

Continuous update of the WCRF-AICR report on diet and cancer

Protocol: Prostate Cancer

Prepared by: Imperial College Team

The current protocol for the continuous update should ensure consistency of approach to the evidence, common approach to the analysis and format for displaying the evidence used as in the literature reviews for the Second Expert Report¹.

The starting point for this protocol are:

- The convention for conducting systematic reviews developed by WCRF International for the Second Expert Report ¹
- The protocol developed by the SLR group on prostate cancer for the Second Expert Report (Bristol) ¹

The peer-reviewed protocol will represent the agreed plan for the Continuous Update. Should departure from the agreed plan be considered necessary at a later stage, this must be agreed by the Continuous Update Panel (CUP) and the reasons documented.

Background.

In the judgment of the Panel of the **WCRF-AICR Second Expert Report**², the factors listed below modify the risk of Prostate cancer. Judgments are graded according to the strength of the evidence.

PROSTATE CANCER		
	DECREASES RISK	INCREASES RISK
Convincing	No factor identified	No factor identified
Probable	Foods containing lycopene Foods containing selenium Selenium	Diets high in calcium
Limited –suggestive	Pulses (legumes) Foods containing Vitamin E Alpha-tocopherol	Processed meat Milk and dairy products

	DECREASES RISK	INCREASES RISK
Limited –no conclusion	Cereals (grains) and their products; dietary fibre; potatoes; non-starchy vegetables; fruits; meat; poultry, fish ; eggs; total fat; plant oils; sugar (sucrose); sugary foods and drinks; coffee; tea; alcohol; carbohydrate;; protein; vitamin A; retinol; thiamine; riboflavin; niacin; vitamin C; vitamin D; gamma-tocopherol; vitamin supplements; iron; phosphorus; zinc; other carotenoids; physical activity; energy expenditure; vegetarian diets; Seventh-day Adventist diets; body fatness; abdominal fatness; birth weight; energy intake	
Substantial effect on risk unlikely	Beta-carotene	

1. Research question

The research topic is:

The associations between food, nutrition and physical activity and the risk of prostate cancer.

2. Review team

Name	Current position at IC	Role within team
Teresa Norat	Research Fellow	Principal investigator
Rui Vieira	Data manager	Responsible of the data management, the design and architecture of the database
Doris Chan	Research Assistant	Nutritional epidemiologist, reviewer
Rosa Lau	Research Assistant	Nutritional epidemiologist, reviewer

Review coordinator, WCRF: Rachel Thompson

3. Timeline.

The review for the Second Expert Report¹ ended in December 30th 2005. A pre-publication update extended the search to June 30th 2006 for exposures and cancer sites with suggestive, probable, convincing associations with the exposure of interest.

In order to ensure the completeness of the database, the ICL will repeat the search conducted for the pre-publication update. Therefore, the continuous update will include the articles added to Medline from January 1st 2006. The reviewer will verify that there are not duplicities in the database. With that purpose, a module for article search has been implemented in the interface for data entry.

List of tasks and deadlines for the continuous update on prostate cancer:

Task	Deadline
Start Medline search of relevant articles	1 st September, 2008
Review abstracts and citations identified in initial electronic search. Select papers for complete review	30 th September, 2008
Review relevant papers. Select papers for data extraction*	30 th October, 2008
Data extraction	1 st November, 2008
Start quantitative analysis	28 th March, 2009
End of quantitative analysis	30 th June, 2009
Send report to WCRF-AICR	30 th July, 2009
Transfer Endnote files to WCRF	30 th July, 2009

4. Search strategy

The Continuous update team will use the search strategy established in the SLR Guidelines with the modifications implemented by the SLR centre (Bristol) for the 2nd Expert Report¹.

The search strategy was refined because of the large number of hits from the original search list of exposures. The SLR centre (Bristol) carried out an exercise in MEDLINE to check that the refinements do not automatically exclude studies that should be included. For each refinement, 100 of the ‘hits’ that would be excluded by the refinement were checked. All 100 were correctly excluded (i.e. they would be out when the titles and abstracts were manually checked).

The complete search strategy and the modifications are in Annex 1.

5. Selection of articles

Only articles that match the inclusion criteria will be updated in the database. Pooled analysis and meta-analysis will be identified in the search, but they will not be included in the database. The results of these studies will be used for support in the preparation of the report.

5.1 Inclusion criteria

The articles to be included in the review:

- Have to be included in Medline from January 1st 2006 (closure date of the database for the Second Expert Report¹).

- Have to present results from an epidemiologic study of one of the following types[†]:
 - Randomized controlled trial
 - Group randomized controlled trial (Community trial)
 - Prospective cohort study
 - Nested case-control study
 - Case-cohort study
 - Historical cohort study
- Must have as outcome of interest prostate cancer incidence or mortality. Studies reporting imprecise anatomical definitions, for example urogenital cancer, which includes prostate cancer, will be included.
- Have to present results on the relevant exposures
- Published in English language^{†††*}

[†] *The selection of these study designs is based, first on the number of articles of cohort studies included in the SLR of prostate cancer (145 prospective cohort studies, 44 nested case control studies, 15 historical cohorts, 31 case cohort studies and 13 controlled trials) and second, because the evidence for exposures graded probable in the 2nd Expert Report was based on the results of cohort studies and trials. Filters for study design will not be implemented in the search strategy.*

** The extent of the update has to be adequate to time and resources. For this reason the proposal is to give priority to articles published in English language. Most, if not all, high quality studies will be published in peer-reviewed journals in English language and referenced in the Medline database.*

5.2 Exclusion criteria

The articles to be excluded from the review:

- Are out of the research topic
- Studies focusing on pre-malignant prostate conditions, for example high grade prostate intra epithelial neoplasia
- Studies on early localised prostate cancer (see 7. Outcome for definition)
- Do not report measure of association between the exposure and the risk of prostate cancer
- The measure of the relationship between exposure and outcome is only the mean difference of exposure
- Are supplement to the main manuscript (e.g. Authors' Reply).
- Are published on-line as "Epub ahead of print" or "In Press". The data of these articles will be extracted after the definitive version is released.
- Are not in English language

Pooled analysis and meta-analysis will be used as support for interpretation, but the data will not be included in the database.

6. Exposures

The continuous update will use the labels and exposure codes listed in the SLR Guidelines for the Second Expert Report¹.

During the SLR for the Second Expert Report¹, the SLR centres assigned subcodes for exposures that were more detailed than the WCRF list of exposures. The codification used was not the same in all centres. These differences did not affect the quality of the review in each centre for the Second Expert Report¹. However, with all databases merged into one, it was necessary to recode the exposures to ensure the identity of exposure codes with the corresponding exposure labels in the merged database.

The process of recodification of sub-exposures for its “harmonization” was carried out at ICL. First, all the codes and labels in the merged database were reviewed by Teresa Norat (ICL), Doris Chan (ICL) and Rachel Thompson (WCRF). Second, a list of codes of sub-exposures was defined following as main criteria to keep the same codes defined in the SLR Guidelines and to introduce the minimum number of changes in the database.

The updated list of sub-exposure and codes is in Annex 2. The codes defined in the SLR Guidelines remained the same. The exposures listed represent the minimum list of exposures to be examined. These exposures are programmed in the interface for data entry to facilitate this process.

The actualization of the database with the new sub-exposure codes was implemented by Rui Vieira (Data manager ICL). This process was concluded on June 2008. The ICL team keeps a copy of the merged database containing the original information generated by the SLR centres.

6.1 Biomarkers of exposure

In the SLR for the Second Expert Report¹, biomarkers of exposure were included under the heading and with the code of the corresponding exposure. Some review centres decided to include only biomarkers for which there was some evidence on reliability or validity, while other centres included in the database results on all the biomarkers retrieved in the search, independently of their validity. During the process of evaluation of the evidence, the Panel of Experts took in consideration the validity of the reported biomarkers.

The SLR centre on prostate cancer (Bristol) prepared a list of biomarkers to be included and excluded, based on data of studies on validity and repeatability of the biomarkers. The list of included and excluded biomarkers and the reasons for exclusion prepared by the SLR centre Bristol are in Annex 3.

The continuous update on prostate cancer will use the same guidelines for exclusion of biomarkers, although the biomarkers excluded from the SLR on prostate cancer may have been included in SLRs of other cancer sites. Results on new biomarkers of exposure will be included in the continuous update.

The excluded biomarkers are:

Vit D: 1.25 (OH)₂D, Alkaline phosphatase activity (serum)

Iron (serum, hair, nails)
Copper (plasma, serum, hair)
Glutathione peroxidase (plasma, serum, erythrocytes, blood)
Zinc, metallotein levels (any)
Lipids: total fats (any)
Cholesterol, LDL (any)
Lipoprotein levels (serum)
Monounsaturated fatty acids (oleic acid) (plasma, adipose tissue)
Saturated fatty acids (palmitic acid, stearic acids) (plasma)
Protein (any)

Biomarkers of effect of exposure and biomarkers of cancer are not included in this review.

7. Outcome

The outcome of interest is prostate cancer encompassing incidence and mortality. Results of studies on incidence and mortality will be presented separately.

Due to PSA testing, a substantial proportion of prostate cancer diagnoses can be of early localised disease. For each result it is very important to extract whether the analyses are restricted to cases of advanced or aggressive disease. The characteristics of the outcome will be recorded. The aim is to do separate analysis for advanced/aggressive cancers.

