BOOK 2

Annexes

Foreword by the first author

Since the Workshop in Nice 6-8th Dec 2006, aspects of the report have been published elsewhere:

> Livesey G, Taylor R, Hulshof T, Howlett J. Glycemic response and health a systematic review and meta-analysis: relations between dietary glycemic properties and health outcomes. Am J Clin Nutr 2008;87:258S-68S.
>
> Livesey G, Taylor R, Hulshof T, Howlett J. Glycemic response and health a systematic review and meta-analysis: the database, study characteristics, and macronutrient intakes. Am J Clin Nutr 2008;87:223S-36S

Minor modifications to the report have also been made to correct typographical errors (transposed numerals, incorrect decimal places, missing negative signs etc, together with general but not exhaustive minor editing. A missing table and a figure omitted during last minute preparation of the draft for the workshop have been reinstated. A number of stylistic changes were made to make the text easier on the eye (in particular referencing to material in the annexes). Some duplicate matter has been removed, and some sentence constructions have been reworked to help them make sense or remove ambiguity. Outputs from statistical analyses have been checked against re-run computer outputs to eliminate transfer errors. The list of abbreviations has been extended to include more of those used and defined in text and tables previously. Some workshop participants requested more information about individual studies, designs, duration of treatment, dose, number of participants etc to be tabulated so as to obtain an overview of the studies. This request has been accommodated by providing an extensive table in the first of the above two references.

Geoff Livesey

Foreword

ILSI Europe Dietary Carbohydrates Task Force

The ILSI Europe Dietary Carbohydrates Task Force commissioned a series of meta-analyses of intervention studies on glycaemic response and health. The resulting report comprised two volumes (books) that describe the work undertaken and present the preliminary results and conclusions. These are described primarily in Book 1 with additional supporting data presented in the tables and figures of Book 2. These served as the working documents for an ILSI Europe Workshop held in Nice in December 2006. After the workshop the meta-analyses and key conclusions were summarised in two papers that, together with papers from other speakers at the workshop, have been published as Supplement (1) to the January 2008 issue of the American Journal of Clinical Nutrition (AJCN, Volume 87). The Supplement focuses on the general approach, outcomes, and conclusions of the meta-analyses, and is available from the Journal's website.
Hard copy of the Supplement can also be obtained without charge from ILSI Europe at publications@ilsieurope.be.

Note that comments, typos, and suggestions for presentation arising during the workshop are not addressed within these books, though are taken into account in the subsequent publications in AJCN. Ideas and findings made first in this work and reported in the books should be credited to ILSI Europe and its authors. Where material is present in both the Books and in the AJCN publication, the peer reviewed AJCN should be cited in any further works. Whereas the papers in AJCN underwent peer review, the additional information in the two workshop books did not. Material in the books but not in the AJCN publications should, therefore, not be used or cited without due caution. Wherever the outcomes of the meta-analyses and workshop are referred to, the papers in AJCN should be cited. In addition, the views expressed herein are those of the individual authors and/or their organisations, and do not necessarily reflect those of ILSI Europe.

Annex 1 (1)

Prior meta-analyses (Brand-Miller, Petocz et al. 2003; Opperman, Venter et al. 2004) (Anderson, Randles et al. 2004) (Kelly, Frost et al. 2004) and reviews (Raben 2002) concerning glycaemic index were visited as they held potential for having citing relevant studies and enabled a relative assessment of search success. Records were imported into Endnotes 7 (www.endnotes.com) to exclude duplicates automatically with finishing manually before scanning titles and abstracts.

PubMed returned with 2093 records (excluding 3 duplicates). CABI identified 291 additional records (excluding 254 as records previously found or duplicates). CINAHL identified 111 additional records (excluding 198 as records previously found or duplicates). SCIRUS identified 287 additional records (excluding 656 as records previously found or duplicates). CENTRAL returned 1 record and added no new records. A combined EMBASE & MEDLINE search performed by the British Library also added no records. No additional studies were included from prior meta-analyses and reviews.

Annex 1 (2)

Search of the International Standard Randomised Controlled Trial Number Register gave notice of 3 ongoing trials, which were identified from 57 trials that returned matching the words <glycaemic> or <index>. Two ongoing trials concerned body weight in overweight/obese patients (Price et al, Australia, and Carels et al, Bowling Green, Ohio USA), and one trial concerned body weight in women with polycystic ovary syndrome (International Standard Randomised Controlled Trial Number Register, UK). A multicentred study concerning insulin sensitivity in insensitive individuals was being undertaken (Food Standards Agency, UK). A study was also being undertaken on a pre-meal drink for the treatment of diabetics (International Standard Randomised Controlled Trial Number Register, UK). A further ongoing trial concerned glycaemic index in diabetics (International Standard Randomised Controlled Trial Number Register, Can). A further study on relevant outcomes under the FSA programme, AN0205, had been undertaken but was incompletely

analysed. After closure of the register early results became available of a 4-week trial of high versus low GI diets on lipid and glucose profiles in type-2 diabetics in China (Sun, JQ, Shanghi Huadong Hospital, China). Except for the details known from Price et al, and Carels et al, none of these studies provided details sufficiently advanced for inclusion in the database at the time.

Annex 2*: Excluded studies.*

Nineteen of the papers obtained gave information that was not extracted and entered into a database. The reasons for exclusion are given below, however these should not be seen as a comprehensive list of studies to type – merely that they were studies with search terms that coincided with the search terms used to ensure included studies would be found:

Studies in patients with hepatic cirrhosis (Barkoukis, Fiedler et al. 2002). Studies in women pregnant (Clapp 2002). Foreign language studies (Ba-Jaber, Al-Fouaz et al. 1998). Acute studies (Chantelau, Sonnenberg et al. 1985; Ritz, Krempf et al. 1991; Rickard, Cleveland et al. 2001; Schafer, Schenk et al. 2003; Diaz, Galgani et al. 2004; Harbis, Perdreau et al. 2004); Studies of historic design (i.e. no control arm) (Morales, Semprun-Fereira et al. 1997; Lorenzo, Petroni et al. 2001). Studies specifically on fiber, fructose or sucrose without information on the total diets GI, (Santacroce, Forlani et al. 1990; Thorburn, Crapo et al. 1990) but not excluding studies in which the presence of unavailable carbohydrate or fructose or sucrose was a part of or attended to a low GI diet that was reported on. Studies referring to change of glycaemic index or load but subsequently dropped were due to replacement of carbohydrate with protein (Dumesnil, Turgeon et al. 2001) and to replacement of carbohydrate with fat (Pereira, Swain et al. 2004). A study with unclear experimental design was excluded (Golay, Koellreutter et al. 1992). A study with measurements differing from those used in the present analyses was excluded (Gilbertson, Thorburn et al. 2003). Reviews thought to be of potential relevance judged from the title and abstract but containing no original data of relevance were excluded at this stage (Haffner 2002; Minehira and Tappy 2002).

Annex 3

Forty studies used randomisation to balance the allocation of participants to treatments. One study used ‘minimisation’ to balance the allocation (Slabber, Barnard et al. 1994). One study had a control-test-control design not requiring a procedure to actively balance the allocation (Jenkins, Wolever et al. 1987b). Four studies (in three publications) were included that did not report (mention) randomisation or an equivalent allocation method. For one publication, the authors subsequently confirmed open randomisation (Calle-Pascual, Gomez et al. 1988; Kelly, Frost et al. 2004). In another publication, all subjects had the same run in diets (wheat based) and similar or insignificant differences in variance and means for fasting glucose, post-prandial glucose, total-, HDL- and LDL- cholesterol, and triglycerides; thus indicating a balanced allocation with respect to these outcomes was achieved (Kurup and Krishnamurthy 1993). Lastly, one parallel study (Spieth, Harnish et al. 2000) was a retrospective cohort study with unmentioned method of allocation under conditions thought likely to encounter allocation bias. This study provided sought information on body weight (only) that was otherwise sparse; its entry in the database includes narrative to report on potential bias when contributing to a combined outcome and to assess the influence statistic.

