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Scientific Advisory Committee on Nutrition

# Framework and methods for the evaluation of evidence that relates food and nutrients to health


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Last updated: January 2023 (Version 23/01)

# Contents

# Introduction

1. This document has been prepared by the Scientific Advisory Committee on Nutrition (SACN) for the evaluation of evidence that relates both food and nutrients to health.

2. It is a ‘living’ document subject to regular review and may be modified or updated as required.

# Terms of reference

3. SACN is a committee of the Office for Health Improvement and Disparities (OHID). It provides independent scientific advice on, and risk assessment of, nutrition and related health issues. It advises the 4 UK governments and is supported by a scientific secretariat based at OHID.

4. SACN’s advice covers the scientific aspects of nutrition and health with specific reference to:
    - nutrient intakes and nutritional status of the population
    - nutrient content of individual foods and advice on individual nutrients and diet as a whole, including the definition of a balanced diet
    - monitoring and surveillance of the above aspects
    - nutritional issues which affect wider public health policy issues, including conditions where nutritional status is one of a number of risk factors (such as cardiovascular disease, cancer, diabetes, oral health, osteoporosis and obesity)
    - research requirements for the above.

5. Consideration of vulnerable groups (such as infants, adolescents and older adults), racially and ethnically diverse groups and health inequality underpins all SACN’s evidence evaluations. Where relevant, and when available evidence allows, SACN also considers beliefs and cultural influences.

# Remit

6. SACN's remit is to:
    - assess the benefits and risks of nutrients, dietary patterns, food, or food components to health by evaluating scientific evidence
    - make dietary recommendations for the UK population (including vulnerable and/or diverse groups) based on its assessment.

7. Before providing advice, SACN assesses possible nutritional or health risks that may be associated with implementing recommendations (such as potential risks of excess intakes or adverse impacts on other health outcomes or nutrients). In addition, principal residual areas of uncertainty are identified and form recommendations for further research.

8. SACN's role is to assess scientific information (risk assessment) to assist policy making and translation into advice (risk management), which is the responsibility of government health departments. The committee does not advise on how recommendations are taken forward for policy nor evaluate their wider implications (for example, agricultural, political, economic).

9. Sustainability issues are also outside SACN's remit but certain aspects may be addressed where relevant or at the request of UK government. For example, in relation to:
    - nutritional implications, such as consideration of both plant and animal sources of nutrients and differences in their bioavailability
    - implications of dietary recommendations to promote more sustainable diets, such as:
        - whether availability of the main dietary sources of nutrients under consideration is likely to be sufficient to meet nutritional recommendations
        - potential alternative dietary sources if availability of the main dietary sources is likely to be insufficient.

10. SACN has a public health focus, therefore the treatment of disease is outside its remit unless specifically requested. Consideration of issues related to alcohol, other than as a source of energy, is also outside the committee's remit.

# SACN subgroups and working groups

11. SACN has two standing subgroups:
    - the **subgroup on maternal and child nutrition** (SMCN) has a continuous work programme. In addition to conducting risk assessments, SMCN provides *ad hoc* scientific advice on maternal, infant and child nutrition issues that are referred to it by the UK health departments and SACN
    - the **subgroup on the SACN framework and methods for the evaluation of evidence that relates foods and nutrients to health** (Framework subgroup) provides ongoing methodological support to SACN (and its working groups) and SMCN. It also keeps the SACN framework under review to ensure it continues to be fit for purpose.

12. A **working group** is established at the start of a new evidence evaluation and is disbanded after publication.

13. SMCN, the Framework subgroup and the working groups comprise SACN members and external experts (appointed or co-opted when additional specialist knowledge is required).

# Relationship with other scientific advisory committees and organisations

14. If an evaluation requires consideration of evidence from scientific areas outside SACN's remit, appropriate expert advice is sought from the relevant scientific advisory committee. For example, advice on potential effects of excessive intakes of a particular nutrient or dietary component will be requested from the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT). Conversely, if another scientific committee requires nutrition advice, or to ensure effective communication between committees in areas of mutual interest, a SACN representative is co-opted onto that committee. An example is the safety assessment of novel foods undertaken by the UK Advisory Committee on Novel Foods and Processes (ACNFP) which includes nutritional assessment.

15. SACN also works with organisations such as the National Institute for Health and Care Excellence (NICE) and the Food Standards Agency (FSA).

16. SACN may conduct joint evidence evaluations with these or other committees and organisations (see paragraph 46).

# Openness and transparency

17. SACN is committed to values of openness and transparency and recognises that these principles underpin public confidence in the scientific evidence evaluation process.

18. In the interest of objectivity, SACN includes lay members and meetings are attended by observers from departments with responsibility for nutrition policy in each UK country.

19. Where possible, meetings of the main committee are held in open session. However, meetings are closed to external observers when members are reviewing ongoing evidence evaluations. This is to allow unconstrained discussion of the evidence and formulation of draft conclusions and recommendations before these are shared and finalised. All SACN working group and subgroup meetings are usually held in closed session for the same reason.

20. The agenda and papers for open sessions of the main committee meetings are published on the SACN website approximately 2 weeks before a meeting. The minutes of SACN, working group and subgroup meetings are also published on the website.

21. SACN is also committed to engagement with interested parties and will usually seek the views of the general public and the wider scientific community at various stages of an evidence evaluation (depending on the type of evaluation; see paragraphs 36 to 47 and Table A1, Annex 1), for example: on the scope of an evaluation; evidence identified through the literature search; and on a draft report. All comments received in response to public consultations are considered.

22. SACN members are required to declare any potential or perceived interests at the time of their appointment and to declare any changes to their interests at the start of every meeting (SACN, its subgroups and working groups). Any changes to a member's declaration of interests are recorded in the minutes of the meeting.

23. Full details of SACN's policy on openness and transparency are available in the SACN Code of Practice.

# Types of evidence

24. SACN's recommendations are based primarily on published evidence from human studies that have been designed *a priori* to identify effects of, or associations between, a nutrient intake, dietary pattern, food, or food component and physiological or behavioural (such as satiety or cognitive function) outcomes relevant to health/disease.

25. The evidence considered by SACN can include intermediate markers (epigenetic, metabolic, and systemic) of nutritional status, health and functional outcomes.

26. To provide biological plausibility of causality, supporting evidence from mechanistic studies in humans, animals, tissues or cells can be used to explain how an exposure may be causally linked to the outcome.

