

Beverages with added sugar

No. 2021/41Fe, The Hague, November 16, 2021

Background document to:

Dutch dietary guidelines for people with type 2 diabetes

No. 2021/41e, The Hague, November 16, 2021

Health Council of the Netherlands



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01 introduction

The current background document belongs to the advisory report *Dutch dietary guidelines for people with type 2 diabetes*.¹ It describes the methodology for the search, selection and evaluation of the literature regarding the relationship of consumption of beverages with added sugar with health outcomes in people with type 2 diabetes. It furthermore describes the scientific evidence on this topic and the conclusions that have been drawn by the Committee on Nutrition of the Health Council of the Netherlands.

The *Dutch dietary guidelines 2015* include a guideline on *sugar-containing beverages*, which is as follows²: Minimise the consumption of sugar-containing beverages.

Tea and filtered coffee without sugar, and water were cited as good alternatives for sugar-containing beverages in these guidelines.

Sugar-containing beverages covers beverages with added sugar as well as fruit juice (with or without added sugar), because the sugar-content of the two is comparable. The present background document covers the evaluation of the scientific literature on beverages with added sugar (including fruit juices with added sugar). The evaluation of the scientific literature on fruit juices without added sugar would have been included in the background document *Fruit and vegetables*. However, scientific literature on fruit juices was not identified by the Committee and thus could not be evaluated.

Data from the most recent Dutch National Food Consumption Survey (2012-2016) shows that the general Dutch population aged 19 to 79 years drinks on average approximately 290 ml of sugar-containing beverages, of which approximately 205 ml of sugar-containing soft drinks and approximately 54 ml of fruit juices.³



02 methodology

2.1 Research question

The Committee aimed to answer the following question: what is the relationship (effect or association) between consumption of beverages with added sugar and health outcomes in people with type 2 diabetes?

The Committee aimed to distinguish between short-term and long-term effects or associations where possible.

2.2 Nutritional topics

Beverages with added sugar are defined as cold drinks made by the addition of sucrose, fructose or glucose. Examples are fruit juice drinks (i.e. fruit juice with added sugar) and ‘nectars’, carbonated drinks (‘pops’ and ‘sodas’), ice tea, vitamin-fortified water and sports drinks made by the addition of sugar.⁴ Fruit juices without added sugar fall outside this definition. In Europe, sucrose is most often used to sweeten beverages. Most people know sucrose as ‘(table) sugar’ (in Dutch: ‘tafelsuiker’ or just ‘suiker’). Drinks sweetened with fructose or glucose are very rare.⁴

2.3 Outcomes

The health outcomes selected by the Committee for this advisory report are presented in the background document *Methodology for the*

evaluation of evidence.⁵ Those included long-term health outcomes, such as all-cause mortality or morbidity from stroke, and surrogate outcomes, such as body weight and fasting blood glucose.

For prospective cohort studies, the Committee included only studies with long-term health outcomes.

2.4 Selection and evaluation of literature

A detailed description of the approach used by the Committee for selecting and evaluating the scientific literature and for drawing conclusions is provided in the background document *Methodology for the evaluation of evidence*.⁵ In short, the Committee aimed to base its evaluation of scientific literature on systematic reviews (SRs), including meta-analyses (MAs), of randomised controlled trials (RCTs) and/or prospective cohort studies examining the relationship of consumption of beverages with added sugar with the selected health outcomes in people with type 2 diabetes. The Committee performed literature searches in PubMed and Scopus in July 2020. The search strategy, flow diagram of the literature search and detailed description of the study selection are provided in **Annex A**.

2.4.1 Selection of randomised controlled trials

The Committee did not retrieve any relevant SR (or MA) of RCTs on the relationship between consumption of beverages with added sugar and health outcomes in people with type 2 diabetes. The Committee found



SRs in which the effect of substitution of fructose with starch or sucrose (mostly isocaloric) on surrogate outcomes was evaluated.⁶⁻⁸ However, the Committee considered those studies not relevant for the evaluation of the effect of beverages with added sugar, because those studies evaluated the effect of (substitution of) different types of carbohydrates but not the effect of beverages with and without sugar. Moreover, the carbohydrates were not administered through drinks in the vast majority of RCTs included in those SRs. Altogether, this means that no (SRs of) RCTs were included in the Committee's evaluation of beverages with added sugar.