The definition of aggressive or advanced cancer was agreed during the SLR of prostate cancer and defined as cancers reported in any of the following:

- (a) stage 3-4 on the AJCC 1992 classification
- (b) advanced cancer
- (c) advanced or metastatic cancer
- (d) metastatic cancer
- (e) stage C or D on the Whitmore/Jewertt scale
- (f) fatal cancer
- (g) high stage or grade
- (h) Gleason grade ≥ 7

8. Databases

Only the Medline database will be searched. Data provided from the SLR Prostate cancer for the Second Expert Report¹ indicates that 95% of the articles included in the review have been retrieved from the Medline database.

9. Hand searching for cited references

For feasibility reasons, journals will not be hand searched in the continuous update.

Hand searching, and searching in other databases will be done after recommendation of the Continuous Update Panel or if there is some evidence that an important study has been missed by the search strategy.

10. Retrieving papers

The abstracts from the initial search results from PubMed will be reviewed by one person to assess each reference as to whether it is relevant and potentially relevant.

The complete papers of relevant and potentially relevant references and of references that cannot be excluded upon reading the title and abstracts will be retrieved. A second assessment will be done after review of the complete papers.

The assessment of papers will be checked by a second reviewer. It is envisaged that 10% of the assessment should be checked.

The IC team uses resources at Imperial College to retrieve the papers identified as satisfying the inclusion criteria. This should cover most of the online journal. For articles not accessible through the IC library, funds provided by WCRF-AICR will be required.

11. Labelling of references

For consistency with the previous data collected during the SLR process for the Second Expert Report¹, the Imperial College team will use the same labelling of references: the unique identifier for a particular reference will be constructed using a 3-letter code to represent the cancer site (e.g. PRO for prostate cancer), followed by a 5-digit number that will be allocated in sequence.

12. Reference Manager Files

Reference Manager databases are generated in the continuous update containing the references of the initial search.

- 1) One of the customized fields (User Def 1) is named 'inclusion' and this field is marked 'included', 'excluded' for each paper, thereby indicating which papers are deemed potentially relevant based on an assessment of the title and abstract.
- 2) One of the customized fields (User Def 2) is named 'reasons' and this field should include the reason for exclusion for each paper.
- 3) The study identifier should be entered under the field titled 'label'.
- 4) One of the customized fields (User Def 3) is named "study design". This field indicates the study design of each paper:

Case-study / case series
Cross-sectional study
Randomised controlled trial
Group randomised control trial
Uncontrolled trial
Ecologic study
Case-control study
Non-randomised control trial

Prospective cohort study
Nested case-control study
Historical cohort study
Case-cohort study
Time series with multiple measurements
Case only study with prospective exposure measurement
Case only study with retrospective exposure measurement

The Reference Management databases will be converted to EndNote and sent to WCRF Secretariat.

13. Data extraction

The Access databases generated during the SLR for the Second Expert Report¹ have been merged into one database at Imperial College.

The IC team will update the merged database using a new interface created at Imperial College. The interface allows the update of all variables included in the Access databases for the SLR for the Second Expert Report¹, including quality characteristics and results, the variables for which the exposure – disease association was adjusted for, the strategy of analysis, the validity of the measurements and whether analyses were performed that attempted to correct for the likely effect of measurement error in the exposure variable.

The study design algorithm devised for use of the SLR centres for the Second Expert Report¹ will be used to allocate study designs to papers (SLR specification manual – version 15 pp 123). In some cases it will be appropriate to assign more than one design to a particular paper because the methods for assessment of different exposures may vary, because the data analyses correspond to more than one study design (e.g. analyses in the entire cohort and nested case-control).

13.1 Quality control

Ideally, data extraction should be performed in duplicate for all papers. This is not feasible with the available resources. Instead, 10% of the data extracted from the studies that are included throughout the year of continuous update will be checked by a second reviewer at Imperial College.

Similarly 10% of the studies indicated as excluded will be checked by a second reviewer.

Some automatic checks will be conducted in the data:

- the confidence interval contains the effect estimate and is symmetrical
- the sum of cases and non case individuals in the categories of exposures add up to the total number of cases and non case individuals (for analysis that are not in subgroups). If these exceed the total number of cases and controls or are lower than 20% the study will be flagged and checked.

13.2 Choice of Result

The effect measure estimated with all the models reported in the paper should be extracted. The models should be labelled as not adjusted, minimally adjusted, intermediately adjusted and maximally adjusted. In addition, the IC reviewer should

indicate a “best model” for inclusion in reports. Unadjusted results will be used only when no others were given.

The best model has to be controlled for confounding by age. The control of confounding by age can be done by adjustment or by matching. Where there is more than one model adjusting for age, the most adjusted one will be considered to be the best model. Exception to this criterion will be “mechanistic” models, adjusting for variables likely to be in the causal pathway. Examples of mechanistic models are:

- 1) results for fruits and vegetables adjusted for vitamin E or selenium
- 2) results for meat adjusted for saturated fatty acids
- 3) results for fish adjusted for n-3 fatty acids
- 4) results for milk and dairy products adjusted for calcium
- 5) results for BMI adjusted for height or weight (or other similar combinations)
- 6) results for waist-to-hip ratio adjusted for either waist or hip circumference

When such results (over adjusted results) are reported, the most adjusted results that are not over adjusted will be extracted.

Potential risk factors of prostate cancer are:

Race
Energy intake
PSA and DRE screening history
Marital status
Height
Socioeconomic status
Physical activity
Body mass index
Smoking status
Personal history of diabetes
Family history of prostate cancer

Sometimes, some of the potential risk factors are not kept in the model because their inclusion does not modify the risk estimates. If this is specified in the article text, this model should also be considered the “best model”.

13.3 Effect modification

The IC team should report whether interaction terms were included in models and extract the results, in particular any statistical tests of heterogeneity across strata. This information was not collected in a standardized way in the SLR. In many cases, a note was added in the database indicating that an interaction term was reported in the article. The IC team envisage developing a module for data entry of results of analysis on effect modifiers and interactions, but this facility is at its early stage of development.

13.4 Gene-nutrient interaction

No attempt was made to critically appraise or analyse the studies that reported gene-nutrient interactions in the Second Expert Report¹. The results of these studies were described in the narrative under the relevant exposures.

A separate protocol to handle gene-nutrient interactions is in the process of being developed.

13.5 Multiple articles

Data should be extracted for each individual paper, even if there is more than one paper from any one study, unless the information is identical. The most appropriate set of data on a particular exposure will be selected amongst the papers published on a study to ensure there is no duplication of data from the same study in an analysis. To facilitate the detection of multiple reports from the same study, the study name in each article should be extracted.

If needed, the IC team should contact the authors for clarification. If the matter remains unresolved the review coordinator of the continuous update will discuss the issue with the WCRF Secretariat and the CUP, if necessary.

14. Reports

14.1 Content of the report:

14.1.1 Results of the search

Information on number of records downloaded, number of papers thought potentially relevant after reading titles and abstracts and number of included relevant papers. The reasons for excluding papers should also be described.

14.1.2 Description of studies identified in the continuous update

Amount of data and study types (i.e. numbers of different types of studies)
Populations studied
Exposures identified
Outcomes identified

14.1.3 Summary of number of studies by exposure and study type, separated on new (studies identified in the continuous update) and total.

14.1.4 Tabulation of study characteristics

Information on the characteristics (e.g. population, exposure, outcome, study design) and results of the study (e.g. direction and magnitude) of the new studies should be summarised in tables using the same format as for the SLR for the Second Expert Report¹.

Within this table the studies should be ordered according to design (trials, cohort studies). The results will be presented separately for advanced/aggressive prostate cancer.

A summary table with number of studies by exposure should be produced:

Exposure Code	Name	Outcome	Number of controlled trials			Number of cohort studies		
			Total	SLR	Continuous update	Total	SLR	Continuous update

A table of study characteristics, in two parts below, should be produced:

Author, Year, country, WCRF Code	Study design	Country, Ethnicity, other characteristics	Age (mean)	Cases (n)	Non cases (n/person-years)	Case ascertainment	Follow-up (years)
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Assessment details	Category of exposure	Subgroup	No cat	OR	(95% CI)	p trend	Adjustment factors						
							A	B	C	D	E	F	G

Where

A : Age

B : Socioeconomic status

C : PSA or DRE screening

D : Anthropometry: Height or BMI

E : Energy intake, other dietary factors

F : Race

G : Others, e.g. family history, smoking, physical activity, marital status

14.2 Data analysis

Meta-analytic and narrative aspects of the data analysis will complement each other. The meta-analyses will not solely focus on simple binary (“high-low”) comparisons but also examine the evidence for dose-response effects. Exposure effect estimates from observational studies may be affected by confounding, selection bias, and error in measurement of exposure variables. The existence of a dose-response relation between exposure and outcome can help address uncertainties about misclassification effects and helps strengthen causal reasoning.

14.2.1 When to do a meta-analysis

A meta-analysis for a particular exposure and outcome will be conducted when 3 or more trials or cohort studies has been published in the year, and if the new and the previous results totalise to more than 3 trials or 5 cohort studies.

The meta-analysis will include also the study results extracted during the SLR and included in the merged database. Special care will be taken to avoid including more than once the results of the same study (e.g. previous analyses and re-analyses after a longer follow-up).

14.2.2 Methods

The methods that will be used to do meta-analyses will be the same methods used for the Second Expert Report¹.

In meta-analysis of “high-low” comparisons, summary RR estimates with their corresponding 95% CIs will be derived with the method of DerSimonian and Laird³ using the assumption of a random effects model that incorporated between-study variability.

To estimate the dose-response relationship, category-specific risk estimates will be transformed into estimates of the relative risk (RR) associated with a unit of increase in exposure by use of the method of generalised least-squares for trend estimation⁴. The unit of increment will be kept as the same unit used in the SLR. We will assign to each exposure category the mid-point for closed categories, and the median for open categories (assuming a normal distribution for exposure)⁵. The relative risk estimates for each unit of increase of the exposure will be combined by use of random-effect meta-analysis³.

