A Framework for Evaluation of Evidence that Relates Food and Nutrients to Health
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Last updated: March 2020*

*SACN agreed in horizon scanning 2018 that the SACN Framework should be regularly reviewed to reflect current practice. This version is a re-fresh of the previous version (dated 2012). A SACN working group is currently considering additional aspects for update.
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Terms of reference

1. The Scientific Advisory Committee on Nutrition (SACN) is an advisory committee set up to provide scientific advice on, and risk assessment of, nutrition and related health issues. It advises the governments of all 4 UK countries and is supported by a Public Health England (PHE) secretariat.

2. SACN’s advice covers the scientific aspects of nutrition and health with specific reference to:
   - nutrient content of individual foods and advice on diet as a whole, including the definition of a balanced diet and the nutritional status of people
   - 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)
   - nutrition of vulnerable groups (such as infants, older adults and ethnic minorities) and health inequality issues
   - research requirements for the above.

3. SACN’s remit is to assess the risks and benefits of nutrients, dietary patterns, food or food components to health by evaluating scientific evidence and to make dietary recommendations for the UK based on its assessment. Conclusions drawn from any evidence considered are those that are applicable to the UK population, including any vulnerable groups which have been identified. Before providing advice, SACN assesses the possible risks that may be associated with implementing particular recommendations such as the 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.

4. The committee does not advise on how recommendations are taken forward for policy; the committee’s role is risk assessment and not risk management. SACN has a public health focus, therefore the treatment of disease is outside SACN’s remit unless specifically requested to consider. Alcohol, other than as a source of energy, is also outside SACN’s remit.

5. This document has been prepared for use by SACN in evaluating evidence that relates both food and nutrients to health. It is a working document that is subject to regular review and may be amended depending upon the nature of the work.
Relationship with other committees

6. If SACN needs to assess evidence from other areas of science, appropriate expert advice will be sought from relevant scientific advisory committees, such as the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT). Conversely, if another scientific committee requires nutrition expertise a SACN representative will be co-opted onto that committee to provide the necessary advice. An example of this is the safety assessment of novel foods undertaken by the UK Competent Authority Advisory Committee on Novel Foods and Processes (ACNFP) which includes nutritional assessment.

Scope of the evaluation

7. Prior to commencing an evaluation, SACN scopes existing literature, such as systematic reviews or expert reports, to assess whether these can inform SACN’s evaluation, for example to help define the issues to be considered or the level of evaluation to be undertaken.

8. To define the scope of the evaluation, inform the terms of reference and identify specific questions the following issues are considered:

- reason for undertaking review, such as:
  - new evidence
  - request from government ministers, UK Health Departments, or other government departments
  - request from interested parties, such as industry or non-governmental organisations
  - issues raised by SACN members, subgroups or working groups
  - developments from other expert bodies
  - changes in legislation
  - emerging issues which can arise from the UK or from international bodies, such as the European Food Safety Authority or World Health Organization

1 SACN has one subgroup - on maternal and child nutrition (SMCN) - which has a continuous work programme. A working group is established to conduct each new risk assessment. SMCN and working groups consist of SACN members and external experts, the latter being appointed or co-opted when additional specialist knowledge is required.
• principal nutrients, dietary patterns, food and/or food components under consideration

• relevant populations and health or disease outcomes of the evaluation; this decision is based on the published literature of health outcomes which are important to public health in the UK

• putative role of nutrients, dietary patterns, food and/or food components in establishing health or disease outcomes

• background/current state of knowledge, including reference to previous UK Health Departments/Food Standards Agency/international reports (such as World Health Organization) and reviews including past SACN/Committee on the Medical Aspects of Food Policy reports, devolved government reports, and/or good quality reviews from non-governmental organisations

• current public health policy on nutrition and health.

Level of evaluation

9. SACN publishes its risk assessments as reports or position statements. The type of risk assessment undertaken is agreed at the outset once the issues have been defined.