## Study types

27. At the outset of an evidence evaluation, each working group specifies the types of evidence to be included. This will vary depending on the question being asked and the evidence available. Different study types have different strengths and limitations and, therefore, value in informing decisions:

    - randomised controlled trials (RCTs): more weight is given to good quality RCTs because these minimise the potential for selection bias and confounding and facilitate assignment of a causal interpretation. RCTs are not always available (due to feasibility or ethical considerations) or there may be too few to draw on, they may be underpowered for the outcome of interest, their duration may be too short to reach clinical endpoints, the interventions may be non-specific, indirectly related to the exposure of interest or incompletely applied
    - observational (non-intervention) or other non-randomised studies: less weight is given to observational studies because these are potentially subject to bias, confounding and/or reverse causality. In the absence of sufficient evidence from appropriate good quality RCTs, evidence from well conducted non-randomised intervention studies and prospective cohort studies is considered. Evidence from other study designs, such as case-control or cross-sectional studies and case reports, is usually not considered.

28. Systematic reviews aim to capture the available primary studies relating to a specific research question according to a pre-defined process and criteria. Well-conducted, comprehensive, high quality systematic reviews reduce the potential for biased study selection or overlooking relevant studies. Systematic reviews with meta-analyses provide a quantitative assessment of the evidence. Systematic reviews with meta-analyses of RCTs (including individual participant data meta-

analyses) provide stronger evidence than those from non-randomised (observational) studies.

29. SACN's preferred approach is to use evidence provided by published systematic reviews and meta-analyses of RCTs (where these are available) and prospective cohort studies (in the absence of systematic reviews/meta-analyses of RCTs) to inform its evaluations rather than conducting its own systematic reviews of the primary evidence. This is because undertaking a systematic review is time and resource intensive. SACN's approach makes use of existing published evidence and draws upon broader scientific expertise. However, there are also limitations since the value of systematic reviews in informing recommendations is dependent on their quality, the quality of the included studies and the analyses conducted. In addition, the relevance and generalisability of the results of systematic reviews are dependent on how closely the systematic review question matches SACN's research question, the specific inclusion or exclusion criteria and comparators.

## Genetic evidence

30. Evidence from genetic association studies may also be considered. The basis for these studies is that an observed association between a genetic polymorphism and a disease state (or other trait) can be used to infer the causal role of the nutrient or dietary factor of interest. This approach has been termed 'Mendelian randomisation'.

31. Genetic association studies are not subject to reverse causality and are less prone to potential confounding than phenotypic observational studies but (in common with other study types) they may be subject to publication bias. There are also specific issues and assumptions that may affect their interpretation and require consideration. They may be subject to bias due to population stratification and inference of a nutritional effect may not always be valid. Gene products may have more than one biological function and it is possible that an association between a genotype and health may operate through a mechanism unrelated to the nutritional effect of the genotype. It is also possible that another variant within a gene (or within another nearby gene), may be influencing the health outcome.

32. Genetic effects are also relevant to interpretation of nutritional status data. Relatively common genetic polymorphisms can result in markedly different concentrations of related nutrients in the blood. Such genetic phenomena have the potential to complicate or confound the interpretation of nutritional data.

## Other evidence

33. SACN's evidence evaluations are also informed by consideration of data from nationally representative surveys, particularly the National Diet and Nutrition Survey (NDNS) rolling programme (a continuous survey of diet and nutrition in adults and children aged 18 months upwards). The NDNS provides important context and background on nutritional intakes and status of the general UK population. It is also useful for identifying nutrients of concern in relation to low (and high) intakes or status.

34. Other surveys that provide useful data include: the Low Income Diet and Nutrition Survey; the UK Diet and Nutrition Survey of Infants and Young Children; the Infant Feeding Survey (IFS); the National Child Measurement Programme; the Health Survey for England; and the Scottish Health Survey.

35. Additional sources of evidence include relevant reports or guidelines from national or international organisations, such as the World Health Organization (WHO), that have systematically considered the evidence.

# Types of evidence evaluation

36. The type of evidence evaluation undertaken by SACN depends on the approach taken to assess the evidence and intended purpose of the evaluation. This is agreed at the outset of an evaluation once the issues (such as nature and availability of the evidence and timeframe for completion of the work) have been considered. The different approaches and nomenclature have changed over time and current practice is described below.

37. All SACN's completed evidence evaluations are published on the SACN website and include:
    - reports
    - rapid reviews
    - position statements
    - joint reports/rapid reviews/position statements
    - updates to reports/rapid reviews/position statements.

38. The processes followed for each approach are tabulated in Annex 1 (Table A1).

## Reports

39. SACN reports are full risk assessments that provide comprehensive evaluations of the available evidence using a systematic and transparent approach. They provide

advice to inform public health policy, identify future research needs and, when the evidence permits, include public health recommendations in relation to diet.

40. They include the following processes:
    - registration of protocol
    - public consultation on draft scope
    - call for evidence
    - formal assessment of evidence quality
    - formal grading of evidence certainty
    - public consultation on draft report (including draft recommendations)
    - publication of final report.

41. All comments received to the public consultation on a draft report are considered before its finalisation and publication. SACN's responses to all comments received at consultation are published at the same time as the final report.

## Rapid reviews

42. Rapid reviews are a type of risk assessment that are conducted in a relatively short timeframe to address more urgent or emerging issues considered to be of high priority.

43. They usually have a narrow focus on a specific question, involve a limited scoping review and a summary of the evidence, without full risk assessment. Evidence is appraised for quality but, due to the rapid nature of the work, use of a formal quality assessment tool and grading is optional. They may include public health recommendations (which may be qualified by the limited nature of the review process) and research recommendations (highlighting limitations/gaps in the evidence). Rapid reviews are usually not subject to public consultation.

## Position statements

44. Position statements convey a concise expert opinion on issues of public health relevance. They generally provide an overview on the nature of the existing evidence for a particular nutritional issue and identify any gaps in the evidence.

45. They may entail a preliminary search of the evidence base to evaluate whether a detailed risk assessment is required (for example, if new evidence has become available that may impact current recommendations) or if it is feasible (for example, if the evidence base is sufficient). They do not usually involve formal quality assessment or grading of the evidence. They do not usually include public

health recommendations but may include research recommendations. They are usually not subject to public consultation.

### Joint reports/rapid reviews/position statements

46. Joint reports/rapid reviews/position statements cover work undertaken jointly by SACN and other scientific committees (for example, COT). Processes such as quality assessment, grading and public consultation should be agreed by both committees at the start of a joint evaluation.

### Updates to reports/rapid reviews/position statements

47. Reports, rapid reviews and position statements may be updated in light of new evidence, new requests, or ongoing interest. The approach will depend on the quantity and nature of any new evidence.

## Scope of an evaluation

48. Prior to commencing an evidence evaluation, SACN agrees the terms of reference and conducts a preliminary survey of existing literature (such as systematic reviews or expert reports) to inform the scope and to decide on the type of evaluation to undertake (see paragraphs 36 to 47).