We will use the “best” (most adjusted risk estimate) from each study. Heterogeneity between studies will be assessed with the I^2 statistic as a measure of the proportion of total variation in estimates that is due to heterogeneity, where I^2 values of 25%, 50%, and 75% correspond to cut-off points for low, moderate, and high degrees of heterogeneity⁶.

When possible, meta-regression should be performed to investigate sources of heterogeneity. The variables that will be examined as sources of heterogeneity are geographic area (North-America –Non black population, North-America –Black population, Europe, Asia, Other); year of publication, outcome (incidence or mortality), stage of disease (all combined or not specified and aggressive/advanced staged).

Other variables that may be considered as source of heterogeneity are characterisation of the exposure (FFQ, recall, diary, anthropometry etc.), exposure range (including correction for measurement error, length of intervention), adjustment for confounders, age at recruitment and time of follow-up. However, the interpretation should be cautious. If a considerable number of study characteristics are considered as possible explanations for heterogeneity in a meta-analysis containing only a small number of studies, then there is a high probability that one or more will be found to explain heterogeneity, even in the absence of real associations with between the study characteristics and the size of associations.

A usual method of assessing and displaying heterogeneity, we will construct and examine forest plots. Publication bias will be examined in funnel plots.

We will use STATA version 9.0 (College Station, TX, USA) to analyse data.

14.2.3 Missing values

The data needed to estimate the dose-response associations are often incompletely reported, which may result in exclusion of results from meta-analyses. Failure to

include all available evidence will reduce precision of summary estimates and may also lead to bias if propensity to report results in sufficient detail is associated with the magnitude and/or direction of associations.

A recent review showed that only 64% of the results of cohort studies provide enough data to be included in dose-response meta-analysis⁷. Moreover, results that showed evidence of an association were more likely to be usable in dose-response meta-analysis than results that found no such evidence. Insufficient detail in reporting of results of observational studies can lead to exclusion of these results from meta-analyses and is an important threat to the validity of systematic reviews of such research.

We will therefore use methods to compute missing data recently summarized⁷. The information required for data to be usable for meta-analysis, for each type of result is:

Dose-response data (regression coefficients)

Estimated odds, risk, or hazard ratio per unit increase in exposure with confidence interval (or standard error of log ratio or p value)
Unit of measurement

Quantile-based or category data

No. of cases and non cases (or person-time denominator for cohort studies) in each group; or total number of cases and non cases (or study size) plus explicitly defined equal-sized groups (for quantile-based data)
Estimated odds, risk, or hazard ratios with confidence intervals (or standard error of log ratio or p value) compared with the baseline group, for each non baseline group (if these are not reported, unadjusted odds ratios can be calculated from the numbers of cases and controls)
Range, mean, or median of exposure in each group
Unit of measurement

The most frequently occurring problems in reporting and suggested solutions to make results usable in a dose-response meta-analysis are:

Type of data	Problem	Assumptions
Dose-response data	Serving size is not quantified or ranges are missing, but group descriptions are given	Use serving size recommended in SLR Prostate ¹ (Annex 4)
	Standard error missing	The p value (either exact or the upper bound) is used to estimate the standard error
Quantile-based data	Numbers of controls (or the denominator in cohort studies) are missing	Group sizes are assumed to be approximately equal
	Odds ratio is missing	Unadjusted odds ratios are calculated by using numbers of cases and controls in each group
	Confidence interval is missing	Standard error and hence confidence interval were calculated from raw numbers (although doing so may result in a somewhat smaller standard error than would be obtained in an adjusted analysis)
	Group mean are missing	This information may be estimated by using the method of Chene and Thompson ⁵ with a normal or lognormal distribution, as appropriate, or by taking midpoints (scaled in unbounded groups according to group numbers) if the number of groups is too small to calculate a distribution
Category data	Numbers of cases and controls (or the denominator in cohort studies) is missing	These numbers may be inferred based on numbers of cases and the reported odds ratio (proportions will be correct unless adjustment for confounding factors considerably alter the crude odds ratios)

14.2.4 Influence of updated studies in the overall results

We will do influence-analyses to assess the effect of each updated study on the summary risk estimates⁸.

References

1. World Cancer Research Fund/ American Institute for Cancer Research. Systematic Literature Review – Support Resource. In : Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective. Washington DC: AICR , 2007
2. World Cancer Research Fund/ American Institute for Cancer Research. Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective. page 305 Washington DC: AICR , 2007
3. DerSimonian R, Laird N (1986) Meta-analysis in clinical trials. *Control Clin Trials* 7:177–188
4. N Orsini, R Bellocco and S Greenland, Generalized least squares for trend estimation of summarized dose-response data, *Stata J* 6 (2006), pp. 40–57
5. Chêne G, Thompson SG. Methods for summarizing the risk associations of quantitative variables in epidemiologic studies in a consistent form. *Am J Epidemiol.* 1996;144(6):610-21.
6. JP Higgins and SG Thompson, Quantifying heterogeneity in a meta-analysis, *Stat Med* 21 (2002), pp. 1539–1558.
7. Bekkering GE et al. How much of the data published in observational studies of the association between diet and prostate or bladder cancer is usable for meta-analysis? *Am J Epidemiol* (2008);167(9):1017-26.
8. A Tobias, Assessing the influence of a single study in meta-analysis, *Stata Tech Bull* 47 (1999), pp. 15–17.

Annex 1.

WCRF - PUBMED SEARCH STRATEGY (with modifications implemented by the SLR centre Bristol)

a) Searching for all studies relating to prostate cancer:

#1 prostatic neoplasms[MeSH Terms]

#2 (prostat* AND cancer*)[tiab]

#3 (prostat* AND neoplasm*)[tiab]

#4 (prostat* AND carcinoma*)[tiab]

#5 (prostat* AND tumo*)[tiab]

#6 #1 OR #2 OR #3 OR #4 OR #5

b) Searching for all studies relating to food, nutrition and physical activity:

#1 diet therapy[MeSH Terms] OR nutrition[MeSH Terms]

#2 diet[tiab] OR diets[tiab] OR dietetic[tiab] OR dietary[tiab] OR eating[tiab] OR intake[tiab] OR nutrient*[tiab] OR nutrition[tiab] OR vegetarian*[tiab] OR vegan*[tiab] OR "seventh day adventist"[tiab] OR macrobiotic[tiab]

#3 food and beverages[MeSH Terms]

#4 food*[tiab] OR cereal*[tiab] OR grain*[tiab] OR granary[tiab] OR wholegrain[tiab] OR wholewheat[tiab] OR roots[tiab] OR plantain*[tiab] OR tuber[tiab] OR tubers[tiab] OR vegetable*[tiab] OR fruit*[tiab] OR pulses[tiab] OR beans[tiab] OR lentils[tiab] OR chickpeas[tiab] OR legume*[tiab] OR soy[tiab] OR soya[tiab] OR nut[tiab] OR nuts[tiab] OR peanut*[tiab] OR groundnut*[tiab] OR (seeds[tiab] and (diet*[tiab] OR food*[tiab])) OR meat[tiab] OR beef[tiab] OR pork[tiab] OR lamb[tiab] OR poultry[tiab] OR chicken[tiab] OR turkey[tiab] OR duck[tiab] OR fish[tiab] OR ((fat[tiab] OR fats[tiab] OR fatty[tiab]) AND (diet*[tiab] or food*[tiab] or adipose[tiab] or blood[tiab] or serum[tiab] or plasma[tiab])) OR egg[tiab] OR eggs[tiab] OR bread[tiab] OR (oils[tiab] AND and (diet*[tiab] or food*[tiab] or adipose[tiab] or blood[tiab] or serum[tiab] or plasma[tiab])) OR shellfish[tiab] OR seafood[tiab] OR sugar[tiab] OR syrup[tiab] OR dairy[tiab] OR milk[tiab] OR herbs[tiab] OR spices[tiab] OR chilli[tiab] OR chillis[tiab] OR pepper*[tiab] OR condiments[tiab] OR tomato*[tiab]

#5 fluid intake[tiab] OR water[tiab] OR drinks[tiab] OR drinking[tiab] OR tea[tiab] OR coffee[tiab] OR caffeine[tiab] OR juice[tiab] OR beer[tiab] OR spirits[tiab] OR liquor[tiab] OR wine[tiab] OR alcohol[tiab] OR alcoholic[tiab] OR beverage*[tiab] OR (ethanol[tiab] and (drink*[tiab] or intake[tiab] or consumption[tiab])) OR yerba mate[tiab] OR ilex paraguariensis[tiab]

#6 pesticides[MeSH Terms] OR fertilizers[MeSH Terms] OR "veterinary drugs"[MeSH Terms]

#7 pesticide*[tiab] OR herbicide*[tiab] OR DDT[tiab] OR fertiliser*[tiab] OR fertilizer*[tiab] OR organic[tiab] OR contaminants[tiab] OR contaminate*[tiab] OR veterinary drug*[tiab] OR polychlorinated dibenzofuran*[tiab] OR PCDF*[tiab] OR polychlorinated dibenzodioxin*[tiab] OR PCDD*[tiab] OR polychlorinated biphenyl*[tiab] OR PCB*[tiab] OR cadmium[tiab] OR arsenic[tiab] OR chlorinated hydrocarbon*[tiab] OR microbial contamination*[tiab]

#8 food preservation[MeSH Terms]

