Effects of Starch on Oral Health: Systematic Review to Inform WHO Guideline

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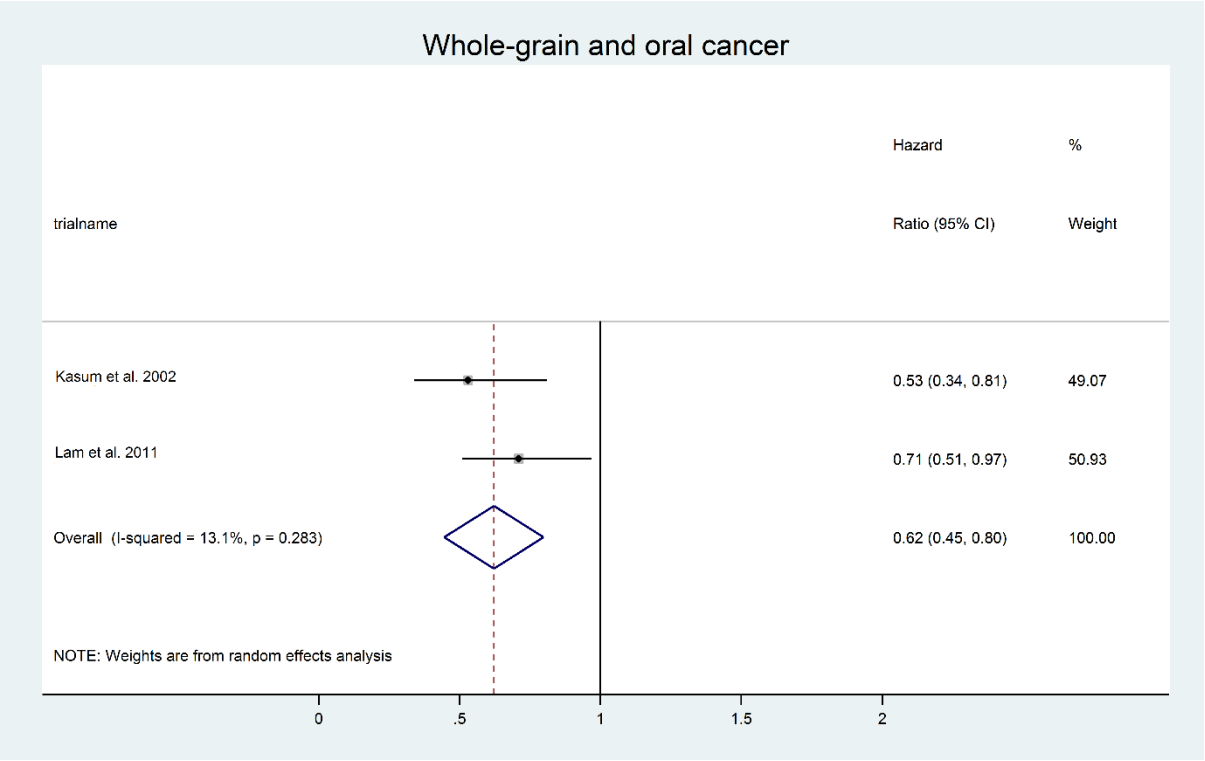
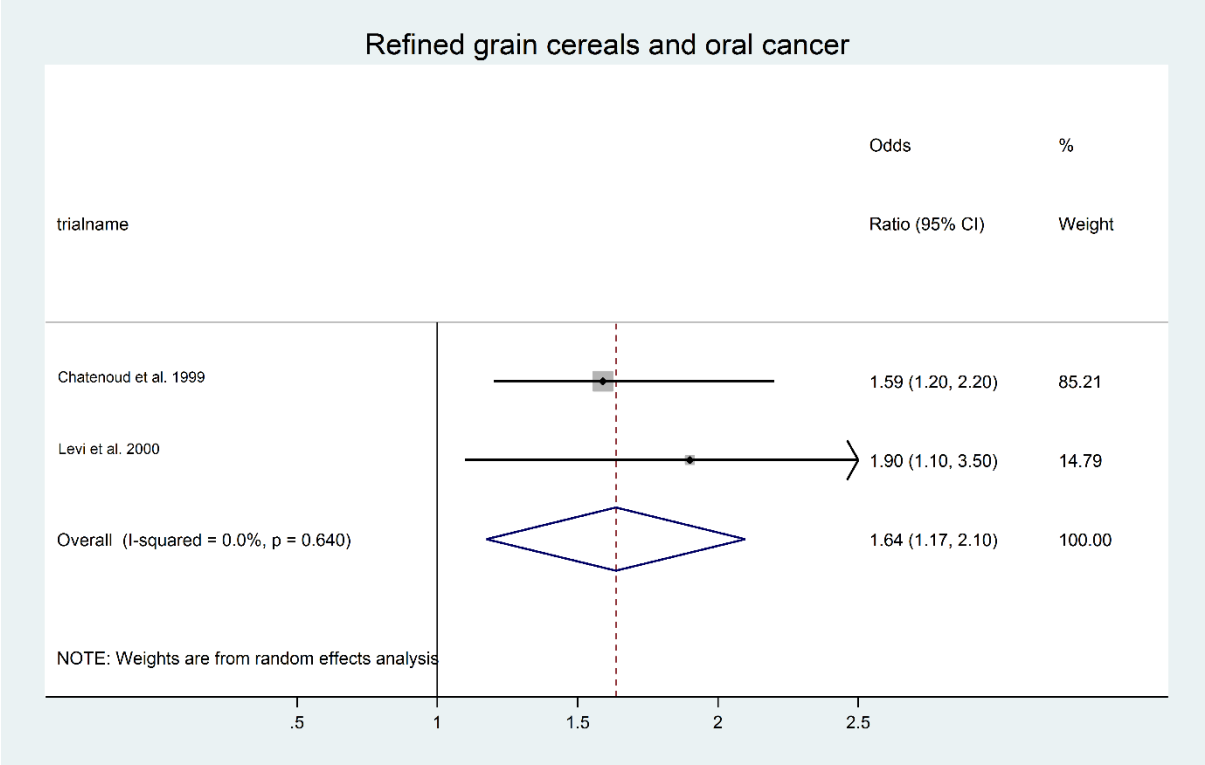
Appendix

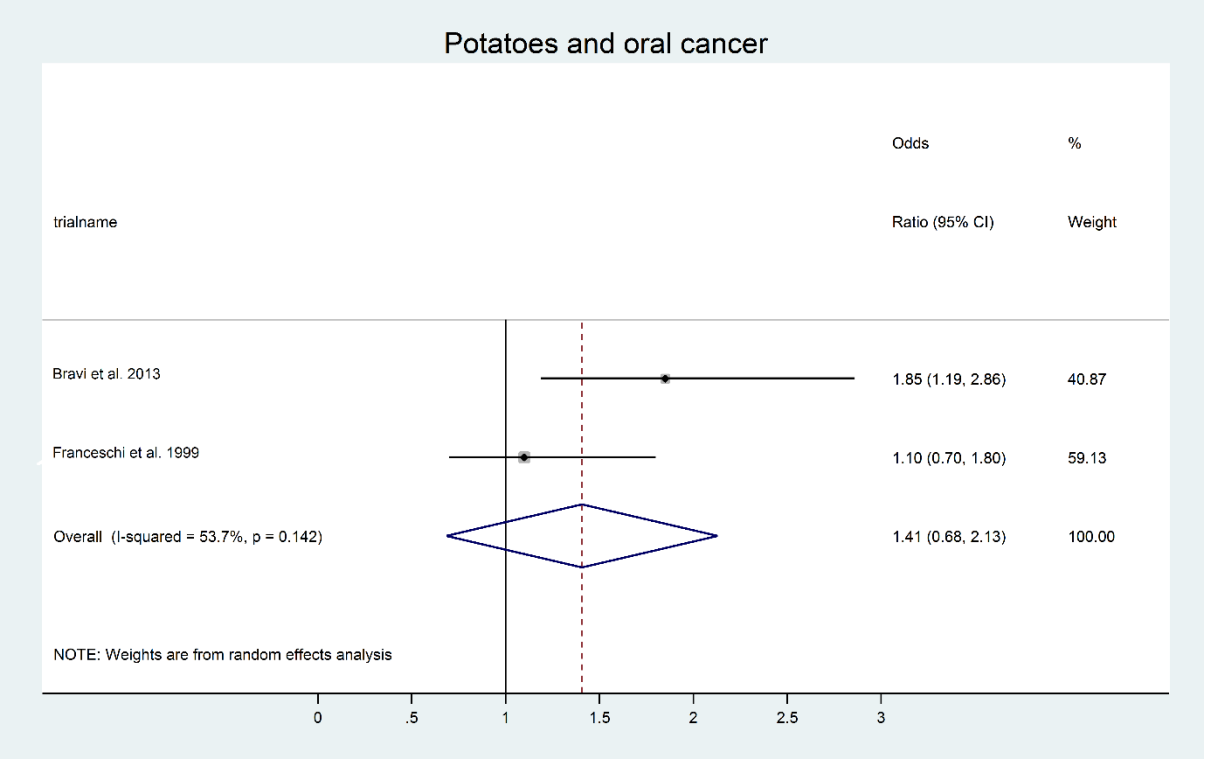
Meta-analyses of Data and Forest Plots



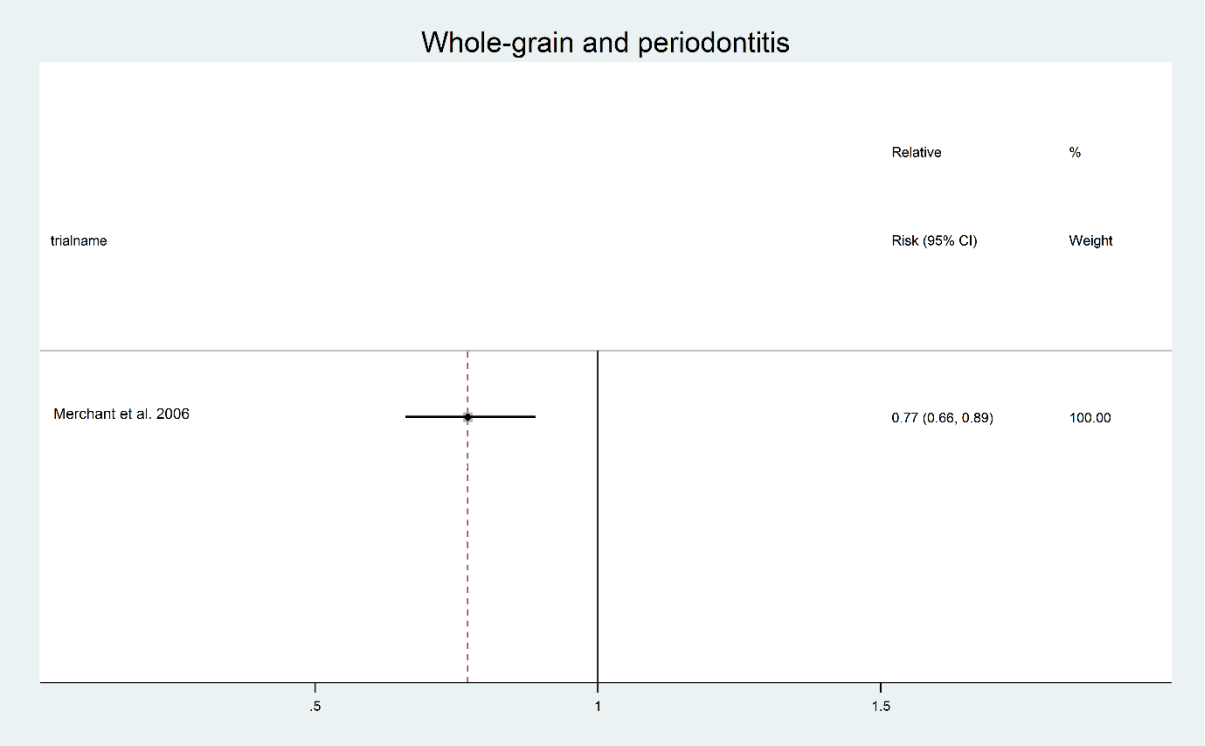
Appendix Figure 1. Crude forest plot of association between high intake of whole-grain and oral cancer in women (cohort studies).



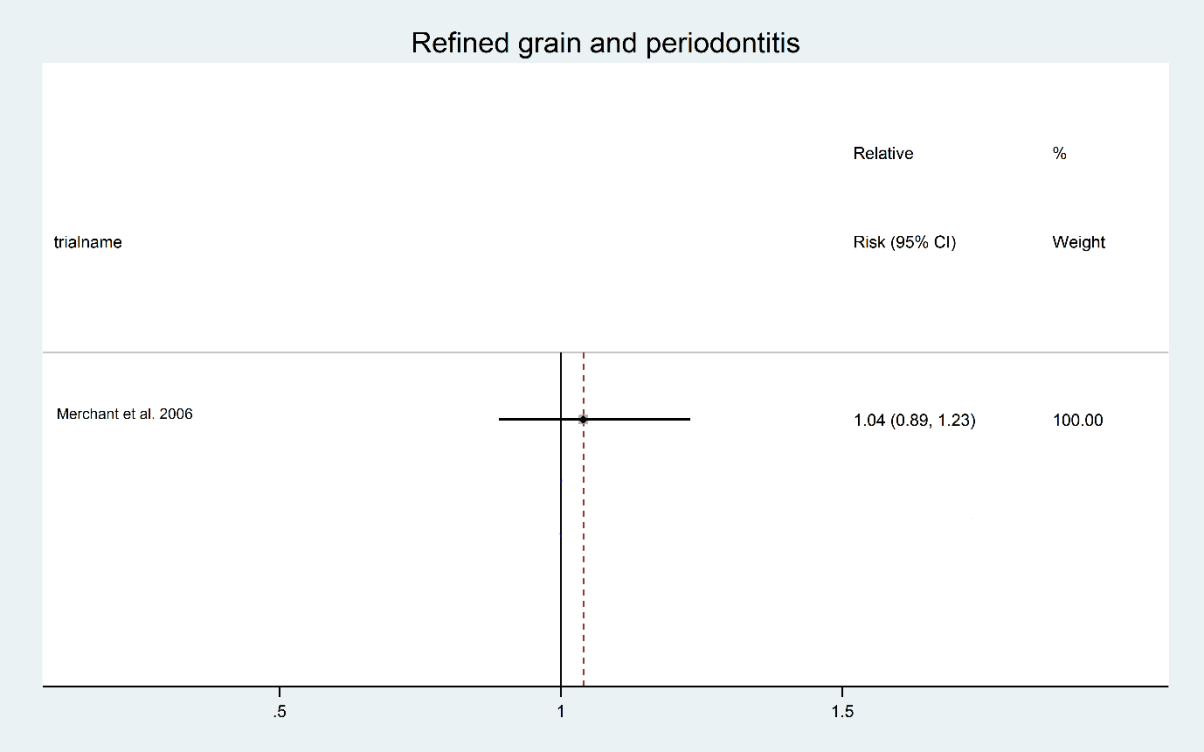
Appendix Figure 2. Crude forest plot of association between high intake of refined cereals and oral cancer (case-control studies).



