A systematic review of the evidence of the benefits and risks of different dietary carbohydrates on cardio-metabolic health and disease

Nutritional Epidemiology Group

University of Leeds

Leeds

July 2012

Contents

Team Members

Dr Victoria Burley (lead)	MSc, PhD
Dr Darren Greenwood	MSc, PhD
Dr Lucinda Summers	MB BS, FRCP, DPhil
Dr Chris Gale	MB BS, MRCP, PhD
Dr Charlotte Evans	MSc, PhD
Ms Iris Gordon	MSc
Ms Cristina Cleghorn	MSc
Ms Diane Threapleton	MSc
Ms Camilla Nykjaer	MSc
Ms Charlotte Woodhead	MSc
Mr James Thomas	BSc

Amendments to project staff:

Lucinda Summers left the project January 2010

James Thomas left the project August 2010

Diane Threapleton reduced from full time to 40% full-time equivalent from November 2010 and left the project in April 2011

Ms Camilla Nykjaer joined the team from October 2009 to March 2011

Ms Charlotte Woodhead joined the team from May 2011 to February 2012

Background to the review

This review was commissioned to update the report produced in the early 1990's by the UK Government's Committee on the Medical Aspects of Food and Nutrition Policy (COMA) from which UK dietary reference values (DRVs) were derived (Committee on Medical Aspects of Food Policy, 1994).

The dietary changes that would help to reduce rates of coronary heart disease (CHD) in the UK population were detailed in the 1994 report from COMA, which concluded that diets high in dietary carbohydrate were associated with higher fasting concentrations of plasma triglyceride and lower HDL cholesterol (Committee on Medical Aspects of Food Policy, 1994). Nonetheless, due to the reciprocal relationship between dietary carbohydrate and dietary fat, such high carbohydrate diets tended to be low in fat and consequently were associated with lower LDL cholesterol levels and low risk of CHD. At that time there was limited evidence that the type of carbohydrate (sugars or starches) was important, although the panel did find evidence that diets rich in non starch polysaccharide were associated with lower post prandial plasma insulin and glucose levels, and LDL cholesterol levels. The panel recommended a reduction in fat intake, particularly saturated fat intake, a reduction in sodium intake and an increase in fruit and vegetable and complex carbohydrate intake.

Somewhat more recently, the World Health Organisation summarised the strength of evidence on lifestyle factors and risk of developing cardiovascular diseases, type 2 diabetes and obesity (World Health Organisation, 2003). They found the evidence *convincing* or *probable* for a decreased risk of these conditions with diets high in dietary fibre and *probable* that a high intake of sugar-sweetened beverages increase the risk of obesity. However, at that time the panel concluded that there was insufficient evidence concerning the relationship between total carbohydrate and risk of cardiovascular disease and that the evidence was indicative of a *possible* decreased risk of obesity with diets composed of low glycaemic index foods.

Since these reports were prepared, further evidence has accrued on these issues. In particular a wealth of studies have been published on the relationship between cardio-metabolic health and dietary glycaemic index and load, wholegrain consumption and other dietary patterns associated with dietary carbohydrates (Baxter *et al.*, 2006;Flight and Clifton, 2006;Harland and Garton, 2008;Livesey *et al.*, 2008;Malik *et al.*, 2006;Vrolix *et al.*, 2008). There is a pressing need for these additional studies to be systematically evaluated and included in the body of evidence that exists to permit the Scientific Advisory Committee on Nutrition to assess whether existing dietary recommendations concerning dietary carbohydrates need to be revised.

Methods

Please refer to the Protocol for this Systematic Literature Review, for details of the search strategy, study selection procedure, inclusion criteria and details of the data analysis plan.

Database searches

The following electronic databases were searched:

- Medline
- Pre-medline (MEDLINE in process)
- Embase
- CAB Abstracts
- BIOSIS
- ISI Web of Science
- The Cochrane Library

Hand-searching

References were obtained by hand-searching the reference lists of key review articles plus existing Reference Manager databases of ‘diet and hypertension’ and ‘carbohydrate and insulin resistance’ held by the review team.

The following journals were also hand-searched to supplement the database searches:

- Journal of Nutrition
- Journal of the American Dietetic Association
- American Journal of Clinical Nutrition
- Diabetes Care
- European Journal of Clinical Nutrition
- British Journal of Nutrition

Removal of Duplicate references

All reference manager files from the different sources were merged in together and electronically de-duplicated with the order of priority: Medline, PREM (MEDLINE In-Process & Other Non-Indexed Citations), Embase, CAB Abstracts, BIOSIS, The Cochrane Library, ISI Web of Science and Hand-searching.

Screening for article relevancy

For each reference, the title and/or abstract were screened once using the guidelines for article relevancy (Protocol appendix III). References that were clearly unrelated to the scope of the review were marked as ‘article not relevant’. All other articles were marked as ‘potentially relevant’ and moved to another database for the next stage of the process. As a quality check, a random

sample (10%) of references that had been identified as 'not relevant', were re-screened by a second team member.

Formal Inclusion or Exclusion

Hard copies of all ‘potentially relevant’ papers were obtained and were reviewed independently by two members of the review team using the Inclusion/Exclusion form and additional details for inclusion (Protocol appendix IV & V). Where any disagreement occurred, a third member of the team arbitrated in the decision.

Papers that did not meet the inclusion criteria were marked with an exclusion code that represents the earliest reason for exclusion based on the Inclusion/Exclusion flow chart, even though some papers were eligible for exclusion based on multiple codes.

Data extraction

Data were entered directly into an Access database which was designed by the Nutrition Epidemiology Group at the University of Leeds. Data from cohort studies and randomised controlled trials (RCT) were extracted onto different style forms so that extraction was tailored specifically towards the design of these study types. Data extraction was completed by one member of the review team.

Quality assessment of RCTs

The review was not restricted on the basis of perceived quality of papers or the process of obtaining data cited in primary studies. However, within included studies, study characteristics that may influence results or are general indicators of study quality have been captured. The quality of included RCTs was assessed using the Cochrane indicators of bias. This was carried out by one reviewer at the point of data extraction and covered the following issues:

1. Sequence generation criteria
2. Allocation concealment
3. Blinding of participants, personnel and outcome assessors
4. Incomplete outcome data
5. Selective outcome reporting
6. Other potential threats to validity

Each paper was categorised as containing bias, no bias or being unclear based on each of the above criteria using a form for guidance (Protocol appendix VI). Assessor blinding for individual outcomes was also captured in addition to overall blinding within the study. Funding sources for RCTs was also recorded and is presented in RCT characteristic tables (detailed below).

Cleaning the extracted data

Data were exported from the Access database and were closely screened in order to identify any unusual results. Any anomalies were then checked against the original papers as necessary.

Amendments to Methods

Amendments and clarifications for Inclusion/ Exclusion process

Detailed guidelines were developed to clarify grey areas of the inclusion and exclusion form in order to assist the review team to deal with any issues in a consistent manner. The following points outline these modifications and clarifications.

Exclusion code 2: Latin-square and counterbalanced sequence of intervention delivery

Studies with these sequences of intervention delivery will not be included unless they clearly state that random allocation was used, as these delivery sequences are often not randomised.

Exclusion code 3: Relevant carbohydrate/diets

For RCT groups, there must be a difference in total carbohydrate content of the diets/supplements ≥5%. Below 5% it was considered that the groups were not sufficiently different in carbohydrate content to obtain a meaningful outcome. N.B, this did not exclude studies with differences in other carbohydrate sources such as a fibre supplementation trial with groups containing similar proportions of macronutrients.