2.4.2 Selection of prospective cohort studies

The Committee found no SRs (or MAs) of prospective cohort studies examining the association between consumption of beverages with added sugar and long-term health outcomes in people with type 2 diabetes that met the eligibility criteria. Therefore, it searched for individual prospective cohort studies in existing external dietary guidelines for diabetes.⁹⁻¹⁴ This yielded one relevant individual prospective cohort study.¹⁵ Through searching the PubMed database for articles citing this study, one additional relevant publication was retrieved. This concerns a pooled analysis of prospective cohort studies.¹⁶ Both studies examined the association with the risk of all-cause mortality (Table 1). The Committee did not find prospective cohort studies within the pre-specified in- and

exclusion criteria for any of the specified chronic diseases and diabetes remission or reversion.

Table 1 Overview of (pooled analyses of) prospective cohort studies selected by the Committee for the evaluation of the associations between consumption of beverages with added sugar and health outcomes in people with type 2 diabetes.

Health outcome ^a	Pooled analysis (of prospective cohort studies)	Individual prospective cohort studies
All-cause mortality	Sluik et al., 2014 ¹⁶	Trichopoulou et al., 2006 ¹⁵

^a The table contains the health outcomes for which (relevant) studies were found. For the health outcomes that are not listed in the table, no (relevant) studies were found.

2.4.3 Drawing conclusions

A detailed description of the approach used for drawing conclusions is provided in the background document *Methodology for the evaluation of evidence*⁵. In short, the Committee drew conclusions on (the certainty of) the evidence regarding the association between consumption of beverages with added sugar and risk of all-cause mortality in people with type 2 diabetes, based on the number of studies, number of participants and number of cases that contributed to the evaluation. Also, it took into account the risk of bias and heterogeneity between studies. The Committee used the decision tree (**Annex B**) as tool to support consistency in drawing conclusions.



03 associations of beverages with added sugar

The scientific evidence for the association between consumption of beverages with added sugar and risk of all-cause mortality in people with type 2 diabetes is described in Table 2.

Table 2 Summary of the association of consumption of beverages with added sugar and the risk of all-cause mortality in people with type 2 diabetes: prospective cohort studies.

Study; study duration	Sluik et al., 2014 ¹⁶ ; 10 years ^a	Trichopoulou et al., 2006 ¹⁵ ; 5 years ^b
Study design	Pooled analysis of 15 cohorts	Individual cohort study
Cohort name	EPIC	EPIC-Greece
Exposure	Soft drinks; juices	Soft drinks and juices (combined)
Dietary assessment method	Self-administered, validated, country-specific dietary questionnaire at baseline, either quantitative dietary questionnaires, semi-quantitative FFQs, or combined dietary methods of food records and questionnaires	Validated, interviewer-administrated FFQ
Number of participants; number of cases	6,384 participants; All-cause mortality: 830	1,013 participants; All-cause mortality: 80
Strength of the association for all-cause mortality: HR (95%CI)	Soft drinks, per 10 g/d higher intake: 1.04 (0.99-1.09) ^c Juices, per 10 g/d higher intake: 0.98 (0.94-1.01) ^c	Soft drinks and juices (combined), per 85 g/d higher intake: 0.82 (0.57-1.17) ^d

Study; study duration	Sluik et al., 2014 ¹⁶ ; 10 years ^a	Trichopoulou et al., 2006 ¹⁵ ; 5 years ^b
Study population	Participants with a confirmed diagnosis of diabetes (type 1 or 2); BMI ^b : 29 ± 5 kg/m ² ; diabetes duration: NR; diabetes medication: NR; men and women; Europe	Participants with self-reported diabetes (type 1 or 2); BMI: <25 (13%), 25-30 (40%), ≥30 kg/m ² (47%); diabetes duration: NR; diabetes medication: oral glucose-lowering medications only (80%), insulin only or insulin and other oral glucose-lowering medications (20%); men and women; Europe

BMI: body mass index; CI: confidence interval; d: days; EPIC: European Prospective Investigation into Cancer and Nutrition; FFQ: food frequency questionnaire; HR: hazard ratio; NR: not reported.

