, as all sugar replacers, maintain tooth mineralisation by decreasing tooth demineralisation if consumed instead of sugars (EFSA, 2011). Based on this scientific opinion, the European Commission authorised the health claim that the consumption of foods containing low

calorie sweeteners instead of sugar contributes to the maintenance of tooth mineralisation (Commission Regulation (EU) No 432/2012).

Furthermore, the regular use of chewing gum containing non-cariogenic sweeteners has a role to play in preventing dental caries because of its non-cariogenic nature and its salivary stimulatory effect (FDI Policy Statement, 2008).

List of evidence in support of this outcome (in alphabetical order):

1. Commission Regulation (EU) No 432/2012 of 16 May 2012 establishing a list of permitted health claims made on foods, other than those referring to the reduction of disease risk and to children's development and health
2. EFSA NDA (EFSA Panel on Dietetic Products Nutrition and Allergies). Scientific opinion on the substantiation of health claims related to intense sweeteners and contribution to the maintenance or achievement of a normal body weight (ID 1136, 1444, 4299), reduction of post-prandial glycaemic responses (ID 4298), maintenance of normal blood glucose concentrations (ID 1221, 4298), and maintenance of tooth mineralisation by decreasing tooth demineralisation (ID 1134, 1167, 1283) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA 2011 Journal 9: 2229
3. FDI World Dental Federation Policy Statement: Sugar substitutes and their role in caries prevention. Adopted by the FDI General Assembly, 26 September 2008, Stockholm, Sweden. Available online here: <http://www.fdiworldental.org/media/11367/Sugar-substitutes-and-their-role-in-caries-prevention-2008.pdf>
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6. Kandelman D, Gagnon G. A 24-month clinical study of the incidence and progression of dental caries in relation to consumption of chewing gum containing xylitol in school preventive programs. *J Dent Res.* 1990; 69: 1771–1775
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10. Szöke J, Banoczy J, Proskin HM. Effect of after-meal sucrose-free gum-chewing on clinical caries. J Dent Res. 2001; 80: 1725–1729

Eating behavior (appetite, satiety)

Overall, the existing evidence supports that the use of low calorie sweeteners shows no consistent association with a heightened appetite for sugar or sweet products in both children and adults. (Bellisle, 2015).

In fact, clinical studies in children showed that low calorie sweeteners use tends to reduce rather than increase the intake of sugar containing foods and to facilitate, rather than impair, weight loss. Moreover, low calorie sweetened drinks have been found to produce similar levels of satiety compared to sugar-sweetened beverages in children. (de Ruyter et al, 2013)

List of evidence in support of this outcome (in alphabetical order):

1. Anderson GH, Saravis S, Schacher R, Zlotkin S, Leiter LA. Aspartame: effect on lunch-time food intake, appetite and hedonic response in children. Appetite 1989; 13: 93–103
2. Bellisle F. Intense Sweeteners, Appetite for the Sweet Taste, and Relationship to Weight Management. Curr Obes Rep 2015; 4(1): 106-110
3. Birch LL, McPhee L, Sullivan S. Children's food intake following drinks sweetened with sucrose or aspartame: time course effects. Physiol Behav 1989; 45: 387–395
4. De Ruyter J, 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;367:1397-1406
5. de Ruyter JC, Katan MB, Kuijper LDJ, Liem DG, Olthof MR. The effect of sugar-free versus sugar-sweetened beverages on satiety, liking and wanting: An 18 month randomized double-blind trial in children. PlosOne 2013; 8(10): e78039
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7. Ventura AK, Mennella JA. Innate and learned preferences for sweet taste during childhood. Curr Opin Clin Nutr Metab Care 2011; 14: 379–384

Additional Comments

Thank you for the opportunity to provide comments.

9. Robert Rankin

Calorie Control Council, United States of America

Comments

Populations

The Calorie Control Council believes that the World Health Organization's Department of Nutrition for Health and Development (NHD) may want to consider that the proposed outcomes may have specific target populations. For example, the population elements considered for the outcome of dental caries may be different from those considered for obesity.