Exclusion code 6: Definition of 'healthy'

Criteria were set for determining the degree of ill health of participants of the studies to be included. Studies were excluded if >50% of participants were ill at baseline and data for any healthy participants were not presented separately. Studies may be included if participants have a combination of illnesses, providing the sample contains at least 50% who are essentially healthy. See 'Additional information sheet 3 and 4' (Protocol appendix V). Studies were excluded if it appeared that the population was specifically selected because of ill health such as type 2 diabetes mellitus or hypertension. Studies whose participants were insulin resistant were not excluded since there is no universally accepted threshold for this.

Exclusion code 7: Upper age threshold

The age range for eligible studies has been modified so there is now no upper limit for age. This ensures that study populations with a mean age lower than 80 years were not excluded because of a minority of older participants. This was primarily relevant for cohort studies such as the Zutphen Elderly Study, where mean baseline age was 75 but ranged from 70-89 years.

The threshold for children has been applied where the population *mean* baseline age was lower than 5 years.

Exclusion code 8: Follow-up 3+ years in cohort studies

Cohort studies were excluded if it could not be determined that the data were analysed prospectively or where there was uncertainty about whether the exposure preceded the outcomes. This was relevant to studies which report average exposure and average outcome over the same time frame. Studies or specific results were excluded if the *average* follow up was less than 3 years even if the *maximum* follow-up had been reported as 3 years. These criteria covered the exclusion of data presented as mean exposure and mean outcome over the same time period since the direction of cause and effect could not be determined.

Exclusion code 9: Does the trial include an appropriate comparison group?

This stage refers to the need to establish that any changes in outcomes which are observed during a trial can be attributed to a change in carbohydrate (be it in terms of amount, type or nature) and not to another influencing lifestyle factor.

- Exclude studies where one group receive no or a minimal intervention and the other group receive an intensive dietary *and* physical activity intervention resulting in marked changes in both carbohydrate content of diet and physical activity level. Any change in outcomes could not be attributed to diet as exercise level differs between the groups
- Include studies where not only carbohydrate intake is different between groups but also sources of fats (SFA/MUFA/PUFA) as change in carbohydrate intake is inevitably accompanied by changes in other macronutrients. This ensures many trials are not excluded due to the differences in fat fractions within trial groups. For example, a low-carbohydrate, high-fat diet (Atkins type) vs. a low fat, high-carbohydrate diet (the typical weight loss diet).

Modifications and clarifications to data extraction

Further work was undertaken on setting clear guidelines for the review team on how to extract the results in the most consistent way. The following points outline these modifications and clarifications to the protocol.

Exposures:

- Serum nutrient levels used as markers of exposure were deemed as insufficient measures of exposure, only dietary information was used.

Outcomes:

- Satisfaction was not included as a satiety outcome as often it was not possible to tell if this related to satisfaction with the amount of food provided or general satisfaction with the overall content of the diet.
- Dietary or eating restraint was not entered as an outcome as it is generally not affected by food intake.
- Heart failure was not entered as an outcome as it is not necessarily connected with cardiovascular health and can be reported as cause of death when cause of death is unknown.

Presentation of results:

- When data were presented in figures only, no attempt was made to read numbers from the graphs as this would introduce unacceptable levels of error. However, the direction of effect and p-values were extracted when reported.

Cohorts:

- If two papers relating to the same study report the same results from different follow-up times, data from the paper with the longest follow-up was extracted. In any case where this data from the longer follow-up was so poor that a dose-response curve could not be generated, the better quality data from the shorter follow-up would be extracted in preference and marked as the best model for this study.
- The follow-up that is mentioned in the abstract or the follow-up that is longest without losing a high proportion of subjects was marked as the best model and would be used in any meta-analysis.
- Results were not extracted that presented data relating to change in intake and exposure over the same time period. This approach was also taken for the World Cancer Research Fund systematic reviews (World Cancer Research Fund and American Institute for Cancer Research, 2007) as direction of association cannot be determined. Data which fall under this category are reported from the Nurses' Health and Health-Professional follow-up (Koh-Banerjee *et al.*, 2004;Liu *et al.*, 2003).

RCTs:

- References with the same authors were cross checked to ensure the same results are not extracted twice. If two papers reported the same result from the same trial, the data from the longest follow-up was extracted.
- Actual dietary intake data were extracted in preference to 'intended diet' of study participants where this information was reported and these data were flagged as 'intended diet' where this had been reported.
- Data for the same result presented in the format of 'difference between groups at follow-up' or 'difference between groups in change from baseline' were marked as best model in preference to values reported in each group at baseline and follow-up.
- If the intervention was supplementation, the dietary information extracted and presented in the trial characteristics table were in relation to these supplements and not the whole diet, where it had been reported in this way.

Follow-up:

- Many trials report outcomes at various time-points. Data for all follow-up periods were extracted but the best model was selected as the follow-up closest to the end of the intervention and not simply the longest follow-up.
- Length of follow-up is defined from the point of randomisation.

Modifications and clarifications to data analysis

Data from the Access database were exported to excel and exposure-outcome pairings with three or more results were then exported to Stata for meta-analysis. All data exported from Access has been included in the results tables of the report.

Where results are presented by diagnostic category e.g. fatal and non-fatal events, but results for the total number of combined events are required to facilitate combination with studies that only present combined results, the method of Hamling *et al*. was used to combine the diagnostic groups prior to performing meta-analysis (Hamling *et al.*, 2008). This method based on the effective cell count used by Greenland and Longnecker method was used to derive the adjusted dose response trend (Greenland and Longnecker, 1992).

Dose response estimates are presented using an increment in exposure equivalent to approximately one standard deviation in a UK or EU population, where possible. This is to allow comparison of the size of the various estimates across different exposures. This is regardless of any skewness in the distribution of intakes. These values are derived from various sources, as detailed in Table A below.

Some studies may not present intake category midpoints, medians or means, or category boundaries from which midpoints can be derived. If the study presents intake split at quantiles (e.g. tertiles, quartiles or quintiles) defined as equal-sized groups, alongside mean and standard deviation of intake, then the category medians will be derived from assuming a normal distribution of intake with given mean and standard deviation. For example, Appleby *et al.* (Appleby *et al.*, 1999) reports dietary fibre intake split into thirds, with mean (SD) intake of 42.4 (8.4) g/day. If the tertiles are at 33% and 67%, then the category medians will be taken as being at 16.7%, 50%, and 83.3% through the normal distribution with the same mean and SD, i.e. 34.3, 42.4, and 50.5 g/day respectively. For Beulens *et al.* (Beulens *et al.*, 2007) which also does not provide intake data, the quartile mean score of glycaemic load divided by the total carbohydrates in grams will be used as an estimate of the mean glycaemic index in each category.

Studies reporting only unadjusted results, or that can only be included in meta-analysis in unadjusted form because of limited data presented, will be excluded from meta-analyses because results that are unadjusted for confounding are liable to potentially substantial bias.

Forest plots will then present results from all studies with some adjustment for potential confounding, with two sets of pooled estimates provided (i) for all such studies, and (ii) for all studies reporting results that are adjusted for at least those characteristics deemed to be key confounders, i.e. age and smoking for blood pressure and cardiovascular outcomes, and age and

anthropometry (e.g. body mass index) for diabetes outcomes. This is because results that are unadjusted for key confounders are liable to potentially substantial bias.
On the forest plots, the horizontal axis (size of association) will be on the log scale (not linear scale) as is common for presenting ratios, providing confidence intervals that are symmetric.

Pooled estimates will not be presented on the forest plots when heterogeneity between the studies is too high for a pooled estimate to be meaningful, i.e. if I^2>75%. This is to avoid over-interpretation of those estimates.