10. All risk assessments involve a consideration of the available evidence using a transparent, systematic approach to assess the potential risk and/or benefit of a particular nutrient intake, dietary pattern, food or food component in terms of health. In evaluating evidence, uncertainties and inconsistencies in the evidence are identified and highlighted.

11. SACN reports are full risk assessments. They are comprehensive considerations of the available evidence and provide advice to inform public health policy, identify future research needs and, when the evidence permits, may lead to public health recommendations on dietary intakes. Draft SACN reports are subject to public consultation and all responses are considered before the evaluation is finalised and published.

12. SACN position statements are not full risk assessments and are therefore not as comprehensive as SACN reports. They can take the form of a scoping exercise where a preliminary search of the evidence is performed to determine whether a risk assessment of a particular nutrient intake, dietary pattern, food or food component is required. They are not subject to public consultation and are conducted when a formal risk assessment is deemed either not appropriate or not feasible (for example, where there are concerns about the sufficiency of the evidence base). Position statements generally
provide commentary on the nature of the evidence base for a particular nutritional issue; they include conclusions and research recommendations but do not make public health recommendations.

## Considering the evidence

13. At the outset, each Working Group specifies which study designs to include in its review. This will vary depending on the question being asked and the evidence available.

14. Evidence can broadly be categorised as either hypothesis-testing or hypothesis-generating. SACN is primarily concerned with making recommendations based on hypothesis-testing evidence, that is from studies that have been designed a priori to identify associations between a nutrient intake, dietary pattern, food or food component and physiological outcomes in humans relevant to health/disease. In addition, 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 linked to the outcome.

15. A ‘hierarchy of evidence’ is used as a framework against which to judge the strength of evidence according to study design. This is because different study designs have different strengths and limitations and, therefore, value in informing decisions. Typically, more weight is given to good quality randomised controlled trials (RCTs) with less weight given to observational (non-intervention) studies when drawing conclusions. This is because observational studies are subject to bias, confounding and/or reverse causality. Guidance provided by the NHS Centre for Reviews and Dissemination (CRD) provides an example of this approach and includes a list of study definitions.²

16. However, RCTs are not always available (it is not always possible or appropriate to conduct RCTs due to feasibility or ethical considerations) or there may be few trials to draw on. In the absence of RCTs, evidence from well-conducted quasi-experimental³ and prospective cohort studies (PCS) is considered stronger evidence than other study designs, such as case control

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² [Systematic Reviews: CRD’s guidance for undertaking reviews in healthcare](https://www.crd.york.ac.uk/guidance/).

³ Quasi-experimental studies are non-randomised intervention studies and include a range of study types such as non-randomised controlled studies, before and after studies, and interrupted time series. See the above CRD guidance for definitions of these specific study types.
or cross-sectional studies.

17. Well-conducted, comprehensive, high-quality systematic reviews (with or without meta-analyses) of RCTs and PCS are mostly used to inform SACN’s deliberations because a systematic review aims to capture the available literature relating to a specific research question according to a pre-defined process and criteria.

18. Systematic reviews of RCTs and PCS are only as good as the methods employed, and their value in informing recommendations is dependent on the quality of included studies and the analyses conducted. SACN bases its recommendations on the totality of the evidence considered and is only able to make population recommendations when the evidence base is sufficiently strong.

19. Judgement on whether a particular nutrient intake, dietary pattern, food and/or food component is contributing to any observed effects on the outcome is based on the quality and quantity of the available evidence. This is of particular importance in drawing conclusions following a risk assessment.
Judging the evidence

Methodology

20. If SACN considers that a full systematic review is required and feasible, it is performed in keeping with established guidelines such as those from CRD or Cochrane Collaboration (see below)

The following guidance provides further details on systematic reviews:

University of York Centre for Review and Dissemination guidance for undertaking reviews
https://www.york.ac.uk/crd/guidance/

Cochrane Handbook for Systematic Reviews of Interventions
https://training.cochrane.org/handbook

http://www.dietandcancerreport.org/?p=slr_specification_manual

Scottish Intercollegiate Guidelines Network (SIGN) developer’s handbook
https://www.sign.ac.uk/sign-50.html