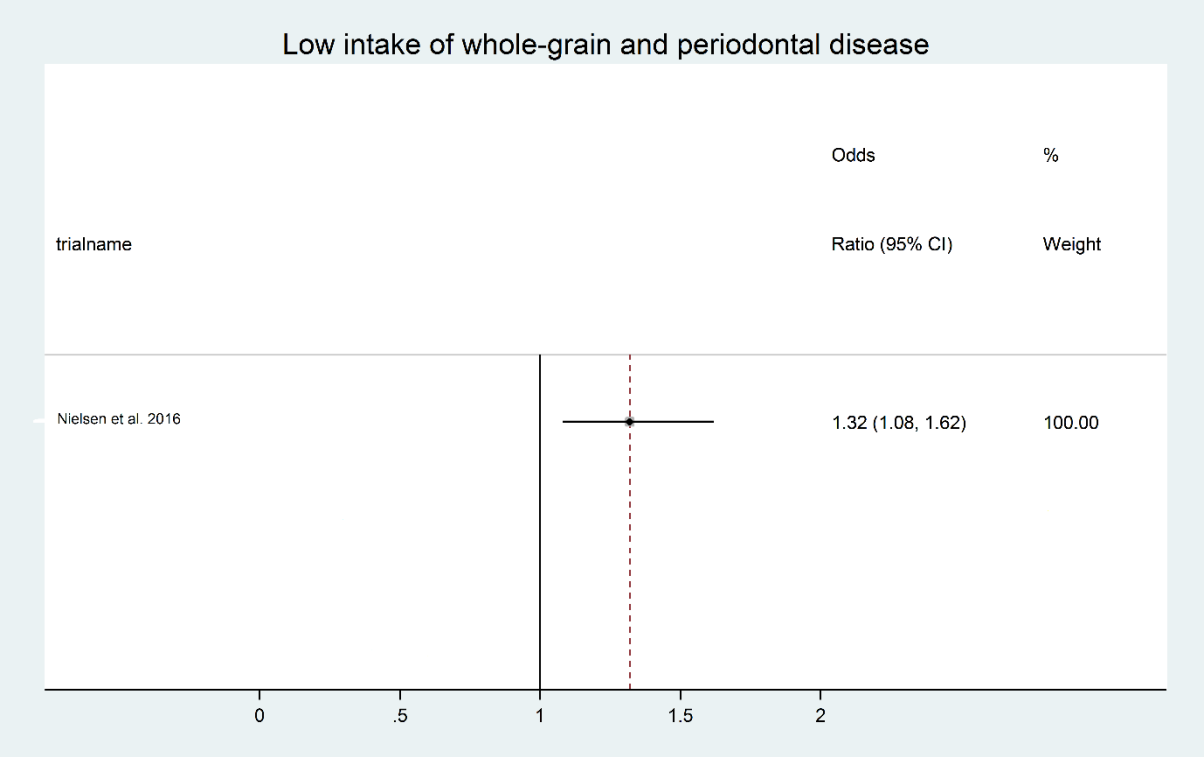
Appendix Figure 3. Crude forest plot of association between high intake of potatoes and oral cancer (case-control studies).



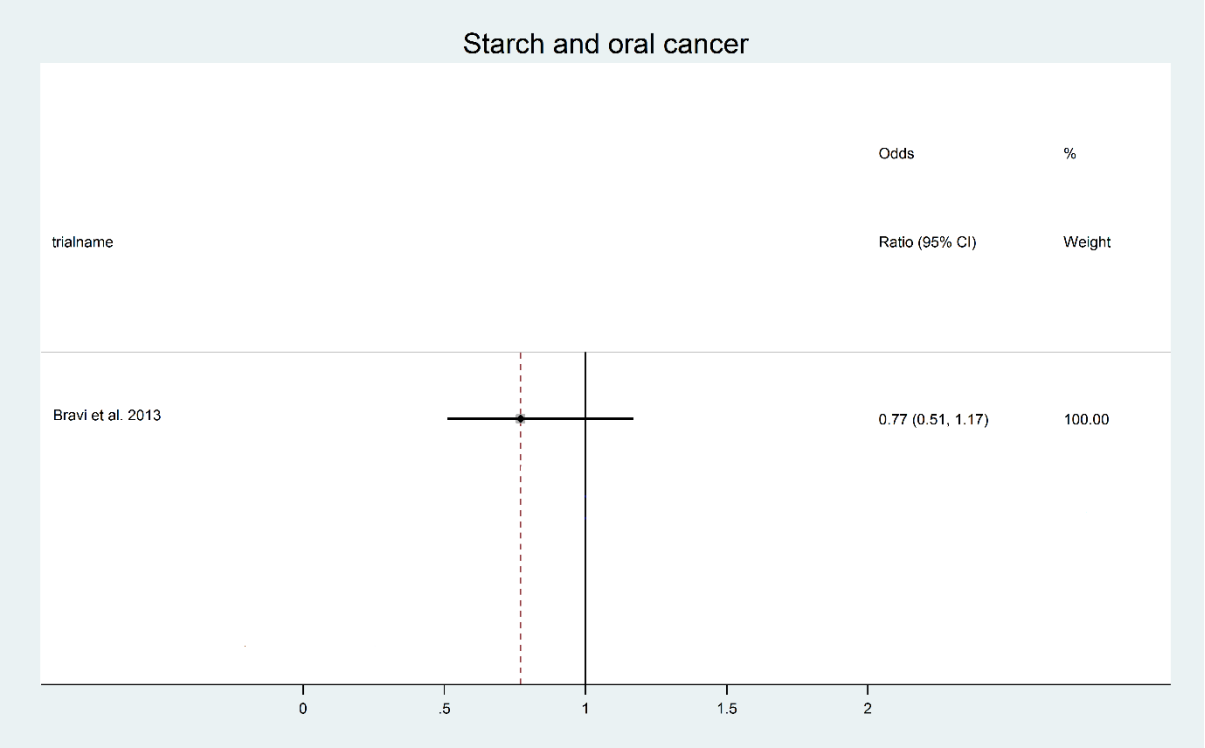
Appendix Figure 4. Crude forest plot of association between high whole-grain intake and periodontitis in men (cohort study).



Appendix Figure 5. Crude forest plot of association between high refined grain intake and periodontitis in men (cohort study).



Appendix Figure 6. Crude forest plot of association between low whole-grain intake and periodontitis risk (cross-sectional study).



Appendix Figure 7. Crude forest plot of association between high intake of starch and risk of oral and pharyngeal cancer (case-control study).

Supplementary Material 1: Protocol

Review scope

To assess the effects on oral health outcomes for adults and children of replacing rapidly digestible starches (RDS) with slowly digestible starches (SDS) in diet(s) (RDS vs. SDS review) and of the dietary intake of total starch (total starch review).

Englyst et al.'s classification (1992) of rapidly digestible starch (RDS), slowly digestible starch (SDS) and resistant starch (RS), in addition to the classification of total starch (TS), is acknowledged, but the comparisons of RDS vs. SDS (see below for full list) may also include refined carbohydrate compared with wholegrain carbohydrate and carbohydrates with higher compared with lower glycaemic response. Starch can be expressed in mg or g per day, kg per year, or as %E from starch.

Review questions

RDS vs. SDS review

The main review question will be: what is the effect of replacing rapidly digestible starches with slowly digestible starches on oral health (including periodontal disease, dental caries and oral cancer)? Sub-questions that will help to address the main review question will include:

1. What is the effect of an increase in intake of slowly digestible starches on oral health?
2. What is the effect of an increase in intake of rapidly digestible starches on oral health?
3. What is the effect of a decrease in intake of slowly digestible starches on oral health?
4. What is the effect of a decrease in intake of rapidly digestible starches on oral health?

Total starch review

The main review question will be: what is the effect of dietary intake of TS on oral health (including periodontal disease, dental caries and oral cancer)? Sub-questions that will help to address the main review question will include:

1. What is the effect of an increase in intake of TS on oral health?
2. What is the effect of a decrease in intake of TS on oral health?

Search strategy

RDS vs. SDS review

Structured search strategy (see 'Search Strategy'), with the following electronic databases to be searched:

- MEDLINE;
- EMBASE;
- Cochrane Database of Systematic Reviews;
- Cochrane Central Register of Controlled Trials;
- Wanfang (Chinese database);
- LILACS - Latin American and Caribbean Health Sciences.

References in any included reviews will also be checked and considered for inclusion.

Total starch review

The review will build upon papers identified for full text screening from the preceding review on RDS vs. SDS (as well as an update of the search for all starch measures using the above strategy). Finally, experts in the field of research will be consulted to identify any missing papers of relevance.

Screening of studies

Records retrieved from the searches will be imported into EndNote X7 software for screening. Title and abstract screening will be conducted by one reviewer to exclude any studies clearly not relevant. Potentially relevant studies will be independently screened two reviewers with full text papers being retrieved in order to make a decision. Any differences between reviewers' decisions will be resolved by discussion but, if not resolvable, a third reviewer will be consulted.

Eligibility criteria

Study design

We will include randomised controlled trials (RCTs), non-randomised intervention studies and observational studies (including cohort, case-control, population, ecological and cross-sectional studies), as well as non-epidemiological studies involving human participants with an experimental/laboratory design assessing aspects relating to dental caries such as percentage of demineralisation and/or change in plaque pH associated with the exposure of tooth surfaces/oral bacteria to starch items.

Animal and incubation studies will be excluded. We will also exclude studies in which no validated/standardised measure of the assessment of dietary intake has been used for the collection of the data (e.g. studies in which researchers have asked subjective questions that do not allow for a clear differentiation between study participants in terms of their actual level of dietary intake (e.g. if researchers merely have asked parents how much their children eat of a particular type of food as represented in broad categories of ‘low’, ‘medium’, ‘high’ intake without specifying intake further, or merely in binary data of e.g. 'consumes daily/does not consume daily')). If studies report both frequency and amount, we will only be interested in outcome measures relating to amount of starch intake as WHO nutrition recommendations are set in terms of amounts of intake of nutrients.

Articles not peer-reviewed and published, narrative reviews without original data, or reviews not published, will be excluded. Where high quality and relatively up to date published systematic reviews address parts of our review scope/questions, we will consider to include the reviews without further work in these particular areas.

Participants

Apparently healthy humans in low-, middle- or high-income countries. Apparently healthy means without acute illness, but may be overweight or have chronic illness such as dental caries,

hypertension or diabetes. An exception will also be made for case-control studies which, by their design, often are hospital-based and include control subjects admitted to the same hospital for other reasons – which sometimes may include acute states – than the case subjects.

Intervention (for RCTs)

Any intervention intended to alter intake of starch in one arm compared to another arm of the study. Interventions may relate to dietary advice, provision of food type supplements and/or provision of a partial or whole diet. To be included, a trial must report starch or starch item achieved in both arms with the effect of the dietary intervention isolated from the effects of other lifestyle or medical interventions (i.e. this will mean the exclusion of a study which alters exercise routines or drug interventions in one arm, but not in the other which is associated with the starch intervention).

Comparison/exposure

For RCTs, see above. For observational studies, intake of starch or change in intake of starch.

<u>RDS vs. SDS review</u>

Comparisons/exposures need to include diet(s)/food product(s) which can be classified as relating to RDS and/or SDS and may include, but may not be limited to:

- Lower versus higher resistant starch intake;
- Lower versus higher legume intakes;
- Higher versus lower starch+sugars;
- Highly processed versus less processed starch foods;
- Starch-influenced diet versus normal diet;
- Refined carbohydrate compared with wholegrain carbohydrate;
- Carbohydrates with higher compared with lower glycaemic response.

Studies that predominantly concentrate on the intake of starch in non-food items – e.g. in the form of medicines, mouthwashes or toothpastes – will be excluded.

Total starch review

For identified studies, they need to include a broad enough classification of starch content to enable an assessment of *total* starch (and not merely broken down by a specific starch types as in the RDS vs. SDS review). This could be in the form of studies that consider the effects of amount of dietary intake of starch as a nutrient and studies that consider a food item containing a high proportion of starch (insofar as that food item can be reasonably assessed to be the sole source of starch in the particular context in which it is being assessed). Included studies also need to enable the effects of starch to be assessed in adequate isolation from other nutrients/food items, but this could include assessing starch in combination with another nutrient (e.g. sugars) in comparison to the other nutrient on its own. As such, comparisons/exposures can comprise, but may not be limited to:

- Higher versus lower intake of TS
- Starch-influenced diet(s) versus normal diet(s)
- TS in isolation versus sugars
- TS in combination with sugars versus sugars

Studies that predominantly concentrate on the intake of starch in non-food items – e.g. in the form of medicines, mouthwashes or toothpastes – will be excluded.

Outcomes

Oral health outcomes relate to general or more specific conditions of the mouth. This ranges from optimal health states represented by the normal performance of the organs of the mouth to evidence of oral diseases and/or cancers. Oral health outcomes may be measured on validated scales/indexes, and/or be represented as events and/or means. We will concentrate on periodontal disease, dental caries and oral cancer, and to be included studies have to consider at least one of these outcomes in relation to intake of starch (as defined above).