Annex 4

Here free-living makes no inference about how the participants were fed or the activity they undertook, merely that they were for large periods of time without supervision (control over food intake is described elsewhere). Indicators used were key words or phrases such as “free-living” (Jarvi, Karlstrom et al. 1999; Tsihlias, Gibbs et al. 2000), “home” (Brand, Colagiuri et al. 1991; Komindr, Ingsriswang et al. 2001), “outpatient” (Gilbertson, Brand-Miller et al. 2001; Frost, Brynes et al. 2004; Giacco, Clemente et al. 2004), “seen weekly” (Wolever, Jenkins et al. 1992a; Wolever, Jenkins et al. 1992b), “away from clinic” (Calle-Pascual, Gomez et al. 1988; Kiens and Richter 1996);“foods delivered” (Kiens and Richter 1996). In other cases a free-living status was judged from general descriptions of the study, for which there was agreement from elsewhere (Kelly, Frost et al. 2004); these were (Fontvieille, Rizkalla et al. 1992; Frost, Wilding et al. 1994; Frost, Leeds et al. 1998; Luscombe, Noakes et al. 1999; Bouche, Rizkalla et al. 2002; Heilbronn, Noakes et al. 2002; Kabir, Oppert et al. 2002; Rizkalla, Taghrid et al. 2004). In other cases the general description of the study together with an absence of indicators of “inpatient” or “in a human nutrition unit” or similar was taken to indicate a free-living status.

Annex 5

Whether or not studies met each criterion was recorded among the “fields” of information in the database created (see below). These noted whether randomisation or an equivalent method was undertaken, the method of randomisation, whether allocation of results of randomisation was concealed, whether participants were blind to the treatments, whether assessors of clinical samples and data were blind to treatments, whether data was from an intention-to-treat analysis or from a compliant to treatment analysis. Quality scores were:

A – When all quality criteria were met there is a low risk of bias.
B – When one or more of the quality criteria were met, all or in part, there is risk of moderate risk of bias.
C – When one or more criteria were not met, there is a high risk of bias.

Three of 45 studies included reported the method of randomisation, coin toss (Wolever and Mehling 2002), computer generated numbers (Gilbertson, Brand-Miller et al. 2001) , and random number tables (Frost, Wilding et al. 1994) . No study reported allocation concealment and either blinding or double blinding. Accordingly, all included studies had one or more criteria not met, so indicating a high risk of bias. No study was dropped due to being of low quality.

Annex 6

Twenty four studies reported numbers completing a study to be the same as the numbers entering the study, suggesting no drop-outs. Studies reporting drop-outs for each treatment were 5 and these indicated similar numbers for the low and high GI treatments (45% and 55% of drop-outs respectively).

Reasons for dropping out were not always given but were various among those reported: Insulin dose modified (Calle-Pascual, Gomez et al. 1988); body weight varied by more than 1% (Calle-Pascual, Gomez et al. 1988); became too busy, no longer attended a clinic, non-compliance to diet , psychological problems, eating disorder (Gilbertson, Brand-Miller et al. 2001); non-compliance to diet, illness unrelated to [entry condition] or time constraint, taking hypoglycaemic agent (Heilbronn, Noakes et al. 2002); not completing diet records (Jimenez-Cruz, Bacardi-Gascon et al. 2003); work commitments (Luscombe, Noakes et al. 1999), not wanting to progress with a next stage of study (Slabber, Barnard et al. 1994); diets too demanding of their time, personal reasons, infection, son hospitalised, lack of compliance to diet, becoming pregnant (Sloth, Krog-Mikkelsen et al. 2004); change of oral glycaemic agents (Tsihlias, Gibbs et al. 2000); and left the area or could not refrain from smoking (Brynes, Mark Edwards et al. 2003). Difficulty finding low GI foods (Jenkins, Wolever et al. 1987b).

Annex 7

*Healthy participants***:** (Agus, Swain et al. 2000) (Bouche, Rizkalla et al. 2002) (Carels, Darby et al. 2005) (Ebbeling, Leidig et al. 2003) (Frost, Leeds et al. 1998) (Herrmann, Bean et al. 2001) (Jenkins, Wolever et al. 1987a) (Kiens and Richter 1996) (Kurup and Krishnamurthy 1993) (Price, unpublished prior to 2005) (Sloth, Krog-Mikkelsen et al. 2004) (Spieth, Harnish et al. 2000).

IGT participants: (Slabber, Barnard et al. 1994) (Wolever and Mehling 2002).

Type 1 diabetes mellitus: (Calle-Pascual, Gomez et al. 1988) (Collier, Giudici et al. 1988) (Fontvieille, Acosta et al. 1988) (Fontvieille, Rizkalla et al. 1992) (Giacco, Parillo et al. 2000) (Gilbertson, Brand-Miller et al. 2001) (Lafrance, Rabasa-Lhoret et al. 1998).

Type 2 diabetes mellitus: (Calle-Pascual, Gomez et al. 1988) (Fontvieille, Rizkalla et al. 1992) (Frost, Wilding et al. 1994) (Heilbronn, Noakes et al. 2002) (Jarvi, Karlstrom et al. 1999) (Jenkins, Wolever et al. 1988; Jimenez-Cruz, Bacardi-Gascon et al. 2003) (Jiménez-Cruz, Turnbull et al. 2004) (Komindr, Ingsriswang et al. 2001) (Luscombe, Noakes et al. 1999) (Rizkalla, Taghrid et al. 2004) (Tsihlias, Gibbs et al. 2000) (Wolever, Jenkins et al. 1992a) (Wolever, Jenkins et al. 1992b) (YinFa, YueXin et al. 2003).

Primary CHD risk: (Brynes, Mark Edwards et al. 2003) (Frost, Leeds et al. 1998) (Frost, Wilding et al. 1994).

Secondary CHD risk: (Frost, Keogh et al. 1996).

Hyperlipdeamia: (Jenkins, Wolever et al. 1987b).

Annex 8

Data on hyperlipaemics (Jenkins, Wolever et al. 1985) had been incorporated in a larger study included in the database (Jenkins, Wolever et al. 1987b). Different aspects of a study in participants with impaired glucose tolerance that had been published separately (Wolever and Mehling 2002; Wolever and Mehling 2003) were combined in Wolever & Mehling 2002 (d1) (d2) (d3) (d4) (contrast identities are given below). Information on two abstract from Taghrid et al (2001, 2003) was incorporated in their full paper (Rizkalla, Taghrid et al. 2004). An abstract from Kabir et al (1999) was incorporated into the full publication (Kabir, Oppert et al. 2002).