^a Median.

^b Mean (± standard deviation).

^c Associations were stratified by age and centre, and adjusted for sex, prevalence of heart disease, cancer or stroke, educational attainment, diabetes medication, and the following when there were no exposure variables: alcohol consumption, smoking behaviour, physical activity and underlying dietary patterns.

^d Associations were adjusted for sex, age, education level, smoking, waist-to-height, hip circumference, physical activity, total energy intake, treatment with insulin, treatment for hypertension and treatment for hypercholesterolemia.

The Committee concluded the following:

There is too little research to draw conclusions regarding the association between consumption of beverages with added sugar and the risk of all-cause mortality in people with type 2 diabetes.

The following considerations were made by the Committee, following the steps of the decision tree, to come to this conclusion:

1. There are no MAs of prospective cohort studies that address the association between consumption of beverages with added sugar and risk of all-cause mortality in people with type 2 diabetes. There is one pooled analysis of 15 cohorts (all from the European Prospective



Investigation into Cancer and Nutrition (EPIC) consortium) and one individual cohort study (the Greek arm of EPIC, which was not included in the pooled analysis) that addresses this topic. In total, more than 500 mortality cases (n=910) were reported. This is the first step required to mark the evidence as strong. However, there were other considerations leading to the conclusion of ‘too little research’, as described below.

2. Both the pooled study and the individual study show no association between consumption of soft drinks, juices or the combination of the two with risk of all-cause mortality. The level of heterogeneity in the pooled analysis is unknown. There is moderate heterogeneity in the direction of the association between the pooled study and the individual study.
3. All cohorts in the pooled analysis are from the same consortium (EPIC) and thus any dependency between cohorts cannot be ruled out. To allow a conclusion of ‘an association is unlikely’, the result of the pooled analysis should therefore be supported by the result of another study. However, since the individual study in this evaluation is from the same consortium (EPIC) as the pooled analysis, the Committee judged the evidence as limited. This impedes a conclusion of ‘an association is unlikely’. Moreover, the exposure in both studies might concern soft drinks/juices with as well as without added sugars, whereas this advisory report focuses on beverages *with* added sugars. Altogether, the Committee downgraded its conclusion and concluded that there is too little research.

Explanation

One pooled analysis of 15 cohorts and one individual cohort study were found that addressed the association between consumption of beverages with added sugar (specifically: soft drinks and juices) and risk of all-cause mortality.

The study by **Sluik et al.**¹⁶ is a pooled analysis of 15 cohorts from the EPIC consortium, covering six European countries. The study included almost 6400 participants with confirmed diabetes. No information was provided on the proportions of the study population that had type 1 diabetes and type 2 diabetes. After a median of 9.9 years of follow-up (interquartile range (IQR): 8.8 to 11.0 years), 830 cases of all-cause mortality were reported. Median (IQR) intakes of soft drinks and juices at baseline were 9 (0-104) and 33 (0-96) g/d, respectively. It was not reported whether those soft drinks and juices all contained added sugar. However, based on other EPIC publications (e.g.^{17,18}) and the fact that a more detailed description of those food groups is lacking, it is likely that those food groups contain both drinks with (e.g. regular soft drinks, nectars) and without (e.g. light soft drinks, pure fruit juice) added sugar. This pooled analysis showed no associations of consumption of soft drinks or juices with risk of all-cause mortality in diabetes patients. In comparison, among non-diabetic persons, there was a lower risk of all-cause mortality with higher consumption of soft drinks and with higher consumption of juices. The authors reported no explanation for this.



Various sensitivity analyses were performed, for example excluding energy misreporters, but these did not substantially affect the results. It is unknown whether or not the non-diabetic persons consumed more non-carbonated (“light”) soft drinks compared to the diabetic persons, which might be an explanation for the different findings in non-diabetic and diabetic persons.