49. To define the scope of an evaluation, the following issues are considered:
    - reason for undertaking evaluation, such as:
        - new evidence on possible diet-health relationships, health benefits, health risks, or nutritional status of the UK population
        - request from government ministers, UK Health Departments or other government departments
        - request from interested parties (such as non-governmental organisations or industry)
        - issues raised by SACN, its subgroups or working groups (for example, through horizon-scanning)
        - changes in legislation
        - emerging issues arising from the UK or international expert bodies, such as the European Food Safety Authority, NICE, or the WHO
    - principal nutrients, dietary patterns, food and/or food components under consideration and their putative role in health or disease outcomes
    - genetic evidence where this is relevant to the interpretation of nutritional information

- relevant populations and health or disease outcomes of the evaluation (based on the published literature of health outcomes important to public health in the UK)
- vulnerable groups (such as infants, adolescents and older adults)
- monitoring and surveillance; for example, through the NDNS and the IFS
- background/current state of knowledge, including reference to previous UK Health Departments/FSA/international reports (such as the WHO) and reviews including past SACN/Committee on the Medical Aspects of Food Policy (COMA) reports, devolved government reports, and/or good quality reviews from non-governmental organisations.

50. The draft scope outlines the terms of reference, background/context, areas to be covered/content and details of the literature search (for example, proposed search terms, proposed inclusion and exclusion criteria, and key publications that have informed the scoping exercise).

51. To provide transparency, the draft scope for a SACN report is published on the SACN website (usually for a 4-week time period) and interested parties are invited to comment on the proposed approach. All responses to the draft scope are considered.

# Process for evaluating the evidence

52. At the outset, once the issues have been defined, the working group for an evidence evaluation:
    - agrees the type of evidence evaluation to be undertaken (see paragraphs 36 to 47) and explains the rationale for this
    - specifies the research question and objectives
    - sets the terms of reference
    - agrees the eligibility criteria
    - indicates the proposed populations, interventions (or exposures), comparators and outcomes of interest (PICO)
    - agrees the search strategy.

53. The outcomes of interest should be identified in advance. For each outcome, the working group should consider whether a positive, negative or no effect/no association implies a benefit or risk for public health. If there is no agreement on this, it would be difficult to interpret results for making recommendations and the working group should consider excluding it from the evaluation.

54. At an early stage, to guide later interpretation, the working group should, where possible and feasible, indicate the direction and size of exposure-outcome effects or associations that would be considered relevant in terms of public health. Specification of a relevant effect size allows conclusions to be drawn on public health (or clinical, where appropriate) importance rather than only statistical significance. The following points should be considered:

- magnitude of effect size (both absolute and relative) that might be considered large enough to be meaningful in public health terms
- magnitude of effect size unlikely to be caused by biases and residual confounding
- the underlying risk/incidence/prevalence in the general population or in unexposed groups.

## Protocol registration

55. Once the protocol for an evidence evaluation has been agreed, it should be registered on PROSPERO or other open access research registration platforms such as Open Science Framework to provide transparency, visibility and searchability of the committee's work.

## Literature search and study selection

56. Literature searches are usually restricted to systematic reviews rather than primary studies (see paragraph 29).

57. The search strategy should include details of search terms (including relevant genotype/polymorphisms), databases to be searched, other sources of information, study designs to include, publication type (for example, those published in peer-reviewed journals), publication date range and language.

58. Grey literature is only considered if the specific types of such publications to be included are agreed *a priori*. Preference is given to data published in peer-reviewed journals but other sources, such as official or expert reports based on peer-reviewed literature and official statistics, may provide valuable information. Where such data are used, the source should be clearly described.

59. Titles and abstracts of the publications identified by the literature search should be screened for eligibility against the inclusion criteria and excluded if it can be determined that they do not meet the criteria. A percentage of these (at least 10%) should be independently screened by 2 reviewers. Any differences between reviewers should be resolved by discussion and consensus or by a third independent reviewer.

60. Full text articles of the studies selected through the screening process should be retrieved and assessed independently by 2 reviewers (or a percentage, depending on number of publications) and any differences resolved by consensus or by a third independent reviewer. Studies not meeting the inclusion criteria after full text assessment should be excluded and the reasons for their exclusion should be clearly documented.

61. Following the literature searches (for a SACN report), a call for evidence is published on the SACN website to check that any relevant research in the field has not been overlooked (for example, recent or imminent publications).

62. When a draft report is made available for public consultation, interested parties are invited to alert SACN to any evidence that it may have missed. Any relevant evidence highlighted through the public consultation (or identified by the secretariat or members as being published after the agreed cut-off dates for the literature searches) is considered. The draft report is amended if newly available evidence published after the literature search cut-off dates, or through the consultation process, may influence the balance of evidence and draft conclusions.

63. A flow diagram detailing the study selection process should be included in evidence evaluations. An example flow diagram can be found in the SACN report on 'Lower carbohydrate diets for adults with type 2 diabetes' (2021) (Figure 4.1, page 36).

## Data synthesis

64. Data from the eligible studies should be tabulated and include the following details: first author, date of publication, country, sample size, duration of study, inclusion and exclusion criteria, dietary assessment method, exposure, outcome, statistical analysis, main results, adjustment for confounders (for observational studies) and source of funding.

65. An example evidence table of data extracted from systematic reviews and meta-analyses included in the SACN report on 'Lower carbohydrate diets for adults with type 2 diabetes' (2021) is provided in Annex 2 (Table A2).

## Assessment of study quality

66. The quality (methodology and potential biases) of studies meeting the eligibility criteria is critically appraised using a formal quality assessment tool.

67. To ensure consistency across SACN's evidence evaluations, the preferred quality assessment tools (appropriate for the study design) are summarised below.

### Systematic reviews: AMSTAR 2

68. AMSTAR 2 (a measurement tool to assess systematic reviews) (Shea et al, 2017) comprises a checklist of 16 domain-related items which form the criteria for evaluation. Comprehensive guidance on using AMSTAR 2 is available on the AMSTAR 2 website.

69. Seven out of the 16 domains are considered 'critical' by the AMSTAR 2 developers because they can critically affect the validity and conclusions of a systematic review. However, they suggest that appraisers can upgrade or remove domains from the 'critical' list as appropriate to the topic. Each working group should decide at the outset of an evidence evaluation which domains are considered critical and these should be described in the protocol.

70. Overall confidence in the systematic review, based on interpretation of weaknesses detected in critical and non-critical domains, is rated as 'high', 'moderate', 'low', or 'critically low'.

### Randomised trials: ROB-2

71. ROB-2 (Cochrane risk of bias revised tool for randomised trials) (Sterne et al, 2019) assesses 5 domains through which bias might be introduced: (1) from the randomisation process; (2) due to deviations from intended interventions; (3) due to missing outcome data; (4) in measurement of the outcome; (5) in selection of the reported result.