Annex 9

Fields of information: [should be in a table not in text] “name” (definition)’ format: “contrast” (a contrast identification (id) number), “source” (author, date, & other information – see study id below), “pub_n” (database source publication number), “location” (city and country of participants), “duration_w” (duration of study in weeks), “meal_n” (number of meals at which the GI was changed), “plane_nutr” (UF or MF or AL -whether participants were underfed or maintenance fed or fed ad-libitum), “allocation” (M or R or O - whether allocation was by minimisation, randomisation, or other method to achieve balanced allocation), “t_allotment” (1, 0, whether allocation was synchronous with the start of treatment or synchronous with the start of a run in period prior to the start of treatments); “m_rand” (R, NR method of randomisation, reported or not reported); m_conceal (R, NR, method of concealment reported or not reported); “blind_party” (R, NR – participants were blinded to treatments, reported or not reported); “blind_asses” (assessors blinded to treatments, reported or not reported); “design_xp” (Parallel or X-over study design), “adlib” (Ad-libitum or Limited Control or Control - over food intake), “advised” (Advised or Provided or Unclear – whether diets were administered by advise with support of a dietician or whether some or all foods were provided to participants), “age” (mean age of participants in years), “health” (Adv CHD or CHD risk or Healthy or Hyperlipidaemic or IGT (impaired glucose tolerant) or Type-1 DM or Type-2 DM – here Adv CHD refers those at risk of secondary CHD while CHD risk refers to those at risk of primary CHD), “duration_w” (duration of treatment in weeks), “duration_diagnosis” (years intervening between diagnosis and study participation), “wt_class” (normal, overweight, obese – according to original authors definitions or as indicated by body mass index <25, 25 to <30 and >30 kg/m^2 for the study groups); “child_adult” (Child or Adult - <18 or ≥18 y); “male_n” (number of compliant male participants); “female_n” (number of compliant female participants); “total_n” (total number of compliant participants); “hgi_n” (number of compliant participants receiving high glycaemic index treatment); “lgi_n” (number of compliant participants receiving low-glycaemic index treatment); “drop_out_hgi_n” (number of non-compliant participants allocated to high GI

diet); “drop_out_lgi_n” (number of non-compliant participants allocated to low GI diet); “drop_out_n” (total number of non-compliant participants), “glu_medium” (Plasma, Blood -medium on which fasting glucose was measured); “glu_source” (venous, capillary – source of medium for fasting glucose analysis). Measurements field listed were “x_unit” (units in which a measurement “x” was expressed); “entry_x_m, entry_x_sd, entry_x_se” (study mean value, standard deviation value and standard error mean value at entry to the study – seldom used); “st_x_hgi_m st_x_hgi_sd st_x_hgi_se st_x_lgi_m st_x_lgi_sd st_x_lgi_se end_x_hgi_m end_x_hgi_sd end_x_hgi_se end_x_lgi_m end_x_lgi_sd end_x_lgi_se” (measurement values “x” at the start “st” or end “end” of a treatment with high glycaemic index “hgi” or low glycaemic index “lgi” and whether mean “m” standard deviation “sd” or standard error mean “se”). Reported calculated change score fields were: “rep_xdiff_t0_hgi_m rep_xdiff_t0_hgi_sd rep_xdiff_t0_hgi_se rep_xdiff_t0_lgi_m rep_xdiff_t0_lgi_sd rep_xdiff_t0_lgi_se” (reported “rep” differences in measurement values “xdiff” fron the start at time 0 “t_0” to the end of the high glycaemic index treatment “hgi” or end of the low glycaemic index treatment “lgi” and whether the reported calculated value was a mean “m”, standard deviation (of difference) “sd” or standard error (of difference) “se”. Reported calculated treatment difference fields were “rep_xdiff_hgi_lgi_m rep_xdiff_hgi_lgi_sd rep_xdiff_hgi_lgi_se” (reported “rep” difference in measurements “xdiff” for treatment end means or differences in change score between dietary treatments “hgi-lgi” and whether the values are means “m”, standard deviations (of difference) “sd” or standard error (of difference) between treatments “se”. Fields completed were for body mass (x = “wt”, kg), body mass index (x = “bmi”, kg/m^2), fasting glucose (x = “fg”, mmol/l), glycated haemoglobin HbA_{1c} (x = ”hb” % total haemoglobin), fructosamine (x = “fr”, mmol/l), high density lipoprotein cholesterol (x = “hdl”, mmol/l), low density lipoprotein cholesterol (x = “ldl”, mmol/l), total cholesterol (x = “chol”, mmol/l), triglycerides (x = “tg”, mmol/l), fasting insulin (x = “fi”, pmol/l), insulin sensitivity (x = “is”, units method dependent), insulin dosage (x = “id”, units publication dependent”), plasminogen activator inhibitor (x = “pai”, mmol/l), and body fat (x = “bf”, units study dependent). Dietary composition intake fields were of syntax “y_when_stat_diet” where y was intakes of either metabolisable energy

(kJ/d) , fat (g/d), protein (g/d), available carbohydrate (g/d), unavailable carbohydrate (g/d) and glycaemic index of available carbohydrate (% glucose), “when” was either “prior” when prior to treatment and “during” when during treatment, “stat” was either the mean “m”, standard deviation “sd” or standard error (se), and diet was either high glycaemic index “hgi” or low glycaemic index “lgi”.

Annex 10

These are fixed identifiers and so are independent of the style of referencing used. The identities are from the databases “source” field and are in an author-date format followed by further details providing information to distinguish between contrasts made within a part of particular study within a publication. These were: expt1, expt2 exptn - for different experiments within a publication. d1, d2 dn - for observations of different durations from the start of treatment irrespective of the duration of treatment. P, C to distinguish parallel and crossover data within a study. Diet1, diet 2, where it was necessary to specify contrasts in multiple diet studies [e.g. Kurup 1992 (expt2 Raggi vs tapioca)], likewise Type II a, Type II b, Type III, or all (types) when identifying data from different types of hyperlipidaemia or all types combined [e.g. . Jenkins et al 1987b (all)]. Study data was also identified by first author-abbreviated year format for graphical presentations.

Annex 11 (1)

The value of r_p was imputed from studies providing sufficient information for its calculation and was allowed to vary with the duration of treatment where this was evident. The relationship between r_p and the commonly recognised and understood paired and unpaired standard error differences is expanded here to derive a practically expedient derivation of the dependent standard errors differences between treatments (Eq.1 to 7).

The population sample standard deviation (SD = σ) was rendered for observations at one time ($_1$) and another ($_2$) and the difference ($_d$) between them. From the general relationship for r_p (Eq. 1) (Deeks J, Higgins J et al. 2002), the σ_1 and σ_2 for times 1 and 2 were pooled (as in ANOVA and t-tests) to obtain the pooled estimate σ_{12} shown in the simpler expression (Eq. 2). Rearrangement and division by n_{12} numbers of paired observations gave Eq.6.

$$r_p = \frac{\sigma_1^2 + \sigma_2^2 - \sigma_d^2}{2 \cdot \sigma_1 \cdot \sigma_2} \qquad \text{Eq. 1}$$

$$r_p = \frac{2\sigma_{12}^2 - \sigma_d^2}{2\sigma_{12}^2} \qquad \text{Eq.2}$$

$$r_p = 1 - \frac{\sigma_d^2}{2\sigma_{12}^2} \qquad \text{Eq. 3}$$

$$\frac{\sigma_d^2}{2\sigma_{12}^2} = 1 - r_p \qquad \text{Eq. 4}$$

$$\sigma_d^2 = 2\sigma_{12}^2 \cdot (1 - r_p) \qquad \text{Eq. 5}$$

$$\frac{\sigma_d^2}{n_{12}} = \frac{2\sigma_{12}^2}{n_{12}} \cdot (1 - r_p) \qquad \text{Eq. 6}$$

For any number (n_{12}) of paired (dependent) observations σ_d^2 / n_{12} equals $SED^2_{dependent}$, the square of the paired (dependent) standard error

difference. Similarly, $2\sigma_{12}^2 / n_{12}$ equals $SED_{dependent}^2$, the square of the unpaired (independent) standard error difference across the time 1 and 2 . A form of Eq.6 used here is Eq. 7 which first takes square roots allowing commonly reported (or calculable) SED quantities to be inter-converted once $\sqrt{1-r_p}$ is imputed from quantities in other studies.

$$SED_{dependent}^2 = SED_{independent}^2 \cdot (1 - r_p) \qquad \text{Eq. 7}$$

The constancy or change of r_p, $(1-r_p)$, and $\sqrt{1-r_p}$ with change in any other study parameter (e.g. duration of treatment) was readily assessed from a plot of $SED_{dependent}/SED_{independent}$ against the other parameter(s).

For cross-over studies the comparisons occur between observations at two time points hence Eq. 8 the square root of Eq. 7 was applied directly. For a parallel study the treatment comparison is the differences between the two change scores, which increases the error by the square root of 2.