#9 mycotoxin*[tiab] OR aflatoxin*[tiab] OR pickled[tiab] OR bottled[tiab] OR bottling[tiab] OR canned[tiab] OR canning[tiab] OR vacuum pack*[tiab] OR refrigerate*[tiab] OR refrigeration[tiab] OR cured[tiab] OR smoked[tiab] OR preserved[tiab] OR preservatives[tiab] OR nitrosamine[tiab] OR hydrogenation[tiab] OR

fortified[tiab] OR additive*[tiab] OR colouring*[tiab] OR coloring*[tiab] OR flavouring*[tiab] OR flavoring*[tiab] OR nitrates[tiab] OR nitrites[tiab] OR solvent[tiab] OR solvents[tiab] OR ferment*[tiab] OR processed[tiab] OR antioxidant*[tiab] OR genetic modif*[tiab] OR genetically modif*[tiab] OR vinyl chloride[tiab] OR packaging[tiab] OR labelling[tiab] OR phthalates[tiab]

#10 cookery[MeSH Terms]

#11 cooking[tiab] OR cooked[tiab] OR grill[tiab] OR grilled[tiab] OR fried[tiab] OR fry[tiab] OR roast[tiab] OR bake[tiab] OR baked[tiab] OR stewing[tiab] OR stewed[tiab] OR casserol*[tiab] OR broil[tiab] OR broiled[tiab] OR boiled[tiab] OR (microwave[tiab] and (diet*[tiab] or food*[tiab])) OR microwaved[tiab] OR re-heating[tiab] OR reheating[tiab] OR heating[tiab] OR re-heated[tiab] OR heated[tiab] OR poach[tiab] OR poached[tiab] OR steamed[tiab] OR barbecue*[tiab] OR chargrill*[tiab] OR heterocyclic amines[tiab] OR polycyclic aromatic hydrocarbons[tiab]

#12 ((carbohydrates[MeSH Terms] OR proteins[MeSH Terms]) and (diet*[tiab] or food*[tiab])) OR sweetening agents[MeSH Terms]

#13 salt[tiab] OR salting[tiab] OR salted[tiab] OR fiber[tiab] OR fibre[tiab] OR polysaccharide*[tiab] OR starch[tiab] OR starchy[tiab] OR carbohydrate*[tiab] OR lipid*[tiab] OR ((linoleic acid*[tiab] OR sterols[tiab] OR stanols[tiab]) AND (diet*[tiab] or food*[tiab] or adipose [tiab] or blood[tiab] or serum[tiab] or plasma[tiab])) OR sugar*[tiab] OR sweetener*[tiab] OR saccharin*[tiab] OR aspartame[tiab] OR acesulfame[tiab] OR cyclamates[tiab] OR maltose[tiab] OR mannitol[tiab] OR sorbitol[tiab] OR sucrose[tiab] OR xylitol[tiab] OR cholesterol[tiab] OR protein[tiab] OR proteins[tiab] OR hydrogenated dietary oils[tiab] OR hydrogenated lard[tiab] OR hydrogenated oils[tiab]

#14 vitamins[MeSH Terms]

#15 supplements[tiab] OR supplement[tiab] OR vitamin*[tiab] OR retinol[tiab] OR carotenoid*[tiab] OR tocopherol[tiab] OR folate*[tiab] OR folic acid[tiab] OR methionine[tiab] OR riboflavin[tiab] OR thiamine[tiab] OR niacin[tiab] OR pyridoxine[tiab] OR cobalamin[tiab] OR mineral*[tiab] OR (sodium[tiab] AND (diet*[tiab] or food*[tiab])) OR iron[tiab] OR ((calcium[tiab] AND (diet*[tiab] or food*[tiab] or supplement*[tiab])) OR selenium[tiab] OR (iodine[tiab] AND and (diet*[tiab] or food*[tiab] or supplement*[tiab] or deficiency)) OR magnesium[tiab] OR potassium[tiab] OR zinc[tiab] OR copper[tiab] OR phosphorus[tiab] OR manganese[tiab] OR chromium[tiab] OR phytochemical[tiab] OR allium[tiab] OR isothiocyanate*[tiab] OR glucosinolate*[tiab] OR indoles[tiab] OR polyphenol*[tiab] OR phytoestrogen*[tiab] OR genistein[tiab] OR saponin*[tiab] OR coumarin*[tiab] OR lycopene[tiab]

#16 physical fitness[MeSH Terms] OR exertion[MeSH Terms] OR physical endurance[MeSH Terms] or walking[MeSH Terms]

#17 recreational activit*[tiab] OR household activit*[tiab] OR occupational activit*[tiab] OR physical activit*[tiab] OR physical inactivit*[tiab] OR exercise[tiab] OR exercising[tiab] OR energy intake[tiab] OR energy expenditure[tiab] OR energy balance[tiab] OR energy density[tiab]

#18 body weight [MeSH Terms] OR anthropometry[MeSH Terms] OR body composition[MeSH Terms] OR body constitution[MeSH Terms]

#19 weight loss[tiab] or weight gain[tiab] OR anthropometry[tiab] OR birth weight[tiab] OR birthweight[tiab] OR birth-weight[tiab] OR child development[tiab] OR height[tiab] OR body composition[tiab] OR body mass[tiab] OR BMI[tiab] OR obesity[tiab] OR obese[tiab] OR overweight[tiab] OR over-weight[tiab] OR over weight[tiab] OR skinfold measurement*[tiab] OR skinfold thickness[tiab] OR DEXA[tiab] OR bio-impedence[tiab] OR waist circumference[tiab] OR hip circumference[tiab] OR waist hip ratio*[tiab]

#20 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR

#12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19
#21 animal[MeSH Terms] NOT human[MeSH Terms]
#22 #20 NOT #21

Annex 2. List of exposure codes

1 Patterns of diet

1.1 Regionally defined diets

*1.1.1 Mediterranean diet

Include all regionally defined diets, evident in the literature. These are likely to include Mediterranean, Mesoamerican, oriental, including Japanese and Chinese, and “western type”.

1.2 Socio-economically defined diets

To include diets of low-income, middle-income and high-income countries (presented, when available in this order). Rich and poor populations within low-income, middle-income and high-income countries should also be considered. This section should also include the concept of poverty diets (monotonous diets consumed by impoverished populations in the economically-developing world mostly made up of one starchy staple, and may be lacking in micronutrients).

1.3 Culturally defined diets

To include dietary patterns such as vegetarianism, vegan diets, macrobiotic diets and diets of Seventh-day Adventists.

1.4 Individual level dietary patterns

To include work on factor and cluster analysis, and various scores and indexes (e.g. diet diversity indexes) that do not fit into the headings above.

1.5 Other dietary patterns

Include under this heading any other dietary patterns present in the literature, that are not regionally, socio-economically, culturally or individually defined.

1.6 Breastfeeding

1.6.1 Mother

Include here also age at first lactation, duration of breastfeeding, number of children breast-fed

1.6.2 Child

Results concerning the effects of breastfeeding on the development of cancer should be disaggregated into effects on the mother and effects on the child. Wherever

possible detailed information on duration of total and exclusive breastfeeding, and of complementary feeding should be included.

1.7 Other issues

For example results related to diet diversity, meal frequency, frequency of snacking, dessert-eating and breakfast-eating should be reported here. Eating out of home should be reported here.

2 Foods

*2.0.1 Plant foods

2.1 Starchy foods

2.1.1 Cereals (grains)

* 2.1.1.0.1 Rice, pasta, noodles

* 2.1.1.0.2 Bread

* 2.1.1.0.3 Cereal

** Report under this subheading the cereals when it is not specified if they are wholegrain or refined cereals (e.g. fortified cereals)*

2.1.1.1 Wholegrain cereals and cereal products

* 2.1.1.1.1 Wholegrain rice, pasta, noodles

* 2.1.1.1.2 Wholegrain bread

* 2.1.1.1.3 Wholegrain cereal

2.1.1.2 Refined cereals and cereal products

* 2.1.1.2.1 Refined rice, pasta, noodles

* 2.1.1.2.2 Refined bread

* 2.1.1.2.3 Refined cereal

2.1.2 Starchy roots, tubers and plantains

* 2.1.2.1 Potatoes

2.1.3 Other starchy foods

**Report polenta under this heading*

2.2 Fruit and (non-starchy) vegetables

Results for “fruit and vegetables” and “fruits, vegetables and fruit juices” should be reported here. If the definition of vegetables used here is different from that used in the first report, this should be highlighted.

2.2.1 Non-starchy vegetables

This heading should be used to report total non-starchy vegetables. If results about specific vegetables are reported they should be recorded under one of the sub-headings below or if not covered, they should be recorded under '2.2.1.5 other'.

2.2.1.1 Non-starchy root vegetables and tubers

*2.2.1.1.1 Carrots

2.2.1.2 Cruciferous vegetables

2.2.1.3 Allium vegetables

2.2.1.4 Green leafy vegetables (not including cruciferous vegetables)

2.2.1.5 Other non-starchy vegetables

*2.2.1.5.13 Tomatoes

*2.2.1.5.1 Fresh beans (e.g. string beans, French beans) and peas

Other non-starchy vegetables' should include foods that are botanically fruits but are eaten as vegetables, e.g. courgettes. In addition vegetables such as French beans that do not fit into the other categories, above.

If there is another sub-category of vegetables that does not easily fit into a category above eg salted root vegetables (ie you do not know if it is starchy or not) then report under 2.2.1.5. and note the precise definition used by the study. If in doubt, enter the exposure more than once in this way.

2.2.1.6 Raw vegetables

This section should include any vegetables specified as eaten raw. Results concerning specific groups and type of raw vegetable should be reported twice i.e. also under the relevant headings 2.2.1.1 –2.2.1.5.