72. Judgements on risk of bias for each domain provide the basis for an overall judgement on risk of bias as: 'low', 'some concerns' or 'high'. Detailed guidance on applying the ROB-2 tool is available from the Cochrane Methods Group on Bias.

### Non-randomised studies: ROBINS-I

73. ROBINS-I (Risk of bias in non-randomised studies - of interventions) (Sterne et al, 2016) assesses 7 domains through which bias might be introduced into non-randomised studies: (1) through confounding; (2) selection of participants; (3) in classification of interventions; (4) deviation from intended interventions; (5) missing data; (6) measurement of outcome; and (7) selection of reported results.

74. Domain-level judgements about risk of bias provide the basis for an overall risk of bias judgement as 'low', 'moderate', 'serious' or 'critical'. Detailed guidance on using the ROBINS-I tool can be found at the Risk of Bias website.

### Published reports or guidelines: AGREE II

75. The quality of published reports or guidelines from national/international organisations can be assessed using the AGREE II tool (Appraisal of Guidelines Research and Evaluation II) (Brouwers et al, 2010; updated 2017).

76. The AGREE II tool comprises 23 items, grouped under 6 domains: 1) scope and purpose; 2) stakeholder involvement; 3) rigour of development; 4) clarity of presentation; 5) applicability; and 6) editorial independence. This is followed by 2 global rating items for an overall assessment. Detailed guidance is available on the AGREE website.

77. The AGREE II developers suggest that relevant domains can be prioritised for quality assessment. It is recommended that working groups decide at the outset of an evidence evaluation which domains (and which items within the domains) are considered relevant and these should be described in the protocol.

## Interpretation of statistical methods and data

78. It is important to consider the statistical methods used in an evaluation. In order to interpret study results, the following should be reported:
    - details of statistical approaches (such as tests used, models built) that are sufficient to guide replication
    - the effect size (including units) and direction
    - 95% confidence intervals
    - exact p-values (where available).

79. Interpretation of study results should also be informed by consideration of study size, assessment of study quality (see paragraphs 66 to 74) and consistency of findings.

80. In systematic reviews with meta-analyses, results of 2 statistical models of meta-analysis, fixed-effect and random-effects, may be reported. There are differences in the underlying assumptions and statistical considerations between these models. Fixed-effect models weight the primary studies in direct proportion to their precision. In the presence of between-study heterogeneity, random-effects models are considered to provide more robust overall estimates but give comparatively more weight to the smaller studies than would fixed-effect models.

81. Where results of only 1 model (that is, fixed-effect or random-effects) are stated, these should be reported and used to draw conclusions. Where results of both models are stated, both should be reported. The following factors should be considered: appropriateness of the model assumptions, between-study heterogeneity (both in design and results), direction and magnitude of the effects, the 95% confidence intervals, statistical significance and level of agreement between the models. Where the results of the 2 models differ, the totality of the evidence and expert judgement should be used to draw conclusions and considered in the final grading of the evidence (see paragraphs 82 to 95).

## Grading the certainty of evidence for the selected outcomes

82. The certainty of a body of evidence is assessed separately for each exposure-outcome relationship.

83. Draft grading is initially conducted by the SACN secretariat for consideration and agreement by working group or subgroup members. Final grades are agreed by SACN.

### Selection of systematic review/meta-analysis for grading the evidence for a specific outcome

84. In general, if a number of systematic reviews/meta-analyses address the same health outcome then, depending on the search inclusion criteria, they would be expected to include many of the same individual studies (published up to that time). The most recent would therefore be expected to include the largest number of studies (and participants) and, consequently, provide the most reliable summary of the evidence.

85. The selection of the systematic review/meta-analysis for grading a specific outcome should also be informed by the quality assessment (which includes risk of bias judgements) and consideration of which systematic review/meta-analysis most closely addresses the research question of interest.

86. If more than 1 systematic review/meta-analysis meets these criteria, including the choice of inclusion/exclusion criteria, all should be graded and then a judgement made on either a combined or separate grades.

87. When evaluating consistency and agreement between systematic reviews/meta-analyses, consideration should be given to the direction and magnitude of effect size, subgroup and sensitivity analyses, heterogeneity and the degree of overlap in the primary studies.

### Grading approach

88. To ensure consistency across SACN's evidence evaluations, the GRADE (Grading of recommendations, assessment, development and evaluation) approach should be used to assess the certainty of a body of evidence for each exposure-outcome relationship under consideration.

89. GRADE specifies 4 levels of certainty for a body of evidence: 'high', 'moderate', 'low' and 'very low' (see Table 1 below).

**Table 1: GRADE certainty ratings**

| CERTAINTY | INTERPRETATION |
|---|---|
| **High** | Very confident that the true effect lies close to that of the estimate of the effect |
| **Moderate** | Moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different |
| **Low** | Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect |
| **Very low** | Very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect |

90. A body of evidence from randomised trials starts with a **high-certainty** rating. The level of certainty can then be decreased by one or two levels after considering the following 5 criteria: (1) risk of bias; (2) imprecision; (3) inconsistency; (4) indirectness; and (5) publication bias.

91. A body of evidence from non-randomised studies (including observational studies) usually starts with a **low-certainty** rating because of potential bias due to lack of randomisation (confounding and selection bias) and recognition that confounding is always a concern in even the most rigorously conducted observational studies. The level of certainty from non-randomised evidence can be upgraded if any of the following 3 criteria are met: (1) large magnitude of effect; (2) clear dose-response gradient; (3) residual confounding is likely to decrease rather than increase the magnitude of effect (where an effect is observed).

92. The initial grade for a body of evidence from non-randomised studies can be rated as **high-certainty** if risk of bias has been assessed using the ROBINS-I tool (see paragraphs 73 to 74) since consideration of selection bias and confounding is an integral part of this tool (Schünemann et al, 2019).

93. Decisions to downgrade or upgrade are based on expert judgements of working group and SACN members. Thresholds for downgrading or upgrading will depend on a number of factors, including the outcome and exposure of interest. These should usually be agreed at an early stage and applied consistently.

94. Judgements on the certainty of the evidence are then used to draw conclusions on the strength of recommendations (see paragraphs 98 to 99). Detailed guidance on using GRADE is available in the GRADE Handbook.

### Assessing certainty of evidence when data are summarised in narrative synthesis

95. Guidance is provided by Murad et al (2017) on how to apply the constructs of the GRADE approach to assess the certainty in evidence when a meta-analysis has not been performed and instead a narrative summary of the data is available.

# Drawing conclusions and making recommendations

## Conclusions

96. Judgement on whether a particular nutrient intake, dietary pattern, food and/or food component causally impacts on the outcome is based on the quality and quantity of the available evidence.