Crossover: $$SED_{dependent} = SED_{indepndent} \cdot \sqrt{(1 - r_p)} \qquad \text{Eq. 8}$$

Parallel: $$SED_{dependent} = SED_{independent} \cdot \sqrt{2 \cdot (1 - r_p)} \qquad \text{Eq. 9}$$

Annex 11(2)

TABLE 1: Methods: Estimates of $\sqrt{(1-r_p)}$ calculated as the paired to unpaired standard error difference ratio between two time points [1]

	Duration	$\sqrt{(1-r_p)}$ [2]	se [2]	min [2]	max [2]	k (n) [3]
Dietary variables [4]						
Metabolisable energy intake	3.4 to 26 w	0.40	0.06	0.23	0.65	6 (7)
Available carbohydrate intake	4 to 8 w	0.45	- [5]	0.45	0.46	2 (2)
Unavailable carbohydrate intake	-	0.7 [6]	-	-	-	-
Fat intake	4 to 12 w	0.38	0.05	0.30	0.49	3 (3)
Protein intake	2 to 26 w	0.54	0.07	0.47	0.68	3 (3)
Glycaemic index	-	0.7 [6]	-	-	-	-
Glycaemic load	-	0.45 [7]	-	-	-	-
Personal variables						
Body weight	4 to 18 w	0.23	0.07	0.03	0.53	6 (8)
Fasting plasma glucose	2 to 16 w	0.43	0.03	0.26	0.61	8 (17)
Fasting insulin	0 to 52 w	0.75	0.06	0.43	1.13	6 (12)
Insulin sensitivity	-	0.7 [6]	-	-	-	-
HOMA %S	-	0.46 [8]	0.05 [8]	-	-	-
HOMA %B	-	0.26 [8]	0.03 [8]	-	-	-
HOMA %D	-	0.46 [8]	0.05 [8]			
Glycated haemoglobin	2 to 52 w	$-0.04 + 0.13 \cdot \ln(w)$ [9]	0.06	0.11	1.22	9 (12)
Fructosamine	2 to 12 w	$0.35 + 0.03w$ [9]	0.10	0.18	0.90	9 (7)
Triglycerides	2 to 12 w	$0.16 + 0.03w$ [9]	0.08	0.17	0.54	9 (19)

1 For cross-over studies, the multiplication of the unpaired standard error difference between treatments with $\sqrt{(1-r_p)}$ provided an estimate of the dependent standard error difference. For parallel design studies the comparison involves two time periods hence $\sqrt{2 \cdot (1-r_p)}$ was used instead.

2 Refers to the mean, standard error, min and max of n number of estimates independently of study size or number of estimates available per study.

3 k (n), the number studies k and number of estimates n (i.e. more than one estimate per study was obtained)

4 The value of $\sqrt{(1-r_p)}$ was applied equally to ad libitum, limited control and controlled food intake studies on the grounds that a large contribution to this variation is likely to occur secondarily to differing energy requirements.

5 See range of the two values obtained.

6 An upper limit of 0.7 is assumed for $\sqrt{(1-r_p)}$ in crossover studies corresponding to $\sqrt{[2 \cdot (1-r_p)]} = 1$ for parallel studies.

7 Value assumed as similar to that for available carbohydrate

8 Values are computed from fractional errors for fasting plasma glucose and insulin and the formula for computing Homa values (see text).

9 The value $\sqrt{(1-r_p)}$ increases with time hence a formula is given in which w is the duration in weeks between measurements, the range of determinant weeks is given in parenthesis.

Annex 12

It is applied usually to the influence on a regression coefficient β and noted $\Delta\hat{\beta}$ij, calculated as the absolute$(\beta_i - \beta_j)/se_j$ where i and j are values with (i) and without (j, jack-knifed) the influential value. Cook's distance (D) is another measure of influence and is based on the standardized residual and leverage of a study value during regression; this is used less often as it is difficult to interpret. Influence statistics less than 1 are considered without sufficient influence on the overall result to warrant consideration of a study belonging to a different dataset (real or erroneous) thereby deleting it from the current assessment. More usually results with both sets of data are provided with comment on the influence. Jackknifed standard errors are errors after truncation of the data by removal of an outlying data.

Annex 13

Conventions used in figures and tables:

A **bubble** in a figure (trend plot) represents at its centre a data point that is the mean treatment difference of an individual study and its area the precision of the study. Precision is given by either one of two methods:

n: When all effect sizes are presented (including repeated measures of effect size) and prior to statistical analysis the precision is represent as $\sqrt{n}$ where n is the average number of participants per treatment arm. Larger bubbles indicate larger studies expected to yield greater precision than smaller studies. Bubble sizes are relative to each other rather than relative to the measurement scale.

Inverse (Tau^2 +SE^2): When a statistical analysis has been made so that an estimate of Tau^2 (the between study variance) is available then precision is represent by this inverse variance. Large bubbles indicate studies with small errors. Bubble sizes are relative to each other rather than relative to the measurement scale.

A **square** in a forest plot (showing a meta-analysis) has the same interpretation as a bubble in a trend plot.

A **diamond** in a figure represents, unless stated otherwise, at its centre a data point that is a combined study weighted mean (or meta-mean). The tips of the diamond along its longest axis indicate the 95% confidence intervals for the combined mean. The area of the diamond is then proportional to the precision of the studies combined mean. Diamond sizes are both relative to each other and relative to the measurement scale.

The **sources** of information for derived data in tables and graphs when given in the footnotes to tables and graphs are original works that contribute to the database with **inclusions** and **exclusions** made post inclusion in the databases. Hence these lists must be considered together with the database

inclusion and exclusion criterion (see text). Not all tables and figure information on the sources. This is to avoid undue repetition. Generally the inclusions and exclusions are implicit, that is all studies in the database are included in the analysis unless they have insufficient data for the statistical analysis made. Sources of information are explicitly included either when agreement (or consistency) among studies is poor and unexplained by determinant factors in the analysis (i.e. when choice of inclusions and exclusions may be more open to question) or when the results provide what is thought to be a key to understanding the relation between glycaemic response and health or communication of this relationship. The included and excluded sources are also not given when there are a good number of independent studies with clearly consistent observations, when the inclusions and exclusions are as implicit as described above. In addition tables and figures may include the source data for the arbitrary reason of illustration, which is due mostly in tables and figures of the earlier chapters.

Annex 14

Explanation of statistics and Sources to figure 3:

Observations are grouped by the category of control over food intake (where total is all categories combined). Each study is represented by a bubble proportional to the inverse (Tau^2+SE^2). To facilitate comparison the curves in each graph show the same bold random effects regression curve for all categories combined as well as the category random effects regression curves.

Sources

Ad-libitum studies include: Brynes et al 2003 (Su), Brynes et al 2003 (st), Ebbeling et al 2003 (d2), Sloth et al 2004 (d5), and Wolever & Mehling 2002a (d4). Excluded are Gilbertson et al 2001 due to no information on energy intake, and Spieth et al 2000 due to no information on either energy intake or glycaemic index.

Limited control food intake studies include: Bouche et al 2002, Collier et al 1988 (d2), Fontvieille et al 1988, Frost et al 1994, Frost et al 1996, Frost et al 1998 (exp1), Frost et al 1998 (exp2), Frost et al 2004, Giacco et al 2000, Herrmann et al 2001 (expt2), Jenkins et al 1987b (all), Jenkins et al 1988, Jimenez-Cruz et al 2003, Jimenez-Cruz et al 2004, Komindr et al 2001, Lafrance et al 1998, Luscombe et al 1999, Rizkalla et al 2004, and Tsihlias et al 2000 (d2). Excluded were Yin-fa (2003) due to no information on energy intake, Slabber et al 1994 (exp2)C due to no information on glycaemic index, and Price (in press 2005) due to neither energy intake or glycaemic index information available at the time of analysis.