21. The eligibility criteria for evidence to be reviewed for a risk assessment or position statement are agreed at the outset. The rationale for the chosen review approach is made clear. This includes:

- scope of the evaluation - including the population, intervention (or exposure), comparator and outcomes (‘PICO’)
- search strategy - including databases to be searched, if hand searching is to be performed, other sources of information, search terms, study designs to include, publication date range
- publication type - for example, published in peer-reviewed journals, after a stated date and English language only.
22. All SACN risk assessments include a detailed description of the methods used, including data sources, databases searched, particular search strategies, and other considerations.

23. Grey literature is only considered if 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 some valuable information. Where such data are used, the source is clearly specified.

24. In addition to the database searches, a call for evidence is issued in order to identify relevant research in the field that may not have been identified (for example, if it has recently been published or is due to be published).

25. When a draft report is made available for public consultation, interested parties are invited to alert the committee to any evidence that it may have missed. The evidence highlighted through the consultation process (or identified by the secretariat or members as being published after the search dates) is considered by the working group and then the full SACN committee. The draft report is amended if newly available evidence adds substantial nuance or update to existing work or changes conclusions.

26. A flow chart is included in risk assessments. An example chart from the SACN report on Saturated Fats and Health (2019) is on the following page.

**Data Synthesis**

27. The main results are tabulated indicating the author, date, country, sample size, duration of study, dietary assessment method, exposure, outcome, main results, adjustment for confounders and sources of funding. Example evidence tables as presented in SACN reports are given in Annex 2.

**Quality assessment of studies**

28. SACN considers the methodologies of included studies in order to assess their quality. Study quality will influence the conclusions that can be drawn; examples of the factors that need to be considered during quality assessment are given in Annex 1.
Data analysis

29. When deliberating whether data analysis can be conducted from information extracted from the studies reviewed, the following issues are considered:

- study duration, power and source of funding
- potential for meta-analysis
• when meta-analysis would be considered appropriate
• the models to be used and rationale such as random vs fixed effect
• consistency of meta-analysis results
• how heterogeneity will be assessed, such as consideration of the $I^2$ statistic and associated criteria
• investigation of publication bias.

30. It may be helpful to present and consider the results graphically, for instance with forest plots.

**Key factors to address while drawing conclusions**

31. When drawing conclusions on whether a relationship exists, a range of issues are considered, including:

a) the relevance and quality of the type of study reviewed

b) the confidence in the observed effects. Particular consideration is given to the magnitude of the relationship and potential confounding by other lifestyle factors (such as physical activity levels and smoking)

c) whether a study is sufficiently powered to detect a pre-defined difference, if one exists

d) 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 linked to the outcome

e) the possibility of reverse causality. That is whether the proposed cause (dietary exposure or lack of it) precedes the observed effect (health or disease outcome)

f) the biological or mechanistic plausibility of the observed relationship

g) the consistency of the association with the outcome(s) under consideration across different population groups, study designs and settings.

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Public consultation

32. Draft SACN reports are issued for public consultation. The comments arising from this process are considered by the working group and then the full SACN committee. Where appropriate, amendments are made before the final report is published. SACN’s responses to comments made at consultation are published at the same time as the final report. Position statements are not subject to this process.
Annex 1: Factors to address when assessing quality of studies

Statistics

33. It is important to consider aspects of the statistical methods used for all study types in the review, in particular:

- statistical methods should be clearly described
- appropriateness of statistical methods, particularly around the use of repeated-measures analysis and handling of baseline values and covariates
- inclusion of information on study power
- whether confounding factors are taken into account in the study design and subsequent analysis
- reduction of systematic bias
- distinction of \textit{a priori} vs post-hoc hypothesis testing and reporting of associated results.
Methodological considerations

There are certain methodological issues that need to be assessed when evaluating the evidence. Important factors to address are listed below.