97. When drawing conclusions on whether there is a causal relationship, a range of issues is considered. These may differ depending on the nature of the evidence base (Howick et al, 2009) and include:

- relevance and quality of the type of research reviewed
- confidence in the observed effects or associations, particularly the magnitude of the relationship and potential confounding by other lifestyle factors (such as physical activity levels and smoking)
- the extent to which research derives from a sufficient number of studies and sufficient number of participants to provide precise estimates and that the findings are generalisable to the population of interest
- whether there is a dose-response relationship. This is not an absolute requirement for causality because a threshold relationship may exist, but if apparent, a dose-response relationship provides additional evidence that the exposure is causally linked to the outcome
- the possibility of reverse causality in observational studies: that is, whether the proposed cause (dietary exposure or lack of it) precedes the observed effect (health or disease outcome)
- the biological or mechanistic plausibility of the observed relationship
- the consistency of the association with the outcome(s) under consideration across different population groups, study designs and settings.

## Recommendations

### Public health recommendations

98. SACN's recommendations for the UK population are based on consideration of the totality of evidence. Expert judgement is applied to determine whether it is appropriate to make any recommendations. In general, recommendations are made when evidence is considered sufficiently strong (graded as **high** or **moderate** certainty).

99. In some cases, expert judgement may be used to make **conditional** recommendations which are based on limited evidence (graded as **low** certainty). If recommendations are based on low certainty of evidence, the rationale and justification for such a decision should be clearly explained (for example, based on the precautionary principle).

### Research recommendations

100. Research recommendations are included in an evaluation if any gaps or limitations in the evidence base are identified or if new hypotheses to be tested are identified.

# Publication

101. SACN's completed evidence evaluations (reports, rapid reviews, position statements, joint evaluations and updated evaluations) are published on the SACN website.

# References


Brouwers M, Kho ME, Browman GP et al. AGREE Next Steps Consortium (2010) AGREE II: advancing guideline development, reporting and evaluation in healthcare. CMAJ. 2010; 182: E839–42. doi: 10.1503/cmaj.090449. Epub 2010 Jul 5.

Howick J, Glasziou P, Aronson JK. The evolution of evidence hierarchies: what can Bradford Hill's 'guidelines for causation' contribute? J R Soc Med. 2009;102(5):186-94.

Murad MH, Mustafa RA, Schünemann HJ, et al. Rating the certainty in evidence in the absence of a single estimate of effect. Evid Based Med. 2017;22(3):85-87. doi: 10.1136/ebmed-2017-110668.

Schünemann HJ, Cuello C, Akl EA et al; GRADE Working Group. GRADE guidelines: 18. How ROBINS-I and other tools to assess risk of bias in nonrandomized studies should be used to rate the certainty of a body of evidence. J Clin Epidemiol. 2019; 111:105-114. doi: 10.1016/j.jclinepi.2018.01.012. Epub 2018 Feb 9.PMID: 29432858.

Shea BJ, Reeves BC, Wells GA et. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017;358:j4008.

Sterne JAC, Hernán MA, Reeves BC et al. ROBINS-I: a tool for assessing risk of bias in non-randomized studies of interventions. BMJ. 2016; 355; i4919; doi: 10.1136/bmj.i4919.

Sterne JAC, Savović J, Page MJ et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019; 366: l4898.

# Annex 1: Types of evidence evaluation

**Table A1 Summary of processes involved in future SACN approaches to evidence evaluation**

| Approach | Report | Rapid review | Position statement | Joint assessment | Update |
|---|---|---|---|---|---|
| Registration of protocol | usually yes | usually yes | usually no | to be agreed by both committees | dependant on nature of update |
| Public consultation on scope | usually yes | usually no | usually no | to be agreed by both committees | usually no |
| Call for evidence | usually yes | usually no | usually no | to be agreed by both committees | usually no |
| Formal quality assessment tool | usually yes | optional | usually no | to be agreed by both committees | dependant on nature of update |
| Grading | usually yes | optional | usually no | to be agreed by both committees | dependant on nature of update |
| Public consultation on draft evaluation | usually yes | usually no | usually no | to be agreed by both committees | usually no |
| Public health recommendations | usually yes | optional | usually no | to be agreed by both committees | dependant on nature of update |
| Research recommendations | yes | optional | optional | to be agreed by both committees | dependant on nature of update |

# Annex 2: Example evidence table

**Table A2 Summaries of systematic reviews with meta-analyses from SACN report on Lower carbohydrate diets for adults with type 2 diabetes (2021)**

| Study | Methods | Included studies | Results of meta-analyses (weighted mean difference in change) (95% CI) | Limitations and study conclusions (assessed by authors) |
|---|---|---|---|---|
| van Zuuren et al (2018)<br><br>Aim: To compare the effects of dietary carbohydrate restriction with fat restriction on markers of metabolic syndrome and quality of life in people with T2D.<br><br>Countries: Australia (2), Europe (14), Israel (2), Japan (2), Mexico (1), US and Canada (15)<br><br>Funding source: Supported by grants from the Dutch Diabetes | Search period: To 21 March 2017<br><br>Databases searched: Medline, PubMed, Embase, Web of Science, Cochrane Library, CENTRAL, Emcare, Academic Search Premier, ScienceDirect, Latin American and Caribbean Health Science Information Database, Indice Bibliografico Espanol en Ciencias de Salud<br><br>Language restrictions: None reported<br><br>Inclusion criteria:<br>• RCTs and CCTs comparing LCD (≤40% TE) with LFD (≤30% TE) ≥4 wks in adults (aged ≥18 y) with T2D<br>• Data from crossover trials with washout of ≥4 wks between interventions. In absence of adequate wash-out period, data only included if able to extract data for 1st phase | Number of studies: 36 (n=2161)<br><br>Study duration: 4 wks to 7 y<br><br>Study population:<br>• Age range (mean): 32 to 65 y<br>• BMI: NR<br>• Sex: male (4), female (3), both (29)<br>• Ethnicity: NR<br>• Medication: insulin (5 trials), oral hypoglycaemic agents (25 trials), anti-hypertensive drugs (3 trials), lipid-lowering medications (10 trials). In 5 trials, anti-diabetic drugs discontinued or reduced;<br>5 trials did not provide details of medication; 2 trials, no medication use | Reported CHO intake: NR<br><br>Retention rates: NR<br><br>Outcomes:<br>HbA1c (%)<br>• ≥16 to 26 wks: -0.26 (-0.50, -0.02), p=0.04, I2=59%<br>• >26 wks: -0.36 (-0.58, -0.14, p=0.001), I2=0%<br>• 2 y: 0.02 (-0.37, 0.41), p=0.93, I2=13%<br>Weight (kg)<br>• ≥16 to 26 wks: -2.51 (-5.42, 0.40), p=0.09, I2=88%<br>• >26 wks: -0.19 (-1.65, 1.27), p=0.80, I2=0%<br>• 2 y: -0.14 (-1.64, 1.35), p=0.85, I2=0%<br>Lipids (mmol/L)<br>LDL-cholesterol<br>• ≥16 to 26 wks: 0.02 (-0.09, 0.13), p=0.75, I2=0% | Limitations:<br>High degree of clinical and methodologic heterogeneity between included studies.<br><br>Energy percentage of macronutrients in prescription diets differed considerably.<br><br>Numerous other aspects differed considerably between studies including calorie content, exercise prescription, provision of food by study centre and reporting of actual food intake.<br><br>Inconsistent methods of quantification and reporting of medication use precluded reliable statistical analyses of changes in drug doses.<br><br>Conclusions: |