The term periodontal disease is, in Medical Subject Headings (MeSH) descriptor data, defined as '[p]athological processes involving the periodontium including the gum (gingiva), the alveolar

bone (alveolar process), the dental cementum, and the periodontal ligament'[1]. As gingivitis is reversible but the more advanced condition of periodontitis is irreversible, we will only consider studies in which periodontitis has been measured/assessed as a proxy for periodontal disease[2].

Dental caries as defined in Moynihan and Kelly (2014)[3]: incidence and/or severity, measured as decayed, missing and filled teeth (DMF Index, DMFT, dmft, DMFS, dmfs, deft, dft or significant caries index), changes in levels of dental caries or comparisons of higher or lower levels of dental caries.

Oral cancers may include cancers of the mouth, pharynx and larynx, but may not be restricted to these forms[4].

Timescale

For RCTs, at least one year for dental caries, at least three months for periodontal disease. For observational studies, any.

Data extraction

Data extraction of included studies will be undertaken by one reviewer and checked by another reviewer. Two data extraction forms will be designed – one for RCTs and one for observational studies. These will be piloted on a few included studies and amended if necessary. The main findings of the data extraction will be presented in summary of included studies tables.

[1] National Library of Medicine - Medical Subject Headings 2016. MeSH descriptor data (for Periodontal Diseases); [accessed 2016 Sep 30]. https://www.nlm.nih.gov/cgi/mesh/2016/MB_cgi

[2] SACN. 2012. Systematic review of evidence: carbohydrates and oral health. Scientific Advisory Committee on Nutrition; [accessed 2016 Sep 20]. https://www.nutritionsociety.org/sites/www.nutritionsociety.org/files/12%20-%20Oral%20health%20review.pdf

[3] Moynihan PJ, Kelly SA. 2014. Effect on caries of restricting sugars intake: systematic review to inform WHO guidelines. J Dent Res. 93(1): 8–18.

[4] Hartman T, Ledikwe J, Mauger D, Martin K, Shaffer M, Murray T, Spaccarotella K, Kronheim L, Camera L. 2006. The associations between food, nutrition and physical activity and the risk of cancer of the mouth, pharynx and larynx and underlying mechanisms. World Cancer Research Fund, submitted by the Review Team at The Pennsylvania State University; [accessed 2016 Sep 20]. http://www.wcrf.org/sites/default/files/SLR_mouth_pharynx_larynx.pdf

For RCTs, we will extract data relating to aims/objectives, setting, participants, interventions, outcomes and trial quality characteristics. For dichotomous outcomes (i.e. caries present or not), data on events in the respective treatment arms will be collected. For continuous outcomes (i.e. DMFT/dmft), we will extract relevant means and standard deviations from each arm. In addition, data on potential effect modifiers will be extracted where reported.

For observational studies, we will extract data relating to aims/objectives, setting, design, details of participant characteristics in high and low exposure groups, similarity at baseline, measurement of the exposure to starch intake, assessment of oral health, participant flow, endpoint criteria and numbers of events or mean. Where applicable, we will extract the relative risk or odds ratio or mean difference comparing the most exposed group/category with the least exposed group/category, including factors adjusted for or any continuous assessment of the association of the outcome with changing starch intake.

Quality assessment

Quality assessment of individual included studies to determine study quality to inform GRADE profile tables (see below) will be undertaken independently by two reviewers. Discrepancies will be resolved by discussion or by consulting a third reviewer.

For individual RCTs, Cochrane criteria will be used to assess the risk of bias (including sequence generation, allocation concealment, blinding of participants, personnel and outcome assessment, incomplete outcome data and selective outcome reporting). Additionally, we will assess the inclusion of dietary interventions (over and above alteration of starch), similarity of type and intensity of intervention in both arms and the methods used to assess the achieved starch intake.

For individual observational studies, we will check whether there is baseline similarity of the most and least exposed groups (or cases/controls), or clearly adjusted for. Otherwise, we will check that adjustment is not needed for:

- oral hygiene (however addressed, i.e. via plaque levels, tooth brushing etc.);
- use of fluoridated toothpaste and water fluoridation;

- method of assessment of starch intake (with observed or measured data assessed as of higher validity than self-reported data);
- method of assessment of oral health valid and reliable (and assessors);

Additionally, for cohort studies, we will assess number lost to follow up in most and least exposed groups.

After assessing the quality of individual RCTs and observational studies, the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach (GRADE Working Group 2004[5]) will be used to assess the quality of the body of evidence and represented in GRADE profile tables relating to the review questions. Primarily studies rated highest based on design will be included in the GRADE profile tables, but any supporting evidence from studies with lower rated design will also be reported on.

Data synthesis

Outcomes to be separated by oral health condition and combined across included studies that address the same/similar condition(s) (i.e. periodontal disease, dental caries, oral cancer). Meta-analyses using random effects models will be conducted if studies are deemed sufficiently homogenous in terms of study design, baseline characteristics of participants and the exposures and outcomes assessed. Data will be synthesised using a narrative approach where outcomes are deemed or shown to be too heterogeneous for meta-analyses (by assessing the chi-squared test and associated p-value, in addition to the I-squared statistic), or where there is insufficient data to combine outcomes across studies.

Where more than one analysis of a specific cohort of participants is relevant to an outcome (for instance, for some cohorts outcomes may be measured at several time points and/or different types of assessment data may be used), only one analysis will be used for that cohort per outcome. The rules for choosing which analysis to use are as follows (in a prioritised order,

[5] GRADE Working Group: Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. 2004. Grading quality of evidence and strength of recommendations. BMJ. 328(7454): 1490.

meaning that once a rule decides then the rest will be ignored or move down until a decision can be reached):

1. Outcome: use the analysis with the most inclusive assessment of starch intake.
2. Sample: the largest population involved in the analysis.
3. Study design: whole cohort analysis over a nested case control analysis, for example.
4. Timescale: the final measure in time.

(Influenced by Moynihan and Kelly 2014, see footnote 3 for full reference).

Evidence of dose response

Within the above analyses, studies may be ordered by difference in starch intake between experimental and control arms to give an indication of the existence of a dose response. If feasible, this can be explored further using meta-regression, with degree of change in starch intake compared to the change in oral health outcomes (in the higher versus lower starch groups/categories).

Evidence of threshold for effect

Plotting starch intake vs. oral health outcomes may provide information about the shape of any relationship, providing some idea of whether a threshold for effect exists and what this might be.

Subgroup analyses

Subgroup analyses may, depending on the available evidence, include subgrouping by:

- Country
- Ethnicity
- Region: urban/rural
- Gender (male, female)
- Age
- Primary and secondary dentition
- Socioeconomic status
- Demographic factors

- Health background and status
- Duration of intervention
- Oral hygiene
- Water fluoridation
- Sanitation

For instance, age may be addressed with a meta-analysis (or using a narrative approach if this is not appropriate), divided into children and adults. If appropriate, subgroups relating to study design (i.e. RCTs, cohort and case-control studies) will then be displayed for each age group.

Where continuous variables (e.g. duration, age) appear to be related to the presence or the extent of an effect, it may be deemed appropriate to explore this relationship further with meta-regression.

Sensitivity analyses

To assess robustness of results relating to study quality, studies deemed to contain the highest risk of bias will be removed in sensitivity analyses. For RCTs, this will relate to the quality assessment criteria as described above. For observational studies, the identification of studies that will be retained in a sensitivity analysis may include whether studies have sufficiently adjusted for factors that appear to be different between lower and higher starch intakes. Where sufficient data exists, funnel plots will be used to assess for evidence of publication bias.

Supplementary Material 2: Search strategy

Ovid MEDLINE(R) 1946 to September Week 2 2016, search conducted on 23.09.16

1	exp Starch/
2	starch$.ab,ti.
3	amylum.ab,ti.
4	(amylose or amylopectin).ab,ti.
5	(banana$ or cereal$ or bread$ or flour$ or pasta$ or rice$ or potato$ or chips or crisps or cracker$ or biscuit$ or cake$ or snack$).ab,ti.
6	(grain$ adj10 (food$ or ingredient$ or cook$ or diet$)).ab,ti.
7	(wholegrain$ or whole-grain$ or (whole adj grain$)).ab,ti.
8	(wholefood$ or whole-food$ or (whole adj food$)).ab,ti.
9	(wholemeal$ or whole-meal$ or (whole adj meal$)).ab,ti.
10	((root$ or tuber$) adj10 (food$ or ingredient$ or cook$ or diet$)).ab,ti.
11	(tapioca$ or legume$ or plantain$).ab,ti.
12	Cariogenic Diet/
13	Diet, Carbohydrate-Restricted/ or Dietary Carbohydrates/
14	exp Dietary Fiber/
15	((cariogenic$ or carbohydrate$ or fibre$ or fiber$ or nutrient$ or nutritive$ or nourish$ or nutritious or nutrition) adj3 diet$).ab,ti.
16	or/1-15
17	Oral Health/
18	(health adj3 (periodontal or dental or oral or tooth or teeth)).ab,ti.
19	exp Periodontal Diseases/ or Mouth Diseases/ or Tooth Diseases/ or Pharyngeal Diseases/ or Laryngeal Diseases/ or Esophageal Diseases/
20	(disease$ adj3 (oral or mouth or periodont$ or gum$ or gingi$ or dental or tooth or teeth or throat or pharyn$ or nasopharyn$ or oropharyn$ or hypopharyn$ or laryn$ or esophag$ or oesophag$)).ab,ti.

21 Tooth Demineralization/ or exp Dental Caries/

22 ((caries or demineral?ation or decay$ or cavit$ or cario$) adj3 (dental or oral or tooth or teeth)).ab,ti.

23 Mouth Neoplasms/ or exp Pharyngeal Neoplasms/ or Laryngeal Neoplasms/ or Esophageal Neoplasms/

24 ((cancer$ or neoplasm$ or tumo?r$) adj3 (oral or mouth or periodont$ or gum$ or gingi$ or dental or tooth or teeth or throat or pharyn$ or nasopharyn$ or oropharyn$ or hypopharyn$ or laryn$ or esophag$ or oesophag$)).ab,ti.

25 exp Dental Health Surveys/

26 (("oral hygiene" or "orthodontic treatment need" or periodontal or plaque or "significant caries") adj3 (index$ or scale$)).ab,ti.

27 ((ohi$ or iotn or pdi or pi or sic or dmf or dmft or dmfs or dft or deft or defs) adj3 (index$ or scale$ or oral or periodont$ or dental or tooth or teeth)).ab,ti.

28 or/17-27

29 16 and 28

30 limit 29 to human

31 remove duplicates from 30

Embase 1980 to 2016 Week 38, search conducted on 23.09.16

1 exp Starch/

2 starch$.ab,ti.

3 Potato Starch/

4 amylum.ab,ti.

5 (amylose or amylopectin).ab,ti.

6 (banana$ or cereal$ or bread$ or flour$ or pasta$ or rice$ or potato$ or chips or crisps or cracker$ or biscuit$ or cake$ or snack$).ab,ti.

7 (grain$ adj10 (food$ or ingredient$ or cook$ or diet$)).ab,ti.

8 (wholegrain$ or whole-grain$ or (whole adj grain$)).ab,ti.

9 (wholefood$ or whole-food$ or (whole adj food$)).ab,ti.

10 (wholemeal$ or whole-meal$ or (whole adj meal$)).ab,ti.

11 ((root$ or tuber$) adj10 (food$ or ingredient$ or cook$ or diet$)).ab,ti.

12 (tapioca$ or legume$ or plantain$).ab,ti.

13 Cariogenic Diet/

14 Carbohydrate Diet/

15 Dietary Fiber/

16 ((cariogenic$ or carbohydrate$ or fibre$ or fiber$ or nutrient$ or nutritive$ or nourish$ or nutritious or nutrition) adj3 diet$).ab,ti.

17 or/1-16

18 Dental Health/

19 (health adj3 (periodontal or dental or oral or tooth or teeth)).ab,ti.

20 exp Periodontal Disease/ or Mouth Disease/ or Tooth Disease/ or Pharynx Disease/ or Larynx Disorder/ or Esophagus Disease/

21 (disease$ adj3 (oral or mouth or periodont$ or gum$ or gingi$ or dental or tooth or teeth or throat or pharyn$ or nasopharyn$ or oropharyn$ or hypopharyn$ or laryn$ or esophag$ or oesophag$)).ab,ti.

22 Dental Caries/

23 ((caries or deminerali?ation or decay$ or cavit$ or cario$) adj3 (dental or oral or tooth or teeth)).ab,ti.

24 Mouth Cancer/ or exp Pharynx Cancer/ or Larynx Cancer/ or Esophagus Cancer/

25 ((cancer$ or neoplasm$ or tumo?r$) adj3 (oral or mouth or periodont$ or gum$ or gingi$ or dental or tooth or teeth or throat or pharyn$ or nasopharyn$ or oropharyn$ or hypopharyn$ or laryn$ or esophag$ or oesophag$)).ab,ti.

26 (("oral hygiene" or "orthodontic treatment need" or periodontal or plaque or "significant caries") adj3 (index$ or scale$)).ab,ti.

27 ((ohi$ or iotn or pdi or pi or sic or dmf or dmft or dmfs or dft or deft or defs) adj3 (index$ or scale$ or oral or periodont$ or dental or tooth or teeth)).ab,ti.