**Randomised Controlled Trials**

a) Sample size/power

b) Method of randomisation

c) Blinding

d) Selection of subjects (for example, age or ethnicity)

e) Other inclusion and exclusion criteria

f) Duration

h) Dose (physiological vs pharmacological)

i) Biomarkers of dietary exposure, nutritional status and/or intermediate health outcome used and their validity

j) Appropriateness of control used

k) Markers of compliance measured (blood, urine etc)

l) Success of intervention in achieving the required change in diet or nutritional status (compliance)

m) Components of diet that have changed (energy, macro and micronutrients, amounts etc) and how change in one component may have influenced other elements of the diet

n) Drop-out rate or loss to follow-up (attrition)

o) Relationship of endpoint measurements with health/disease outcome(s) under consideration

p) Baseline nutritional status

q) Other *a priori*-hypothesised sources of variance including polymorphisms in functionally relevant genes.
Prospective cohort studies

a) Sample size/power

b) Method of drawing sample

c) Method of recruiting participants

d) Response to recruitment

e) Length of follow-up

f) Dietary methodology used and the reported validity and reproducibility of that method

g) Biomarkers of dietary exposure, nutritional status and/or intermediate health outcome used and their validity and comparability

h) Drop-out rate or loss to follow-up (attrition)

i) Components of diet that have changed (energy, macro and micronutrients, amounts etc) and how change in one component may have influenced other elements of the diet

j) Outcome assessment method used and whether this is self-reported, measured or clinically assessed – and if intermediate the strength of its relationship to health outcome

k) Data analysed according to validation of exposure assessment

l) Baseline nutritional status

m) Other a priori and post-hoc considered sources of variance including polymorphisms in functionally-relevant genes.
Social Science

Social science can be quantitative or qualitative and draws on a range of academic disciplines including sociology, psychology and anthropology. It is most often used to explore a topic in depth, collect information on perceptions, knowledge and behaviours and to evaluate policies and interventions. In addition to the considerations already discussed above, the following questions may also be asked of the research:

Study purpose/scoping
- Are the research objectives clearly defined
- Is reference made to previous research and theory

Design and sampling
- Is the research design (including sampling) discussed adequately and appropriate to address the research questions
- Is the research design justified with any limitations discussed

Data collection and ethics
- Were the data collected appropriately
- Have ethical issues been considered and addressed

Analysis
- Is the approach to analysis described and is it systematic and appropriate
- Does the data support any subgroup analysis
- Is the scope for drawing wider inference discussed

Reporting
- Are conclusions supported by evidence
- Does the summary accurately reflect findings
- Is there any discussion on whether the findings support or contradict existing research
- Has the study been peer reviewed and any concerns addressed
**Animal and cellular/molecular studies**

If animal or in vitro studies are to be evaluated, the following issues need to be considered:

Animal studies:

a) Reasons for selection of studies
b) Extent to which data from animal studies are likely to be relevant to humans
c) Statistical power of the study
d) Consistency of data and the extent of impact of micronutrients, macronutrients and whole diet
e) Suitability of animal model (anatomy/metabolism/pathophysiology) for the particular diet-disease relationship of interest
f) Comparability of micronutrients, macronutrients and whole-diet exposures to human dietary intake levels (particularly in the UK)
g) Components of diet that have been altered, for example energy, macronutrient intake
h) Consistency of age/stage of growth of the animal with the age of appearance of the disease in humans.

In vitro, ex vivo and molecular studies:

i) Evidence for direct effects of nutrients or their metabolites on cellular processes (for example, cell signalling mechanisms, transcription factors, gene and protein expression, cell proliferation, differentiation, apoptosis)
j) Extent to which in vitro or ex vivo data are likely to be relevant to humans
k) Appropriateness of models to the human tissue(s) of interest, such as possessing functionally-relevant genes, receptors and proteins
l) Use of physiological levels of nutrients, metabolites or nutrient-sensitive endocrine exposures in cell studies, taking appropriate account of their bioavailability and bio-accessibility
m) Influence of polymorphisms in functionally-relevant genes
n) Appropriate statistical analysis and control for multiple outcome measures (for instance in ‘-omics’ studies).
Annex 2: Example evidence tables

An example of data extracted from systematic reviews and meta-analysis taken from the SACN Saturated Fats and Health (2019).