Control food intake studies include: Brand et al 1991, Calle-Pascual 1988 (exp1_T2), Calle-Pascual 1988 (exp2_T2), Carels et al 2005, Fontvieille et al 1992 ('exp1'), Fontvieille et al 1992 ('exp2'), Heilbronn 2002 (d2), Jarvi et al 1999, Jenkins et al 1987a (d2), Kiens et al 1996 (d4), Kurup 1992 (raggi vs. rice), Kurup 1992 (expt2 raggi vs. tapioca), Wolever et al 1992a (d3), Wolever et al 1992b (d2). Excluded are Kabir et al 2002 due to no information on metabolisable energy intake and Agus et al 2000 due to no information on glycaemic index.

Annex 15: Table 2 including statistical details

TABLE 2: Macronutrients Intakes: Difference in metabolisable energy intakes in intervention studies related to difference in glycaemic index$_{ac}$ achieved, by category of food intake control.

	All studies combined	Control	Limited control	Ad libitum
k (df)	38 (36)	14 (12)	19 (17)	5 (3)
Slope (kJ/GI%glu)	13.5	-0.8	24	113
SEE	9.7	0.6	16	37
P>|kh-t|	0.17	0.9	0.2	0.005
3P	-	>0.99	0.6	0.015
Constant (kJ/d)	150	48	244	1009
SEE	170	148	302	445
P>|kh-t|	0.38	0.75	0.47	0.11
3P	-	>0.99	>0.99	0.33
I^2 (J^2/J^2)	0.77	0	0.21	0.69
Tau (kJ/d)	412	0	447	430
P>Q	0.001	0.999	0.001	0.001
P>X	0.001	1.000	0.001	0.001

[1] Model: difference in metabolisable intake = slope (SEE) x difference in GI + constant (SEE) + Tau + SE

[2] Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 16

Table 3 with more statistical details.

TABLE 3: Macronutrients Intakes: Difference in available carbohydrate intakes in intervention studies related to difference in glycaemic $index_{ac}$ achieved, by food intake control.

	All studies combined	Control	Limited control	Ad libitum
k (df)	38 (36)	14 (12)	19 (17)	5 (3)
Slope (g/GI%glu)	1.12	0.66	1.44	3.35
SEE	0.43	0.39	0.80	1.87
P>|kh-t|	0.013	0.11	0.09	0.17
3P	-	0.33	0.27	0.51
Constant (g/d)	17.6	14.8	20.2	34.6
SEE	7.2	7.2	13.4	21.3
P>|kh-t|	0.021	0.063	0.15	0.20
3P	-	0.189	0.45	0.60
I^2 (g2/g2)	0.99	0.99	0.99	0.99
Tau (g/d)	21	13	25	26
P>Q	0.001	0.001	0.001	0.001
P>X	0.001	0.001	0.001	0.001

1 Model: difference in available carbohydrate intake = slope (SEE) x difference in GI + constant (SEE) + Tau + SE

2 Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 17(1)

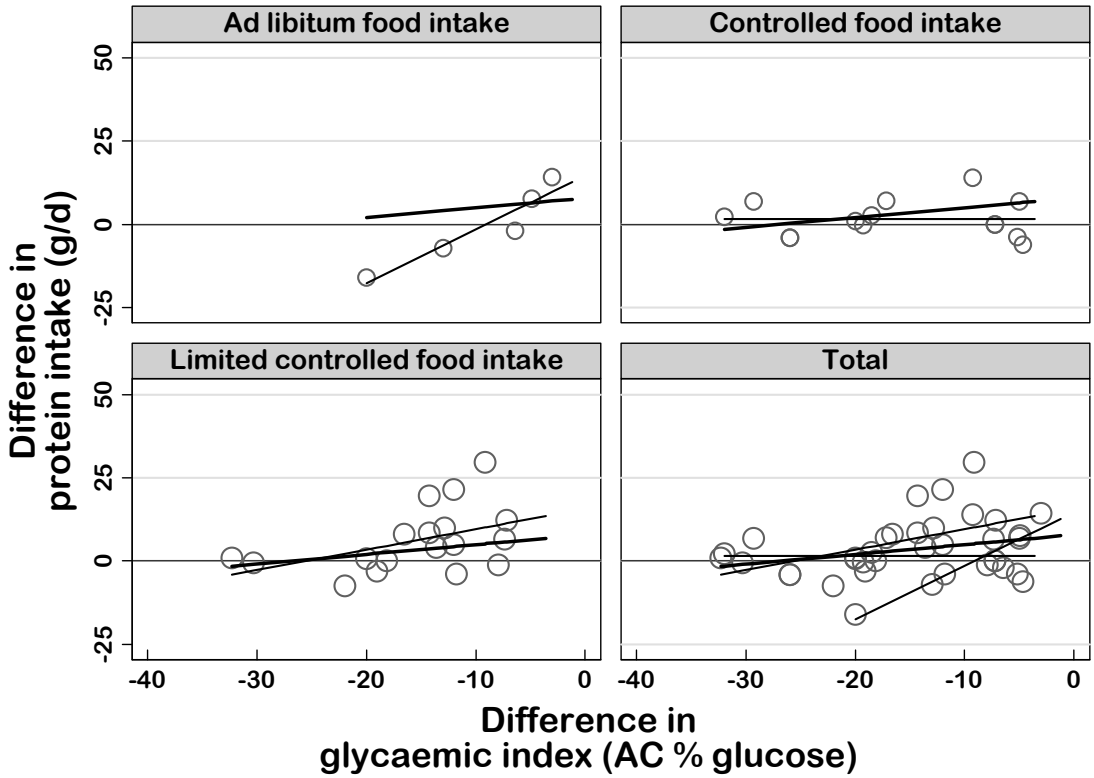

FIG 4: Macronutrient Intakes: Difference in protein intake associated with difference in glycaemic index achieved. Observations are grouped by the category of control over food intake (where total is all categories combined). Each study is represented by a bubble proportional to the inverse (Tau^2+SE^2). To facilitate comparison the curves in each graph show the same bold random effects regression curve for all categories combined as well as the category random effects regression curves.

Annex 17(2)

Table 4(1): Difference in protein intakes in intervention studies related to difference in glycaemic $index_{ac}$ achieved, by category of food intake control.

	All studies combined	Control	Limited control	Ad libitum
k (df)	37 (35)	14 (12)	18 (16)	5 (3)
Slope (g/GI%glu)	0.29	-0.002	0.61	1.608
SEE	0.18	0.16	0.30	0.324
P>|kh-t|	0.09	0.99	0.06	0.016
3P	-	>0.99	0.18	0.048
Constant (g/d)	7.5	1.5	15.6	14.5
SEE	2.9	3.1	5.1	3.6
P>|kh-t|	0.014	0.62	0.008	0.029
3P	-	>0.99	0.036	0.087
I^2 (g2/g2)	0.49	0.99	0.99	0.93
Tau (g/d)	8.6	5.7	9	4.3
P>Q	0.001	0.001	0.001	0.001
P>X	0.001	0.001	0.001	0.001

1 Model: difference in protein intake = slope (SEE) x difference in GI + constant (SEE) + Tau + SE

2 Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 18(1)