WHO defined general population as:

- Adults and children (> 2 years)
- Male and female
- Generally healthy
 - o Healthy BMI (18.5-24.9 kg/m²) for adults and percentile (5th – 85th) for children
 - o Healthy metabolic parameters (such as, but not limited to, glucose, insulin, HbA1c, triglycerides, healthy BMI)

Suggested criteria specific to outcomes of overweight/obese:

- Additional biological parameters for underlying co-morbidities should be adjusted or sub-grouped for:
 - o Diabetes
 - o Dyslipidemia
 - o Cardiovascular disease
- At-risk for unhealthy weight gain (adults, children)

Suggested criteria specific to outcome of prediabetes and type 2 diabetes:

- Clearly defined clinically diagnosed prediabetes or diabetes
 - o Glucose, insulin, HbA1c
 - o Control groups within healthy range with no baseline differences

Suggested criteria specific to outcome of dental caries:

- Sub-group analysis of adults with a) increased risk for root caries, b) xerostomia, and c) intake of medications that impact saliva production as these differences could affect the outcome
- Stratification on the basis of additional socioeconomic factors, including a) geography (rural vs. urban) and b) access to medical and dental care

Interventions

The Council believes that the intervention element should be defined as follows:

Individual sweetener (e.g., aspartame, acesulfame potassium, saccharin, sucralose, advantame, neotame, cyclamate, stevia, thaumatin, brazzein)

Sweeteners used in combination

% total sweetener intake

Consumption of beverages with non-nutritive sweeteners.

Consumption of foods with non-nutritive sweeteners.

Use of oral care products containing sweeteners (i.e., Sugar-free chewing gum)

The Council believes that grouping low-calorie sweeteners by artificial vs. natural is irrelevant as this may imply that natural is preferable to artificial. Further, for the remaining proposed outcomes, this should be clarified and NHD may want to consider if metabolism may be more relevant.

Energy intake should also be considered for both the control and the intervention groups. If non-sugar sweeteners are used in addition rather than in substitution of caloric sweeteners, this should be reported.

Caution should be taken with regard to self-reporting questionnaires in prospective cohort studies as the collection strategy for primary outcomes as underreporting is typical and may skew the results.

Further, less weight should be given to such observational studies with more weight given to randomized controlled trials (RCTs), where intake is specifically known.

Comparators

With regard to the proposed comparators for subgroup by solids (non-sugar sweetened vs sugar sweetened), the Council requests some additional clarity on how these would be grouped. Many solid foods, such as ice creams, breads and other confectionaries, contain both sugar and non-sugar sweeteners, as well as various digestible carbohydrates. Further clarity on how these products would be treated would be appreciated.

Additionally, the Council requests clarity regarding the proposed comparator for non-sugar sweetened beverages vs water related to level of sweetness. How would such an assessment be measured? As not all beverages have a standardized sweetness level, such a measurement might prove difficult.

Further, the Council believes that comparators for consideration should be:

Non-sugar sweeteners vs. cariogenic sweetener (sucrose, high fructose corn syrup (HFCS))

Non-sugar sweetener intake vs. standard of care/fluoride use (for dental caries)

Non-sugar sweetener intake vs. placebo (regardless of food form)

Outcomes

The Council believes NHD may want to consider reviewing short-term energy intake studies (RCT) for several of the outcomes, including those related to overweight/obesity and eating behavior.

Specifically for overweight/obesity, primary outcomes should be weight change with the secondary outcomes being total energy intake, diet quality, metabolic parameter changes (blood lipids, glucose/insulin) and satiety/food intake regulating hormones (GLP-1, CCK, PYY, ghrelin).

Relative to dental caries, the Council believes that the NHD should consider the primary outcome as caries risk using the International Caries Detection and Assessment System (IDCAS) criteria.

Reduction in caries incidence has also been measured by decay missing filled surfaces (DMFS) increment; however, this is a low sensitivity measure. Surrogate measures include plaque pH and re-mineralization.

Additional Comments

The Council believes that the systematic review should be evaluated by leading experts in several fields, including statistics, endocrinology (specifically energy balance, metabolism and diabetes) and toxicology with a number of methodological experts in evidence-based reviews. This will help to reduce risk of individual bias. Expertise in the area of evaluating the quality of evidence, such as the GRADE system, should also be included.