The exploration of heterogeneity through the use of subgroup analyses and meta-regression will only be conducted where sufficient studies exist for this to be anything like robust, i.e. only when there are five or more studies in a meta-analysis. The following study characteristics (defined in advance) will then be explored where appropriate: subjects' gender, subjects' gender compared in same study, whether a cardiovascular outcome includes non-fatal events or not, the standard used for defining glycaemic index and load, the definition used for fibre exposures, the definition used for wholegrain exposures, length of follow-up, geographic location, and whether results were adjusted age, alcohol, anthropometry, energy intake, family history of the disease outcome, physical activity, sex, smoking, both age & smoking (for blood pressure and cardiovascular outcomes) or both age and anthropometry (for diabetes outcomes). Because the number of studies included in most meta-analyses is low, these subgroup analyses should be interpreted cautiously and as exploratory in nature.

Small study effects, such as publication bias, will be investigated using contour-enhanced funnel plots, but only when there are sufficient studies for this to be informative, i.e. when there are ten or more studies in a meta-analysis. Contour-enhanced funnel plots are more informative than standard funnel plots in that they allow the reader to identify whether potentially unreported results are in the non-significant region, thereby providing information on whether small study effects are likely to be caused by publication bias or not, under the assumption that publication bias is driven by statistical significance of results.

At the end of each chapter that has multiple meta-analyses of cohort data, the pooled estimates from each cohort study meta-analysis are presented in a summary forest plot for each outcome, including the pooled estimates of each exposure. As for the individual meta-analyses, estimates are not included where heterogeneity is too high for the pooled estimate to be meaningful, i.e. if I^2>75%. Comparison of the dose-response association across different exposures is made possible by using increments that are equivalent to approximately one standard deviation. Approximately four standard deviations cover the majority of the range of intakes. These are also presented alongside an approximate mean population intake, to facilitate interpretation from a

public health perspective. These values are derived from various sources, as detailed in the table below.

Where exact figures were not available, or where different sources were contradictory, approximate values have been used that ensure consistency with similar exposure categories. Numbers are rounded. For fibre, the mean and standard deviation depends on whether it was calculated using the Association of Official Analytical Chemist (AOAC) method, or not. The figures used are approximate estimates of the values for AOAC fibre in the UK or EU population.

Table A: Sources of approximate standard deviation used for dose-response increments.

Exposure	**≅1 sd**	**Mean**	**Source**
total carbohydrate	70 g/day	240 g/day	(Bates *et al.*, 2009)
% energy from carbohydrate	8% energy	44% energy	(Bates *et al.*, 2009)
total sugars	50 g/day	100 g/day	(Bates *et al.*, 2009)
glucose	10 g/day	20 g/day	for consistency with total sugars
fructose	20 g/day	40 g/day	for consistency with total sugars
sucrose	20 g/day	40 g/day	for consistency with total sugars
lactose	10 g/day	10 g/day	for consistency with total sugars
fibre	7 g/day	19 g/day	(Bates *et al.*, 2009)*1.33
soluble fibre	4 g/day	4 g/day	(Bates *et al.*, 2009)
insoluble fibre	7 g/day	15 g/day	(Bates *et al.*, 2009) + resistant starch + lignin
fibre in cereals	7 g/day	12 g/day	(Bates *et al.*, 2009) & (Larsson *et al.*, 2009)*
fibre in fruit	4 g/day	2 g/day	(Bates *et al.*, 2009) & (Larsson *et al.*, 2009)*
fibre in vegetables	4 g/day	4 g/day	(Bates *et al.*, 2009) & (Larsson *et al.*, 2009)*
fibre in legumes	1 g/day	0.5 g/day	(Bates *et al.*, 2009) & (Larsson *et al.*, 2009)*
total cereals	0.5 servings/day	0.5 servings/day	for consistency with grains
high fibre breakfast cereals	0.5 servings/day	0.5 servings/day	(Bates *et al.*, 2009)
wholegrain bread	0.5 servings/day	0.5 servings/day	(Bates *et al.*, 2009)
potatoes	0.5 servings/day	0.5 servings/day	(Bates *et al.*, 2009)
starch	50 g/day	130 g/day	(Bates *et al.*, 2009)
sugary drinks	1 serving/day	0.5 servings/day	(Bates *et al.*, 2009)
fruit juice	1 serving/day	0.5 servings/day	(Bates *et al.*, 2009)
beans & legumes	0.25 servings/day	0.25 servings/day	(Bates *et al.*, 2009)
wholegrains	0.5 servings/day	0.5 servings/day	(Lang *et al.*, 2003)
refined grains	0.5 servings/day	0.5 servings/day	(Lang *et al.*, 2003)
glycaemic index	2 GI units	55 GI units	(van Bakel *et al.*, 2009)
glycaemic load	20 GL units	120 GL units	(van Bakel *et al.*, 2009)

* Also used (Streppel *et al.*, 2008) & (Pietinen *et al.*, 1996).

Results of searches

All searches were undertaken from the publication year 1990 until the date of searching, which was between November and December 2009.

In total 42,518 references were obtained from both electronic and hand-searching (Table B).

Table B: Identified and included references by source

Database	Date of Search	Number of references identified	Number of references included in the review
Medline	26/11/2009	7765	316
PREM (MEDLINE In-Process & Other Non-Indexed Citations)	26/11/2009	356	6
Embase	26/11/2009	12501	21
CAB Abstracts	07/12/2009	4293	1
BIOSIS	26/11/2009	6032	7
The Cochrane Library	17/11/2009	3342	7
ISI Web of Science	27/11/2009	7751	18
Hand-searching	Nov to Dec 2009	478	20
TOTAL		42518	396

Inclusion Process

After removal of duplicates from electronic searching, 23,165 unique references remained. On first screening 1,736 of these references were deemed to be potentially relevant and 21,429 were marked as not relevant for this review. Just over 10% of references (2,214) marked as not relevant were screened independently by a second reviewer. Of this checking sample, 0.8% (17 articles) were identified as potentially relevant and these were transferred back into the potentially relevant file. The number identified in this process was lower than our pre-specified cut-off of 1% and no further checking was carried out.

At this stage, the 16 unique references additionally identified during hand-searching were included into the potentially relevant file, bringing the total to 1,769.

Hand-search references were de-duplicated and included into the potentially relevant folder at the final stage and it has therefore been possible to track whether the ‘potentially relevant’ papers were also identified during hand-searching and cross-check methods. Of the 17 papers identified during the quality check process, five were eventually included into the review. Four of these five

papers eligible for inclusion were also identified during journal hand-searching and through screening reference lists of relevant literature reviews (details in Table C).

Table C: Articles identified during checking process that were eligible for inclusion in the review

Reference	Inclusion code	Also identified in reference cross-check/ through hand-searching?
(Appel *et al.*, 2005) Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the OmniHeart randomized trial	C: RCT, blood pressure outcomes	Identified from reference cross check of: *Effect of High-Carbohydrate Versus High-Cis-Monounsaturated Fat Diets on Blood Pressure: A Meta-Analysis* (Shah *et al.*, 2007)
(Barton *et al.*, 2005) The relationship of breakfast and cereal consumption to nutrient intake and body mass index: the National Heart, Lung, and Blood Institute Growth and Health Study	A: Cohort study	Identified during hand-searching of: *Journal of the American Dietetic Association*
(Carels *et al.*, 2005) Education on the glycemic index of foods fails to improve treatment outcomes in a behavioural weight loss program	B: RCT, weight loss outcomes	Identified from reference cross check of: *Carbohydrate intake and obesity* (Van Dam and Seidell, 2007)
(Ells *et al.*, 2005) Postprandial glycaemic, lipaemic and haemostatic responses to ingestion of rapidly and slowly digested starches in healthy young women	D: RCT, satiety outcomes	Identified during hand-searching of: *British Journal of Nutrition*
(Vido *et al.*, 1993) Childhood obesity treatment: double blinded trial on dietary fibres (glucomannan) versus placebo	CD: RCT, other outcomes & satiety	Not identified during cross-check or through hand-searching

Included references were marked as A, B, C or D depending on the outcomes reported (Table D) and 396 papers, reporting on 321 studies were included in this review. Breaking this down by cohort and RCTs, 69 cohort studies were reported in 143 papers and 221 RCTs were reported in 253 papers.