The study by **Trichopoulou et al.**¹⁵ was performed among the 1,030 participants with self-reported diabetes from the Greek arm of the EPIC consortium. It was not reported whether it concerned type 1 or type 2 diabetes patients; it likely is a combination of the two. During the 5-year follow-up, 80 cases of mortality were reported. Mean (\pm standard deviation) consumption of soft drinks and juices (combined) at baseline was 60 ± 86 g/d. Similar to the study by Sluik et al., Trichopoulou et al. did not report whether the food group of soft drinks and juices concerned drinks with or without added sugar, or both. It is assumed that it concerned both. No association of consumption of soft drinks and juices with risk of all-cause mortality was observed.

Funding or author’s conflicts of interest likely did not affect the study findings of the studies included in this evaluation (**Annex C**).



04 summary of conclusions

The Committee's conclusion regarding the association between consumption of beverages with added sugar and all-cause mortality in people with type 2 diabetes is summarised in Table 3.

Table 3 Overview of conclusions regarding the association between consumption of beverages with added sugar and the risk of all-cause mortality in people with type 2 diabetes, based on prospective cohort studies.

Health outcome ^a	Conclusion
All-cause mortality	Too little research

^a The table contains the health outcomes for which (relevant) studies were found. For the health outcomes that are not listed in the table, no (relevant) studies were found.



references

- ¹ Health Council of the Netherlands. *Dutch dietary guidelines for people with type 2 diabetes*. The Hague: Health Council of the Netherlands, 2021; publication no. 2021/41e.
- ² Health Council of the Netherlands. *Dutch dietary guidelines 2015*. The Hague: Health Council of the Netherlands, 2015; publication no. 2015/26E.
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- ⁴ Gezondheidsraad. *Dranken met toegevoegd suiker - Achtergronddocument bij Richtlijnen goede voeding 2015*. Den Haag: Gezondheidsraad, 2015; publicatienr. A15/08.
- ⁵ Health Council of the Netherlands. *Methodology for the evaluation of evidence. Background document to Dutch dietary guidelines for people with type 2 diabetes*. The Hague: Health Council of the Netherlands, 2021; publication no. 2021/41Ae.
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- ⁷ Cozma AI, Sievenpiper JL, de Souza RJ, Chiavaroli L, Ha V, Wang DD, et al. *Effect of fructose on glycemic control in diabetes: a systematic review and meta-analysis of controlled feeding trials*. *Diabetes Care* 2012; 35(7): 1611-1620.
- ⁸ Sievenpiper JL, Carleton AJ, Chatha S, Jiang HY, de Souza RJ, Beyene J, et al. *Heterogeneous effects of fructose on blood lipids in individuals with type 2 diabetes: systematic review and meta-analysis of experimental trials in humans*. *Diabetes Care* 2009; 32(10): 1930-1937.
- ⁹ Nederlandse Diabetes Federatie. *NDF Voedingsrichtlijn Diabetes*. Amersfoort, November 2020.
- ¹⁰ Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, et al. *2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD*. *Eur Heart J* 2020; 41(2): 255-323.
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- ¹² Diabetes UK 2018 Nutrition Working Group. *Evidence-based nutrition guidelines for the prevention and management of diabetes*. United Kingdom, 2018.
- ¹³ Diabetes Canada Clinical Practice Guidelines Expert Committee, Sievenpiper JL, Chan CB, Dworatzek PD, Freeze C, Williams SL. *Nutrition Therapy*. *Can J Diabetes* 2018; 42 Suppl 1: S64-S79.