Additionally, the Council believes that assessments should take into consideration both human and animal data, including long-term studies conducted in the evaluation of sweeteners as part of safety assessments as it relates to the “Cancer” outcome listed in the PICO document. Data from animal toxicology studies provide insights into the safety of non-sugar sweeteners, as have been confirmed by leading health and regulatory agencies around the world. However, relative to nutrition-related health outcomes, WHO NUGAG should heavily rely on RCTs.

The Council also believes that care should be taken with how the communications of consultation findings are written. Non-sugar sweeteners have been determined to be safe and suitable as sugar replacements by leading global authorities and can be used as tools by clinicians worldwide in the management of overweight and nutritional therapy for patients, including those with diabetes.

Further, care should be taken in communications to ensure that the public is not under the impression that it would be better to replace non-sugar sweeteners with caloric sweeteners.

Specifically for overweight/obesity, key research questions may include:

Does substitution of sugar products with NSS support maintenance of healthy weight?

Does substitution of sugar products with NSS support reduction of body weight in overweight/obese?

Does substitution of sugar products with NSS result in reduced caloric intake?

Does substitution of sugar products with NSS result in improved eating patterns?

Does substitution of sugar products with NSS result in greater control over eating, cravings compared to water substitution?

Specifically for prediabetes/type 2 diabetes, key questions may include:

Does substitution of sugar products with NSS result in improved fasting and postprandial glycemic/insulemic control in pre-diabetics and diabetics?

Does substitution of sugar products with NSS aid in improved dietary adherence for disease control?

Specifically for dental caries, key research questions may include:

In the general population, does total non-sugar sweetener intake from solid foods compared to those with caloric sweeteners (sucrose, HFCS) result in a reduction in caries incidence per ICDAS criteria?

For those individuals with lower SES levels from isolated rural populations, does total non-sugar sweetener intake compared to intake of total caloric sweeteners (sucrose, HFCS) result in a reduction in caries incidence per ICDAS criteria?

For those individuals using medication which may affect saliva production, does total intake of non-sugar sweeteners compared to intake of caloric sweeteners (sucrose, HFCS) result in a reduction in caries incidence per ICDAS criteria?

For those with increased caries risk (such as those 60 years or older), does total non-sugar sweetener intake compared with total intake of caloric sweeteners (sucrose, HFCS) result in reduction in caries incidence per ICDAS criteria?

In addition to the comments above, the Council believes that the NHD should consider the following references in the systematic review and development of the guidelines for non-sugar sweeteners.

Overweight/Obesity (Adults)

1. Rogers PJ, Hogenkamp PS, de Graaf K, et al. Does low-energy sweetener consumption affect energy intake and body weight? A systematic review, including meta-analyses, of the evidence from human and animal studies. *Int J Obes* 2016; 40(3): 381-94.

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12. Raben A, Richelsen B. Artificial sweeteners: a place in the field of functional foods? Focus on obesity and related metabolic disorders. *Curr Opin Clin Nutr Metab Care* 2012; 15: 597â€“604
13. Fitch C, Keim KS, Academy of Nutrition and Dietetics. Position of the Academy of Nutrition and Dietetics: use of nutritive and nonnutritive sweeteners. *J Acad Nutr Diet* 2012; 112: 739â€“758
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- American Heart Association and the American Diabetes Association. *Circulation* 2012; 126:509â€“519
15. Munsters MJ, Saris WH. The effect of sugar-sweetened beverage intake on energy intake in an ad libitum 6-month low-fat high-carbohydrate diet. *Ann Nutr Metab* 2010; 57: 116â€“123
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 17. de la Hunty A, Gibson S, Ashwell M. A review of the effectiveness of aspartame in helping with weight control. *Nutr Bull* 2006; 31: 115â€“128
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Dental Caries (Adults)

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Prediabetes/Type 2 Diabetes (Adults)

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Overweight/Obesity (Children)

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Eating Behavior (Children)

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Dental Caries (children)

1. US FDA. Health claims: dietary noncariogenic carbohydrate sweeteners and dental caries. 21 C.F.R. Â§ 101.80. 2016.

10. Anne Roulin

Nestlé, Switzerland

Comments

Populations

Children will be considered from which age?