| Study | Methods | Included studies | Results of meta-analyses (weighted mean difference in change) (95% CI) | Limitations and study conclusions (assessed by authors) |
|---|---|---|---|---|
| Foundation and Sanofi<br><br>Declarations of interest: None | Exclusion criteria:<br>• Studies that included adults with other chronic diseases (except hypertension or CVD), any disease requiring hospital care<br>• Studies that included those with an eating disorder or other disease re special dietary requirements<br>Outcome measures:<br>• Primary: HbA1c, whole blood and FPG and lipids (triacylglycerol, LDL-c, HDL-c)<br>• Secondary: weight, BMI, waist circumference, BP, QoL<br>Statistical analysis:<br>• Random-effects model<br>• Heterogeneity assessed using I2 statistic (I2>50% indicative of substantial heterogeneity)<br>• Several sensitivity analyses to explore sources of heterogeneity<br>• Repeated analyses using fixed-effects model in MAs with between study heterogeneity | • Physical activity: 8 trials encouraged increase in physical activity<br>Intervention:<br>LCD (CHO ≤40% TE)<br>• Ranged from 10 to 40% TE/<20 to <130 g<br>Comparator: LFD (≤30% TE)<br>• Fat intake ranged from 10 to 30% TE<br>• CHO intake ranged from 45 to 70% TE<br>Authors' evaluation:<br>Risk of bias<br>RCTs (n=33): 19, high risk; 14, unclear risk<br>CCTs (n=3): moderate to serious | • >26 wks: -0.07 (-0.23, 0.09), p=0.41, I2=50%<br>• 2 y: 0.06 (-0.08, 0.21), p=0.39, I2=0%<br>HDL-cholesterol<br>• ≥16 to 26 wks: 0.09 (-0.03, 0.22), p=0.13, I2=91%<br>• >26 wks: 0.11 (0.05, 0.18), p<0.0007, I2=66%<br>• 2 y: 0.12 (0.07, 0.17), p<0.00004, I2=0%<br>Triacylglycerols<br>• ≥16 to 26 wks: -0.22 (-0.37, -0.08), p=0.002, I2=41%<br>• >26 wks: -0.25 (-0.47, -0.04), p=0.02, I2=73%<br>• 2 y: -0.19 (-0.32, -0.05), p=0.007, I2=0% | Low to moderate certainty of evidence that dietary CHO restriction to maximum of 40% yields slightly better metabolic control of uncertain clinical importance than reduction in fat to a maximum of 30% in people with T2D. |

| Study | Methods | Included studies | Results of meta-analyses (weighted mean difference in change) (95% CI) | Limitations and study conclusions (assessed by authors) |
|---|---|---|---|---|
| | Study quality: GRADE (to assess certainty of evidence) and Cochrane risk of bias tool.<br>Publication bias: Paucity of studies evaluating any of the outcomes at same timepoints did not permit assessment. | | | |

| Study | Methods | Included studies | Results of meta-analyses (weighted mean difference in change) (95% CI) | Limitations and study conclusions (assessed by authors) |
|---|---|---|---|---|
| Korsmo-Haugen et al (2018)<br><br>Aim: To compare the effects of low carbohydrate diets on body weight, glycaemic control, lipid profile and BP with those observed on higher carbohydrate diets in adults with T2D<br><br>Countries: Australia (5), Europe (5), Israel (3), Japan (1), New Zealand (1), North America (8)<br><br>Funding source: No particular funding received<br><br>Declarations of interest: None | Search period: 1983 to 31 January 2016<br><br>Databases searched: Medline, Embase, CINAHL, CENTRAL, Food Science Source and SweMed<br><br>Language restrictions: English, Danish, Norwegian, Swedish<br><br>Inclusion criteria:<br>• RCTs with more than 3 m duration comparing diet below to a diet above 40% TE from CHO<br>• Comorbidities accepted but studies including individuals with impaired glucose tolerance and/or T1D only included if separate data provided for T2D individuals<br>Exclusion criteria:<br>• Complex interventions consisting of elements with potential to interfere with effect of dietary interventions (such as parenteral administration or promotion of physical activity)<br>Outcome measures: | Number of studies: 23 (n=2178)<br>Study duration: 3 m to >3 y<br>Study population:<br>• Age range: NR<br>• BMI: NR<br>• Sex: NR<br>• Ethnicity: NR<br>• Medication: insulin therapy (12 trials), anti-hypertensive drugs (8 trials), lipid-lowering drugs (10 trials) and oral hypoglycaemic agents such as metformin (10), sulfonylurea (10), thiazolidinedione (4)<br>• Physical activity: several trials promoted general recommendations for physical activity<br>Intervention: LCD (CHO <40% TE)<br>• Ranged from 5 to 40% TE<br>Comparator:<br>Variety of diets: LFD (n=8), standard diabetes care (n=4), HCD (n=3), LPD | Reported CHO intake (mean):<br>• 9/18 studies CHO intakes in LCD were 5% TE within prescribed intakes<br>• 7/9 trials that observed low compliance, participants were on VLCD (CHO intakes of 5 to 22% TE)<br>Attrition rates: LCD vs HCD<br>• No detectable difference in attrition rates between diets:<br>RR=1.08 (95% CI, 0.92, 1.27; I2=0%)<br>Outcomes:<br>HbA1c (%)<br>• 3 to 6 m: -0.17 (-0.27, -0.08), p=NR, I2=0%<br>• >12 m: 0.00 (-0.10, 0.09), p=NR, I2=0%<br>Weight (kg)<br>• 3 to 6 m: -0.87 (-1.88, 0.15), p=NR, I2=33%,<br>• >12 m: 0.14 (-0.29, 0.57), p=NR, I2=0%<br>Sensitivity analyses showed less difference between LCDs and HCDs in studies with low RoB than in those with high RoB. | Limitations:<br>Ability to follow diet with very low CHO content was generally poor.<br>Changes in medications over time may have blurred effects of differences in diet composition.<br>Conclusions:<br>The proportion of daily energy provided by CHO intake is not an important determinant of response to dietary management, especially when considering longer-term trials. |