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- ¹⁵ Trichopoulou A, Psaltopoulou T, Orfanos P, Trichopoulos D. *Diet and physical activity in relation to overall mortality amongst adult diabetics in a general population cohort*. Journal of Internal Medicine 2006; 259(6): 583-591.
- ¹⁶ Sluik D, Boeing H, Li K, Kaaks R, Johnsen NF, Tjønneland A, et al. *Lifestyle factors and mortality risk in individuals with diabetes mellitus: are the associations different from those in individuals without diabetes?* Diabetologia 2014; 57(1): 63-72.
- ¹⁷ InterAct C, Romaguera D, Norat T, Wark PA, Vergnaud AC, Schulze MB, et al. *Consumption of sweet beverages and type 2 diabetes incidence in European adults: results from EPIC-InterAct*. Diabetologia 2013; 56(7): 1520-1530.
- ¹⁸ Slimani N, Fahey M, Welch AA, Wirfalt E, Stripp C, Bergstrom E, et al. *Diversity of dietary patterns observed in the European Prospective Investigation into Cancer and Nutrition (EPIC) project*. Public Health Nutr 2002; 5(6B): 1311-1328.



annex A

search strategy, study selection and flow diagram

Systematic reviews including meta-analyses

The Committee performed a literature search to identify relevant systematic reviews (SRs) including meta-analyses (MAs) on the relationship between carbohydrate-containing food sources and health outcomes in people with type 2 diabetes. Literature searches were performed in PubMed and Scopus on 20th and 29th July 2020, respectively, using the following search strategies:

PubMed

("diabetes mellitus, type 2"[MeSH] OR Diabet*[tiab] OR T2DM[tiab] OR NIDDM[tiab]) AND (("Dietary Fiber"[Mesh] OR "Dietary Carbohydrates"[Mesh] OR "Starch"[Mesh] OR "Polysaccharides"[Mesh] OR "Fructans"[Mesh] OR "Inulin"[Mesh] OR "Dietary sugars"[Mesh] OR (dietary[tiab] AND (fiber*[tiab] OR fibre*[tiab] OR carbohydrates[tiab] OR starch*[tiab] OR fructan[tiab] OR inulin[tiab] OR sugar*[tiab]))) OR (("edible grain"[MeSH] OR "edible grain"[tiab] OR cereals[tiab] OR "Whole Grains"[Mesh] OR grain*[tiab] OR wheat*[tiab] OR oat[tiab]) OR

(fruit[MeSH] OR fruit[tiab] OR fruits[tiab]) OR (vegetables[MeSH] OR vegetables[tiab]) OR (((sugars[MeSH] OR sugars[tiab] OR sugar[tiab] OR sweetened[tiab] OR sweetener[tiab]) AND (beverages[MeSH] OR beverages[tiab] OR drink*[tiab] OR juice*[tiab] OR soda*[tiab]))) OR (fabaceae[MeSH] OR fabaceae[tiab] OR legume[tiab] OR legumes[tiab] OR bean*[tiab] OR "Soybean Proteins"[Mesh] OR soy[tiab] OR soya[tiab])) AND (Systematic review[publication type] OR Meta-analysis[publication type] OR review[tiab] OR "meta-analysis"[tiab] OR meta analysis[tiab] OR metaanalysis[tiab] OR quantitative review[tiab] OR quantitative overview[tiab] OR systematic review[tiab] OR systematic overview[tiab] OR methodologic review[tiab] OR methodologic overview[tiab])

Limit: from 2000 + English

Scopus

((((KEY ("diabetes mellitus, type 2") OR TITLE-ABS-KEY (t2dm) OR TITLE-ABS-KEY (niddm))) OR (TITLE-ABS ("diabetes mellitus, type 2") OR TITLE-ABS (diabet*) OR TITLE-ABS (t2dm) OR TITLE-ABS (niddm))) AND (((TITLE-ABS-KEY ("Dietary Fiber") OR TITLE-ABS-KEY ("Dietary Carbohydrates") OR TITLE-ABS-KEY ("Starch") OR TITLE-ABS-KEY ("Polysaccharides") OR TITLE-ABS-KEY ("Fructans") OR TITLE-ABS-KEY ("Inulin")))) OR ((TITLE-ABS (dietary)) AND (TITLE-ABS (fiber*) OR TITLE-ABS (fibre*) OR TITLE-ABS (carbohydrates) OR TITLE-ABS