Table D: Included articles

Inclusion Code	Number of articles	Number of studies	Description
A	143	69	Cohort references
B	32	31	RCTs with outcomes relating to body composition, with at least 12 month follow-up
C	163	140	RCTs with any other relevant outcomes (except satiety) and interventions at least 6 weeks in duration
D	176	162	RCTs relating to satiety with interventions longer than 3 days. A large proportion of these studies relate to energy intake with consumption of specified diets and not simply to hunger or appetite

N.B. References may be allocated multiple inclusion codes based on the outcomes of interest.

During formal inclusion of papers 1,372 references were excluded from the review for various reasons (Table E). One additional reference was excluded as the British Library could not source the article.

Table E: Excluded articles

Exclusion Code	Number of references	Description of the types of papers excluded or reasons for exclusion
1	50	Reviews, news articles, abstracts and study summaries where no original data were presented
2	411	Cross-sectional and case-control studies. Single-group trials and trials where allocation to groups was not randomised. N.B. Latin-square and counterbalanced trials which do not state random allocation to treatment sequences have been excluded here, but flagged (n=29)
3	322	The study did not report any carbohydrate intake
4	35	The study did not report an outcome relevant to the review
5	27	The study did not report carbohydrate intake in relation to an outcome (i.e. Cohort studies where baseline CHO intake is reported but not explored in relation to a relevant outcome)
6	136	The participants were suffering from outright illnesses or a marginally ill population was specifically recruited into the study and their baseline levels (e.g. BP, cholesterol) exceeded the pre-specified thresholds
7	20	The mean age of participants at baseline was less than 5 years
8	42	Cohort studies with follow-up shorter than 3 years
9	41	RCTs where the groups were deemed non-comparable since the effects of carbohydrate change could not be separated from other differences. This was usually where the intervention was multi-component vs. a control group or where the prescribed diets changed not only carbohydrate content but also the proportion of saturated, poly- or monounsaturated fats.
10	105	Satiety studies where the duration of the intervention was less than 3 days.
11	160	RCTs with an intervention duration of less than 6 weeks
12	14	Weight loss trials with follow-up duration shorter than 12 months
13	10	Studies which presented no unique data. The outcomes were presented with longer follow-up in another included article.

Animal Searches

Searches for animal data were carried out in November 2009 in Medline, Pre-Medline, Embase, CAB and BIOSIS. Animal searches were not conducted in ISI Web of Science as there was no filter to specify either human or animal studies.

Summary of evidence base for included studies

Studies identified within this review have been reported in six separate chapters, covering different types of outcome:

Chapter 1: Incident cardiovascular disease
Chapter 2: Markers of cardiovascular disease
- Part 1: Incident hypertension and blood pressure
- Part 2: Hyperlipidaemia and blood lipids
- Part 3: Markers of vascular function

Chapter 3: Markers of inflammation
Chapter 4: Incident diabetes and glycaemia
Chapter 5: Obesity
Chapter 6: Energy intake and eating motivation

At the start of each chapter a summary of the evidence base for each group of outcomes is presented.

For the 143 articles reporting results from observational studies, details of each cohort are included in a summary table at the start of each relevant section. A summary description of the included studies is also provided above these tables, to describe the general evidence base. This description details average study follow-up duration, age of participants, location of studies, participant recruitment and methods used to assess dietary intake.

An example cohort result table is provided below (Table F), including a detailed key, to display the various methods by which data were presented in included studies. This table and key should be used to interpret cohort results tables throughout the report to understand the types of data presented under each separate column header.

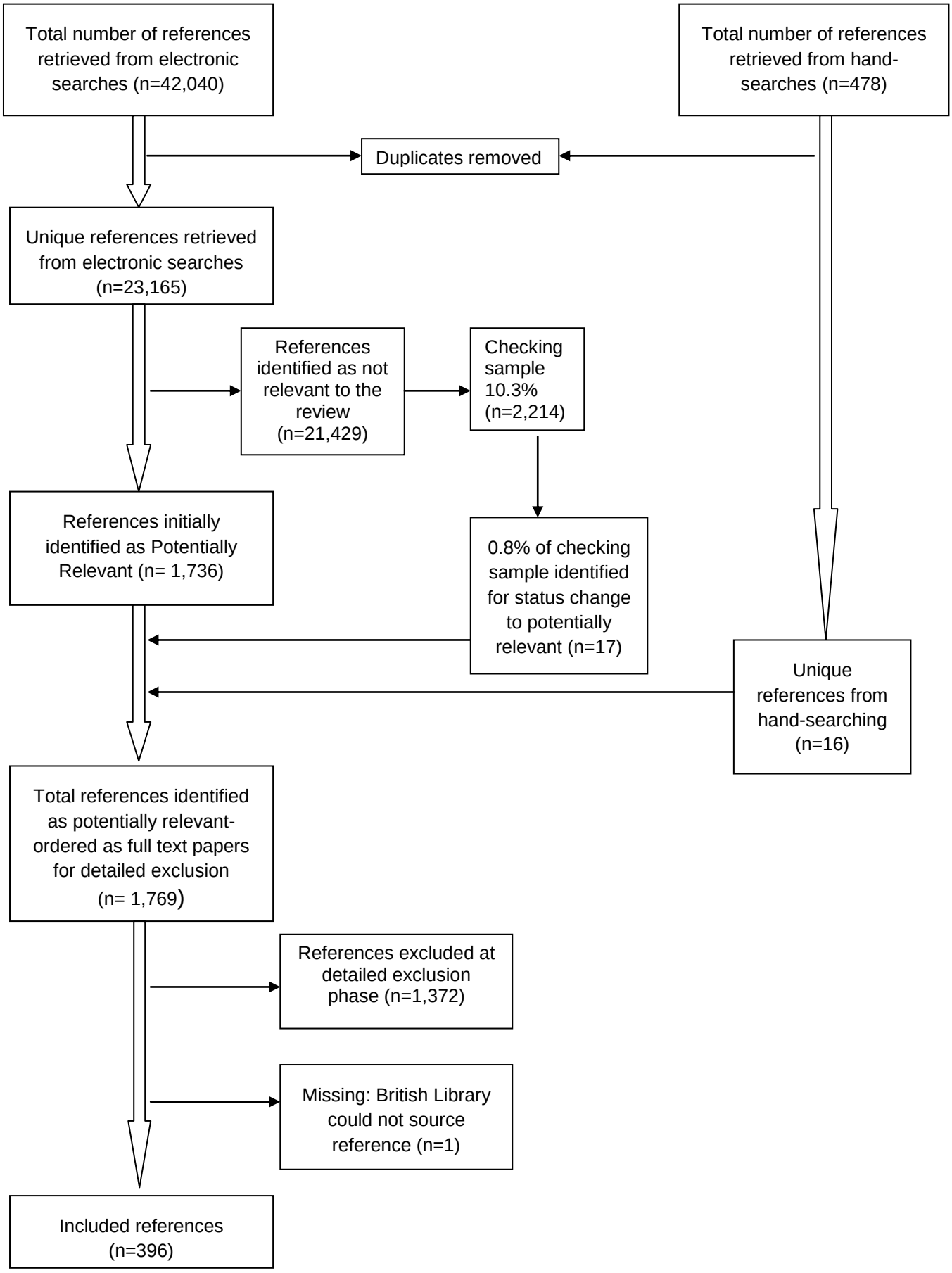
Similar summaries for the evidence base from the 253 included RCTs are presented within each separate outcome section. These summaries detail study designs, location and age of participants, by each outcome type.