<table>
<thead>
<tr>
<th>Study</th>
<th>Research methods</th>
<th>Analysis</th>
<th>Results</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>Hoope et al.</td>
<td>Research question: What is the effect of reducing saturated fat intake and replacing it with carbohydrate, PUFA, MUFA and/or protein on mortality and cardiovascular morbidity? Selection criteria: Search dates: July 2010 to March 2014 (plus search from Hoope 2012 – inception to June 2010). Study design: RCTs only. Inclusion criteria: &gt;18yrs at any risk of CVD, with/without existing CVD, using/not using lipid-lowering medication; aim to reduce saturated fat intake or alter dietary fats and achieve reduction in saturated fats; intervention dietary advice, supplementation of fats, oils or modified or low-fat foods or a provided diet and the control group usual diet, placebo or a control diet;</td>
<td>Analysis: Random effects meta-analysis to assess risk ratios. Low vs high % of energy from saturated fats. Incremental changes in % of energy from saturated fats. Subgroup analysis: Saturated fat substitution with PUFA, MUFA, and carbohydrate. Evaluation of study quality: Cochrane ‘risk of bias’ tool used. Additional characteristics assessed include: studies being free of systematic differences in care, a study aiming to reduce diet;</td>
<td>12 RCTs; n=59,000; duration: 2-&gt;8y; age: 45-66y; gender: M(7), F(3), M/F(5); health at baseline:: with or without CVD; country: USA (7), Europe (8), Australia/New Zealand (2). Lowest saturated fat compared with usual saturated fat: CVD mortality (10 RCTs) RR 0.95 (95% CI 0.80, 1.12); Combined CV events (11 RCTs) RR 0.83 (95% CI 0.72, 0.96); Myocardial infarctions (11 RCTs) RR 0.90 (95% CI 0.80, 1.01); Non-fatal MI (9 RCTs) RR 0.95 (95% CI 0.80, 1.13); CHD mortality (10 RCTs) RR 0.98 (95% CI 0.84, 1.15); CHD events (12 RCTs) RR 0.87 (95% CI 0.74, 1.03); Subgroup analysis</td>
<td>Findings suggest a small but potentially important reduction in risk of CVD on reduction of saturated fat intake. Replacing energy from saturated fats with PUFA appears to be a useful strategy but replacement with carbohydrate appears to be less useful. Effects of replacement with MUFA unclear due to inclusion of only one trial. Limitations: Although the Cochrane Central Register of Controlled Trials,</td>
</tr>
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### Study

**Declarations of interest**
None to declare.

**Dietary assessment methods:** Not reported.

**Exclusion criteria:** Pregnant, acutely ill or breastfeeding subjects; allocation not truly randomised; multifactorial trials.

**Duration:** ≥ 24 months; mortality or cardiovascular morbidity data available; no language restrictions.

**Research methods**

- Saturated fat intake, achieving saturated fats reduction, and achieving total serum cholesterol reduction.
- Evidence assessed using GRADE system, sensitivity analyses, and heterogeneity examined using $I^2$ test.

**Results**

Analysis suggested reductions in CV events in studies where saturated fat intake was greater than 9% of energy in control groups and less than 9% of energy in intervention groups.

Reduction in CV events was seen in studies that primarily replaced calories from saturated fats with PUFA; no effect was seen in studies that replaced saturated fats with carbohydrate or protein. Effects in studies replacing with MUFA were unclear.

**Analysis**

Narrative review, results of the quality assessment of the individual studies were summarised to evaluate the quality and strength of the overall evidence in relation to the posed research questions. The evidence for each exposure-outcome association was categorised according to predetermined categories: convincing, probable, limited-5 PCS (6 publications); n=185,049; duration: 7-22y; age: 30-84y; gender: M (1), F (2), M/F (3); health at baseline: healthy (6); country: USA (4), Denmark (2).