28 or/18-27

29 17 and 28

30 limit 29 to human

31 remove duplicates from 30

Cochrane Database of Systematic Reviews: Issue 9 of 12, September 2016; Cochrane Central Register of Controlled Trials: Issue 8 of 12, August 2016 (search conducted on 23.09.16)

#1 MeSH descriptor: [Starch] explode all trees

#2 starch*:ti,ab,kw (Word variations have been searched)

#3 amylum:ti,ab,kw (Word variations have been searched)

#4 (amylose or amylopectin):ti,ab,kw (Word variations have been searched)

#5 (banana* or cereal* or bread* or flour* or pasta* or rice* or potato* or chips or crisps or cracker* or biscuit* or cake* or snack*):ti,ab,kw (Word variations have been searched)

#6 (grain* near/10 (food* or ingredient* or cook* or diet*)):ti,ab,kw (Word variations have been searched)

#7 (wholegrain* or whole-grain* or (whole next grain*)):ti,ab,kw (Word variations have been searched)

#8 (wholefood* or whole-food* or (whole next food*)):ti,ab,kw (Word variations have been searched)

#9 (wholemeal* or whole-meal* or (whole next meal*)):ti,ab,kw (Word variations have been searched)

#10 ((root* or tuber*) near/10 (food* or ingredient* or cook* or diet*)):ti,ab,kw (Word variations have been searched)

#11 (tapioca* or legume* or plantain*):ti,ab,kw (Word variations have been searched)

#12 MeSH descriptor: [Diet, Cariogenic] this term only

#13 MeSH descriptor: [Diet, Carbohydrate-Restricted] this term only

#14 MeSH descriptor: [Dietary Carbohydrates] this term only

#15 MeSH descriptor: [Dietary Fiber] explode all trees

#16 ((cariogenic* or carbohydrate* or fibre* or fiber* or nutrient* or nutritive* or nourish* or nutritious or nutrition) near/3 (diet*)):ti,ab,kw (Word variations have been searched)

#17 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16

#18 MeSH descriptor: [Oral Health] this term only

#19 (health near/3 (periodontal or dental or oral or tooth or teeth)):ti,ab,kw (Word variations have been searched)

#20 MeSH descriptor: [Mouth Diseases] this term only

#21 MeSH descriptor: [Periodontal Diseases] explode all trees

#22 MeSH descriptor: [Tooth Diseases] this term only

#23 MeSH descriptor: [Pharyngeal Diseases] this term only

#24 MeSH descriptor: [Laryngeal Diseases] this term only

#25 MeSH descriptor: [Esophageal Diseases] this term only

#26 (disease* near/3 (oral or mouth or periodont* or gum* or gingi* or dental or tooth or teeth or throat or pharyn* or nasopharyn* or oropharyn* or hypopharyn* or laryn* or esophag* or oesophag*)):ti,ab,kw (Word variations have been searched)

#27 MeSH descriptor: [Tooth Demineralization] this term only

#28 MeSH descriptor: [Dental Caries] explode all trees

#29 ((caries or deminerali?ation or decay* or cavit* or cario*) near/3 (dental or oral or tooth or teeth)):ti,ab,kw (Word variations have been searched)

#30 MeSH descriptor: [Mouth Neoplasms] this term only

#31 MeSH descriptor: [Pharyngeal Neoplasms] explode all trees

#32 MeSH descriptor: [Laryngeal Neoplasms] this term only

#33 MeSH descriptor: [Esophageal Neoplasms] this term only

#34 ((cancer* or neoplasm* or tumo?r*) near/3 (oral or mouth or periodont* or gum* or gingi* or dental or tooth or teeth or throat or pharyn* or nasopharyn* or oropharyn* or hypopharyn* or laryn* or esophag* or oesophag*)):ti,ab,kw (Word variations have been searched)

#35 MeSH descriptor: [Dental Health Surveys] explode all trees

#36 (("oral hygiene" or "orthodontic treatment need" or periodontal or plaque or "significant caries") near/3 (index* or scale*)):ti,ab,kw (Word variations have been searched)

#37 ((ohi* or iotn or pdi or pi or sic or dmf or dmft or dmfs or dft or deft or defs) near/3 (index* or scale* or oral or periodont* or dental or tooth or teeth)):ti,ab,kw (Word variations have been searched)

#38 #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37

#39 #17 and #38

LILACS (Latin American and Caribbean Health Sciences), search conducted on 29.09.16

tw:((tw:((mh:(mh:"Starch")) OR (tw:((tw:(starch*)) OR (tw:(amylum)) OR (tw:(amylose OR amylopectin)) OR (tw:(banana* OR cereal* OR bread* OR flour* OR pasta* OR rice* OR potato* OR chips OR crisps OR cracker* OR biscuit* OR cake* OR snack*)) OR (tw:(grain* (food* OR diet*))) OR (tw:(wholegrain* OR whole-grain* OR "whole grain" OR "whole grains")) OR (tw:(wholefood* OR whole-food* OR "whole food" OR "whole foods")) OR (tw:(wholemeal* OR whole-meal* OR "whole meal" OR "whole meals")) OR (tw:((root* OR tuber*) (food* OR diet*))) OR (tw:((tapioca* OR legume* OR plantain*))))) OR (mh:(mh:"Diet, Cariogenic")) OR (mh:(mh:"Diet, Carbohydrate-Restricted")) OR (mh:(mh:"Dietary Carbohydrates")) OR (mh:(mh:"Dietary Fiber")) OR (tw:((cariogenic* OR carbohydrate* OR fibre* OR fiber* OR nutrient* OR nutritive* OR nourish* OR nutritious OR nutrition) (diet*))) AND (mh:(mh:"Oral Health")) OR (tw:((health) (periodontal OR dental OR oral OR tooth OR teeth))) OR (mh:(mh:"Mouth Diseases")) OR (mh:(mh:"Periodontal Diseases")) OR (mh:(mh:"Tooth Diseases")) OR (mh:(mh:"Pharyngeal Diseases")) OR (mh:(mh:"Laryngeal Diseases")) OR (sh:(mh:"Esophageal Diseases")) OR (tw:((disease*) (oral OR mouth OR periodont* OR gum* OR gingi* OR dental OR tooth OR teeth OR throat OR pharyn* OR nasopharyn* OR oropharyn* OR hypopharyn* OR laryn* OR esophag* OR oesophag*))) OR (mh:(mh:"Tooth Demineralization")) OR (mh:(mh:"Dental Caries")) OR (tw:((caries OR deminerali?ation OR decay* OR cavit* OR cario*) (dental OR oral OR tooth OR teeth))) OR (mh:(mh:"Mouth Neoplasms")) OR (mh:(mh:"Pharyngeal Neoplasms")) OR (mh:(mh:"Laryngeal Neoplasms")) OR (mh:(mh:"Esophageal Neoplasms")) OR (tw:((cancer* OR neoplasm* OR tumo?r*) (oral OR mouth OR periodont* OR gum* OR gingi* OR dental OR tooth OR teeth OR throat OR pharyn* OR nasopharyn* OR oropharyn* OR hypopharyn* OR laryn* OR esophag* OR oesophag*))) OR (mh:(mh:"Dental Health Surveys")) OR (tw:(("oral hygiene" OR "orthodontic treatment need" OR periodontal OR plaque OR "significant caries") (index* OR scale*))) OR (tw:((ohi* OR iotn OR pdi OR pi OR sic OR dmf OR dmft OR dmfs OR dft OR deft OR defs) (index* OR scale*

OR oral OR periodont* OR dental OR tooth OR teeth)))) AND (instance:"regional")) AND (limit:(humans)))

This search strategy was then combined with different subject categorisations available through the LILACS database in order to capture relevant papers.

Wanfang database, English search conducted on 29.09.16, Simplified Chinese on 30.09.16

Due to the limited search fields available to operate searches for this database, searches concentrated on the search term ‘oral health’ and terms capturing the main outcomes of interest to the review (‘periodontal disease’, ‘dental caries’ and ‘oral cancer’). These search terms were combined in many rounds with all the different terms used in the other databases relating to and capturing starch. Searches were conducted both by using English language and simplified Chinese language.

Supplementary Material 3: Tables of included studies

Epidemiological studies

Chronological, by study type

Appendix Table 1: Included caries studies; total starch

Scheinin and Mäkinen (1975)	
Study question	Examined the effects of substituting sucrose in diets with either xylitol (a sugar alcohol not fermented by oral bacteria) or fructose on the incidence of caries.
Study design	Non-randomised intervention study
Study population	155 participants aged <15 to ≥45 years in Finland over 2 years
Exposure	Thirty-three participants consumed a diet sweetened with sucrose, 35 with fructose and 47 with xylitol. Starch intake in the three groups were not restricted and stayed stable. Sugar was removed from the diet in the xylitol group, with participants also instructed to avoid noticeably sweet fruits (with raisins, dried figs and dates mentioned as examples) as the sugars in these food items could not be substituted.
Dental outcome	8 dental examinations measuring DMFS increment. This expressed caries activity in terms of indices showing total quantitative and qualitative development
Statistics	Kruskal-Wallis test for overall comparison of differences, Mann Whitney U-test for differences between the sugar groups
Results	The mean increment of the DMFS-index (decayed, missed and filled tooth surfaces) was 7.2 in the sucrose group and 3.8 in the fructose group, and 0.0 in the xylitol experimental condition (with little or no new caries shown by a secondary analysis of the total quantitative and qualitative development of caries). The high incidence of caries associated with the sucrose group when compared to the xylitol group may suggest that starch in combination with sugars (rather than starch alone) may increase the risk of dental caries.
Discussion/ limitations	Reproducibility of examinations was tested using the procedure suggested by COCSTOC (1973) and Fleisch et al (1968). Poor initial reproducibility was improved by the use of a decision table however there are several issues relating to inconsistency in the classification and recording of the dental data. Xylitol may have a slight inhibitory effect on caries but it is highly unlikely that the caries inhibiting properties of xylitol accounted for the observed reduction in caries activity
Rugg-Gunn et al (1987)	

Study question	To examine the relative cariogenicity of starch and sugars (calculated as mean intake g/day)
Study design	Two-year prospective cohort study
Study population	405 schoolchildren (12-14 years old) in England
Exposure	Measured using five separate three day diet diaries with interview on fourth day with a dietician. Twenty-seven of the participants were categorised in a high-starch/low-sugars diet group with an average intake of starch per day of 186.7g and an average intake of sugars of 86.7g, while 32 of the participants were categorised in a low-starch/high-sugars diet group with an average intake of starch per day of 124.5g and an average intake of sugars of 143.4g
Dental outcome	Annual dental exams to measure caries increment (DMFS), (included bite-wing radiographs)
Statistics	Pearson's correlation coefficient to rank the dietary variables. Bivariate correlation then used to examine the association between caries increments and diet. Stepwise regression analysis was then applied.
Results	Participants in the high-starch/low-sugars group developed fewer caries (DMFS = 2.8) than the participants in the low-starch/high-sugars group (DMFS = 4.1) over the two-year-period. However, this result was not statistically significant ($p = 0.23$).
Discussion/ limitations	Thorough and validated dietary assessment, although 'sugars intake' included all dietary sugars. The authors suggest that the small size of the caries increment may partly explain the low correlation. Studies of three years minimum are suggested to help overcome this.
Campain et al. (2003)	
Study question	To determine whether food-level sugar-starch combinations are predictors of dental caries in a low-risk adult population.
Study design	Two-year prospective cohort study.
Study population	645 participants aged 12-13 years at baseline in Australia. Half from a non-Anglo-Saxon background.
Exposure	Four diet records, each lasting four days. Food groups were categorised according to their sugars and starch content and classified as e.g. high sugar-low starch, low sugar-medium starch.
Dental outcome	Dental caries was measured annually by one of two calibrated examiners. This was by clinical inspection only according to WHO criteria.

Statistics	Multivariate logistic regression.
Results	Foods classified in a low sugar-high starch food group with a high proportion of starch (median % = 50.2) but relatively low levels of sugar (median % = 2.4), were found to be predictive of caries risk (Multivariate Relative Risk (95% CIs) = 1.23 (1.05–1.44). However, this group included 'pastries' and muffin (see Discusssion).
Discussion/ limitations	No reporting of how individual foods were classified. The quantification of starch intake in the different food groups provided by this study is questionable and suggests no association between starch and dental caries. In particular, the low sugar–medium starch food group included a higher mean daily intake (g) of starch (= 77.3 (41.1)) than the low sugar-high starch food group (mean daily intake (g) = 53.3 (38.1)); yet, suggested a non-significant result in relation to caries risk (Multivariate Relative Risk (95% CIs) = 1.06 (0.92–1.22).
Marshall et al. (2005)	
Study question	Examined the relationship between caries experience and meal, snack and daily total exposures to beverages/foods, based on data from the Iowa Fluoride Study.
Study design	Prospective cohort study - three-day diaries were used, when participants were 1, 2, 3, 4 and 5 years old, to determine beverage and food exposures, which were subsequently averaged into a 1-5 years estimate.
Study population	Recruitment from 1992 to 1995, 398 children in Iowa, USA followed from aged 1 to aged 6.8 years from generally high-income and well-educated families (results adjusted for total fluoride intake).
Exposure	Starches (includes "baked starch with sugar, presweetened cereals, unsweetened cereals, processed snacks and unprocessed starches"
Dental outcome	Presence of a cavitated (d2-3) or filled surface.
Statistics	Logistic regression models used.
Results	A potential protective effect was indicated of the highest quartile of intake of 'starches' (otherwise unspecified in terms of amount eaten) for 1-5 year old children (OR = 0.90); yet, this result failed to reach statistical significance (95% CIs = 0.42–1.94).
Discussion/ limitations	Higher socio-economic families under examination not representative of general population.
Kaye et al. (2015)	

