

Scientific Advisory Committee on Nutrition

Paper for discussion: Agenda Item 3

A Systematic Approach to the Evaluation of Evidence that relates Food and Nutrients to Health

Please see attached paper for consideration. The following annex is also attached:

Annex 1: Suggested systematic approach to assessment of evidence

Background papers were provided at the previous meeting.

Scientific Advisory Committee on Nutrition

A Systematic Approach to the Evaluation of Evidence that relates Food and Nutrients to Health

Background papers were provided at the SACN meeting held on 27th September 2001.

BACKGROUND

1. At its last meeting on 27 September, SACN proposed a subgroup to discuss the most appropriate framework for risk assessment for use by the Committee. Members suggested that the subgroup should compile a 'checklist' to ensure that evidence from a range of different sources was considered in a systematic manner for each issue. The assessment should be documented in such a way that it is open to scrutiny and such that different assessors of the same topic would be expected to reach the same conclusion.
2. A meeting of the risk assessment subgroup chaired by Professor John Cummings took place on 12 November 2001. Professor Christine Williams and Dr Tim Key of SACN attended with Dr Peter Bennett from Economics and Operational Research Division, Department of Health. Representatives of DH and FSA secretariat were also present.

MINUTES OF THE RISK ASSESSMENT SUBGROUP

3. The subgroup agreed that the traditional toxicological approach to risk assessment is not entirely appropriate to public health nutrition, and that SACN should take a more positive approach, examining issues in relation to positive health outcomes, as well as negative. This would be appropriate when assessing the role of diet in the promotion of good health.

4. The subgroup used as its reference sources the Codex proposed draft working principles for risk analysis, Review of Risk Procedures used by Government's advisory committees dealing with Food Safety, Interdepartmental Liaison Group on Risk Assessment Ministers' Report and the Southwood Report.
5. The subgroup considered that any risk assessment structure used by SACN should:
 - be systematic and transparent
 - assess the quality of evidence against an explicit set of criteria, e.g. causal criteria.
 - acknowledge gaps in evidence
 - state reasons for omitting studies from consideration
 - consider the use of scoring systems for evidence on a case by case basis. Ratings can be attributed to studies based on the quality of the study design. However, limitations associated with using such scoring systems should be stated where necessary. An example of a scoring system used for the COMA Report of the Working Group on Diet and Cancer is attached as at Annex 2.
 - consider the generalisability of evidence, including, gender, age, ethnicity, pregnancy, genotype.
 - consider evidence in relation to environmental and lifestyle factors, such as smoking, exercise and social class.
 - consider confounders, the quality of study design, use of statistics, and measurement issues
 - consider estimation of attributable and absolute risk where possible.
 - consider possible public health recommendations that might be made in relation to a specific diet-health relationships, and possible adverse effects of any recommendations for other diet-health relationships (e.g. meat/ cancer versus meat/ anaemia, folic acid and NTD versus folic acid and hidden pernicious anaemia).

In addition:

- It may be necessary to obtain additional analysis from external researchers, selected on the basis of expertise and independence with regard to interests

involved. Procedures and criteria used to select research should be documented (including a public declaration of potential conflicts of interest).

- The health effects examined should include acute, chronic (including long-term), cumulative and/or combined.
 - Risk/benefit assessment should be based on realistic exposure scenarios, with consideration of different situations and of susceptible or high risk population groups.
6. Initial steps when considering an issue should include:
- Area of interest to be clearly identified
 - Subject for evaluation defined
7. Causal criteria are a useful basis for assessing evidence for recommendations in nutrition. To establish causality, a minimum set of criteria are required: consistency, strength of association, dose response, plausibility and temporality (see Potischman et al, AJCN, 1999).

- **Consistency**

Rarely can any single epidemiological study be considered definitive. Only by observing similar findings consistently from a large set of diverse studies can a case for causal association be made.

- **Strength of Association**

Strong associations are more likely to indicate a causal relationship than weak associations. However, weak associations are common in dietary studies, and weak causal associations may have important public health implications.

- **Dose-response**

The presence of a statistically significant increasing trend strengthens the evidence in favour of causality. Such a situation is not always seen in nutrition, and interpretation may be complicated by threshold effects.

- **Biological plausibility**

Assessed via consistency of putative mechanisms indicated by animal models, in vitro cell systems, human metabolic and clinical studies. Use of genetic and other biological markers as exposures or endpoints is increasing. Where the

biological functions of dietary constituents are not well studied, or not known at all, it is wise to be cautious when making public health recommendations. Potischman et al suggest that '*where biological evidence is unavailable and yet recommendations based on epidemiologic evidence seem prudent, it is wise to make clear that some recommendations are more tentative than others*' because emerging evidence may lead to a reassessment of recommendations.

- **Temporality**

Consideration of the extent to which the data support the contribution of variability in dietary intake/ nutritional status as an influencing factor prior to diagnosis of disease.

8. The types of evidence that should be considered:

- *Epidemiological evidence*
 - **Ecological Studies** - Which investigate diet and disease at the population level
 - **Case-control** – Individuals with recently diagnosed disease are interviewed regarding their dietary intake and compared to a control group
 - **Cohort Studies** – A group of individuals are identified and their exposures to health effects of interest are measured. Individuals are followed over time to examine the association between dietary factors and the incidence of disease
 - **Randomised Controlled Trials** – Participants randomly assigned to receive dietary intervention and then followed for health effects
- *Mechanistic studies*
 - Human physiological studies, including healthy & clinical subjects
 - Genetic/molecular/cellular work

- *Animal studies*

9. The subgroup agreed that levels of evidence should not be ranked, nor should a generic scoring system be created. It agreed that although in some circumstances, randomised controlled trials might be considered a 'gold standard', it will be rare to have many randomised controlled trials relating dietary change to disease outcome. This is due to the complexity, labour intensiveness and cost of such trials. Therefore, all types of evidence must be considered, acknowledging the strengths and weaknesses of each type.
10. The subgroup acknowledged that it may be asked to look at issues which have already been thoroughly examined by others. In such situations, the subgroup proposed that requests for SACN to consider new evidence should be accompanied by a formal submission in which evidence is presented according to the basic criteria agreed by the committee (Annex 1). The committee will assess the relevance of any new evidence to the situation in the UK.
11. Reports should be prepared, made available to interested parties for review and conveyed in a readily understandable form. Constraints, uncertainties, assumptions and their impact on the risk/benefit assessment should be highlighted, as should minority opinions. Formal records should draw a distinction between information provided by others and the SACN conclusions. Conclusions regarding any adverse health consequences should not be modified out of anxiety not to cause public alarm. The Reports should then be forwarded for the purposes of risk management.

Members are invited to:

Agree to the proposed general framework, enabling a systematic approach to each issue.

Annex 1

Suggested systematic approach to assessment of evidence

1. Establish clear definitions

- Identify area of interest
- Define subject for evaluation

2. Use causal criteria to assess evidence

- Consistency
- Strength of association
- Dose-response
- Biological plausibility
- Temporality

3. Assess a range of study types

If a type of evidence is not to be considered, this should be clearly stated, giving reasons.

- **Epidemiological evidence**
 - Ecological Studies
 - Case-control
 - Cohort Studies
 - Randomised Controlled Trials
- **Mechanistic studies**
 - Human physiological studies examined to include healthy & clinical subjects
 - Genetic/molecular/cellular work
- **Animal studies**