1 RCT; n=48,835; duration: 8.1y; age: 50-79y; gender: F; health at baseline: healthy; country: USA.

Majority of PCS – no association between intake of saturated fats and risk of CVD outcomes (grade B evidence).

**Secondary analysis**

RCT: Lower saturated fat intake associated with decreased risk of CHD in women (men not included in RCT), (grade B evidence).

**Comments**

MEDLINE and EMBASE were searched, due to limited resources, filters were applied to limit to core clinical journals (MEDLINE) and priority journals (EMBASE).

**Limitations**

Focus on new evidence since previous edition of Nordic Nutrition Recommendations (NNR), hence why studies pre-2000 not included, however several systematic reviews and meta-analyses included in previous publications. Strict criteria for both study quality and evidence grading resulting in a relatively

### Study

**Schwab et al. (2014)**
(Systematic narrative review)

**Funding source**
Supported by the Nordic Council of Ministers.

**Research question**
What are the effects of intake of total fat and various combinations and proportions of fatty acid classes in the diet, considering intake of other nutrients on: well-established indicators of clinical outcomes such as plasma or serum total lipids and lipoprotein concentrations, plasma or serum glucose and insulin concentrations, and blood pressure? clinical outcomes including body weight, type 2 diabetes, CVD, and cancer?

**Selection criteria**

- **Search dates:** January 2000 - February 2012.
- **Analysis**
  - Narrative review, results of the quality assessment of the individual studies were summarised to evaluate the quality and strength of the overall evidence in relation to the posed research questions. The evidence for each exposure-outcome association was categorised according to predetermined categories: convincing, probable, limited-

- 5 PCS (6 publications); n=185,049; duration: 7-22y; age: 30-84y; gender: M (1), F (2), M/F (3); health at baseline: healthy (6); country: USA (4), Denmark (2).

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- Majority of PCS – no association between intake of saturated fats and risk of CVD outcomes (grade B evidence).

- **Secondary analysis**
  - RCT: Lower saturated fat intake associated with decreased risk of CHD in women (men not included in RCT), (grade B evidence).

- **Comments**
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  - Focus on new evidence since previous edition of Nordic Nutrition Recommendations (NNR), hence why studies pre-2000 not included, however several systematic reviews and meta-analyses included in previous publications. Strict criteria for both study quality and evidence grading resulting in a relatively
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</tr>
</thead>
</table>
| **Declarations of interest**  
None to declare. | Study designs: RCT and PCS.  
*Inclusion criteria:* 18-70y, healthy (subjects with dyslipidaemia, glucose intolerance, or overweight (mean BMI of study population not exceeding 30kg/m²) were included); ≥10 participants for RCTs; dietary assessment method: food record, FFQ, dietary recall, biomarkers; duration ≥ 4 weeks (RCTs), ≥6 months (body weight and body composition studies); PCS follow-up >4y, studies >5y for cancers; RCT dropout <30% in 6 months, <40% on 12 months, <50% in 24 months; intervention: amount and/or quality of dietary fat; updated/relevant nutrient databases.  
*Exclusion criteria:* Studies without Caucasians or Caucasians a clear minority; study aim outside scope of review; exposure food pattern or a whole food; included non-healthy subjects, obese subjects.  
**Dietary assessment methods**  
Food record, FFQ, dietary recall, valid biomarkers. | suggestive, and limited-no conclusion.  
**Evaluation of study quality**  
Primary evidence assessed for quality but method not stated.  
Quality categories included:  
A) high quality with very low risk of bias;  
B) good quality, some risk of bias but not enough to invalidate results;  
C) low quality with significant bias and weaknesses which may invalidate results. | 2 PCS: saturated fats reduced and replaced with carbohydrate: associated with increased risk of CVD outcomes (grade B evidence).  
1 PCS: Increased risk of CVD outcomes with simple carbohydrate (high glycaemic index) but not complex carbohydrate (low glycaemic index) (grade B evidence). | conservative estimate of the evidence.  
Many questions remain unresolved due to conflicting results from studies and lack of high quality-controlled studies. |