Details of individual RCT characteristics are also presented within each relevant section and an example table, with key, is included below (Table G). An example of the RCT bias information collected within each chapter is also included below (Table H).

Individual RCT results are presented in each section throughout the report. Owing to the various methods of result reporting by the included RCTs, an example table plus key is presented below to aid interpretation of how each type of data is presented under the various column headers, throughout this report (Table J).

Results of Searches and Inclusion Process: flowchart

Figure A: Flowchart of Review Progress



Example tables for cohort results and RCT trial descriptions, results and risk of bias

Table F: Example cohort study result table

This table and key below detail the information presented in each column of cohort result tables, which appear throughout the report.

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Result ID/ Reference/ Cohort Name	**Country, Ethnicity, Inclusion criteria**	**Age range (mean) %Male**	**(Cases) / Total**	**Follow Up (% loss)**	**Diet Assess-ment**	**Exposure**	**Fatal / Non-fatal Events**	**Outcome/ Assessment Details**	**Sub-group Detail**	**Contrast (mean)**	**Exposure Units**	**RR (CI)**	**Mean Exposure (SD)**	**Mean Outcome (SD)**	**Beta**	**p**	**p trend**	**Adjustments**
14115 (Esrey *et al.*, 1996) Lipid Research Clinics Prevalence Follow-Up Study	Canada, Age 30-79y, No CHD	30-79 (46) %M 52	(40) /4904	12.4 y	Dietary recall	Carbo-hydrate, total (g/day)	Fatal Events	CHD events (unspecified) Medical records/ autopsy	Age 60-79y		g/d		Cases: (n: 40) 42.9 (10.1) Non-cases: (n: 581) 42.4 (9.6)					
14630 (Liu *et al.*, 2000) NHS	USA, No T2DM, Without angina or heart attack	38-63 %M 0	75521	10 y (2)	FFQ (126)	Carbo-hydrate, total (% energy)	Fatal + Non-fatal Events	CHD events (unspecified) Medical records/ autopsy		Continuous risk estimate	5% Energy	1.02 (0.96, 1.08)				0.5		Age, Alcohol, Aspirin, BMI, energy intake, Fibre, Folate, Hyperchol-esterolaemia, hypertension, Menopausal Status, physical activity, Parental CHD, protein intake, Smoking, Supplements, Vit E
13485 (Beulens *et al.*, 2007) Prospect-EPIC Utrecht	The Netherlands, No CHD, No T2DM	49-70 %M 0	(556) /17357	9 y (10)	FFQ (178)	Carbo-hydrate, total (g/day)	Fatal + Non-fatal Events	CHD events (unspecified) Registry data		Q4 vs Q1		1.17 (0.78, 1.77)					0.35	Age, Alcohol, BMI, Smoking, physical activity, Hyperchol-esterolaemia, HTN, Menopausal Status, Nutrient intake, occupation, systolic blood pressure

N.B: Blank cells indicate this value was not reported for the study

1) Cohort name: Standard cohort names have been included for ease of cohort identification. Cohort names were created where there was no common name in use for the study.
2) Inclusion Criteria: A list of criteria relevant to this systematic review which were applied to participants at the point of entering the cohort (e.g. No diabetics or persons with coronary heart disease were recruited into the cohort).
3) Age ranges, means and percent of males within the cohorts
4) The number of cases for the incident event is reported in brackets and 'Total' represents the total number of participants recruited into the cohort study at baseline
5) % loss: Percent of participants lost during follow-up
6) Dietary assessment method. Numbers in brackets relate to FFQ items
7) Exposure: Details of the dietary data provided by the study
8) The result relates to fatal, non-fatal or combined fatal and non-fatal events
9) Outcome details plus method used to assess outcomes. 'Multiple Methods' means that combinations of the following assessment methods were used: Self-reporting, Confirmed self-reporting, Medical testing, Registry data, Medical records/autopsy.
10) Sub group details: The result represents analysis carried out on a sub-group of the cohort
11) Contrast: Always in the format maximum consumption category from referent vs. referent (The majority of these results are highest vs. lowest category, with some being presented as lowest vs. highest).
    Continuous risk estimate: Risk scores which have been generated from continuous exposure values.
12) Units of exposure
13) Risk score (Confidence Intervals)
14) Where no risk score was reported, this column reports mean intake of exposures in cases and non-cases. Numbers of cases and non-cases are presented where this was reported.
15) Where no risk score was reported, this column reports mean outcomes or number of cases by exposure category (e.g. Weight change by intake quintile).
16) Beta coefficient for exposures which were analysed as continuous variables
17) P value
18) P trend
19) Adjustments for each result. Some abbreviations have been used here to keep tables concise. Please see Abbreviations section for details.

Table G: Example trial characteristics table

This table and key below detail the information presented in each column of trial characteristics tables, which appear at the beginning of each chapter, throughout the report.

N.B: Blank cells mean this value was not reported for the study

1	2	3	4	5	6	7	8	9	10	11	12
Authors, study name	Subject Inclusion criteria	Characteristics of participants	Trial Design (washout duration)	Length of intervention	Intervention Style	Total # of Participants	Intervention group names	Intervention Description	Diet/Supplement nutritional characteristics	Actual diet consumed reported?	Funding source
(Abete *et al.*, 2008)	No medical conditions which influence outcomes No medication Weight stable	Spain 56% Male Age: (36) BMI: (32)	Parallel Group	8 weeks	Free living diet plan	32	1. Higher GI diet 2. Lower GI diet	1. Individually prescribed diet within a strict dietary frame-work repeated on a 3 day rotation basis. 84% of CHO provided by rice and potatoes. 2. Individually prescribed diet within a strict dietary frame-work repeated on a 3 day rotation basis. 84% of CHO provided by pasta and legumes.	1. %E: C 47.8 P 19.6 F 32.6 Fibre g/d:18.5 2. %E: C 50.2 P 18.3 F 31.5 Fibre g/d:24.9	Yes	Government funding
(Anderss on *et al.*, 2007) Uppsala Wholegra in Trial	≥ 1 CHD risk factor Age 30-70y BMI 26-35	Sweden 27% Male Age: 35 - 70(59) BMI: (28)	Crossover (washout 6 weeks)	6 weeks	Supplement	34	1. Wholegrain products 2. Refined grain products	1. Usual diet + whole grain foods (Bread, crisp bread, muesli & pasta) Minimum 50% wholegrain in provided foods = 112g wholegrain/day 2. Usual diet + refined grain foods (Bread, crisp bread, muesli & pasta)	1. g/d: C 143 P 28 F 8 Energy: 3180kJ/d Fibre g/d:18 2. g/d: C 145 P 23 F 14 Energy: 3340kJ/d Fibre g/d:6	Yes	Swedish diabetes association and government and research institute funding
(Bantle *et al.*, 2000)	Age >18y BMI <32 No CHD Normal glucose tolerance Not hyperlipidaemic/ cholesterolaemic	USA 50% Male Age: (41) BMI: (25)	Crossover (washout not reported)	6 weeks	All food provided	24	1. High-fructose diet 2. High-glucose diet	1. 55% of energy as carbohydrate, 15% of energy as protein, and 30% of energy as fat (17% total energy as fructose). Crystalline fructose was added to diet. 2. 55% of energy as carbohydrate, 15% of energy as protein, and 30% of energy as fat (3% total energy as fructose). Crystalline glucose was added to diet.	1. g/d: C 276 P 76 F 66 Energy 2004 kcal/d Fibre g/d:23 2. g/d: C 276 P 76 F 66 Energy 2001 kcal/d Fibre g/d:23	No-Intended diet only	NIH