2.2.2 Fruits

*2.2.2.0.1 Fruit, dried

*2.2.2.0.2 Fruit, canned

*2.2.2.0.3 Fruit, cooked

2.2.2.1 Citrus fruit

2.2.2.1.1 Oranges

2.2.2.1.2 Other citrus fruits (e.g. grapefruits)

2.2.2.2 Other fruits

*2.2.2.2.1 Bananas

*2.2.2.2.4 Melon

*2.2.2.2.5 Papaya

*2.2.2.2.7 Blueberries, strawberries and other berries

*2.2.2.2.8 Apples, pears

*2.2.2.2.10 Peaches, apricots, plums

*2.2.2.2.11 Grapes

If results are available that consider other groups of fruit or a particular fruit please report under 'other', specifying the grouping/fruit used in the literature.

2.3 Pulses (legumes)

*2.3.1 Soya, soya products

- *2.3.1.1 Miso, soya paste soup
- *2.3.1.2 Soya juice
- *2.3.1.4 Soya milk
- *2.3.1.5 Tofu

*2.3.2 Dried beans, chickpeas, lentiles

*2.3.4 Peanuts, peanut products

Where results are available for a specific pulse/legume, please report under a separate heading.

2.4 Nuts and Seeds

To include all tree nuts and seeds, but not peanuts (groundnuts). Where results are available for a specific nut/seed, e.g. brazil nuts, please report under a separate heading.

2.5 Meat, poultry, fish and eggs

Wherever possible please differentiate between farmed and wild meat, poultry and fish.

2.5.1 Meat

This heading refers only to red meat: essentially beef, lamb, pork from farmed domesticated animals either fresh or frozen, or dried without any other form of preservation. It does not refer to poultry or fish.

Where there are data for offal (organs and other non-flesh parts of meat) and also when there are data for wild and non-domesticated animals, please show these separately under this general heading as a subcategory.

2.5.1.1 Fresh Meat

2.5.1.2 Processed meat

- *2.5.1.2.1 Ham
- *2.5.1.2.1.7 Burgers
- *2.5.1.2.8 Bacon
- *2.5.1.2.9 Hot dogs
- *2.5.1.2.10 Sausages

Repeat results concerning processed meat here and under the relevant section under 4. Food Production and Processing. Please record the definition of 'processed meat' used by each study.

2.5.1.3 Red meat

- *2.5.1.3.1 Beef
- *2.5.1.3.2 Lamb
- *2.5.1.3.3 Pork
- *2.5.1.3.6 Horse, rabbit, wild meat (game)

Where results are available for a particular type of meat, e.g. beef, pork or lamb, please report under a separate heading.

Show any data on wild meat (game) under this heading as a separate sub-category.

2.5.1.4 Poultry

Show any data on wild birds under this heading as a separate sub-category.

*2.5.1.5 Offals, offal products (organ meats)

2.5.2 Fish

- *2.5.2.3 Fish, processed (dried, salted, smoked)
- *2.5.2.5 Fatty Fish
- *2.5.2.7 Dried Fish
- *2.5.2.9 White fish, lean fish

2.5.3 Shellfish and other seafood

2.5.4 Eggs

2.6 Fats, oils and sugars

2.6.1 Animal fats

- *2.6.1.1 Butter
- *2.6.1.2 Lard
- *2.6.1.3 Gravy
- *2.6.1.4 Fish oil

2.6.2 Plant oils

2.6.3 Hydrogenated fats and oils

*2.6.3.1 Margarine

Results concerning hydrogenated fats and oils should be reported twice, here and under 4.3.2 Hydrogenation

2.6.4 Sugars

This heading refers to added (extrinsic) sugars and syrups as a food, that is refined sugars, such as table sugar, or sugar used in bakery products.

2.7 Milk and dairy products

Results concerning milk should be reported twice, here and under 3.3 Milk

*2.7.1 Milk, fresh milk, dried milk

*2.7.1.1 Whole milk, full-fat milks

*2.7.1.2 Semi skimmed milk, skimmed milk, low fat milk, 2% Milk

*2.7.2 Cheese

*2.7.2.1 Cottage cheese

*2.7.2.2 Cheese, low fat

*2.7.3 Yoghurt, buttermilk, sour milk, fermented milk drinks

*2.7.3.1 Fermented whole milk

*2.7.3.2 Fermented skimmed milk

*2.7.7 Ice cream

2.8 Herbs, spices, condiments

*2.8.1 Ginseng

*2.8.2 Chili pepper, green chili pepper, red chili pepper

2.9 Composite foods

Eg, snacks, crisps, desserts, pizza. Also report any mixed food exposures here ie if an exposure is reported as a combination of 2 or more foods that cross categories (eg bacon and eggs). Label each mixed food exposure.

*2.9.1 Cakes, biscuits and pastry

*2.9.2 Cookies

*2.9.3 Confectionery

*2.9.4 Soups

*2.9.5 Pizza

*2.9.6 Chocolate, candy bars

*2.9.7 Snacks

3 Beverages

3.1 Total fluid intake

3.2 Water

3.3 Milk

For results concerning milk please report twice, here and under 2.7 Milk and Dairy Products.

3.4 Soft drinks

Soft drinks that are both carbonated and sugary should be reported under this general heading. Drinks that contain artificial sweeteners should be reported separately and labelled as such.

3.4.1 Sugary (not carbonated)

3.4.2 Carbonated (not sugary)

The precise definition used by the studies should be highlighted, as definitions used for various soft drinks vary greatly.

*3.5 Fruit and vegetable juices

*3.5.1 Citrus fruit juice

*3.5.2 Fruit juice

*3.5.3 Vegetable juice

*3.5.4 Tomato juice

3.6 Hot drinks

3.6.1 Coffee

3.6.2 Tea

Report herbal tea as a sub-category under tea.

3.6.2.1 Black tea

3.6.2.2 Green tea

3.6.3 Maté

3.6.4 Other hot drinks

3.7 Alcoholic drinks

3.7.1 Total

3.7.1.1 Beers

3.7.1.2 Wines

3.7.1.3 Spirits

3.7.1.4 Other alcoholic drinks

4 Food production, preservation, processing and preparation

4.1 Production

4.1.1 Traditional methods (*to include 'organic'*)

4.1.2 Chemical contaminants

Only results based on human evidence should be reported here (see instructions for dealing with mechanistic studies). Please be comprehensive and cover the exposures listed below:

4.1.2.1 Pesticides

- 4.1.2.2 DDT
- 4.1.2.3 Herbicides
- 4.1.2.4 Fertilisers
- 4.1.2.5 Veterinary drugs
- 4.1.2.6 Other chemicals
 - 4.1.2.6.1 Polychlorinated dibenzofurans (PCDFs)
 - 4.1.2.6.2 Polychlorinated dibenzodioxins (PCDDs)
 - 4.1.2.6.3 Polychlorinated biphenyls (PCBs)

4.1.2.7 Heavy metals

- 4.1.2.7.1 Cadmium
- 4.1.2.7.2 Arsenic

4.1.2.8 Waterborne residues

4.1.2.8.1 Chlorinated hydrocarbons

4.1.2.9 Other contaminants

Please also report any results that cover the cumulative effect of low doses of contaminants in this section.

4.2 Preservation

4.2.1 Drying

4.2.2 Storage

4.2.2.1 Mycotoxins

- 4.2.2.1.1 Aflatoxins
- 4.2.2.1.2 Others

4.2.3 Bottling, canning, vacuum packing

4.2.4 Refrigeration

4.2.5 Salt, salting

4.2.5.1 Salt

4.2.5.2 Salting

4.2.5.3 Salted foods

4.2.5.3.1 Salted animal food

4.2.5.3.2 Salted plant food

4.2.6 Pickling

4.2.7 Curing and smoking

4.2.7.1 Cured foods

4.2.7.1.1 Cured meats

4.2.7.1.2 Smoked foods

For some cancers e.g. colon, rectum, stomach and pancreas, it may be important to report results about specific cured foods, cured meats and smoked meats. N-nitrosamines should also be covered here.

4.3 Processing

4.3.1 Refining

Results concerning refined cereals and cereal products should be reported twice, here and under 2.1.1.2 refined cereals and cereal products.

4.3.2 Hydrogenation

Results concerning hydrogenated fats and oils should be reported twice, here and under 2.6.3 Hydrogenated fats and oils

4.3.3 Fermenting

4.3.4 Compositional manipulation

4.3.4.1 Fortification

4.3.4.2 Genetic modification

4.3.4.3 Other methods

4.3.5 Food additives

4.3.5.1 Flavours

Report results for monosodium glutamate as a separate category under 4.3.5.1 Flavours.

4.3.5.2 Sweeteners (non-caloric)

4.3.5.3 Colours

4.3.5.4 Preservatives

4.3.5.4.1 Nitrites and nitrates

4.3.5.5 Solvents

4.3.5.6 Fat substitutes

4.3.5.7 Other food additives

Please also report any results that cover the cumulative effect of low doses of additives.

Please also report any results that cover synthetic antioxidants

4.3.6 Packaging

4.3.6.1 Vinyl chloride

4.3.6.2 Phthalates

4.4 Preparation

4.4.1 Fresh food

4.4.1.1 Raw

Report results regarding all raw food other than fruit and vegetables here. There is a separate heading for raw fruit and vegetables (2.2.1.6).

4.4.1.2 Juiced

4.4.2 Cooked food

4.4.2.1 Steaming, boiling, poaching

4.4.2.2 Stewing, casseroles

4.4.2.3 Baking, roasting

4.4.2.4 Microwaving

4.4.2.5 Frying

4.4.2.6 Grilling (broiling) and barbecuing

4.4.2.7 Heating, re-heating

Some studies may have reported methods of cooking in terms of temperature or cooking medium, and also some studies may have indicated whether the food was cooked in a direct or indirect flame. When this information is available, it should be included in the SLR report.