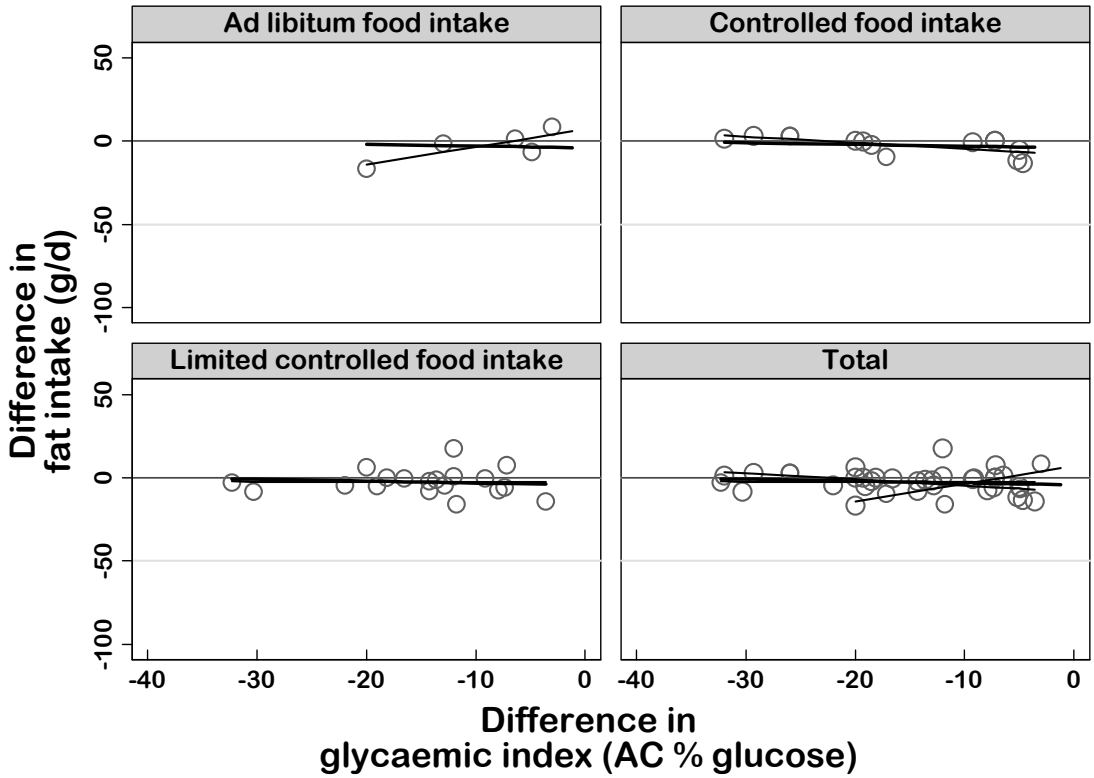

FIG 6: Macronutrient Intakes: Difference in fat intake associated with difference in glycaemic index achieved. Observations are grouped by the category of control over food intake (where total is all categories combined). Each study is represented by a bubble proportional to inverse (Tau^2+SE^2). To facilitate comparison the curves in each graph show the same bold random effects regression curve for all categories combined as well as the category random effects regression curves.

Annex 18(2)

TABLE 4 (2): Macronutrients Intakes: Difference in fat intakes in intervention studies related to difference in glycaemic $index_{ac}$ achieved

	All studies combined	Control	Limited control	Ad libitum
k (df)	38 (36)	14 (12)	19 (17)	5 (3)
Slope (g/GI%glu)	-0.1	-0.36	-0.01	1.07
SEE	0.14	0.13	0.25	0.46
P>|kh-t|	0.45	0.013	0.96	0.10
3P	-	0.039	>0.99	0.30
Constant (g/d)	-4.1	-8.3	-2.7	-7.1
SEE	2.3	2.3	4.40	5.3
P>|kh-t|	0.09	0.004	0.52	0.27
3P	-	0.012	>0.99	0.81
I^2 (g2/g2)	0.99	0.96	0.99	0.97
Tau (g/d)	6.9	4.2	7.7	6.3
P>Q	0.001	0.001	0.001	0.001
P>X	0.001	0.001	0.001	0.001

[1] Model: difference in fat intake = slope (SEE) x difference in GI + constant (SEE) + Tau + SE

[2] Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 19(1)

Effects of unavailable carbohydrates

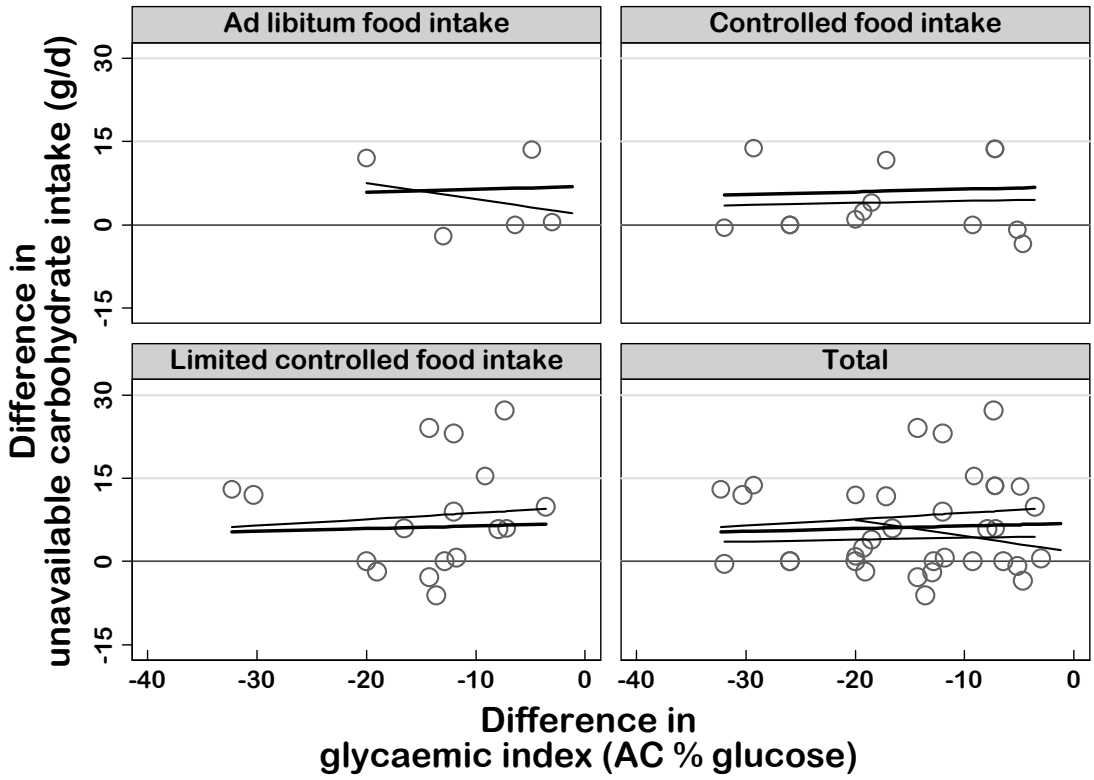

FIG 7: Macronutrient Intakes: Difference in unavailable carbohydrate intake associated with difference in glycaemic index achieved. Observations are grouped by the category of control over food intake (where total is all categories combined). Each study is represented by a bubble proportional to the inverse (Tau^2+SE^2). To facilitate comparison the curves in each graph show the same bold random effects regression curve for all categories combined as well as the category random effects regression curves.

Annex 19(2)

TABLE 5: Macronutrient Intakes: Difference in unavailable carbohydrate intakes in intervention studies related to difference in glycaemic index$_{ac}$ achieved, by difference in food intake control.