1) Reference information and trial name (trials reported in more than one paper have been given unique names so multiple papers from single studies can be identified)
2) Participant inclusion criteria for the trial
3) Characteristics of trial participants: country, percentage of male participants, age range (mean) and BMI range (mean)
4) Design of the trial, either parallel groups or crossover design (washout duration for crossover trials)
5) Duration of intervention
6) Style of intervention: the intervention involved a free-living diet plan, supplementation to the diet, substitution of foods already within the diet or all food during the trial was provided to participants
7) Total number of participants randomised
8) Names of trial groups. N.B. these names will appear in the results tables
9) Description of diets in study groups
10) Nutritional detail for the study groups. N.B. for supplements and substitution trials this detail is specific to the food or supplement where this information was provided. Carbohydrate, protein and fat are presented as g/day or percent of total energy. Energy intake and fibre content of the diets are presented where this was reported. These data represent reported dietary intake rather than the intended intake.
11) Actual diet consumed reported: Where ‘intended diet’ appears, data in column 10 represents the intended consumption for study participants as dietary compliance was not assessed or reported.
12) Funding source detail.

Table H: Example trial bias information table

1	2	3	4	5	6	7	8
Authors	Allocation sequence generation	Allocation concealment	Participant blinding	Researcher Blinding	Incomplete outcome data	Selective outcome reporting	Any other bias
(Abete *et al.*, 2008)	Unclear	Unclear	Unclear	Unclear	Bias	No Bias	No Bias
(Aller *et al.*, 2004)	Unclear	Unclear	Unclear	Unclear	No Bias	No Bias	No Bias
(Andersson *et al.*, 2007)	Unclear	Unclear	Bias	Bias	No Bias	No Bias	No Bias
(Bantle *et al.*, 2000)	No Bias	Unclear	Unclear	Unclear	No Bias	No Bias	No Bias
(Bell *et al.*, 1990)	Unclear	Unclear	No Bias	No Bias	No Bias	No Bias	No Bias
(Bellisle *et al.*, 2007)	Unclear	Unclear	Bias	Bias	No Bias	No Bias	No Bias

1) Reference information
2) Risk of bias in sequence generation for randomising participants
3) Risk of bias in concealing randomisation sequence from researchers
4) Risk of bias: were participants blind to allocation
5) Risk of bias: were researchers blind to allocation
6) Risk of bias: were incomplete data accounted for (intention to treat analysis) or missing data were likely related to outcomes
7) Risk of bias: the paper presents selective outcomes (study aims are not fully represented by the outcomes reported?)
8) Risk of bias: did the paper present any other causes for concern in terms of bias?

Table J: Example trial result table

This table and key below detail the information presented in each column of trial results tables, which appear throughout the report.

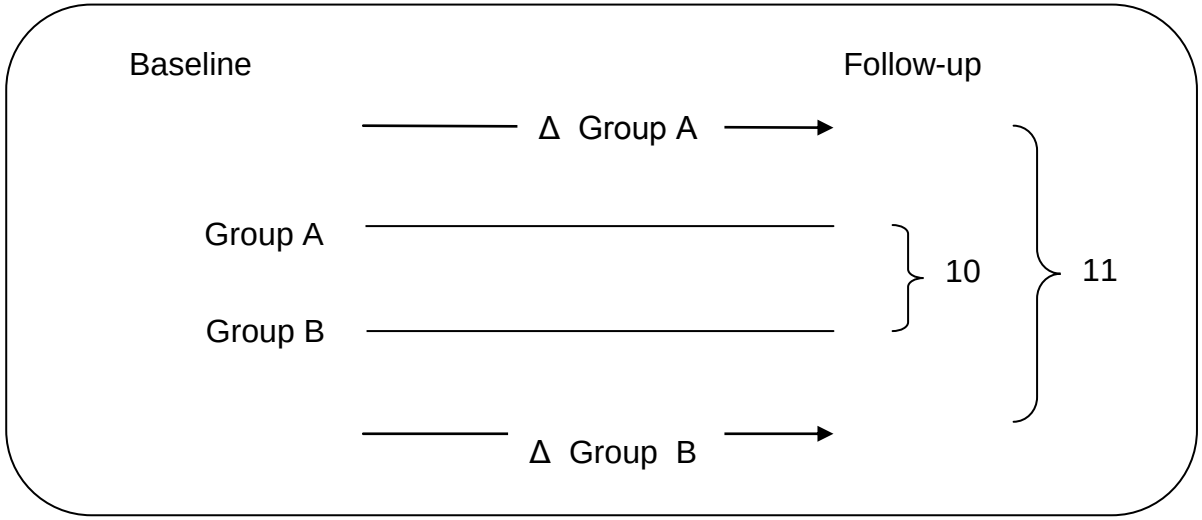
N.B: Blank cells mean this value was not reported

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Result ID/ Author	**Subgroup Detail**	**Intervention group names**	**Comple-ters/ Allocated**	**Baseline**	**Follow-up**	**Within group Δ from baseline**	**p-value Within group Δ from baseline**	**p-value difference between groups**	**Difference between groups at follow-up**	**Difference between groups in Δ from baseline**	**p-value difference between groups**	**Outcome/ Assessment method**	**Result/ Outcome details**	**Result-specific follow-up**	**Group Weight Change**	**Outcome Assess-ment Bias**
14782 (Salas-Salvado *et al.*, 2008)		Mixed soluble fibre twice a day minus Placebo	Intervention: 53/66 Placebo: 55/66							0.04 (CI -0.64, 0.72)		Blood glucose (OGTT 120 min)	(mmol/L)	16 weeks		No bias
14783 (Salas-Salvado *et al.*, 2008)		Mixed soluble fibre 3 times a day minus Placebo	Intervention: 58/58 Placebo: 55/66							0.07 (CI -0.58, 0.72)		Blood glucose (OGTT 120 min)	(mmol/L)	16 weeks		No bias
15295 (Due *et al.*, 2008)		Control	24/25	4.78 (CI 4.6, 5.0)	4.90 (CI 4.7, 5.1)	0.11 (CI -0.05, 0.27)						Glucose	Fasting Serum, (pmol/L)	6 months	Increase	unclear
		High MUFA	39/52	4.98 (CI 4.8, 5.1)	4.91 (CI 4.8, 5.0)	-0.06 (CI -0.19, 0.07)		NS							Increase	
		Low fat	43/48	4.82 (CI 4.7, 4.9)	4.91 (CI 4.8, 5.0)	0.09 (CI 0.01, 0.18)		NS							Increase	
15986 (Dale *et al.*, 2009)		High MUFA diet minus high carbohydrate diet	High MUFA: 85/100 High CHO: 89/100							-0.06 (CI -0.14, 0.03)		Glucose	Fasting (mmol/L)	2 years		unclear
17116 (Landin *et al.*, 1992)		Guar gum minus placebo	Cross-over: 25/25							-0.02 (CI -0.11, 0.06)	<0.001	Glucose	Fasting Whole blood, (mmol/L)	6 weeks		No bias
14579 (Pereira *et al.*, 2004)		Hypo-energetic low fat diet	11/23	92.4 (SE 9.47)	102.3 (SE 8.11)	16.2% (SE 5.24%)						Triglycerides	Fasting Serum, (mg/dL)	67 days	Decrease	unclear
		Hypo-energetic low GL diet	14/23	78.3 (SE 8.4)	72.4 (SE 7.19)	-3.5% (SE 4.63%)		0.01							Decrease	