(starch*) OR TITLE-ABS (fructan) OR TITLE-ABS (inulin) OR TITLE-ABS (sugar)))) OR ((TITLE-ABS-KEY (“edible grain”)) OR ((TITLE-ABS-KEY (cereals) OR KEY (“Whole Grains”) OR TITLE (grain*) OR ABS (grain*) OR TITLE (wheat*) OR ABS (wheat*) OR TITLE (oat) OR ABS (oat))) OR (KEY (fruit) OR TITLE-ABS (fruit) OR TITLE-ABS (fruits)) OR (KEY (vegetables) OR TITLE-ABS (vegetables)) OR (KEY (sugars) OR TITLE-ABS (sugar) OR TITLE-ABS (sugars) OR TITLE-ABS (sweetened) OR TITLE-ABS (sweetener) OR KEY (beverages) OR TITLE-ABS (beverages) OR TITLE-ABS (drink*) OR TITLE-ABS (juice*) OR TITLE-ABS (soda*) OR KEY (fabaceae) OR TITLE-ABS (fabaceae) OR TITLE-ABS (legume) OR TITLE-ABS (legumes) OR KEY (“Soybean Proteins”) OR TITLE-ABS (soy) OR TITLE-ABS (soya)))) AND (((TITLE-ABS-KEY (“Systematic review”) OR TITLE-ABS-KEY (“Meta-analysis”))) OR (TITLE-ABS (review) OR TITLE-ABS (meta-analysis) OR TITLE-ABS (meta analysis) OR TITLE-ABS (“quantitative review”) OR TITLE-ABS (“quantitative overview”) OR TITLE-ABS (“systematic overview”) OR TITLE-ABS (“methodologic review”) OR TITLE-ABS (“methodologic overview”)))

Limit: from 2000 + English

In total, 2054 publications were found in PubMed and 3887 publications in Scopus. After removal of duplicates, 4527 publications remained and were screened for title and abstract. A total of 172 publications remained for

full-text assessment, of which 19 were selected for the Committee’s evaluation of high-carbohydrate foods.

Of those 19 publications, 3 SRs⁶⁻⁸ focused on fructose (a monosaccharide that can be used, but in Europe is rarely used, to sweeten drinks) compared to other carbohydrates, but the Committee considered those studies irrelevant for the evaluation of consumption of beverages with added sugar (compared to consumption of beverages without added sugar or a lower consumption of beverages with added sugar).

No SRs remained for the Committee’s evaluation.



Prospective cohort studies

Since no SR or MA of (multiple) cohort studies were found, the Committee searched for individual prospective cohort studies on associations between consumption of beverages with added sugar and health outcomes in external dietary guidelines for diabetes of the following organisations:

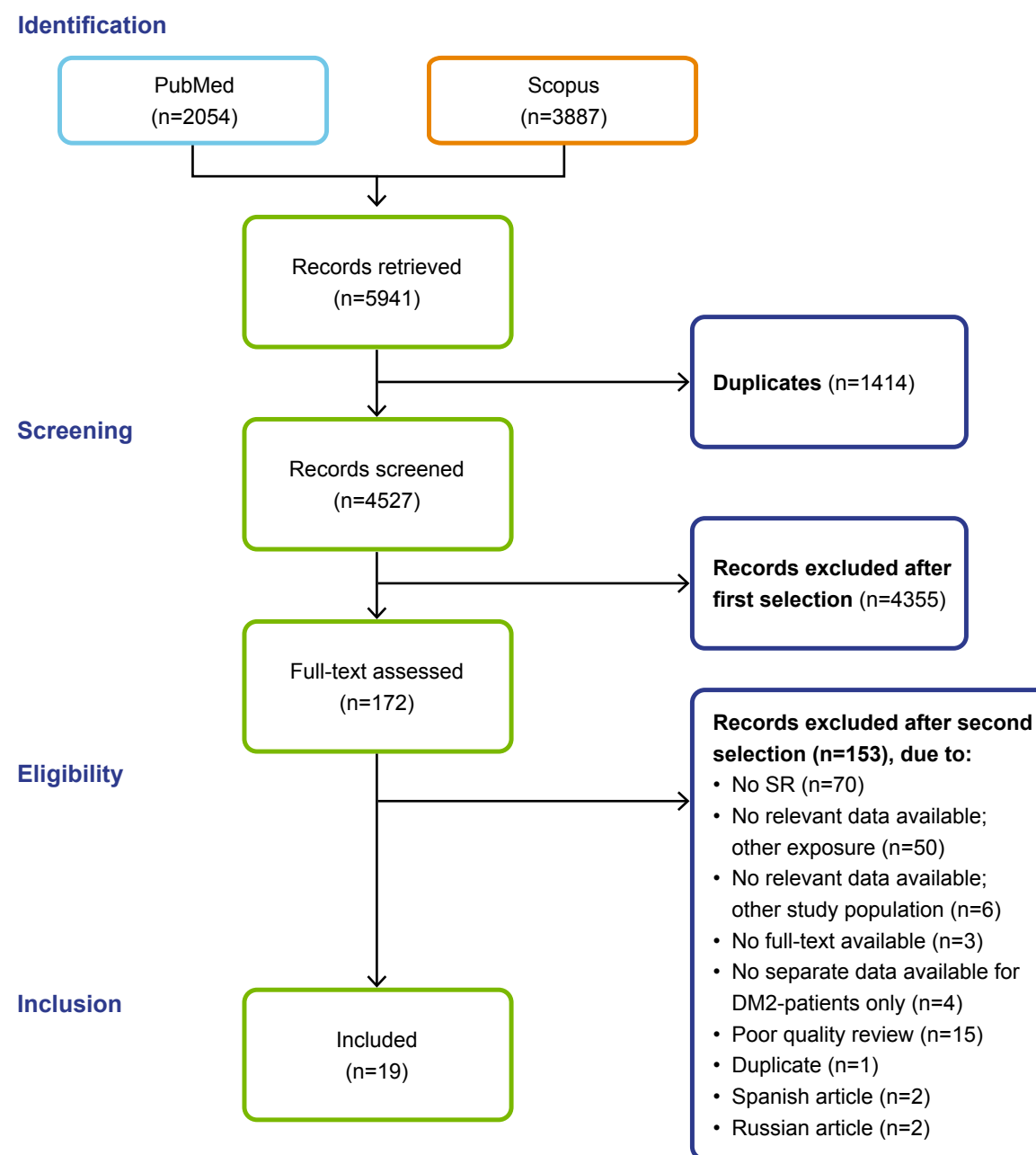
- Dutch Diabetes Federation (Nederlandse Diabetes Federatie (NDF)), 2020⁹
- European Association for the Study of Diabetes (EASD) & European Society of Cardiology (ESC), 2020¹⁰
- American Diabetes Association (ADA), 2019¹¹
- Diabetes UK, 2018¹²
- Diabetes Canada, 2018¹³
- Swedish Council, 2010¹⁴

One prospective cohort study¹⁵ was retrieved via the dietary guidelines of the Swedish Council.¹⁴ Articles citing this study were searched in PubMed. This yielded one additional relevant publication: a pooled analysis of prospective cohort studies.¹⁶

The Committee selected the following prospective cohort studies for its evaluation of beverages with added sugar:

- Sluik et al., 2014¹⁶ (pooled analysis of prospective cohort studies)
- Trichopoulou et al., 2006¹⁵