| Study | Methods | Included studies | Results of meta-analyses (weighted mean difference in change) (95% CI) | Limitations and study conclusions (assessed by authors) |
|---|---|---|---|---|
| | • Weight, HbA1c, lipids (triacylglycerol, total cholesterol, LDL-c, HDL-c), BP, compliance to dietary intervention<br>Statistical analysis:<br>• Random effects model<br>• Lipid profile qualitatively evaluated<br>• Heterogeneity assessed using I2 statistic (I2>50% or value of Cochrane Q test <0.1 associated with heterogeneity) and subgroup analyses to explore possible reasons for heterogeneity<br>• Post hoc subgroup and sensitivity analyses to explore impact of study duration (6 vs 12 m), varying CHO content (VLCD 21 to 70 g vs LCD 30 to 40% TE) and risk of bias (low vs high)<br>Study quality: GRADE and Cochrane risk of bias tool.<br>Publication bias: Funnel plot | (n=1), Med (n=2), HCD/LFD (n=2), High wheat fibre (n=1), Low GI (n=2), High GI (n=1)<br>• CHO intake ranged between 42 and 65%.<br>Authors' evaluation:<br>Risk of bias: Overall, 3 studies classified as low risk, 10 as high risk and 10 as unclear risk<br>Publication bias: Not indicated | Lipids (mmol/L)<br>Total cholesterol<br>• 3 to 6 m: -0.06 (-0.41, -0.30); p=NR, I2=57%,<br>• >12 m: 0.07 (-0.04, 0.19); p=NR, I2=23%<br>LDL-cholesterol<br>• 3 to 6 m: -0.08 (-0.29, 0.14); p=NR, I2=50%,<br>• >12 m: 0.03 (-0.10, 0.16); p=NR, I2=51%<br>HDL-cholesterol<br>• 3 to 6 m: -0.01 (-0.07, 0.04); p=NR, I2=15%<br>• >12 m: 0.06 (-0.01, 0.13);p=NR, I2=71%<br>Triacylglycerols<br>• 3 to 6 m: -0.18 (-0.36,0.00); p=NR, I2=20%<br>• >12 m: -0.10 (-0.23, 0.03); p=NR, I2=61% | |

| Study | Methods | Included studies | Results of meta-analyses (weighted mean difference in change) (95% CI) | Limitations and study conclusions (assessed by authors) |
|---|---|---|---|---|
| Sainsbury et al (2018)<br><br>Aim: To compare effectiveness of carbohydrate-restricted diets with high carbohydrate diets on glycaemic control in adults with T2D<br><br>Countries: Austria (1), Australia (6), Canada (2), Czech Republic (1), Israel (2), Japan (2), New Zealand (1), Sweden (1), UK (2), US (7)<br><br>Funding source: Did not receive specific grant from funding agencies in public, commercial or not-for-profit sectors<br><br>Declarations of interest: None | Search period: 1 January 1980 to 31 August 2016<br><br>Databases searched: Medline, Embase, CINAHL, Global Health, Cochrane<br><br>Language restrictions: English<br><br>Inclusion criteria:<br>• RCTs comparing CHO-restricted diet (≤45% TE) to HCD (>45% TE) for glycaemic control in adults (≥18 y) with T1D or T2D<br>• Studies had to report on change in HbA1c and minimum duration of 3 m<br>• Studies of individuals with and without diabetes only included if ≥80% had diabetes or if subgroup analysis for this group<br><br>Exclusion criteria:<br>• 1 intervention group included a non-dietary weight loss component (such as physical activity advice, pharmaceutical intervention) while other group did not<br>• Trials with meal replacement drinks or enteral feeds | Number of studies: 25 (n=2412)<br><br>Study duration: 3 to 24 m<br><br>Study population:<br>• Age range: 52 to 63 y<br>• BMI: 25.8 to 38.1 kg/m2 (median, 36.7)<br>• Sex: male and female<br>• Ethnicity: NR<br>• Medication: majority on diabetes medication and/or insulin (1 study, diet treatment only); 11 studies allowed medication adjustments during intervention, with 5 reporting that they accounted for this in analysis<br>• Physical activity: 15 studies included advice (to maintain or increase level)<br><br>Intervention: CHO-restricted diet (≤45% TE)<br>• LCD <130 g or <26% TE) (10 studies) | Reported CHO intake: NR<br><br>Retention rates:<br>• 3 to 6 m (n=10): >70%<br>• 12 to 24 m: 50 to 69% (n=6); ≥70% (n=8)<br><br>Outcomes:<br><br>HbA1c (%)<br>• 3 m: -0.19 (-0.33, -0.05), p=0.008, I2=28%<br>• 6 m: -0.15 (-0.31, 0.02), p=0.09, I2=50%<br>• 12 m: -0.09 (-0.21, 0.03), p=0.12, I2=16%<br>• 24 m: -0.11 (-0.38, 0.15), p=NR, I2=NR<br><br>Weight change (kg)<br>• 3 m: -1.08 (-1.93, -0.23), p=0.01, I2=69%<br>• 6 m: -0.14 (-0.94 to 0.65), p=0.72, I2=48%<br>• 12 m: -0.43 (-0.93, 0.07), p=0.09, I2=0%<br><br>Lipids<br>• 3 to 6 m: no change or small reductions in total cholesterol and LDL-c on both CHO-restricted diet and HCD. Greater increase in | Limitations:<br><br>Due to high risk of performance and detection bias and inconsistency in estimates of effect across studies, the evidence of HbA1c change was graded low quality<br><br>High variability in methods of analysis across studies<br><br>CHO quantity based on prescribed rather than actual intake<br><br>Did not consider effect that altering fat and protein proportions may have had on outcomes<br><br>Conclusions:<br><br>Over the short term (3 to 6 m) CHO-restricted diets (≤45% TE) produce greater reductions in HbA1c than HCD (>45% TE). These effects primarily driven by LCDs (<26% TE) with no significant difference between MCDs (26 to 45% TE) and HCDs. The short- |