1) Unique result ID/ Reference information
2) This column is filled when the results are presented by subgroup
3) Intervention group names: Group names are stacked one above the other when data are presented by group or as A minus B when the difference between groups is presented
4) Number of completers within the group/total allocated to group
5) Baseline value
6) Follow-up value
7) Change within group between baseline and follow-up
8) P-value for within group change from baseline
9) P-value for difference between groups at follow-up
10) See diagram below. Difference between groups in follow-up values
11) See diagram below. Difference between groups in change from baseline value
12) P-value for difference at follow-up or difference of change
13) Outcome (assessment method details)
14) Outcome details plus units
15) Follow-up period for the result
16) Weight change experienced within groups
17) Outcome specific bias: Was the researcher blind to group allocation

Figure B: Illustration to explain result data presented for RCTs

Data is often reported in publications in different formats: Outcome data are often the difference between groups (column 10) or the difference between groups in respect of the separate values of change from baseline, with each group (11).



Abbreviations

%E	Percent energy
ACS	Acute coronary syndrome
AOAC	Association of official analytical chemists
ATBC	Alpha-Tocopherol, Beta-Carotene Cancer Prevention
AUC	Area under the curve
BMI	Body mass index
BP	Blood pressure
CHD	Coronary heart disease
CHO	Carbohydrate intake
Chol	Cholesterol
CI	Confidence Interval
COB	Country of birth
COMA	Committee on medical aspects of food policy
CRP	C-reactive protein
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DEXA	Dual-energy X-ray absorptiometry
DMT2	Diabetes Mellitus Type 2
Ed	Education
EI	Energy intake
EPIC	European Prospective Investigation into Cancer
Eth	Ethnicity
F	Female
F&V	Fruit and vegetables
FA	Fatty acid
FABP	Fatty acid binding protein
FAT	Fat intake
FDA	US Food and Drug Administration
FFQ	Food frequency questionnaire
FH	Family history of
GI	Glycaemic index
GL	Glycaemic Load
H	History of
HDL-C	High-density lipoprotein cholesterol
HDL	High-density lipoprotein
HEI	Healthy eating index
Hip	Hip circumference
HMW	High molecular weight
HPFS	Health Professionals' Follow-Up Study
HR	Hazard ratio
HRT	Hormone replacement therapy
hsCRP	High-sensitivity C-reactive protein
hsIL	High-sensitivity Interleukin
HTN	Hypertension
ICAM	Intecellular adhesion molecule
ICAM	Inter-cellular adhesion molecule
IGT	Impaired glucose tolerance
IHD	Ischaemic heart disease
IL	Interleukin
IOTF	International obesity task force
ITT	Intention to treat analysis
LDL	Low-density lipoprotein
LDL-C	Low-density lipoprotein cholesterol
LMW	Low molecular weight
M	Male
MCP	Monocyte chemotactic protein

Meds	Medication
Met	Methionine
Mg	Magnesium
MI	Myocardial Infarction
mo	Month
MUFA	Monounsaturated fatty acid intake
NCEP	National Cholesterol Education Program
NHS	Nurses' Health Study
NMES	Non-milk extrinsic sugar
NS	Not Statistically Significant
NSP	Non starch polysaccharide
OCP	Oral contraceptive pill
PA	Physical activity
PAI	Plasminogen activator inhibitor
PHS	Physician's Health Study
PRO	Protein intake
PUFA	Polyunsaturated fatty acid intake
RCT	Randomised controlled trial
RR	Relative risk
RTEC	Ready-to-eat cereal
SAA	Serum amyloid A
SBP	Systolic blood pressure
SD	Standard deviation
SE	Standard error
SES	Socio-economic Status
SFA	Saturated fat intake
SICAM	Soluble intercellular adhesion molecule
SSB	Sugar-sweetened beverages
TAG	Triacylglycerol
TC	Total cholesterol
TFA	Trans fatty acid intake
TG	Triglycerides
TNF	Tumour necrosis factor
tPA	tissue plasminogen activator
UCP-3	Uncoupling protein 3
UK	United Kingdom
US	United States
VCAM	Vascular-cellular adhesion molecule
Veg	Vegetables
Vit	Vitamin
VLCD	Very low calorie diet
VLDL	Very low density lipoprotein
VLED	Very low energy diet
W:H	Waist to hip ratio
Waist	Waist circumference
WHO	World Health Organization
wks	Weeks
Yr	Year

References

Abete I, Parra D, Martinez JA (2008) Energy-restricted diets based on a distinct food selection affecting the glycemic index induce different weight loss and oxidative response. *Clin Nutr* **27** (4): 545-551

Aller R, de Luis DA, Izaola O, la CF, del OL, Fernandez L, Arranz T, Hernandez JM (2004) Effect of soluble fiber intake in lipid and glucose levels in healthy subjects: a randomized clinical trial. *Diabetes Research & Clinical Practice* **65** (1): 7-11

Andersson A, Tengblad S, Karlstrom B, Kamal-Eldin A, Landberg R, Basu S, Aman P, Vessby B (2007) Whole-grain foods do not affect insulin sensitivity or markers of lipid peroxidation and inflammation in healthy, moderately overweight subjects. *J Nutr* **137** (6): 1401-1407

Appel LJ, Sacks FM, Carey VJ, Obarzanek E, Swain JF, Miller ER, III, Conlin PR, Erlinger TP, Rosner BA, Laranjo NM, Charleston J, McCarron P, Bishop LM, OmniHeart Collaborative Research Group (2005) Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the OmniHeart randomized trial. *JAMA* **294** (19): 2455-2464

Appleby PN, Thorogood M, Mann JI, Key TJ (1999) The Oxford Vegetarian Study: an overview. *Am J Clin Nutr* **70** (3:Suppl): Suppl-531S

Bantle JP, Raatz SK, Thomas W, Georgopoulos A (2000) Effects of dietary fructose on plasma lipids in healthy subjects. *Am J Clin Nutr* **72** (5): 1128-1134

Barton BA, Eldridge AL, Thompson D, Affenito SG, Striegel-Moore RH, Franko DL, Albertson AM, Crockett SJ (2005) The relationship of breakfast and cereal consumption to nutrient intake and body mass index: the National Heart, Lung, and Blood Institute Growth and Health Study. *J Am Diet Assoc* **105** (9): 1383-1389

Bates, B., Lennox, A, and Swan, G. National Diet and Nutrition Survey: Headline results from Year 1 of the rolling programme. [Online]. 2009. 21-2-2011.