Study question	Relationship between root caries increment and a number of dietary variables, including starch.
Study design	Prospective cohort study extended over 20 years.
Study population	533 men between aged between 47 and 90 years from the Veterans Affairs Dental Longitudinal Study in the greater Boston, Massachusetts, area (US).
Exposure	'DASH' (Dietary Approach to Stop Hypertension) diet analysed including a number of dietary variables including starch defined as "[t]otal carbohydrate minus dietary fiber and sugars" (p. 1816). Detailed and repeated food frequency questionnaires were used to obtain dietary information.
Dental outcome	Root caries incidence and increment.
Statistics	Generalised linear and negative binomial models used to examine associations between root caries increment and DASH adherence scores.
Results	Level of root caries increment was not significant when the highest quartile of starch intake (of 31.1–44.4 percentage of kcal/d, mean score (95% CIs) = 2.67 (2.10–3.40) was compared with the lowest quartile of starch intake.
Discussion/ limitations	Sugars were also included but it was not possible to determine whether sugars were consumed at the same time as starch (or with any other foods, e.g. only at meal times or between meals). Higher absolute incidence rate of root caries compared to similar populations but this may have been due to closer inspection and longer follow up.
Papas et al. (1995)	
Study question	To report on the relationship between root caries and diet in middle aged and older adults.
Study design	Cross-sectional.
Study population	275 adults (range = 44 to 64 years) in Boston, US. Recruited from hospitals, clinics and responders to advertisements. Predominantly white (95%) and well-educated. 55% male.
Exposure	The authors calculated the mean frequency of exposure to various food groups, which included starches and sugars in isolation and sugars and starches combined (with the compositions of these groups unreported).
Dental outcome	Decayed and filled root surfaces (root -DFS) was measured by one calibrated examiner according to the Adult Survey Diagnostic Criteria of the National Institute of Dental Research.
Statistics	Stepwise multiple logistic regression used to assess which of the nutritional variables differentiate the healthy and diseased groups.
Results	For subjects who had detected gingival recession and at least one active root carious lesion (n=107), on average 40% more sugars and 32% more starch had been consumed than for those who were

	classified as 'healthy subjects' in the study (n=48). 'Starches' alone was not a factor in the development of root caries (t-test 'diseased' vs. 'healthy' P = 0.27, with odds ratio and 95% CIs not estimated and/or reported).
Discussion/ limitations	Food groups only described as e.g. 'starches' or 'sugars and starches' without further breakdown of food groups.
Arcellea et al. (2002)	
Study question	Investigated the association between frequency of carbohydrate intake and dental caries (DMFT).
Study design	Cross sectional.
Study population	193 teenagers (age range 13 to 19 years, with majority 15 to 17 years) from a single secondary school in Rome, Italy. 74% female.
Exposure	Starch and sugars content calculated over 14 consecutive days by using The Italian National Tables of Food Composition, with the weight/volume and content of starch and sugars of new or previously undocumented recipes/products that participants consumed retrieved from the recipes/products' packaging labels. Diaries verified three times weekly through interviews.
Dental outcome	Two examiners measured DMFT (enamel and dentine caries) using WHO methods.
Statistics	Differences tested using the t-test or F-test. Pearson's correlation coefficient used as a measure of association between caries and diet. Stepwise forward linear regression analysis used to study interrelations between DMFT and frequency of eating events (and age).
Results	The frequency of separate eating events of the variable 'high sugars and high starch events' accounted for about 8% of the DMFT variance in the sample, with 'high sugars and low starch' accounting for about 4% of the DMFT variance and 'low sugars and high starch' accounting for about 3% of the DMFT variance. This suggests that diets rich in both starch and sugars may be more likely to cause dental caries than diets rich in either sugars or starch in isolation.
Discussion/ limitations	Authors acknowledge limitation of cross-sectional studies to compare current diet habits with caries which developed earlier (diet may have changed since caries developed).
Holloway et al. (1963) and Fisher (1968)	
Study question	Compared dental health of population with dietary habits
Study design	Ecological: Holloway et al (1963) carried out a dental health survey of inhabitants of the Island of Tristan da Cunha in 1960s and compared with data on the islands' population in 1937. Fisher (1968) carried out a survey of nutritional habits.

Study population	Population of Tristan da Cunha, sub divided into age groups 1-5 years, 13-19 years, 20-29 years, 30-39 years and 40-49 years. 219 subjects participated in 1962
Exposure	Before the Second World War potatoes had been the main constituent of the diet, with some fish and very occasional meat and other vegetables. Following the Second World War potatoes and fish remained the staple diet but large amounts of sugar and sweetened foods were imported and frequently consumed. The study therefore measured dental caries when intake of starch was high but sugars low and examined the effect of adding sugar to the population's diet when starch intake remained relatively stable.
Dental outcome	'Carious, filled and extracted teeth' (included radiographic assessment of caries into dentine).
Statistics	Statistical analysis not applied.
Results	Several previous studies reported that the Tristan da Cunha islanders were caries free up until 1938. The next dental examination of the islanders took place in 1952 and caries prevalence had increased dramatically, particularly in children. The 1962 survey reported that over 80% of the islanders revealed that only 12% of those examined remained caries free. Starch was by far the main component of the islanders' diet before 1938 when caries was not observed. The dramatic increase in caries occurred after sugar was introduced to the diet.
Discussion/ limitations	Difficulty of ecological studies in equating causation with association but examination of other dietary factors, coupled with the 88% prevalence of caries reported in the 1963 paper, is highly suggestive that the previous 'starch only' diet was not cariogenic.

Appendix Table 2: Included caries studies; SDS vs RDS

Campain et al. (2003)	
As per entry for total starch. No direct comparison between SDS and RDS although some suggestion that diets containing more RDS may contribute to an increase in caries.	
Chankanka et al. (2011)	
Study question	To examine the risk factors, including dietary intake, for children having new cavitated caries between 5 and 9 years old (Iowa Fluoride Study.
Study design	Prospective cohort study.
Study population	198 children – subjects of the Iowa Fluoride Study (population differed in terms of fluoride concentration of water). Mainly Caucasian of relatively high socio-economic status.
Exposure	A three-day food and drink diary was sent to parents every 1.5 to 6 months from aged 1.5 months to aged 8.5 years. Detailed diet diaries

	were abstracted by dieticians. Food categories included 'baked starch with sugar', 'unprocessed starches' and 'processed starches'.
Dental outcome	Children were examined for clinically evident caries at aged 5 and again at around aged 8.5 years. Surface-specific transitions combined counts of new cavitated caries from 4 primary second molars, 8 permanent incisors and 4 permanent molars.
Statistics	Univariable logistic regression to model each dietary/other variable. Dietary variables with P<0.15 then selected for multivariate logistic regression model.
Results	Multivariable logistic regression showed 'unprocessed starches' (SDS) were not association with dental caries. Higher processed starch (RDS) intake at snack frequency was associated with new carious cavities. OR (95% CIs) = 3.87 (0.93-16.16). This was significant to p=0.07. Significance was accepted at p<0.10 as the simultaneous inclusion of previous caries experience in a multivariable model in which caries was also the outcome reduced the contribution of the other factors such that no relationships were found at the 5% level (and previous caries have the same risk factors as new caries).
Discussion/ limitations	This study was part of the larger 'Iowa Fluoride Study' which offered identification and subsequent follow-up of participants from birth and the inclusion of different water fluoride levels, which is an important non-modifiable factor. Unprocessed starches' (SDS) included 'boiled potato, bread, rice, etc. 'Processed starches' was inadequtely defined as 'potato chips, etc'.
Sreebny (1983)	
Study question	Study of the relationship between national cereal availability and dental caries
Study design	Ecological
Study population	National data on cereal supplies were compared with caries prevalence of 12-year-old children in 47 nations and 5 and 6 year old children from 23 countries.
Exposure	The study differentiated between three different cereal types (wheat, rice and maize).
Dental outcome	Dental caries – DMFT/dmft obtained from the WHO global oral epidemiology bank
Statistics	Linear regression analysis of caries prevalence with each type of cereal
Results	Found differences in the relationship of each cereal type with dental caries. Linear regression suggested that the consumption of wheat is associated with increased prevalence of dental caries (r): 0.45; P-value: 0.001), while maize consumption is associated with decreased prevalence (r): -0.37; P-value: 0.005 Linear regression of

	consumption of rice suggested no significant correlation (r): -0.07; P-value: 0.68).
Discussion/ limitations	In addition to the weakness of all ecological studies of attributing causation to association, the availability of sugars has not been controlled for as a confounder for the significance of wheat consumption on dental caries prevalence. Later analysis controlling for sugars availability nulled the relationship between wheat and caries.
Llena and Forner (2008)	
Study question	Aimed to explore any association between caries experience and potentially cariogenic foods.
Study design	Cross-sectional.
Study population	369 children (59.6% male). All children aged between 6 and 9 years who first attended a (state run) dental clinic in Valencia.
Exposure	Attempted to measure food frequency as food types such as foods 'rich in semi-hydrolysed starch'. However, the food frequency questionnaire used contained broad, subjective frequency measures with no indication of amounts of different food types consumed apart from weekly intake by age group.
Dental outcome	Dental caries (DMFS/dmfs) by visual examination with mirror and probe (no radiographs) by one calibrated examiner.
Statistics	Logisitic regression used to calculate odds ratio between food consumption frequency and caries experience adjusted by age, sex and tooth brushing frequency.
Results	The paper suggested that foods 'rich in semi-hydrolysed starch' increases the risk of dental decay OR 1.137 (1.049-1.232) - see limitations below.
Discussion/ limitations	The food frequency questionnaire used contained broad, subjective frequency measures with no indication of amounts of different food types consumed apart from weekly intake by age group. It is difficult to be confident that participants differed in consumption of the different food types reported.

Appendix Table 3: Included periodontal disease studies; SDS vs RDS

Merchant et al. (2006)	
Study question	To assess the relationship of wholegrain and fibre intakes with periodontitis risk (but comparisons made between whole-grain and refined grain).
Study design	Prospective cohort study.
Study population	34,160 in the US. All male health professionals aged 40-75 at the outset over 12 years.
Exposure	Wholegrain can be assumed to contain proportionally more SDS, whereas refined grain – due to processing – can be assumed to

	contain proportionally more RDS. The food items contained under the category 'whole-grain' were breakfast cereal with ≥ 25% whole-grain content by weight, cooked cereal, brown rice, dark breads, popcorn, wheat germ, bran and other grains. 'Refined grain' incorporated refined grain breakfast cereals, white bread and rice plus sweetened bakery items (cakes, muffins etc.). Food Frequency Questionnaire completed every 4 years and validated by comparing with two week diet records at 4 different times of the year by a subset of the population.
Dental outcome	Participants asked every two years 'Have you had professionally diagnosed periodontal disease with bone loss?'(Validated against blinded review of radiographs amongst dentists).
Statistics	Cox proportional hazard model to estimate RRs, controlling for age, smoking, BMI, alcohol use, physical activity and total energy consumption.
Results	Wholegrain intake appeared protective against periodontal disease. Those in the highest quintile of wholegrain consumption were 23% less likely to develop periodontitis (multivariate relative risk (95%CI) = 0.77 (0.66 to 0.89). However, periodontitis was not significantly associated with the intake of refined grains; those in the lowest quintile of refined grain intake versus the highest quintile of intake had a multivariate relative risk (95%CI) = 1.04 (0.89 to 1.23).
Discussion/ limitations	Large sample and 12 year follow up. However, generalisability is restricted by the study population of adult and male US health professionals (including 58% dentists). Oral hygiene practices not adjusted for as a potential confounder.
Nielsen et al. (2016)	
Study question	To examine the relation of dietary fibre (including whole-grain) intake with periodontal disease (NHANES 2009-2012 – National Health And Nutrition Examination Survey).
Study design	Cross-sectional.
Study population	Nationally representative sample of 6,052 in the US. Adults, >30 years of age. Men=2945; Women=3107.
Exposure	Whole-grains: 'all grain-based products made from 100% whole grains or their flour' (p. 2532).
Dental outcome	Periodontitis: According to the CDC/American Academy of Periodontology. Trained dentists conducted oral examinations, with the examiners being periodically calibrated by the survey experts.
Statistics	Logistic, multinomial logistic and regression modelling.
Results	The *lowest* intake category of whole-grain (n = 1731, 0 ounce equivalents) was associated with a statistically significant risk of periodontitis (Fully adjusted OR (95% CIs) = 1.32 (1.08 to 1.62)).

Discussion/ limitations	A limitation was that food and nutrient estimates stemmed from only two 24-hour recalls, as well as the failure to adjust for and/or report alcohol consumption as a potential confounder in the analyses.

No studies on periodontal disease were identified for inclusion in the total starch review.

Appendix Table 4: Included oral cancer study; total starch

Bravi et al. (2013)	
Study question	Analyse the role of selected food groups, macronutrients and micronutrients on oral cavity and pharyngeal cancer.
Study design	Case control – participants interviewed by trained personnel using a structured questionnaire including information on sociodemographic characteristics, anthropometric measures and lifestyle habits, with dietary habits during the 2 years before cancer diagnosis or hospitalisation assessed through a food frequency questionnaire (FFQ) that included weekly consumption of 78 foods, recipes and beverages.
Study population	768 cases/2078 controls in Italy and Switzerland aged 19-79 years followed between 1997-2009 ("adjusted for age, sex, centre, education, year of interview, body mass index, tobacco smoking and alcohol drinking [and] nonalcoholic energy").
Exposure	Intake of starch (g), portions per week mean (and standard deviation) among controls = 136.6 (63.4)
Dental outcome	Histologically confirmed squamous cell carcinoma cases – oral and pharyngeal cancer.
Statistics	ORs logistic regression
Results	Highest quintile of starch intake showed a non-significant association with oral and pharyngeal cancer (OR (95% CI) = 0.77 (0.51–1.17)).
Discussion/ limitations	The authors reflect on the possibility that dietary habits of hospital controls are not necessarily representative of the general population, although this potential bias may have been limited by the fact that patients with acute conditions not associated with long-term dietary modifications were selected amongst the controls, and all diagnoses associated with tobacco smoking and alcohol drinking were excluded.

Appendix Table 5: Included oral cancer studies; RDS vs. SDS

Kasum et al. (2002)	
Study question	To examine the association between whole-grain intake and incidence of upper aerodigestive tract cancer (Iowa Women's Health Study).