	All studies combined	Control	Limited control	Ad libitum
k (df)	35 (33)	13 (11)	17 (15)	5 (3)
Slope (g/GI%glu)	0.05	0.03	0.11	-0.28
SEE	0.17	0.20	0.34	0.58
P>|kh-t|	0.78	0.87	0.74	0.65
3P	-	>0.99	>0.99	>0.99
Constant (g/d)	6.9	4.6	9.9	1.7
SEE	2.9	3.8	5.4	6.5
P>|kh-t|	0.025	0.26	0.09	0.81
3P	-	0.78	0.27	>0.99
I^2 (g2/g2)	0.99	0.89	0.99	0.91
Tau (g/d)	8.3	6.2	10.0	7.5
P>Q	0.001	0.001	0.001	0.001
P>X	0.001	0.001	0.001	0.001

1 Model: difference in unavailable carbohydrate intake = slope (SEE) x difference in GI + constant (SEE) + Tau + SE.

2 Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 20(1)

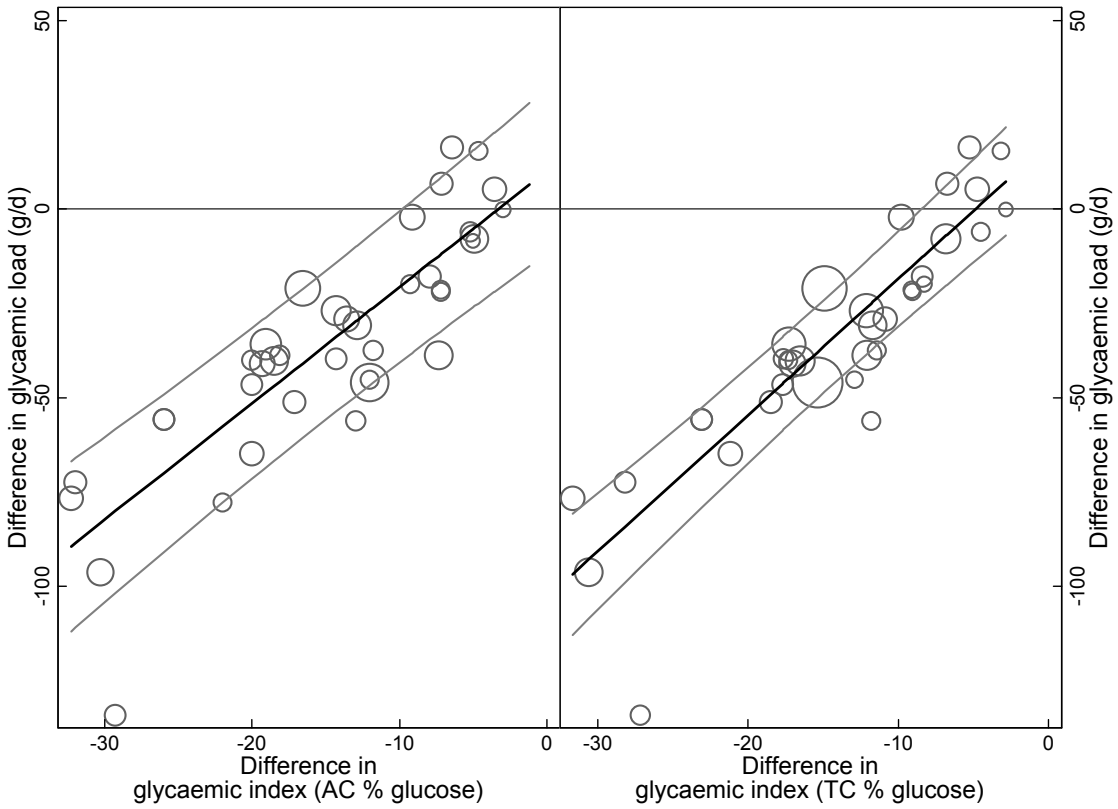

FIG 9: Macronutrient Intakes: Difference in glycaemic load associated with difference in glycaemic index of both available and total carbohydrate achieved. Observations are for all food intake categories combined. Each study is represented by a bubble proportional to inverse (Tau^2+SE^2). Curves are the regression line and the 95% confidence intervals for the population of studies. Abbreviations: AC, available carbohydrate; UC unavailable carbohydrate.

Annex 20(2)

TABLE 6: Macronutrient Intakes: Difference in glycaemic load in intervention studies related to difference in glycaemic index$_{ac}$ achieved, by food intake control.

	All studies combined	Control	Limited control	Ad libitum
k (df)	37 (35)	14 (12)	19 (17)	5 (3)
Slope (g/GI%glu)	3.1	3.2	2.9	4.5
SEE	0.4	0.6	0.50	1.3
P>|kh-t|	0.001	0.001	0.001	0.046
3P	-	0.001	0.001	0.138
Constant (g/d)	10.2	13.2	7	21.9
SEE	6.4	12	9.3	16.1
P>|kh-t|	0.122	0.298	0.439	0.268
3P	-	0.894	>0.99	0.804
I^2 (g2/g2)	0.67	0.24	0.78	0.81
Tau (g/d)	11	10	12	16
P>Q	0.001	0.20	0.001	0.31
P>X	0.001	0.23	0.001	0.26

1 Model: difference in glycaemic load = slope (SEE) x difference in GI + constant (SEE) + Tau + SE

2 Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 21

TABLE 7: Macronutrient Intakes: Difference in glycaemic load in intervention studies related to difference in glycaemic index$_{tc}$ achieved, by food intake control.

	All studies combined	Control	Limited control	Ad libitum
k (df)	35 (33)	13 (11)	17 (15)	5 (3)
Slope (g/GI%glu)	3.6	3.9	3.3	4.4
SEE	0.4	0.7	0.39	1.2
P>|kh-t|	0.001	0.001	0.001	0.041
3P	-	0.001	0.001	0.120
Constant (g/d)	17.5	20.0	13.8	22.0
SEE	5.5	12.1	86.5	15.6
P>|kh-t|	0.003	0.128	0.051	0.25
3P	-	0.384	0.225	0.75
I^2 (g2/g2)	0.85	0.80	0.89	0.75
Tau (g/d)	12	16	9	16
P>Q	0.001	0.390	0.001	0.008
P>X	0.001	0.470	0.001	0.014

1 Model: difference in glycaemic load = slope (SEE) x difference in GI + constant (SEE) + Tau + SE.

2 Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I_2 variation among studies (Tau^2) as a proportion of total variation (Tau_2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 22(1)

TABLE 8: Macronutrient Intakes: Difference in available carbohydrate intake in intervention studies related to difference in unavailable carbohydrate intake found, by food intake control.

	All studies combined	Control	Limited control	Ad libitum
k (df)	35 (33)	13 (11)	17 (15)	5 (3)
Slope (g/g)	-1.09	-1.31	-1.00	-1.37
SEE	0.45	0.58	0.67	2.44
P>|kh-t|	0.021	0.046	0.16	0.61
3P	-	0.14	0.48	>0.99
Constant (g/d)	8.9	9.6	8.3	9.4
SEE	4.7	4.4	8.1	19.9
P>|kh-t|	0.07	0.051	0.32	0.67
3P	-	0.15	0.96	>0.99
I^2 (g2/g2)	0.99	0.99	0.99	0.99
Tau (g/d)	22	13	26	36
P>Q	0.001	0.001	0.001	0.001
P>X	0.001	0.001	0.001	0.001

1 Model: difference in available carbohydrate intake = slope (SEE) x difference in unavailable carbohydrate intake + constant (SEE) + Tau + SE.