Ref Type: Online Source

Baxter AJ, Coyne T, McClintock C (2006) Dietary patterns and metabolic syndrome--a review of epidemiologic evidence. *Asia Pacific Journal of Clinical Nutrition* **15** (2): 134-142

Bell LP, Hectorn KJ, Reynolds H, Hunninghake DB (1990) Cholesterol-lowering effects of soluble-fiber cereals as part of a prudent diet for patients with mild to moderate hypercholesterolemia. *Am J Clin Nutr* **52** (6): 1020-1026

Bellisle F, Dalix AM, De Assis MA, Kupek E, Gerwig U, Slama G, Oppert JM (2007) Motivational effects of 12-week moderately restrictive diets with or without special attention to the Glycaemic Index of foods. *Br J Nutr* **97** (4): 790-798

Beulens JW, de Bruijne LM, Stolk RP, Peeters PH, Bots ML, Grobbee DE, van der Schouw YT (2007) High dietary glycemic load and glycemic index increase risk of cardiovascular disease among middle-aged women: a population-based follow-up study. *J Am Coll Cardiol* **50** (1): 14-21

Carels RA, Darby LA, Douglass OM, Cacciapaglia HM, Rydin S (2005) Education on the glycemic index of foods fails to improve treatment outcomes in a behavioral weight loss program. *Eating Behaviors* **6** (2): 145-150

Committee on Medical Aspects of Food Policy (1994) *Nutritional aspects of cardiovascular disease*. HMSO: London

Dale KS, McAuley KA, Taylor RW, Williams SM, Farmer VL, Hansen P, Vorgers SM, Chisholm AW, Mann JI (2009) Determining optimal approaches for weight maintenance: a randomized controlled trial. *Can Med Assoc J* **180** (10): E39-E46

Due A, Larsen TM, Mu H, Hermansen K, Stender S, Astrup A (2008) Comparison of 3 ad libitum diets for weight-loss maintenance, risk of cardiovascular disease, and diabetes: a 6-mo randomized, controlled trial. *Am J Clin Nutr* **88** (5): 1232-1241

Ells LJ, Seal CJ, Kettlitz B, Bal W, Mathers JC (2005) Postprandial glycaemic, lipaemic and haemostatic responses to ingestion of rapidly and slowly digested starches in healthy young women. *Br J Nutr* **94** (6): 948-955

Esrey KL, Joseph L, Grover SA (1996) Relationship between dietary intake and coronary heart disease mortality: lipid research clinics prevalence follow-up study. *J Clin Epidemiol* **49** (2): 211-216

Flight I, Clifton P (2006) Cereal grains and legumes in the prevention of coronary heart disease and stroke: a review of the literature. *European Journal of Clinical Nutrition* **60** (10): 1145-1159

Greenland S, Longnecker MP (1992) Methods for trend estimation from summarized dose-response data, with applications to meta-analysis. *Am J Epidemiol* **135** (11): 1301-1309

Hamling J, Lee P, Weitkunat R, Ambuhl M (2008) Facilitating meta-analyses by deriving relative effect and precision estimates for alternative comparisons from a set of estimates presented by exposure level or disease category. *Stat Med* **27** (7): 954-970, doi:10.1002/sim.3013 [doi]

Harland JI, Garton LE (2008) Whole-grain intake as a marker of healthy body weight and adiposity. *Public Health Nutrition* **11** (6): 554-563

Koh-Banerjee P, Franz M, Sampson L, Liu S, Jacobs DR, Jr., Spiegelman D, Willett W, Rimm E (2004) Changes in whole-grain, bran, and cereal fiber consumption in relation to 8-y weight gain among men. *Am J Clin Nutr* **80** (5): 1237-1245, doi:80/5/1237 [pii]

Landin K, Holm G, Tengborn L, Smith U (1992) Guar gum improves insulin sensitivity, blood lipids, blood pressure, and fibrinolysis in healthy men. *Am J Clin Nutr* **56** (6): 1061-1065

Lang R, Thane CW, Bolton-Smith C, Jebb SA (2003) Consumption of whole-grain foods by British adults: findings from further analysis of two national dietary surveys. *Public Health Nutr* **6** (5): 479-484, doi:10.1079/PHN2002453 [doi];S136898000300065X [pii]

Larsson SC, Mannisto S, Virtanen MJ, Kontto J, Albanes D, Virtamo J (2009) Dietary fiber and fiber-rich food intake in relation to risk of stroke in male smokers. *Eur J Clin Nutr* **63** (8): 1016-1024

Liu S, Willett WC, Manson JE, Hu FB, Rosner B, Colditz G (2003) Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle-aged women. *Am J Clin Nutr* **78** (5): 920-927

Liu S, Willett WC, Stampfer MJ, Hu FB, Franz M, Sampson L, Hennekens CH, Manson JE (2000) A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *Am J Clin Nutr* **71** (6): 1455-1461

Livesey G, Taylor R, Hulshof T, Howlett J (2008) Glycemic response and health--a systematic review and meta-analysis: relations between dietary glycemic properties and health outcomes. *American Journal of Clinical Nutrition* **87** (1): 258S-268S

Malik VS, Schulze MB, Hu FB (2006) Intake of sugar-sweetened beverages and weight gain: a systematic review. *American Journal of Clinical Nutrition* **84** (2): 274-288

Pereira MA, Swain J, Goldfine AB, Rifai N, Ludwig DS (2004) Effects of a low-glycemic load diet on resting energy expenditure and heart disease risk factors during weight loss. *JAMA* **292** (20): 2482-2490

Pietinen P, Rimm EB, Korhonen P, Hartman AM, Willett WC, Albanes D, Virtamo J (1996) Intake of dietary fiber and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Circulation* **94** (11): 2720-2727

Salas-Salvado J, Farres X, Luque X, Narejos S, Borrell M, Basora J, Anguera A, Torres F, Bullo M, Balanza R, Fiber in Obesity-Study Group (2008) Effect of two doses of a mixture of soluble fibres on body weight and metabolic variables in overweight or obese patients: a randomised trial. *Br J Nutr* **99** (6): 1380-1387

Shah M, Adams-Huet B, Garg A (2007) Effect of high-carbohydrate or high-cis-monounsaturated fat diets on blood pressure: a meta-analysis of intervention trials. *Am J Clin Nutr* **85** (5): 1251-1256, doi:85/5/1251 [pii]

Streppel MT, Ocke MC, Boshuizen HC, Kok FJ, Kromhout D (2008) Dietary fiber intake in relation to coronary heart disease and all-cause mortality over 40 y: the Zutphen Study. *Am J Clin Nutr* **88** (4): 1119-1125

van Bakel MM, Slimani N, Feskens EJ, Du H, Beulens JW, van der Schouw YT, Brighenti F, Halkjaer J, Cust AE, Ferrari P, Brand-Miller J, Bueno-de-Mesquita HB, Peeters P, Ardanaz E, Dorronsoro M, Crowe FL, Bingham S, Rohrmann S, Boeing H, Johansson I, Manjer J, Tjonneland A, Overvad K, Lund E, Skeie G, Mattiello A, Salvini S, Clavel-Chapelon F, Kaaks R (2009) Methodological challenges in the application of the glycemic index in epidemiological studies using data from the European Prospective Investigation into Cancer and Nutrition. *J Nutr* **139** (3): 568-575, doi:jn.108.097121 [pii];10.3945/jn.108.097121 [doi]

Van Dam RM, Seidell JC (2007) Carbohydrate intake and obesity. *Eur J Clin Nutr* **61 Suppl 1** S75-S99, doi:1602939 [pii];10.1038/sj.ejcn.1602939 [doi]

Vido L, Facchin P, Antonello I, Gobber D, Rigon F (1993) Childhood obesity treatment: double blinded trial on dietary fibres (glucomannan) versus placebo. *Padiatr Padol* **28** (5): 133-136

Vrolix R, van Meijl LE, Mensink RP (2008) The metabolic syndrome in relation with the glycemic index and the glycemic load. *Physiol Behav* **94** (2): 293-299

World Cancer Research Fund, American Institute for Cancer Research (2007) *Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective*. AICR: Washington DC

World Health Organisation (2003) *Joint WHO/FAO Expert Consultation. Diet, nutrition and the prevention of chronic diseases*. WHO: Geneva