Flow diagram for the selection of systematic reviews including meta-analyses

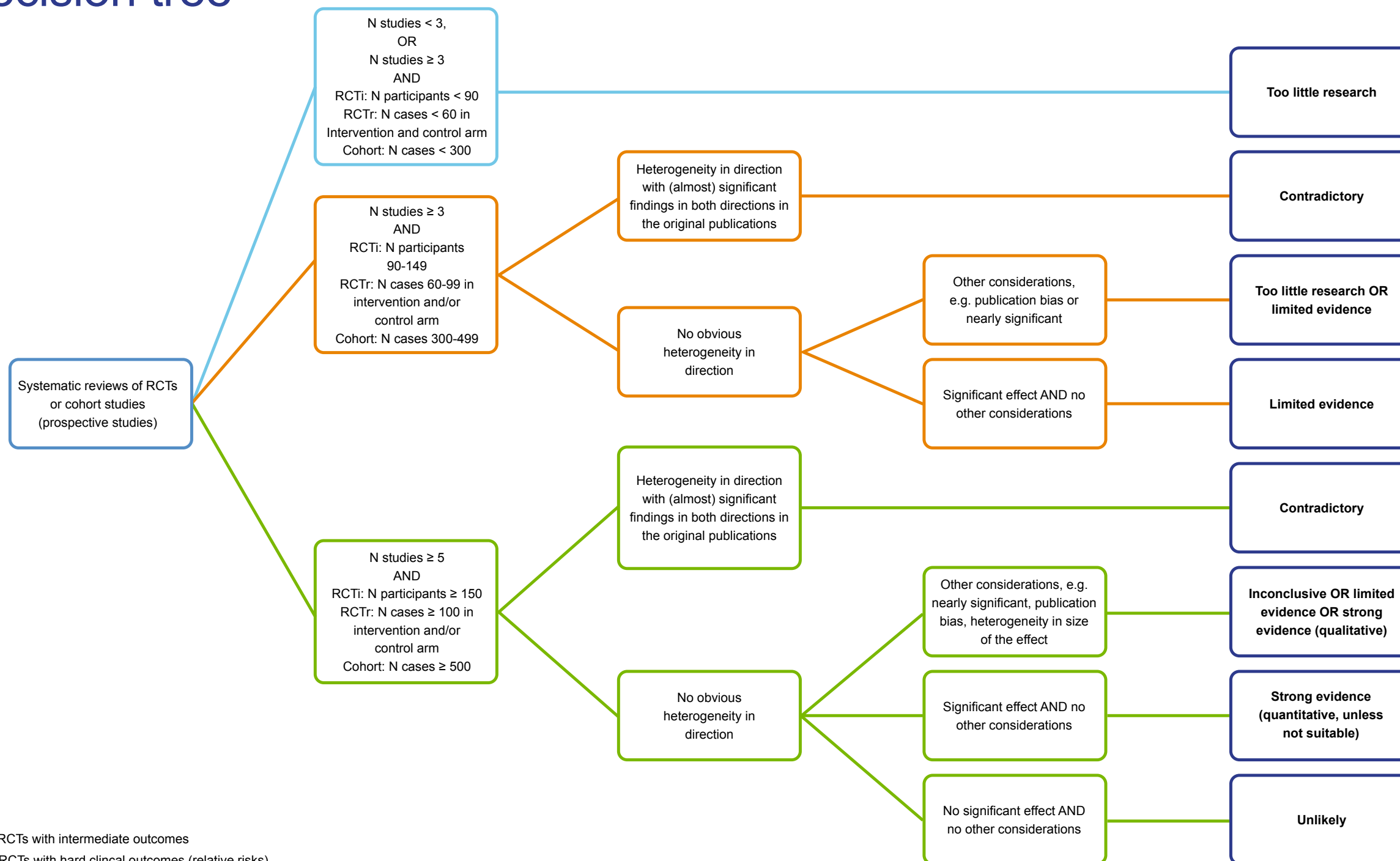


DM2: type 2 diabetes.



annex B

decision tree



RCTi: RCTs with intermediate outcomes
 RCTr: RCTs with hard clinical outcomes (relative risks)



annex C

funding sources and conflicts of interest regarding the articles used in this background document

In the table below, the funding sources of the studies listed in this background document and conflicts of interests of authors contributing to those studies are reported.

Study's first author, year	Funding of the work	Conflicts of interest of authors
Sluik, 2014 ¹⁶	This study was supported by a European Foundation for the Study of Diabetes (EFSD)/Sanofi-Aventis grant.	The authors declared to have no conflicts of interests.
Trichopoulou, 2006 ¹⁵	This study was supported by the European Commission, the Greek Ministries of Health and Education and the University of Athens.	The authors declared to have no conflicts of interests.



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