Study design	Prospective cohort study – with a mailed questionnaire including a 127-item food-frequency questionnaire and assessment of other cancer risk factors circulated to participants at baseline in 1986.
Study population	A random sample of 34,651 postmenopausal, initially cancer-free women aged 55–69 years in the US were extracted from the 1985 Iowa driver's license list. Participants were followed from 1986 to 1999 (analyses were adjusted for age, energy intake, alcohol use and smoking).
Exposure	'Whole-grain consumption [SDS] was assessed by 8 items: dark bread, whole-grain breakfast cereal, popcorn, cooked oatmeal, wheat germ, brown rice, bran and other grains. Whole-grain breakfast cereals were defined as having >25% whole-grain or bran content by weight'. Intake of whole-grain (servings/week): Lowest whole-grain intake tertile = 0–6.5 (mean intake=3.3, n=11,961); Highest whole-grain intake tertile = 13.0–108.5 (mean intake=21.5, n=11,709).
Dental outcome	Occurrence of cancers of the upper aerodigestive tract (Health Registry of Iowa).
Statistics	Multivariate analyses/regression. Estimates from proportional hazard regression models adjusted for all variables presented in table" [including other food groups including refined grains and yellow/orange vegetables (servings/week), alcohol (drinks/day), smoking (20 pack-years), age (10 years) and Energy intake (250 kcal/day)].
Results	A significant effect was found for the highest tertile in whole-grain group (36 cases) and decreased risk of upper aerodigestive tract cancer (HRR (95% CI) = 0.53 (0.34-0.81)) Association between highest tertile of refined grain [RDS] consumption (9.5-78.0 servings/week – 61 cases) and upper aerodigestive tract cancer was not significant **(**HRR (95% CI) = 1.03 (0.67-1.58)).
Discussion/ limitations	Restricted to postmenopausal women. The authors also acknowledge that the number of cases was small compared to many case-control studies and that the study was observational with possible selection bias and residual confounding present. The authors also reflect on whether the relationships studied may have been underestimated as the dietary variables were imperfectly measured.
Lam et al. (2011)	
Study question	To examine dietary fibre and grain consumption in relation to head and neck cancer (National Institutes of Health (NIH)-AARP Diet and Health Study).
Study design	Prospective cohort study – a self-administered 124-item food-frequency questionnaire (FFQ) assessing participants' usual frequency of intake and portion size (over the last 12 months).
Study population	494,991 men and women aged 50–71 years old in six US states (California, Florida, Louisiana, New Jersey, North Carolina, and

	Pennsylvania) and two metropolitan areas (Atlanta and Detroit) were followed between 1996-2004 ("Adjusted for age at entry, education, body mass index, physical activity, alcohol intake, cigarette smoke dose, red meat intake, and total energy intake")
Exposure	Whole-grains and refined grains (groups compared are, however, total grains vs. total fibre, so no separate n or age for these consumption groups).
Dental outcome	Head and neck cancer (Cancers identified by anatomic site and histologic code of the *International Classification of Disease for Oncology*, with cases restricted to squamous cell carcinomas).
Statistics	Multivariate Cox proportional hazards regression models. Adjusted for age at entry, education, body mass index, physical activity, alcohol intake, cigarette smoke dose, red meat intake, and total energy intake. In analyses of total fibre and grains, these variables were mutually adjusted".
Results	For both women and men, a statistically significant association was shown between the highest quintile of whole-grains (women = 59 cases, men = 233 cases) and decreased risk of head and neck cancer (women HR (95% CI) = 0.71 (0.51–0.97); men = 0.85 (0.72–1.01)). For women, a statistically significant association was shown between the highest quintile of refined grains and decreased risk of head and neck cancer (56 cases, HR (95% CI) = 0.71 (0.51–0.97)), but this association was not significant for men (244 cases = 0.87 (0.73–1.04)).
Discussion/ limitations	The authors acknowledge that the findings might be due to chance as they investigated multiple subtypes of fibre, grains, and cancer sites that they lack information on smoking duration and passive smoke exposure as a potential confounder and that a modest number of cases were identified.
McLaughlin et al. (1988)	
Study question	To examine risk factors, including diet, for oral and pharyngeal cancer
Study design	Case control – questionnaires with dietary section containing 61 food items and interviews conducted by trained personnel.
Study population	871 cases and 979 controls aged 18-79 years in the US State of New Jersey, metropolitan Atlanta, Los Angeles County, and Santa Clara and San Mateo Counties (south of San Francisco-Oakland), followed between January 1, 1984 to March 31, 1985 (adjusted for alcohol habits and smoking).
Exposure	Quartiles of legume intake.
Dental outcome	Pathologically confirmed incident cases of oral and pharyngeal cancer (*International Classification of Diseases*).
Statistics	Logistic regression.
Results	The relationship between highest intake of legume and risk of oral and pharyngeal cancer was not significant for either men or women (men: OR = 1.3, women: OR = 1.5, but the authors reported (without

	specifying further) that none of these ORs were statistically significant as the 95% CIs did not exclude 1).
Discussion/ limitations	Restricted to Caucasian sample, only adjusted for alcohol habits and smoking and lower and upper limits of 95% CIs not reported.
Chatenoud et al. (1999)	
Study question	To examine the association between the frequency of consumption of refined cereals and the risk of selected cancers.
Study design	Case-control.
Study population	583 cases and 3526 controls younger than 75 years in Northern Italy (including Milan) between 1983-1993 (adjusted for "center, age, sex, education, smoking habits, alcohol intake, BMI, and intake of fruit, vegetables, and whole grains").
Exposure	Refined cereals (RDS) (bread, pasta or rice): lowest intake = 0-14 portions/week; highest intake = > 22 portions/week.
Dental outcome	Histologically confirmed cancers of the oral cavity and pharynx, oesophagus and larynx.
Statistics	Unconditional multiple logistic regression.
Results	A statistically significant association between highest intake of refined cereals (316 cases/1166 controls) and increased risk of cancers of the oral cavity and pharynx, oesophagus and larynx was found (OR (95% CI) = 1.59 (1.2-2.2)).
Discussion/ limitations	It is possible that a diet rich in refined cereals may also be poor in nutrients which have been demonstrated to provide a protective effect against cancer, so that it is not necessarily the high intake of refined cereals *per se* that is causing the effect but a lack of other nutrients.
Franceschi et al. (1999)	
Study question	To examine the role of dietary habits and food groups on cancer of the oral cavity and pharynx.
Study design	Case-control – a structured questionnaire including an interviewer-administered food frequency questionnaire (FFQ) based on 78 foods, food groups or recipes to assess subjects' habitual diet estimated as average weekly frequency of consumption.
Study population	598 cases/1491 controls aged <40->70 years in the province of Pordenone in north-eastern Italy and those of Rome and Latina and followed between January 1992 - November 1997 (adjusted for "age, centre, sex, education, smoking habit, total energy and alcohol intake".
Exposure	Quintiles of intake for e.g. pulse (SDS), potatoes and white bread (RDS).
Dental outcome	Histologically confirmed cancer of the oral cavity and pharynx.
Statistics	Multiple logistic regression.
Results	Pulse and potatoes did not indicate a statistically significant association between highest intake and oral and pharyngeal cancer (Pulse: OR (95% CI) = 2.1 (1.0–4.2); Potatoes: OR (95% CI) = 1.1 (0.7–1.8)), while

	highest intake of white bread indicated a statistically significant result towards decreased risk (OR (95% CI) = 0.4 (0.2–0.6)).
Discussion/ limitations	Inconsistent results in relation to RDS reported, with e.g. a significant decreased risk for white bread but not for potatoes.
Bosetti et al. (2000)	
Study question	To examine risk factors for oral and pharyngeal cancer.
Study design	Case-control – data collected by trained interviewers using structured questionnaires that included information on socio-demographic characteristics and lifestyle habits, medical history, frequency of intake of selected food items, menstrual and reproductive factors, and use of oral contraceptives and hormone replacement therapy in menopause.
Study population	195 cases and 1113 controls (female population) aged <45->65 years in the provinces of Milan, Pordenone and Rome (Italy) and the Swiss Canton of Vaud were followed between 1984–1997 ("adjusted for education, body mass index, tobacco and alcohol consumption").
Exposure	Wholegrain foods, low and moderate intake (79 cases and 592 controls, results for high intake group not reported).
Dental outcome	Histologically confirmed oral and pharyngeal cancer.
Statistics	Conditional multiple logistic regression models.
Results	No statistically significant relationship between moderate intake of wholegrain foods and risk of oral and pharyngeal cancer (OR (95% CI) = 0.63 (0.30-1.32)).
Discussion/ limitations	Restricted to female population, no results reported for high intake group of wholegrain foods and only moderate intake group could be considered in the analyses.
Levi et al. (2000)	
Study question	To investigate the possible different role of refined and whole-grain cereals on the risk of upper digestive and respiratory tract neoplasms
Study design	Case control – trained interviewers administered a structured questionnaire, with information on socio-demographic characteristics and lifestyle habits. A food frequency questionnaire (FFQ) including 79 items assessed subjects' habitual diet.
Study population	297 cases (of which the oral cavity and pharynx = 156) and 349 controls aged 34-74 years in Lausanne (Switzerland) between 1992 and 1999 (adjusted for "age, sex, education, smoking habits, and vegetables, fruits, alcohol and energy intake").
Exposure	Whole-grain (defined as i.e. whole wheat bread and cereals) = <4 times/week (lowest intake); >10 times/week (highest intake). Refined grain (defined as i.e. white bread and biscuits, pizza, pasta and rice) = <9 times/week (lowest intake); >17 times/week (highest intake).
Dental outcome	Histologically confirmed cancer cases (including oral and pharyngeal cancer) admitted to hospital.
Statistics	Unconditional multiple logistic regression.

Results	A statistically significant association was found between highest intake of refined grain and increased risk of oral and pharyngeal cancer (71 cases, OR (95% CI) = 1.9 (1.1-3.5)), while no statistically significant association was found between highest intake of whole-grain and oral and pharyngeal cancer (31 cases, OR (95% CI) = 0.6 (0.3-1.2)).
Discussion/ limitations	The identified association of cancer with refined cereals may have been confounded by the higher rate of digestion amongst this group as compared to other components of diet such as whole grain.
Aune et al. (2009)	
Study question	To explore the association between legume intake and cancer risk.
Study design	Case-control study – participants administered a structured questionnaire by two trained social workers, with the questionnaire including a detailed food frequency questionnaire (FFQ) with 64 food items (covering dietary intake one year before diagnosis).
Study population	539 cancer cases and 2032 hospital controls, aged 26-89 years, drawn from four major public hospitals of Montevideo (Uruguay) and followed between 1996 and 2004 (adjusted for "age, sex, residence, education, income, interviewer, smoking status, age at starting smoking, years since quitting smoking, cigarettes per day, duration of smoking, alcohol intake, intake of grains, dairy products, fatty foods (eggs, cake, custard, butter), fruits and vegetables, total meat, mate drinking status, energy intake, and BMI").
Exposure	Total legumes (SDS) calculated as sum of beans and lentils, lowest tertile of legume intake = 0-2.7 g/day, highest intake = 5.41-164 g/day.
Dental outcome	Newly diagnosed and microscopically confirmed primary cancers of the oral cavity and pharynx.
Statistics	Unconditional logistic regression.
Results	Highest intake of legumes (63 cases/664 controls) showed a statistically significant relationship with decreased risk or oral and pharyngeal cancer (ORs (95% CIs) = 0.48 (0.34-0.68)).
Discussion/ limitations	Participants generally of a low socioeconomic status, physical activity not adjusted for and since multiple cancer sites were investigated (beyond oral cancers) there is also a possibility that some of the findings may have been due to chance.
Bravi et al. (2013)	
Study question	Analyse the role of selected food groups, macronutrients and micronutrients on oral cavity and pharyngeal cancer.
Study design	Case control – participants interviewed by trained personnel using a structured questionnaire including information on sociodemographic characteristics, anthropometric measures and lifestyle habits, with dietary habits during the 2 years before cancer diagnosis or hospitalisation assessed through a food frequency questionnaire (FFQ) that included weekly consumption of 78 foods, recipes and beverages.

Study population	768 cases/2078 controls in Italy and Switzerland aged 19-79 years followed between 1997-2009 ("adjusted for age, sex, centre, education, year of interview, body mass index, tobacco smoking, alcohol drinking and non-alcohol energy intake").
Exposure	Intake of potatoes, portions per week, median (interquartile range) among controls = 1.5 (1.0-2.5).
Dental outcome	Histologically confirmed squamous cell carcinoma cases – oral and pharyngeal cancer.
Statistics	ORs logistic regression
Results	Highest quintile of potato intake showed a statistically significant association with increased risk of oral and pharyngeal cancer (OR (95% CI) = 1.85 (1.19-2.86)).
Discussion/ limitations	The authors reflect on the possibility that dietary habits of hospital controls are not necessarily representative of the general population, although this potential bias may have been limited by the fact that patients with acute conditions not associated with long-term dietary modifications were selected amongst the controls, and all diagnoses associated with tobacco smoking and alcohol drinking were excluded.
Chen et al. (2016)	
Study question	To examine the association between diet and oral cancer.
Study design	Case-control – personal interviews with a standard questionnaire.
Study population	313 cases/575 controls (cases male with controls matched in gender and age) in China (Union Hospital of Fujian Medical University) between 20-85 years of age, followed in the time period between September 2010 and December 2014.
Exposure	Edible beans (SDS) (frequency of eating beans 1 time or more per day).
Dental outcome	Oral cancer confirmed by pathological diagnosis.
Statistics	Logistic regression.
Results	Association between frequency of eating beans 1 time or more per day and the risk of oral cancer was not statistically significant (OR (95% CIs) = 0.725 (0.411–1.278)).
Discussion/ limitations	Restricted to male population. Broad measurements of potential confounding factors such as smoking and alcohol consumption, with smoking simply determined by having smoked over 100 times in the participant's lifetime, while alcohol consumption was measured by whether the participant had been drinking alcohol once a week or more over the last 6 month period.
Giraldi et al. (2016)	
Study question	To examine the association between adherence to Mediterranean diet and head and neck cancers.
Study design	Case control - dietary information obtained with validated food frequency questionnaire (FFQ) containing 27 items of foods and beverages, with patients asked to focus on intake one year prior to the interview when answering questions.

Study population	500 cases and 433 controls aged <60->70 years in Rome (Italy) between 2002-2014 ("adjusted for age, sex, tobacco smoking, alcohol drinking, and total energy intake").
Exposure	Legumes (SDS), lowest tertile: n=55; highest tertile: n=115.
Dental outcome	Patients with tumours (including oral cavity and pharynx) enrolled at hospital.
Statistics	Logistic regression.
Results	A statistically significant relationship was found between the highest intake of legumes and decreased risk of oral and pharyngeal cancer (OR (95% CI) = 0.05 (0.01–0.25)).
Discussion/ limitations	Caution needs to be exhibited when interpreting the finding on the statistically significant decreased risk of cancer related to legume intake, as legume comprised only one of the food components of a specific Mediterranean diet.