Results linked to mechanisms e.g. heterocyclic amines, acrylamides and polycyclic aromatic hydrocarbons should also be reported here. There may also be some literature on burned food that should be reported in this section.

5 Dietary constituents

Food constituents' relationship to outcome needs to be considered in relation to dose and form including use in fortified foods, food supplements, nutrient supplements and specially formulated foods. Where relevant and possible these should be disaggregated.

5.1 Carbohydrate

5.1.1 Total carbohydrate

5.1.2 Non-starch polysaccharides/dietary fibre

5.1.2.1 Cereal fibre

5.1.2.2 Vegetable fibre

5.1.2.3 Fruit fibre

5.1.3 Starch

5.1.3.1 Resistant starch

5.1.4 Sugars

*5.1.5 Glycemic index, glycemic load

This heading refers to intrinsic sugars that are naturally incorporated into the cellular structure of foods, and also extrinsic sugars not incorporated into the cellular structure of foods. Results for intrinsic and extrinsic sugars should be presented separately. Count honey and sugars in fruit juices as extrinsic. They can be natural and unprocessed, such as honey, or refined such as table sugar. Any results related to specific sugars e.g. fructose should be reported here.

5.2 Lipids

5.2.1 Total fat

5.2.2 Saturated fatty acids

5.2.3 Monounsaturated fatty acids

5.2.4 Polyunsaturated fatty acids

5.2.4.1 n-3 fatty acids

Where available, results concerning alpha linolenic acid and long chain n-3 PUFA should be reported here, and if possible separately.

5.2.4.2 n-6 fatty acids

5.2.4.3 Conjugated linoleic acid

5.2.5 Trans fatty acids

5.2.6 Other dietary lipids, cholesterol, plant sterols and stanols.

For certain cancers, e.g. endometrium, lung, and pancreas, results concerning dietary cholesterol may be available. These results should be reported under this section.

5.3 Protein

5.3.1 Total protein

5.3.2 Plant protein

5.3.3 Animal protein

5.4 Alcohol

This section refers to ethanol the chemical. Results related to specific alcoholic drinks should be reported under 3.7 Alcoholic drinks. Past alcohol refers, for example, to intake at age 18, during adolescence, etc.

*5.4.1 Total Alcohol (as ethanol)

*5.4.1.1 Alcohol (as ethanol) from beer

*5.4.1.2 Alcohol (as ethanol) from wine

*5.4.1.3 Alcohol (as ethanol) from spirits

*5.4.1.4 Alcohol (as ethanol) from other alcoholic drinks

* 5.4.1.5 Total alcohol (as ethanol), lifetime exposure

* 5.4.1.6 Total alcohol (as ethanol), past

5.5 Vitamins

- *5.5.0 Vitamin supplements
- *5.5.0.1 Vitamin and mineral supplements
- *5.5.0.2 Vitamin B supplement

5.5.1 Vitamin A

- 5.5.1.1 Retinol
- 5.5.1.2 Provitamin A carotenoids

5.5.2 Non-provitamin A carotenoids

Record total carotenoids under 5.5.2 as a separate category marked Total Carotenoids.

5.5.3 Folates and associated compounds

- *5.5.3.1 Total folate
- *5.5.3.2 Dietary folate
- *5.5.3.3 Folate from supplements

Examples of the associated compounds are lipotropes, methionine and other methyl donors.

- 5.5.4 Riboflavin
- 5.5.5 Thiamin (vitamin B1)
- 5.5.6 Niacin
- 5.5.7 Pyridoxine (vitamin B6)
- 5.5.8 Cobalamin (vitamin B12)
- 5.5.9 Vitamin C
- 5.5.10 Vitamin D (and calcium)
- 5.5.11 Vitamin E
- 5.5.12 Vitamin K
- 5.5.13 Other

If results are available concerning any other vitamins not listed here, then these should be reported at the end of this section. In addition, where information is available concerning multiple vitamin deficiencies, these should be reported at the end of this section under 'other'.

5.6 Minerals

- 5.6.1 Sodium
- 5.6.2 Iron
- 5.6.3 Calcium (and Vitamin D)
- 5.6.4 Selenium
- 5.6.5 Iodine
- 5.6.6 Other

Results are likely to be available on other minerals e.g. magnesium, potassium, zinc, copper, phosphorus, manganese and chromium for certain cancers. These should be reported at the end of this section when appropriate under 'other'.

5.7 Phytochemicals

- 5.7.1 Allium compounds
- 5.7.2 Isothiocyanates
- 5.7.3 Glucosinolates and indoles
- 5.7.4 Polyphenols
- 5.7.5 Phytoestrogens eg genistein
- 5.7.6 Caffeine
- 5.7.7 Other

Where available report results relating to other phytochemicals such as saponins and coumarins. Results concerning any other bioactive compounds, which are not phytochemicals should be reported under the separate heading 'other bioactive compounds'. Eg flavonoids, isoflavonoids, glycoalkaloids, cyanogens, oligosaccharides and anthocyanins should be reported separately under this heading.

5.8 Other bioactive compounds

6 Physical activity

6.1 Total physical activity (overall summary measures)

6.1.1 Type of activity

6.1.1.1 Occupational

6.1.1.2 Recreational

6.1.1.3 Household

6.1.1.4 Transportation

6.1.2 Frequency of physical activity

*6.1.2.1 Frequency of occupational physical activity

*6.1.2.2 Frequency of recreational physical activity

6.1.3 Intensity of physical activity

*6.1.3.1 Intensity of occupational physical activity

*6.1.3.2 Intensity of recreational physical activity

6.1.4 Duration of physical activity

*6.1.4.1 Duration of occupational physical activity

*6.1.4.2 Duration of recreational physical activity

6.2 Physical inactivity

6.3 Surrogate markers for physical activity e.g. occupation

7 Energy balance

7.1 Energy intake

*7.1.0.1 Energy from fats

*7.1.0.2 Energy from protein

- *7.1.0.3 Energy from carbohydrates
- *7.1.0.4 Energy from alcohol
- *7.1.0.5 Energy from all other sources

7.1.1 Energy density of diet

7.2 Energy expenditure

8 Anthropometry

8.1 Markers of body composition

8.1.1 BMI

8.1.2 Other weight adjusted for height measures

8.1.3 Weight

8.1.4 Skinfold measurements

8.1.5 Other (e.g. DEXA, bio- impedance, etc)

8.1.6 Change in body composition (including weight gain)

8.2 Markers of distribution of fat

8.2.1 Waist circumference

8.2.2 Hips circumference

8.2.3 Waist to hip ratio

8.2.4 Skinfolds ratio

8.2.5 Other e.g. CT, ultrasound

8.3 Skeletal size

8.3.1 Height (and proxy measures)

8.3.2 Other (e.g. leg length)

8.4 Growth in fetal life, infancy or childhood

8.4.1 Birthweight,

8.4.2 Weight at one year

Annex 3. Tables of excluded and included biomarkers proposed by the SLR centre Bristol.

Extracted from: Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective
Systematic Literature Review – Support Resource
SLR Prostate Cancer (pp 1185-1186)

The reviewers of the SLR centre Bristol used two chapters (Willet: Nutritional epidemiology (Chapter 9), 1998; Margetts and Nelson: Design concepts in nutritional epidemiology (Chapter 7), 1997) to guide their decisions. If there was no info, the biomarker was excluded. If one of the chapters stated the biomarker was useful, the data on validity were checked. Biomarkers with a correlation >0.20 were included. If the chapters stated that there were no good biomarkers for a nutrient or that the biomarker was valid for certain range of intake only, the biomarker was excluded. It was assumed that if biomarkers measured in plasma were valid, this would also be true for serum and vice versa.

The reviewers of the SLR centre Bristol have been more inclusive with respect to the validation required for biomarkers of important nutrients and have therefore added serum/plasma retinol, retinol binding protein, vit B6, ferritin, magnesium, erythrocyte superoxide dismutase (more details below). They have also included biomarkers where validity is not possible: this happens in the case of toxins and phytochemicals where dietary data are sparse. Various contaminants, such as cadmium, lead, PCBs in the serum are also included now although validity data are not available. The level of these chemicals in human tissues is often the only available measure of ingestion.

Measured in	Include	Exclude
Serum	Provit A carotenoids: Carotene, B-carotene, Alpha-carotene Nonprovit A carotenoids: Carotenoids, Lycopene, Cryptoxanthin (B-), Lutein+zeaxanthin Vit E: alpha-tocopherol, gamma tocopherol Selenium n-3 fatty acids: EPA (Eicosapentaenoic), DHA (Docosahexaenoic) Magnesium Vit A: Retinol & Retinol Binding Protein Pyridoxic acid (vit B6) Phytoestrogen: Genistein, Daidzein Chemical food contaminants Polychlorinated biphenyls (PCBs) Phytochemicals	Prealbumin Minerals: Zinc, Copper, Copper/zinc ratio, Zinc/retinol ratio Other dietary lipids: Cholesterol, Triglycerides Saturated fatty acids, Monounsaturated fatty acids, Polyunsaturated fatty acids Lipids (as nutrients), Total fat (as nutrients), Total protein
Urine	4-pyridoxic acid (vit B6) in 24-h urine	Nitrosamines Xanthurenic acid in 24-h urine Arsenic Ferritin
Saliva		Other dietary lipids: Cholesterol, Triglycerides
Erythrocyte	Linoleic acid Selenium Superoxide dismutase Cadmium	Minerals: Zinc, Copper Monounsaturated fatty acids n-3 fatty acids: EPA (Eicosapentaenoic), DHA (Docosahexaenoic) n-6 fatty acids (other than linoleic acid) Polyunsaturated fatty acids, Saturated fatty acids Glutathione peroxidase