| Study | Methods | Included studies | Results of meta-analyses (weighted mean difference in change) (95% CI) | Limitations and study conclusions (assessed by authors) |
|---|---|---|---|---|
| | • Studies of prediabetes, gestational diabetes, pregnant or lactating women<br>Outcome measures:<br>• Primary: HbA1c<br>• Secondary: weight; lipid profile (triacylglycerol, total cholesterol, LDL-cholesterol, HDL-cholesterol)<br>Statistical analysis:<br>• Random-effects model to estimate HbA1c change at 3, 6, 12, 24 m. Subgroup analysis conducted at each time-point to test effect of different levels of CHO restriction on HbA1c<br>• Lipid profile qualitatively evaluated<br>• Heterogeneity assessed using I2 statistic<br>Study quality: GRADE and Cochrane risk of bias tool.<br>Publication bias: Funnel plot and Egger's test | • MCD (130 to 225 g or 26 to 45% TE) (15 studies)<br>(4 studies increased % of protein, 6 increased % of fat, 4 increased % of both protein and fat as proportion of TE, 14 studies isocaloric.)<br>Comparator:<br>• HCD (>225 g or >45% TE)<br>Authors' evaluation:<br>Risk of bias: Overall 9 studies classified as being low risk, 7 at high risk and 9 at unclear risk<br>Publication bias: Present at 3 m (p=0.005) but not at 6 m (p=0.125) or 12 m (p=0.052). Not tested at 24 m (n=3) | HDL-c for CHO-restricted diet in 9/20 studies with 3 reporting significant difference between groups<br>• 12 to 24 m: 6 studies reported significantly greater increase in HDL-c and 5 reported significantly greater reductions in triacylglycerols for CHO-restricted diet compared with HC diet. | term glycaemic improvements on LCDs appear to be due to weight loss with no significant difference in HbA1c change between diets when restricted to studies with equal weight loss. |

| Study | Methods | Included studies | Results of meta-analyses (weighted mean difference in change) (95% CI) | Limitations and study conclusions (assessed by authors) |
|---|---|---|---|---|
| Huntriss et al (2018)<br><br>Aim: To evaluate the clinical effect of a low carbohydrate diet in the management of T2D<br><br>Countries: NR<br><br>Funding source: Completed within a National Institute of Health Research funded Masters in Clinical Research<br><br>Declarations of interest: None | Search period: until June 2016<br><br>Databases searched: Medline, Embase, CINAHL, Cochrane, ISRCTN, ProQuest, opengrey.eu. Reference lists of selected papers<br><br>Language restrictions: English<br><br>Inclusion criteria:<br>• RCTs in adults aged: ≥18 y with T2D<br>• LCD group must have achieved lower CHO intake than control group<br>• Control group usual care (on variety of diets)<br><br>Exclusion criteria:<br>• Studies that enrolled individuals with T1D, pre-diabetes or included pregnant women<br><br>Outcome measures:<br>• Primary: HbA1c<br>• Secondary: Change in diabetes medication, weight, total cholesterol, LDL-c, HDL-c, triacylglycerol, BP, dietary adherence<br><br>Statistical analysis:<br>• Random-effects model | Number of studies: 18 (n=2204)<br><br>Study duration: 12 wks to 4 y<br><br>Study population:<br>• Mean age: NR<br>• BMI: NR<br>• Sex: NR<br>• Ethnicity: NR<br>• Medication: Participants in 14/18 studies on diabetes medication; 2 studies did not include participants on medication; 2 did not report medication changes<br>• Physical activity: NR<br><br>Intervention:<br>• CHO: <20 to 70 g/d /14 to 52% TE<br>• All authors described intervention as low CHO<br>• 10 studies prescribed LCD (<130 g/d or <26% TE) | Dropout: NR<br><br>Reported CHO intake (mean): 106 g/d<br><br>Outcomes (1 y)<br><br>HbA1c (%)<br>• -0.28% (-0.53, -0.02), p=0.03, I2=54%<br><br>Body weight (kg):<br>0.28 (-1.37, 1.92), p=0.74, I2=75%<br><br>Blood lipids (mmol/L)<br><br>Total cholesterol:<br>• -0.08 (-0.23, 0.08), p=0.35, I2=60%<br><br>LDL-c<br>• 0.05 (-0.10, 0.19), p=0.54, I2=0%<br><br>HDL-c<br>• 0.06 (0.04, 0.09), p<0.00001, I2=1%<br><br>Triacylglycerols<br>• -0.24 (-0.35, -0.13,) p<0.0001, I2=0%<br><br>Diabetes medication: Out of 14 studies, 9 reported statistically significant reduction in diabetes medication in LCD group (p≤0.05).<br><br>Dietary adherence: 12/18 trials reported CHO intake at trial end in | Limitations:<br><br>Varied CHO prescription across studies<br><br>Lack of blinding of participants and study personnel<br><br>True effect of LCD group on HbA1c could not be observed due to medication adjustments<br><br>Study design heterogeneity present<br><br>Some studies prescribed lower calorie allowance to control group<br><br>Several studies provided insufficient information and could not be included in the MAs, limiting number of studies and participants that could be included in pooled analysis<br><br>Conclusions:<br><br>Statistically significant superiority of LCD in improving HbA1c, HDL-c, triacylglycerol at 1 y and in reducing diabetes |

| Study | Methods | Included studies | Results of meta-analyses (weighted mean difference in change) (95% CI) | Limitations and study conclusions (assessed by authors) |
|---|---|---|---|---|
| | • MA performed for change in each outcome at 1 y<br>• Studies <48 wks or with marked design heterogeneity not included in MA<br>Study quality: Assessed for risk of bias using Cochrane Risk of Bias tool<br>Publication bias: Not assessed | • 5 prescribed MCD (130 to 225 g/d or 26 to 45% TE)<br>• 1 prescribed HCD (>225 g/d or 45% TE)<br>• 1 prescribed up to 50% TE from CHOs<br>Comparator:<br>Usual care, which included variety of diets<br>• CHO: 50 to 60% TE<br>• Fat: ≤30% TE<br>Authors' evaluation:<br>Risk of bias: 15/18 studies at high RoB in 1 or more of the 6 criteria [random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment), incomplete outcome data, selective reporting. 15/18 studies at high risk of performance bias. | LCD. Two reported that they achieved prescribed intake in the intervention arm, 1 that prescribed LCD and 1 that prescribed up to and including HCD. | medication. No difference in weight loss, total cholesterol or LDL-c at 1 y.<br>Reducing CHO intake may promote favourable health outcomes in management of T2D in context of a healthy diet. |

# Abbreviations

| | |
|---|---|
| ACNFP | Advisory Committee on Novel Foods and Processes |
| AGREE II | Appraisal of Guidelines Research and Evaluation II |
| AMSTAR 2 | A Measurement Tool to Assess Systematic Reviews 2 |
| COT | Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment |
| FSA | Food Standards Agency |
| GRADE | Grading of recommendations, assessment, development and evaluations |
| IFS | Infant Feeding Survey |
| NDNS | National Diet and Nutrition Survey |
| NICE | National Institute for Health and Care Excellence |
| OHID | Office for Health Improvement and Disparities |
| RCT | Randomised controlled trial |
| ROB-2 | Cochrane risk of bias revised tool for randomised trials - 2 |
| ROBINS-I | Risk of bias in non-randomised studies - of interventions |
| SACN | Scientific Advisory Committee on Nutrition |
| SMCN | Subgroup on Maternal and Child Nutrition |
| WHO | World Health Organization |