Hebert et al. (1993)	
Study question	To examine nutritional predictors of oral and oesophageal cancer mortality rates.
Study design	Ecological study – using secondary sources from the United Nations (UN), the World Health Organization (WHO) and the World Bank.
Study population	Data from 59 countries with population aged 45-74 years.
Exposure	Pulses, Calories, kcal/day: Mean = 47, Minimum = 2, Maximum = 183, IQR = 20, 71.
Dental outcome	Oral cancer mortality rates.
Statistics	Exploratory analyses – regression models.
Results	Intake of pulses unspecified decrease the risk of oral cancer mortality significantly for males (Pearson correlation coefficients of -0.27), but the correlation coefficients were not significant for females (-0.14, with < - 0.25 significant at $p < 0.05$ in these analyses).
Discussion/ limitations	The cross-national design of the study may increase generalisability of findings relating to legumes; however, the study design (ecological) in addition to being a relatively old study (from 1993) may limit the reliability on which conclusions can be drawn.

Supplemental Material 4 Grade Evidence Profiles

Appendix Table 6

Question: What is the effect of an increase/decrease in total starch on dental caries?

QUALITY ASSESSMENT						NO OF PARTICIPANTS		EFFECT	QUALITY
No of studies	**Design**	**Risk of bias**	**Consistency**	**Directness**	**Other modifying factors**	**Experimental**	**Control**		
Dental caries									
4	Observational (cohort studies[6])	No serious risk of bias	No serious inconsistency	No serious indirectness	No significant modifying factors	-/2217[7]		Not pooled	Low

[6] Marshall *et al.* (2005), Campain *et al.* (2003), Rugg-Gunn *et al.* (1987), Kaye *et al.* (2015)
[7] Total from all studies

Appendix Table 7

Question: What is the effect of an increase/decrease in total starch on oral cancer?

QUALITY ASSESSMENT						NO OF PARTICIPANTS		EFFECT (95% CIs)	QUALITY
No of studies	**Design**	**Risk of bias**	**Consistency**	**Directness**	**Other modifying factors**	**Experimental**	**Control**		
Oral cancer									
1	observational (case control study[8])	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious risk of imprecision[9]	768 cases; 2078 controls		OR[10] 0.77 (0.51 to 1.17)	Very low

[8] Bravi *et al.* (2013)
[9] Single study (Bravi *et al.*, 2013) with relatively wide confidence intervals with upper limit just above the null value of 1 (starch may reduce odds of cancer if sample size larger)
[10] Odds Ratio

Appendix Table 8

Question: What is the effect of an increase in intake of RDS on dental caries?

QUALITY ASSESSMENT						NO OF PARTICIPANTS		EFFECT	QUALITY
No of studies	**Design**	**Risk of bias**	**Consistency**	**Directness**	**Other modifying factors**	**Experimental**	**Control**		
Dental caries									
2	Observational (cohort studies[1])	No serious risk of bias[2]	No serious inconsistency[3]	No serious indirectness[4]	No significant modifying factors[5]	702[6]		Not pooled	Low

[1] Chankanka *et al.* (2011) and Campain *et al.* (2003)
[2] Prospective cohort design, continuous dietary assessment with calibrated outcome measures at start and end of study. Potential for recall bias likely to be non-differential and minimal as little general understanding of the effects of starch on caries.
[3] No evidence of inconsistency. Both studies found higher caries with an increase in processed starch. Insufficient data for pooling results.
[4] Both studies include some outcomes on adult dentition but both may also include outcomes on primary dentition.
[5] No justification for upgrading or downgrading based on precision or effect size
[6] Total number of participants from both studies

Appendix Table 9

Question: What is the effect of an increase in intake of SDS on oral cancer?

QUALITY ASSESSMENT						NO OF PARTICIPANTS		EFFECT	QUALITY
No of studies	**Design**	**Risk of bias**	**Consistency**	**Directness**	**Other modifying factors**	**Experimental**	**Control**	(95% CIs)	
Oral cancer									
2	Observational (cohort studies[1])	No serious risk of bias[2]	No serious inconsistency[3]	No serious indirectness[4]	No significant modifying factors[5]	36518[6]		HR[7] = 0.62 (0.46 - 0.79)	Low
Oral cancer									
4	Observational (case-control studies[8])	No serious risk of bias[9]	No serious inconsistencies[10]	No serious indirectness	No significant modifying factors[11]	9025 total[12]		Not pooled	Low

[1] Kasum *et al*. (2002), Lam *et al*. (2011)
[2] Dietary intake assessed only at baseline; any effect of dietary changes throughout follow up would be unlikely to be differential in terms of outcome as prospective design
[3] Significant effect only seen in females, and not males, in Lam *et al*. (2011)
[4] Insufficient data to pool results for oral cancer specifically and confidence intervals are only reported for 'Upper Aerodigestive Tract' (Kasum *et al.*, 2002);
[5] Only Lam *et al*. (2011) reports confidence intervals for oral cancer specifically
[6] Total number of participants from both studies
[7] Hazard Ratio
[8] Bosetti *et al.* (2000), Aune *et al.* (2009), Giraldi *et al.* (2016), McLaughlin *et al.* (1988)
[9] Used recognised dietary assessment methods; some bias associated with these but already graded 'low' due to case-control design
[10] Different food groups but risks either non-significant or decreased for food types classified as SDS
[11] All studies except McLaughlin *et al.* (1988) reported odds ratios with 95% confidence intervals
[12] Total number of participants from both studies

Appendix Table 10

Question: What is the effect of an increase in intake of RDS[1] on oral cancer?

QUALITY ASSESSMENT						NO OF PARTICIPANTS		EFFECT	QUALITY
No of studies	**Design**	**Risk of bias**	**Consistency**	**Directness**	**Other modifying factors**	**Experimental**	**Control**		
Oral cancer									
4	Observational (case control[2])	No serious risk of bias[3]	Opposite effects reported[4]	No serious indirectness[5]	No significant modifying factors	4292[6]		Total not pooled[7]	Very low

[1] This group was the most difficult to classify and these studies included results for white bread, potatoes and 'refined cereals'
[2] Chatenoud *et al*. (1999), Levi *et al*. (2000), Bravi *et al*. (2013), Franchesci *et al*. (1999)
[3] Used recognised dietary assessment methods; some bias associated with these but already graded 'low' due to case-control design
[4] Franceschi *et al.* (1999) report a significant decreased risk for white bread, Levi *et al.* (2000) reported a significant increased risk for refined cereals and the evidence was downgraded to 'very low' based on such inconsistency
[5] Studies reported on oral/pharyngeal cancer except Chatenoud *et al.* (1999) which reports results for oral cavity, pharynx, larynx and oesophagus
[6] Total number of participants from both studies
[7] Some results pooled according to more specific food groups (see main report); this table gives an overall assessment of the evidence coming from included studies which potentially answer the question of the effects of RDS on oral cancer

Appendix Table 11

Question: What is the effect of an increase in intake of SDS on periodontal disease?

QUALITY ASSESSMENT						NO OF PARTICIPANTS		EFFECT	QUALITY
No of studies	**Design**	**Risk of bias**	**Consistency**	**Directness**	**Other modifying factors**	**Experimental**	**Control**		
Periodontal disease									
1	Observational (cohort study[1])	Serious[2] risk of bias	No serious inconsistency	Serious[3] indirectness	No significant modifying factors	5,683 (median of 3.4 servings per day/whole-grain)	8,210 (median of 0.3 servings per day/whole-grain)	Whole-grain: Multivariate RR=0.77, 95%CI=0.66 to 0.89	Very low

RR = Relative Risk

[1] Merchant et al. (2006).

[2] Participants merely asked every two years whether they had been professionally diagnosed with periodontal disease with bone loss, and oral health practices as a potential confounder not adjusted for in the analyses (although these may not have varied between groups).

[3] Study sample restricted to adult and male US health professionals (including 58% dentists).

Appendix Table 12

Question: What is the effect of an increase in intake of RDS on periodontal disease?

QUALITY ASSESSMENT						NO OF PARTICIPANTS		EFFECT	QUALITY
No of studies	**Design**	**Risk of bias**	**Consistency**	**Directness**	**Other modifying factors**	**Experimental**	**Control**		
Periodontal disease									
1	Observational (cohort study[1])	Serious[2] risk of bias	No serious inconsistency	Serious[3] indirectness	No significant modifying factors	5,717 (median of 4.2 servings per day/refined grain)	8,059 (median of 0.7 servings per day/ refined grain)	Refined grain: Multivariate RR=1.04, 95%CI=0.89 to 1.23	Very low

RR = Relative Risk

[1] Merchant et al. (2006).

[2] Participants merely asked every two years whether they had been professionally diagnosed with periodontal disease with bone loss, and oral health practices as a potential confounder not adjusted for in the analyses (although these may not have varied between groups).

[3] Study sample restricted to adult and male US health professionals (including 58% dentists).

Appendix Table 13

Question: What is the effect of a decrease in intake of SDS on periodontal disease?

QUALITY ASSESSMENT						NO OF PARTICIPANTS		EFFECT	QUALITY
No of studies	**Design**	**Risk of bias**	**Consistency**	**Directness**	**Other modifying factors**	**Experimental**	**Control**		
Periodontal disease									
1	Observational (cross-sectional study[1])	Serious[2] risk of bias	No serious inconsistency	No serious indirectness	No significant modifying factors	Lowest quartile of whole-grain, n = 1731	Highest quartile of whole-grain, n = 1368	OR=1.32, 95% CI=1.08 to 1.62	Very low

OR = Odds Ratio

[1] Nielsen et al. (2016).

[2] Food and nutrient estimates stemmed from only two 24-hour recalls and alcohol consumption was not adjusted for and/or reported as a potential confounder in the authors' analyses.

Supplementary Material 5: Excluded Studies

The studies to be assessed at title and abstract were the same for the SDS/RDS review and for the total starch review. The following gives reasons for exclusion from the SDS/RDS review followed by a list of studies excluded from the total starch review for completion (these are mainly duplicated from the SDS/RDS review).

Exclusions at full paper stage from the RDS/SDS review

Not starch (39) = No clear breakdown from e.g. carbohydrates to starch or starch-influenced food product(s) in the assessments of the researchers conducting the individual studies.

Starch not isolated (9) = Starch in general or starch-influenced food product(s) have been considered, but the effects of the starch cannot be singled out from the effects of other nutritional types.

Unclear starch type (27) = Starch in general or starch-influenced food product(s) have been considered, but it is not possible based on the researchers' descriptions to determine whether RDS and/or SDS is being assessed.

Not recognised dietary assessment method (11) = No validated/standardised measure of the assessment of dietary intake has been used for the collection of the data (e.g. studies in which researchers have asked subjective questions that do not allow for a clear differentiation between study participants in terms of their actual level of dietary intake (e.g. if researchers merely have asked parents how much their children eat of a particular type of food as represented in broad categories of 'low', 'medium', 'high' intake without specifying intake further, or merely in binary data of e.g. 'consumes daily/does not consume daily')).

Nasopharynx (5) = Researchers only consider the impact of dietary intake on cancer in relation to the nasopharynx and no other parts of the pharynx and/or the oral cavity or the larynx.

No outcomes (2) = None of the oral health outcomes of main interest to this review have been clearly represented in the analysis.

Not human study (1) = Animal or incubation study.

Review with no original data (16) = Researchers present a review, but it does not include any original data (e.g. in a meta-analysis of previous studies).

Opinion paper (5) = Papers with expert opinion etc., but which have not collected original data.

Not peer-reviewed (1) = The paper has not been peer-reviewed, e.g. is part of a book or a journal in which papers do not go through a peer-review process.

Appendix Table 14: Summary of excluded studies

Reference	Main reason for exclusion
Aires, C.P., Del Bel Cury, A.A., Tenuta, L.M., Klein, M.I., Koo, H., Duarte, S. and Cury, J.A. (2008) 'Effect of starch and sucrose on dental biofilm formation and on root dentine demineralization', *Caries Research*, 42(5), pp. 380-6.	Unclear starch type
Aizawa, S., Miyasawa-Hori, H., Nakajo, K., Washio, J., Mayanagi, H., Fukumoto, S. and Takahashi, N. (2009) 'Effects of alpha-amylase and its inhibitors on acid production from cooked starch by oral streptococci', *Caries Research*, 43(1), pp. 17-24.	Unclear starch type
Akarslan, Z.Z., Sadik, B., Sadik, E. and Erten, H. (2008) 'Dietary habits and oral health related behaviors in relation to DMFT indexes of a group of young adult patients attending a dental school', *Medicina Oral, Patologia Oral y Cirugia Bucal*, 13(12), pp. E800-7.	Starch not isolated
Amtha, R., Zain, R., Razak, I.A., Basuki, B., Roeslan, B.O., Gautama, W. and Purwanto, D.J. (2009) 'Dietary patterns and risk of oral cancer: a factor analysis study of a population in Jakarta, Indonesia', *Oral Oncology*, 45(8), pp. e49-53.	Not starch
Arcella, D., Ottolenghi, L., Polimeni, A. and Leclercq, C. (2002) 'The relationship between frequency of carbohydrates intake and dental caries: a cross-sectional study in Italian teenagers', *Public Health Nutrition*, 5(4), pp. 553-60.	Unclear starch type
Basir, L., Kartalaie, M.M., Shaddel, M., Imani, Z. and Heidari, M.A. (2016) 'The relationship between diet and DMFT / DMFT indexes in 2-12 years old children referred to dental clinics in Ahvaz in 2015', *International Journal of Pharmacy and Technology*, 8(2), pp. 11652-11664.	Unclear starch type
Bassir, L., Amani, R., Khaneh Masjedi, M. and Ahangarpor, F. (2014) 'Relationship between dietary patterns and dental health in type i diabetic children compared with healthy controls', *Iranian Red Crescent Medical Journal*, 16 (1) (no pagination)(e9684).	Unclear starch type
Bibby, B.G. and Mundorff, S.A. (1975) 'Enamel demineralization by snack foods', *Journal of Dental Research*, 54(3), pp. 461-70.	Not human study
Bidoli, E., Pelucchi, C., Polesel, J., Negri, E., Barzan, L., Franchin, G., Franceschi, S., Serraino, D., De Paoli, P., La Vecchia, C. and Talamini, R. (2013) 'Fiber intake and risk of nasopharyngeal	Nasopharynx