Measured in	Include	Exclude
Plasma	Vit D Vit E: alpha-tocopherol, gamma tocopherol Vit C Provit A carotenoids: Carotene, Alpha-carotene, B-carotene Nonprovit A carotenoids: Lycopene, Cryptoxanthin (B-), zeaxanthin, Lutein Selenium, Selenoprotein Folate, Iron: ferritin Vit A Retinol: Retinol Binding Protein Cadmium, Cadmium/zinc ratio EPA DHA fatty acids	Alkaline phosphatase Minerals: Zinc, Copper, caeruloplasmin Other dietary lipids: Cholesterol, Triglycerides, LDL, HDL
Adipose tissue	n-3 fatty acids: EPA (Eicosapentaenoic), DHA (Docosahexaenoic) n-6 fatty acids Trans fatty acids , Polyunsaturated fatty acids, Saturated fatty acids	Unsaturated fat, Monounsaturated fatty acids n-9 fatty acids other measures of polyunsat fa: M:S ratio, M:P ratio, n3-n6 ratio
leucocyte	Vit C	Zinc
Erythrocyte membrane	n-6 fatty acids: linoleic	n-6 fatty acids (other than linoleic) n-3 fatty acids: EPA (Eicosapentaenoic), DHA (Docosahexaenoic)
Hair		Minerals: Zinc, Copper, Manganese, Iron Cadmium
Toenails or fingernails	Selenium	Cadmium, zinc

Reasons for exclusion and inclusion of biomarkers proposed by the SLR centre Bristol.

Extracted from: Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective

Systematic Literature Review – Support Resource

SLR Prostate Cancer (pp 1187-1189)

(Source: Willett: Nutritional epidemiology (Chapter 9), 1998; Margetts and Nelson: Design concepts in nutritional epidemiology (Chapter 7), 1997)

Exposure	Measured in	Valid?	Reason (Willett)	Reason (Margetts / Nelson)
Retinol	Plasma/serum	Yes	Can be measured adequately, but limited interpretability in well-nourished population (p 190).	Main biochemical marker of vit A intake is serum retinol (p 194) although in western countries dietary intake of this vitamin is only a very minor determinant of its plasma levels.
Retinol-Binding protein	Serum	Yes	Retinol levels are highly correlated to RBP(p192).	May be measure of physiologically available form. Not if certain disease processes exist (p 192).
Beta-carotene	Plasma	Yes	Yes (p 194) although blood levels much more responsive to supplemental beta-carotene than beta-carotene from food sources (p 193)	Yes (p 197)
Alpha-carotene Beta-cryptoxanthin Lutein+zeaxanthin Lycopene	Plasma	Yes	Yes (p 194)	There is some evidence for interaction between carotenoids during intestinal absorption, which may complicate relationship between intake and blood levels (p 198)
Vit E	Plasma	Yes	Yes (p 196) NB. Strong confounding with serum cholesterol and total lipid concentrations (p 196).	Plasma, red and white blood cells. Yes, if used for vit E supplements. Yes, although if used for diet, associations are only moderate (p199)

Exposure	Measured in	Valid?	Reason (Willett)	Reason (Margetts / Nelson)
Vit D: D25 (OH)D	Plasma Serum	Yes	Yes (P 198/199) NB. Seasonal variation exists, especially in elderly populations, decreasing in winter and rising during summer (p 198) Sunshine exposure is most important determinant; level is better marker of dietary intake in subjects with low sun exposure	Both can be used to measure vit D status, but the higher plasma concentration and lesser metabolic control of d25 makes this, by far, the better option (p 198).
Vit D: 1.25 (OH)2D		No	No. Influenced by calcium and phosphate levels and parathyroid hormone (p 199).	
Vit D: Alkaline phosphatase activity	Serum	No	No. Is indirect measure of vit D status and is susceptible to other disease processes (p 199)	No info
Vit C	Plasma Leukocyte Serum	Yes	Yes (p 200). Leukocyte may be preferred for long-term intake and plasma and serum reflects more recent intake (p 201)	Yes (p 209), vit C exhibits the strongest and most significant correlation between intake and biochemical indices. Known confounders are: gender, smoking
Vitamin B6	Plasma	Yes	Yes response to supplementation shows response in PLP. PLP better measure of short term rather than long term	Recent studies show that there is unlikely to be a strong correlation between dietary intake and plasma pyridoxal phosphate levels (PPL)
PLP and 4 Pyridoxic acid	Urinary	Yes	Urinary B6 may be more responsive to recent dietary intake than plasma PLP. Random samples of urine 4-pyridoxic acid correlate well with 24 hour collections	
Folacin (folate)	Serum Erythrocyte	Yes	Yes good correlation with dietary folate in both serum and erythrocytes	Used for assessing folate status Table 7.11p
Magnesium	Serum	Yes	Yes stronger correlation with supplement users than with dietary Mg	
Iron	Serum Hair/nails	No No	No, short-term variability is very high (p 208). No, remains to be determined	
Iron: Ferritin	Serum	Yes	Meat intake predicts serum ferritin level (p 208)	No marker of iron intake is satisfactory (p. 192)

Exposure	Measured in	Valid?	Reason (Willett)	Reason (Margetts / Nelson)
Copper : Superoxide dismutase	Erythrocyte	Yes	Among four men fed a copper deficient diet for 4 months, erythrocyte S.O.D declined for all 4. Copper repletion restored S.O.D levels	
Copper	Plasma/serum	No	No (p 211): large number of lifestyle factors/pathologic conditions probably alter blood copper concentrations (smoking, infections)	
Copper	Hair	No	No evidence (212) and data suggests influenced by external contamination	No. Copper-dependent enzyme superoxide dismutase in erythrocytes and copper-protein complex caeroplasmin in serum have been shown to be associated with copper intake, but these markers may be influenced by nondietary factors (p 193)
Selenium	Blood components Toenails	Yes	Yes. Erythrocyte is probably superior to serum as measure of long-term intake (p 206). Lower influence of environment in countries where wearing shoes is norm (toenails). Selenium status is reduced by smoking, also in older persons (p 207); Relationship of selenium with disease may be modified by other antioxidants (vit E and C)	Yes (p 193). Relationship between selenium intake and biomarkers is reasonably good. Urine: reasonable marker, plasma reflects intake provided that the range of variation is large. Red cell and glutathione peroxidase are markers of longer-term intakes. Hair and toenails are alternative possibilities, although contamination of hair samples with shampoo must be controlled for
Glutathione peroxidase	Plasma Serum Erythrocytes Blood	No	Is poor measure of selenium intake among persons with moderate and high exposure (p 206)	

Exposure	Measured in	Valid?	Reason (Willett)	Reason (Margetts / Nelson)
Zinc Metallothionein levels	Any	No No	No (p 212) May be marker of short-term intake (p 213)	No biochemical marker is a good indicator of zinc intake (p 192/193). This is, in general terms, also true for other trace metal nutrients such as copper, manganese, chromium, etc
Lipids: total fats	Any	No	No (p 213)	No, there are no markers of total fat intake (p 215)
Cholesterol, LDL Lipoprotein levels	Serum	No	No, but may be useful to predict dietary changes but not for dietary intake (p 215)	No, relationship dietary cholesterol and lipoprotein levels of cholesterol are complex and appears to vary across range of intake (p218)
Linoleic acid	Plasma Adipose tissue	No Yes	Plasma linoleic acid can discriminate between groups with relatively large differences in intake but performs less well on an individual basis (p 220) Yes (p 220)	No consistent relation between dietary linoleic acid intake and plasma linoleic acid (p 220). Across the range of fatty acids in the diet, fatty acids levels in blood and other tissue (adipose tissue) reflect the dietary levels. NB levels are not comparable across tissues
Marine omega-3 fatty acids (EPA, DHA)	Serum Plasma Adipose tissue	Yes	Yes (p 222/223), although dose-response relation remains to be determined	
Monounsatur fatty acids (oleic acid)	Plasma Adipose tissue	No No	No, plasma levels are poor predictors of oleic acid intake, but adipose tissue may weakly reflect oleic acid intake (p. 224). Validity is too low	
Polyunsatur fatty acids	Adipose tissue	Yes	Yes (p 220)	No info

Exposure	Measured in	Valid?	Reason (Willett)	Reason (Margetts / Nelson)
Saturated fatty acids (Palmitic acid, stearic acids)	Adipose tissue Plasma	Yes No	Yes, long term sat fatty acid intake may be reflected in adipose tissue levels (p 224) No, levels of palmitic and stearic acids in plasma do not provide a simple index of intake (p 224).	No info
Trans-fatty acids	Adipose tissue	Yes	Yes (p 225)	No info
Protein	Any	No	No (p 226)	No info
Nitrogen	Urine	Yes	Yes, but several 24-h samples are needed to provide a stable estimate of nitrogen intake (p 227) Nitrogen excretion increases with body size and exercise and decreased caloric intake	Yes (p 219) One assumes that subjects are in nitrogen Balance

Data on validity and reliability of included biomarkers

Extracted from: Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective
 Systematic Literature Review – Support Resource
 SLR Prostate Cancer (pp 1187-1189)