It would be relevant to include a third group with pregnant women, as the effects on health in this subgroup is a recurrent question.

Interventions

Which lengths of intervention will be included? It will be important to distinguish the outcomes of acute studies (test meal design) vs longer term interventions (>6 days)

“Capture sugars intake as intermediate outcome (check studies to see if adjusted for sugars intake)”: the meaning of this is not very clear.

Comparators

No comments provided.

Outcomes

Adults

- Cardiovascular diseases should be given a higher importance, given that increased blood lipids is one of the main proven effect of high-sugar diets.

Children

- Growth should be one of the outcome, as replacing a caloric sweetener (sugar) by a non-caloric one can affect growth (ref: Ebbeling et al, NEJM 2010: lower growth with non-sugar sweeteners)

Pregnant women

- Gestational diabetes
- Weight gain
- Blood lipids

Additional Comments

No comments provided.

Additional comments (covering all topics)

Thank you for the opportunity to contribute to this consultation.

11. Laurence Rycken

International Dairy Federation, Belgium

Comments

Populations

No comments provided.

Interventions

No comments provided.

Comparators

No comments provided.

Outcomes

No comments provided.

Additional Comments

No comments provided.

Additional comments (covering all topics)

The International Dairy Federation (IDF) would like to thank the WHO for this public call and we appreciate the opportunity to submit comments on the scope of the proposed update of WHO guidelines on the intake of carbohydrates, polyunsaturated fatty acids and non - sugar sweeteners. If, as stated the objective of this work is to ensure that WHO guidelines on these critical nutrients and associated dietary practices are comprehensive and informed by the most recent scientific data, we would suggest a 'whole food' and 'dietary approach', rather than an 'isolated nutrients' approach is taken.

Because:

1. Foods and diets are clearly far more than the sum of their single nutrients. Single nutrients are not consumed in isolation – many factors within a food influence the effects of a single nutrient and it is inaccurate to generalise about the effects of a single nutrient without considering the food it is present in.
2. Foods are not a matrix that we can adjust at will. Their composition is sometimes mainly defined by the raw material meaning by nature itself. Thus, in recommending decreasing or increasing the consumption of a single nutrient it will result in a modification of the diet itself. However, this major issue is not addressed if a nutrient approach is taken.

Instead of the suggested approach, the WHO evidence review should focus on foods and dietary patterns (rather than isolated nutrients) and on actual disease risk (rather than considering various

markers of risk in isolation).

People eat whole foods not single nutrients in isolation and food based recommendations are more practical for the general public than nutrient-based dietary advice. We would therefore urge WHO to provide clear guidelines on how to translate these recommendations into practical advice for consumers.

Moreover, the GRADE system appears more relevant to developing guidelines for pharmaceutical drug use than for food based dietary guidelines. For example, short term randomised controlled trials measuring short term changes in a small number of indicators of risk will be given higher priority than long term observational studies assessing dietary intake over many years and risk of developing NCDs.

12. Rusidah Selemat

Nutrition Division, Ministry of Health, Malaysia

Comments

Populations

Suggest to also include elderly.

Interventions

The scope of non-sugar sweetener. Suggest not to group non-sugar sweeteners which are from two different sources together such as aspartame and stevia

Scope/definition of sugar should also be defined.

Comparators

Scope/definition of sugar should also be defined.

Outcomes

No comments provided.

Additional Comments

No comments provided.

13. Pankaj Shah

SRMC & RI, SRU, India

Comments

Populations

Great.

Interventions

non question format

Comparators

Great.

Outcomes

Great.

Additional Comments

No comments provided.

Additional comments (covering all topics)

Dear Sir/Madam,

Thank you for the opportunity provided.

I feel along with PICO methods of the systematic review and possibility of meta-analysis should be included. As this research method is also very important along with PICO. For example- method of literature review, data extraction, assessment of heterogeneity, publication bias, independent work by review authors etc are also very important.

Also I suggest for registration of protocol with Prospero.

Thank you,

With regards,

Pankaj