carcinoma: a case-control study', *Nutrition & Cancer*, 65(8), pp. 1157-63.	
Biral, A.M., Taddei, J.A.d.A.C., Passoni, D.F. and Palma, D. (2013) 'Cárie dentária e práticas alimentares entre crianças de creches do município de São Paulo', *Rev. nutr*, 26(1), pp. 37-48.	Not starch
Bradshaw, D.J. and Lynch, R.J. (2013) 'Diet and the microbial aetiology of dental caries: new paradigms', *International Dental Journal*, 63 Suppl 2, pp. 64-72.	Review with no original data
Bravo Rivera, L., Torres Chianale, F., Fierro Monti, C. and Pérez Flores, M.A. (2010) 'Estado de salud bucal en preescolares con sobrepeso de Concepción, Chile', *Int. j. odontostomatol. (Print)*, 4(3), pp. 267-270.	Not starch
Brownlee, I. (2014) 'The impact of dietary fibre intake on the physiology and health of the stomach and upper gastrointestinal tract', *Bioactive Carbohydrates and Dietary Fibre*, 4(2), pp. 155-169.	Review with no original data
Burt, B.A., Kolker, J.L., Sandretto, A.M., Yuan, Y., Sohn, W. and Ismail, A.I. (2006) 'Dietary patterns related to caries in a low-income adult population', *Caries Research*, 40(6), pp. 473-80.	Not starch
Chaffee, B.W., Feldens, C.A., Rodrigues, P.H. and Vitolo, M.R. (2015) 'Feeding practices in infancy associated with caries incidence in early childhood', *Community Dentistry & Oral Epidemiology*, 43(4), pp. 338-48.	Starch not isolated
Chapple, I.L. (2009) 'Potential mechanisms underpinning the nutritional modulation of periodontal inflammation', *Journal of the American Dental Association*, 140(2), pp. 178-84.	Review with no original data
Chatenoud, L., Tavani, A., La Vecchia, C., Jacobs, D.R., Jr., Negri, E., Levi, F. and Franceschi, S. (1998) 'Whole grain food intake and cancer risk', *International Journal of Cancer*, 77(1), pp. 24-8.	Not recognised dietary assessment method
Chu, C.H., Wong, A.W.Y., Lo, E.C.M. and Courtel, F. (2008) 'Oral health status and behaviours of children in rural districts of Cambodia', *International Dental Journal*, 58(1), pp. 15-22.	Not starch
Chyou, P.H., Nomura, A.M. and Stemmermann, G.N. (1995) 'Diet, alcohol, smoking and cancer of the upper aerodigestive tract: a prospective study among Hawaii Japanese men', *International Journal of Cancer*, 60(5), pp. 616-21.	Unclear starch type
Coogan, M.M., Jones, R.L., Meyer, D.H. and Viljoen, H.W. (1988) 'Starch and dental caries', *Journal of the Dental Association of South Africa*, 43(11), pp. 515-9.	Unclear starch type
Deakin, T. (2013) 'Starchy carbohydrates with every meal is good advice', *Practical Diabetes*, 30(4), pp. 164-166a.	Opinion paper
Deneo-Pellegrini, H., Boffetta, P., De Stefani, E., Correa, P., Ronco, A.L., Acosta, G., Mendilaharsu, M., Silva, C. and Luaces, M.E. (2013) 'Nutrient-based dietary patterns of head and neck quamous cell	Unclear starch type

cancer: A factor analysis in Uruguay', *Cancer Causes and Control*, 24(6), pp. 1167-1174.	
Dikshit, R.P., Boffetta, P., Bouchardy, C., Merletti, F., Crosignani, P., Cuchi, T., Ardanaz, E. and Brennan, P. (2005) 'Lifestyle habits as prognostic factors in survival of laryngeal and hypopharyngeal cancer: a multicentric European study', *International Journal of Cancer*, 117(6), pp. 992-5.	Not starch
Duarte, S., Klein, M.I., Aires, C.P., Cury, J.A., Bowen, W.H. and Koo, H. (2008) 'Influences of starch and sucrose on Streptococcus mutans biofilms', *Oral Microbiology & Immunology*, 23(3), pp. 206-12.	Unclear starch type
Edefonti, V., Bravi, F., Garavello, W., La Vecchia, C., Parpinel, M., Franceschi, S., Dal Maso, L., Bosetti, C., Boffetta, P., Ferraroni, M. and Decarli, A. (2010) 'Nutrient-based dietary patterns and laryngeal cancer: evidence from an exploratory factor analysis', *Cancer Epidemiology, Biomarkers & Prevention*, 19(1), pp. 18-27.	Unclear starch type
Edefonti, V., Bravi, F., La Vecchia, C., Randi, G., Ferraroni, M., Garavello, W., Franceschi, S., Talamini, R., Boffetta, P. and Decarli, A. (2010) 'Nutrient-based dietary patterns and the risk of oral and pharyngeal cancer', *Oral Oncology*, 46(5), pp. 343-8.	Unclear starch type
Edefonti, V., Hashibe, M., Ambrogi, F., Parpinel, M., Bravi, F., Talamini, R., Levi, F., Yu, G., Morgenstern, H., Kelsey, K., McClean, M., Schantz, S., Zhang, Z., Chuang, S., Boffetta, P., La Vecchia, C. and Decarli, A. (2012) 'Nutrient-based dietary patterns and the risk of head and neck cancer: a pooled analysis in the International Head and Neck Cancer Epidemiology consortium', *Annals of Oncology*, 23(7), pp. 1869-80.	Not starch
Edefonti, V., Nicolussi, F., Polesel, J., Bravi, F., Bosetti, C., Garavello, W., La Vecchia, C., Bidoli, E., Decarli, A., Serraino, D., Calza, S. and Ferraroni, M. (2015) 'Nutrient-based dietary patterns and nasopharyngeal cancer: evidence from an exploratory factor analysis', *British Journal of Cancer*, 112(3), pp. 446-54.	Nasopharynx
Elangovan, A., Mungara, J. and Joseph, E. (2012) 'Exploring the relation between body mass index, diet, and dental caries among 6-12-year-old children', *Journal of the Indian Society of Pedodontics & Preventive Dentistry*, 30(4), pp. 293-300.	Unclear starch type
Escribano Uzcudun, A., Rabanal Retolaza, I., Bravo Fernandez, P., Sanchez Hernandez, J.J., Garcia Grande, A., Garcia Garcia, A., Miralles Olivar, L., De Diego Sastre, I., Gonzalez Baron, M. and Gavilan Bouzas, J. (2002) 'Nutrition and pharyngeal cancer: Results from a case-control study in Spain', *Head and Neck*, 24(9), pp. 830-840.	Not starch
Escribano Uzcudun, A., Rabanal Retolaza, I., Garcia Grande, A., Miralles Olivar, L., Garcia Garcia, A., Gonzalez Baron, M. and Gavilan Bouzas, J. (2002) 'Pharyngeal cancer prevention: evidence	Not starch

from a case--control study involving 232 consecutive patients', *Journal of Laryngology & Otology*, 116(7), pp. 523-31.	
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Supplementary Material 6: Experimental studies

Appendix Table 15: Included non-epidemiological studies on dental caries

Author and year	Study design	Type of starch exposure	Dental outcome	Enables assessment of total starch, RDS or SDS or RDS vs SDS	Evidence for increase starch type and proxy measures of caries	Notes: All studies on adults
Edgar et al. (1975)	Plaque pH Harvesting technique	White bread Whole meal bread Plain crackers Potato crisps Apple Banana	Minimum pH Reached over 30 minutes (= best outcome)	RDS, SDS No statistical comparison conducted.	Did not decrease plaque pH to <5.7 for 30 minutes. Minimum PH reached for banana and whole meal bread were >5.7 but <5.9.	19 young adults A number of sugars containing foods measured too. Whole meal bread contained corn syrup and honey.
Harper et al. (1985)	Plaque pH touch electrodes	Potato crisps Sponge cake 'Sandwich biscuits/cookies' Milk chocolate	Minimum plaque pH, 'area under pH 5.5'	RDS (Crisps), compared with sugars containing starch foods	Crisps (the primary starch test food) had a higher pH compared with sponge cake but a similar plaque pH to other foods.	Only 5 subjects with large variability in results
Lingstrom and Birkhed (1993)	Plaque pH indwelling electrode	Only product that contained starch without sugars was potato crisps. No added sugar cheese doodles contained 3% sugar mostly lactose from cheese and 0.4% sugars	Minimum pH reached (subgroup analysis by low and normal saliva exposure) (best outcome)	Compared RDS starch or sucrose only with individual foods	Starch only, potato crisps or 'doodles' (a form of cheese-flavoured puff snack) did not decrease plaque pH to <5.7 with normal saliva flow. With low flow min pH was ≈5.6 and 5.5, respectively.	Ten volunteers 30-71 year old adults Could be relevant to older people with exposed roots and low saliva flow
Lingström et al. (1994)	Plaque pH indwelling electrode	Crossover periods of 'Starch product' (bread, crisps and potato combined with very low sugar) and 'sugar products' (boiled sweets with high sugar) 12-15 times per day and compared with a control period (normal diet)	Changes in plaque pH of the	RDS Compares an increase in frequency of starch compared to sucrose and normal diet (control). Nb starch was highly gelatinized	Plaque pH for starch did not go below 5.7.	N=8 Edentulous elderly wore slabs in prosthesis.
Pollard (1995)	Plaque pH harvesting technique	Pasta Banana Rice	Minimum pH reached (best outcome)	Anova showed no difference between foods	Minimum pH of starch foods did not go below 5.7 for 30 mins.	Ten participants 20-35 years old

		White bread Whole meal bread Weetabix			Pasta and banana went below 5.9, others did not.	Sugar content of bread unknown. Weetabix is 4% sugar.
Lingstrom et al. (2000)	Plaque pH touch electrode (up to 60 minutes)	Three types of bread with no added sugar, one sweetened wheat-rye bread Barley kernel bread (BKB), Sourdough-fermented, White wheat bread and Sweetened wheat-rye bread	Minimum pH reached (best outcome)	BKB was only compared with sweetened breads.	None of the non-sweetened breads decreased plaque pH below 6.0. Minimum pH was 5.75 for sweetened	Ten participants 19-52 years
Brudevold et al. (1985)	Enamel slab	Gelatinised wheat starch	Demineralisation of enamel by increase in Ip, mineralisation by decrease in Ip	Comparison of cooked versus raw starch	Cooked starch caused some demineralisation in all subjects, including two statistically significant. Raw starch caused no demineralisation (four of five statistically significant)	N=5 dentulous males (age range 29-73 years), with teeth in good condition
Brudevold et al. (1988)	Enamel slab – of 45 mins duration	Gelatinised wheat starch of different concentrations	Demineralisation using Iodide permeability. (final pH of biofilm on slab also measured)	Measured different concentrations of gelatinized starch - RDS	3 and 5% starch rinses were not statistically significantly different from control (no rinsing). 10, 15, and 20% caused demineralisation over 45 min study period.	N=6 dentate males
Lingström et al. (1994)	Enamel and dentine slabs	Bread, crisps and potato (combined) 12-15 times per day and compared with a control period normal diet	Surface microhardness and transverse microradiograph. PH of plaque on experimental slabs also measured using an indwelling electrode	RDS: compares an increase in frequency of starch compared to sucrose and normal diet (control). NB starch was highly gelatinized	Demineralisation with the starch test diet did not differ to control diet	N=8 Edentulous elderly wore slabs in prosthesis.
Kashket et al. (1994)	Enamel Slab	Wheat starch in unsweetened cookies (compared with sweetened cookies)	Demineralisation measured using iodide permeability. (PH of biofilm on intra-oral device also measured)	RDS Compared starch with or without sugar	Results show RDS if left in mouth for 45 mins can cause demineralisation (takes time) and decrease pH on plaque on an intra-oral device to below pH 5.	22-75 years. N= at least 5 per test.

Kashket et al. (1996)	Starch hydrolysis	Of the test foods only crisps were high starch without sugars	Oral retention time.	RDS And starch with sugars	Potato crisps retained up to 10 mins. Starch was hydrolysed to maltose and maltotriose in this time and this corresponded with acid production.	N=5 laboratory personnel.
Linke and Birkenfeld (1999)	Measured hydrolysis of starch – up to 2 hours post consumption	Whole meal crackers, bread stick Cornflakes and pretzel – with non-disclosed sugars concentration. Popcorn and crisps – assume sugars free.	Glucose and lactic acid concentrations measured in oral fluid collected using small filter paper from 5 sites	RDS	Shows that RDS are hydrolysed to glucose and that lactic acids concentrations increase within 30 mins and remain at around 25% of the 30 min level at 2 hours.	N=7. No drinks were allowed over 2 hours to aid oral clearance. Sugars content of test foods not disclosed. Findings indicate that oral retentiveness of RDS foods is important.
Ribeiro et al. (2005)	Enamel slab	Water/2% starch/10% sucrose/2% starch plus 10% sucrose	Demineralisation measured by cross sectional microhardness	RDS RDS and sucrose	No significant difference between water and starch alone, sucrose alone showed significantly more demineralisation than starch alone, sucrose plus starch showed significantly more demineralisation than starch alone	15 volunteers aged 18-33 years old but used enamel from primary teeth
Aires et al. (2008)	Dentine slabs	2% starch/10% sucrose/2% starch + 10% sucrose/2% starch + delayed 10% sucrose	Dentine demineralization (Surface hardness and cross sectional hardness)	Compares starch plus sugar with starch/sugar separately	Starch alone caused a non-significant reduction in surface hardness. Sucrose (in any combination of starch or with no starch) caused significant reduction in surface hardness	11 volunteers (20-34 years old)
Other study designs						

Linke and Birkenfeld (1999)	Measured hydrolysis of starch – up to 2 hours post consumption	Whole meal crackers, bread stick Cornflakes and pretzel – with non-disclosed sugars concentration. Popcorn and crisps – assume sugars free.	Glucose and lactic acid concentrations measured in oral fluid collected using small filter paper from 5 sites	All foods were 'starches' so no comparison made	Shows that starch is hydrolysed to glucose and that lactic acids concentrations increase within 30 mins and remain at around 25% of the 30 min level at 2 hours.	N=7. No drinks were allowed over 2 hours to aid oral clearance. Sugars content of test foods not disclosed. Findings indicate that oral retentiveness of starchy foods is important.

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