Nutrient	Biologic tissue	Val./reproduc	Coef	Details
Retinol	Plasma	Validity	0.17	Borderline Correlation between pre-formed vit A intake and plasma retinol. However plasma retinol is a recognized marker of vit A nutritional status for undernourished populations
Beta-carotene			0.51	Correlation between plasma beta-carotene level (averaged from 2 samples taken 1 week apart) and a 7-day diet record estimate of beta-carotene in 98 non-smoking women (Willett, p 194).
			0.38	Cross-sectional correlation between dietary intake of carotene and plasma betacarotene in 902 adult females. In males (n=880): r=0.20 (Margetts, table 7.9a).
	Plasma	Reproducibility	0.45	Correlation for carotene (80% beta-carotene, 20% alpha-carotene) between two measurements taken 6 years apart (Willett, p 194).
Beta-cryptoxanthin	Plasma	Validity	0.49	Correlation between plasma beta-carotene level (averaged from 2 samples taken 1 week apart) and a 7-day diet record estimate of beta carotene in 98 non-smoking women (Willett, p 194)
Lutein+zeaxanthin	Plasma	Validity	0.31	
Lycopene	Plasma	Validity	0.50	
Alpha-carotene	Plasma	Validity	0.58	
Alpha-carotene	Plasma	Validity	0.43	Cross-sectional correlation between dietary intake of carotene and plasma alphacarotene in 902 adult females. In males (n=880): r=0.41 (Margetts, table 7.9a).
Carotenoids	Plasma	Reproducibility	≥080	Within-person variability of plasma levels over 1 week (Willett, p 194).
Vitamin E	Plasma	Validity	0.53	Lipid-adjusted alpha-tocopherol measurements and estimated intake (incl. supplements). After excluding supplement users: r=0.35 (Willett, p 196)
	Plasma	Reproducibility	0.65	Unadjusted repeated measures over a 6-year period (p 188). Adjusting for serum cholesterol reduced correlation to r=0.46 (p 188). Also r=0.65 was found over a 4-year period in 105 adults in Finland (Willett, p 196).
	Plasma	Validity	0.20	Cross-sectional correlation between dietary intake of vit E and plasma vit E in 880 adult males. In females (n=906): r=0.14 (Margetts, table 7.9a)

Nutrient	Biologic tissue	Val./reproduc	Coef	Details
Vitamin D: D25 (OH)D	Plasma	Validity	0.35	Correlation between FFQ estimate of vit D intake (including supplements) with plasma D25 (OH)D (n=139). Correlation excluding supplement users: r=0.25 (Willett, p 199)
			0.18	Cross-sectional correlation between dietary intake of nutrients and biochemical markers in UK pre-school child study in females (n=350). In males (n=365) r=0.06 (Margetts, table 7.9b).
	Serum	Validity	0.24	Correlation between estimated vit D intake from food and supplements (based on 24 h recall) and serum D25 (OH)D (n=373 healthy women). Food only: r=0.11 (Willett, p 199).
Vitamin C	Plasma	Validity	0.43	Unadjusted correlation between questionnaire-derived dietary ascorbic acid intake and plasma ascorbic acid concentration in a heterogeneous population. Diet only: r=0.38 (Table 9.1). Correlation is 0.31 for leukocyte ascorbic acid concentration.(Willett, p 200)
		Reproducibility	0.28	Repeated measures in men obtained 6 years apart (Willett, p 201)
		Validity	0.43	Cross-sectional correlation between dietary intake of nutrients and biochemical markers in UK pre-school child study in males (n=369). In females (n=354) r=0.39 (Margetts, table 7.9b).
	Serum	Validity	0.55	Correlation between food-frequency questionnaire estimate of vit C intake and serum vit C values (in smokers) in 196 men in Scotland (adjusted for total energy intake, BMI and serum cholesterol level). Non-smokers: 0.58 (Willett, p 200/201)
	Leukocyte	Validity	0.49	Correlation between one week of intake data and a single leukocyte ascorbate measurement for men. For women: r=0.36. Nutrition survey of elderly in UK (Margetts, p 211)
Vitamin B6	Plasma	Validity	0.37	Correlation between B6 and plasma pyridoxal phosphate levels in 280 healthy men =0.37 (Willett p203)
	Urinary	Validity	-	
Folacin	Serum Erythrocyte	Validity	0.56	Correlation of 0.56 in Framington Heart study 385 subjects (serum)
			0.51	Correlation in 19 elderly subjects (erythrocyte) (Willett p204)
Magnesium	Serum	Validity	0.27	Correlation between intake with supplements 0.27 in 139 men and 0.15 without supplements (Willett p211)

Nutrient	Biologic tissue	Val./reproduc	Coef	Details
Iron (ferritin)	Serum	Validity	0.16	Borderline 0.16 correlation with heme intake but only r=0.15 with total iron intake (Willett p 208). Included as marker of iron storage
Copper (Superoxide dismutase)	Erythrocyte	-	-	S.O.D levels reflect both depletion and repletion of Cu (Willett p 212)
Selenium	Serum	Validity	0.63	Correlation between selenium intake and serum selenium in South Dakotans (n=44)(Willett, p 186)
		Reproducibility	0.76	Average correlation between repeated measurements at four 3-month intervals in 78 adults (Willett, p 188)
	Toenails	Validity	0.59	Correlation between selenium intake and toenail selenium level in South Dakotans (n=44) (Willett, p 186)
		Reproducibility	0.48	Correlation for selenium levels in toenails collected 6 years apart from 127 US women (Willett, p 206)
	Whole blood	Validity	0.62	Correlation between selenium intake and whole blood selenium in South Dakotans (n=44) (Willett, p 186)
		Reproducibility	0.95	Average correlation between repeated measurements at four 3-month intervals in 78 adults (Willett, p 188)
Linoleic acid	Adipose tissue	Validity	0.57	Correlation between dietary linoleic acid intakes determined from 7-day weighted diet records and the relative proportion of linoleic acid in adipose tissue in Scottish men (n=164). Also correlation between linoleic acid measured in adipose tissue and calculated from FFQ in 118 Boston-area men (Willett, p 220)
Eicosapentaenoic (n-3)	Adipose tissue	Validity	0.40	Correlation with intake estimated from three 7-day weighted food records (Willett, p 223).
		Reproducibility	0.68	Correlation over 8 months in 27 men and women aged 20-29 (Willett, p 223).
	Plasma	Validity	0.23	Correlation of cholesterol ester fraction and intake in 3,570 adults (Willett, p 223)
		Reproducibility	0.38	Correlation of two measurements taken 6 years apart in study of 759 Finnish youths (Willett, p 219)

Nutrient	Biologic tissue	Val./reproduc	Coef	Details
Docosahexaenoic (n-3)	Adipose Tissue	Validity	0.66	Correlation with intake estimated from three 7-day weighted food records (Willett, p 223)
		Reproducibility	0.93	Correlation over 8 months in 27 men and women aged 20-29 (Willett, p 223).
	Plasma	Validity	0.42	Correlation of cholesterol ester fraction and intake in 3,570 adults (Willett, p 223)
		Reproducibility	0.38	Correlation of two measurements taken 6 years apart in study of 759 Finnish youths (Willett, p 219)
Polyunsaturated fatty acids	Adipose tissue	Validity	0.80	Correlation between % of polyunsaturated fatty acid relative to total fatty acid intake and relative % of adipose tissue polyunsaturated fatty acid (Willett, p 220)
Palmitic acid	Adipose tissue	Validity	0.27	Correlation adipose tissue measurement with a FFQ estimate among 118 men. A correlation of 0.14 was reported among women. Among 20 healthy subjects, correlations between normal intake of total saturated fatty acids and fatty acid composition of triglycerides in adipose tissue was 0.57 (Willett, p 224)
Stearic acid	Adipose tissue	Validity	0.56	Among 20 healthy subjects, correlations between normal intake of total saturated fatty acids and fatty acid composition of triglycerides in adipose tissue (Willett, p 224)
Trans fatty acids	Adipose tissue	Validity	0.40	Correlation between adipose trans and intake estimated from the average of two FFQ among 140 Boston-area women. Previous study: 115 Boston area women, correlation of 0.51 between trans intake estimated from a single FFQ and a fatty acid measurement. Among 118 Boston-area men: correlation of 0.29 between trans fatty acid measured in adipose and by FFQ (Willett, p 225)
Nitrogen	Urine	Validity	0.69	Correlation between nitrogen intakes estimated from weighted food records of 16 days and the average of six 24-h urine nitrogen levels (160 women) (Willett, p 227)
Phyto Oestrogens Genistein, daidzein	Plasma 24 hr urine	Validity	0.97 0.92	Urinary excretion (24 h) and plasma concentrations of PO were significantly related to measured dietary PO intake (r 0.97, P<0.001 and r 0.92, P<0.001 respectively). These findings validate the PO database and indicate that 24 h urinary excretion and timed plasma concentrations can be used as biomarkers of PO intake. Br J Nutr. 2004 Mar;91(3):447-57

Nutrient	Biologic tissue	Val./reproduc	Coef	Details
Enterodiol Enterolactone	Serum Urine	Validity	0.13 to 0.29	Urinary enterodiol and enterolactone and serum enterolactone were significantly correlated with dietary fiber intake ($r = 0.13-0.29$) Cancer Epidemiol Biomarkers Prev. 2004 May;13(5):698-708

Annex 4. List of conversion units

In cases where the units of measurement differed between results the units would be converted, where possible, such that all results used the same measurement. Where assumptions had to be made on portion or serving sizes an agreement was reached after discussion between team members and consultation of various sources. The following general sizes were agreed upon:

Beer	400ml serving
Cereals	60g serving
Cheese	35g serving
Dried fish	10g serving
Eggs	55g serving (1 egg)
Fats	10g serving
Fruit & Vegetables	80g serving
Fruit Juice	125ml serving
General drinks inc soft & hot drinks	200ml serving
Meat & Fish	120g serving
Milk	50ml serving
Milk as beverage	200ml serving
Processed cheese slice	10g serving
Processed meat	50g serving
Shellfish	60g serving
Spirits	25ml serving
Staple foods (rice, pasta, potatoes, beans & lentils, foods boiled in soy sauce)	150g serving
Water & Fluid intake	8oz cup
Wine	125ml serving