2 Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 22(2)

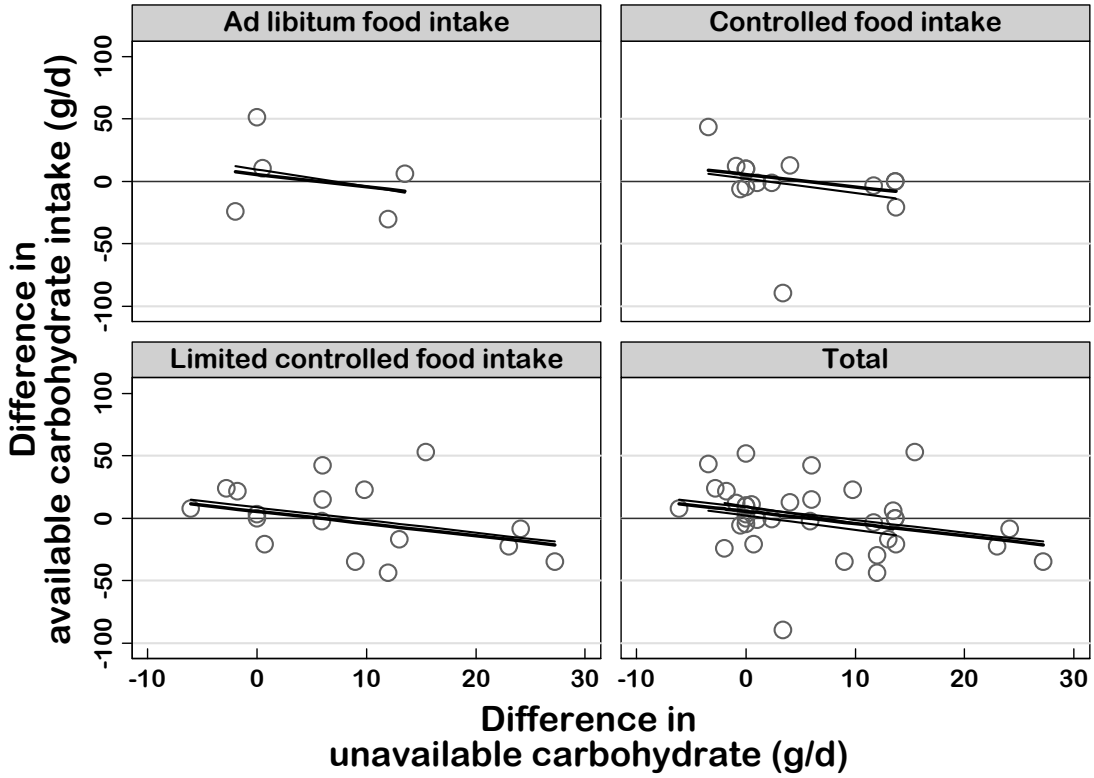

FIG 11: Macronutrient Intakes: Difference in available carbohydrate associated with difference in unavailable carbohydrate achieved. Observations are grouped by the category of control over food intake (where total is all categories combined). Each study is represented by a bubble proportional to inverse (Tau^2+SE^2). To facilitate comparison the curves in each graph show the same bold random effects regression curve for all categories combined as well as the category random effects regression curves. Outlying data of Agus et al (2000) is identified.

Ad-libitum studies include: Brynes et al 2003 (Su), Brynes et al 2003 (st), Ebbeling et al 2003 (d2), Sloth et al 2004 (d5), and Wolever & Mehling 2002a (d4). Excluded are Gilbertson et al 2001 and Spieth et al 2000 due to no information on either available or unavailable carbohydrate intake or glycaemic index.

Limited control food intake studies include: Bouche et al 2002, Collier et al 1988 (d2), Fontvieille et al 1988, Frost et al 1994, Frost et al 1996, Frost et al 1998 (exp1), Frost et al 1998 (exp2), Frost et al 2004, Giacco et al 2000, Jenkins et al 1987b (all), Jenkins et al 1988, Jimenez-Cruz et al 2003, Jimenez-Cruz et al 2004, Lafrance et al 1998, Luscombe et al 1999, Rizkalla et al 2004, and Tsihlias et al 2000 (d2). Excluded were Herrmann et al 2001 (expt2), Komindr et al 2001, and Slabber et al 1994 (exp2)C due to no information on unavailable

carbohydrate intake and Yin-fa (2003) and Price (in press 2005) due to no information on either available or unavailable carbohydrate intake.

Control food intake studies *i*nclude: Agus et al 2000, Brand et al 1991, Calle-Pascual 1988 (exp1_T2), Calle-Pascual 1988 (exp2_T2), Fontvieille et al 1992 ('exp1'), Fontvieille et al 1992 ('exp2'), Heilbronn 2002 (d2), Jarvi et al 1999, Jenkins et al 1987a (d2), Kiens et al 1996 (d4), Kurup 1992 (raggi vs rice), Kurup 1992 (expt2 raggi vs tapioca), Wolever et al 1992a (d3), Wolever et al 1992b (d2). *Excluded*: Kabir et al due to no information on either available or unavailable carbohydrate intake.

Annex 23

TABLE 9: Macronutrient Intakes: Difference in metabolisable energy intakes in intervention studies related to difference in glycaemic load achieved, by food intake control.

	All studies combined	Control	Limited control	Ad libitum
k (df)	38 (36)	14 (12)	19 (17)	5 (3)
Slope (kJ/ g eq)	8.0	0.1	15.2	23.4
SEE	2.4	1.8	3.8	3.7
P>|kh-t|	0.002	0.978	0.001	0.008
3P	-	>0.99	0.003	0.024
Constant (kJ/d)	245	67	472	420
SEE	115	108	176	163
P>|kh-t|	0.041	0.55	0.016	0.08
3P	-	>0.99	0.048	0.24
I^2 (J^2/J^2)	0.72	0.00	0.71	0.00
Tau (kJ/d)	346	0.00	303	0.00
P>Q	0.001	0.999	0.001	0.46
P>X	0.001	1.000	0.001	1.00

1 Model: difference in metabolisable energy intake = slope (SEE) x difference in GI + constant (SEE) + Tau + SE.

2 Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 24(1)

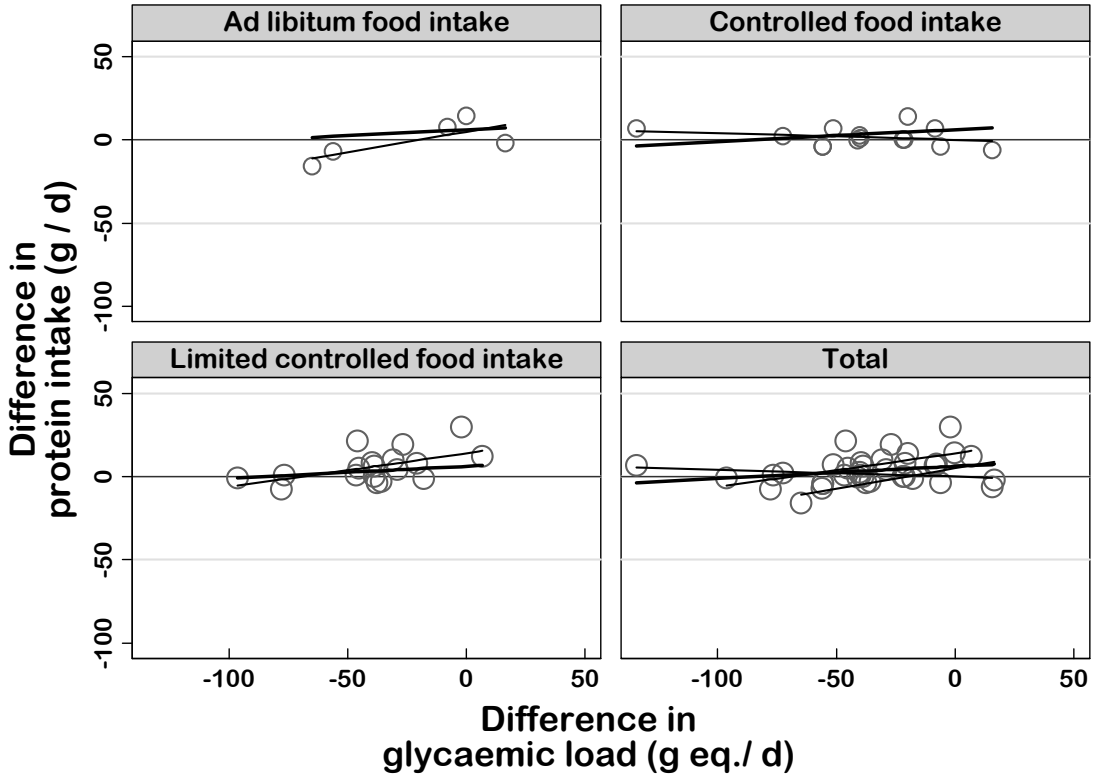

Fig 13: Macronutrient intakes: Difference in protein intake associated with difference in glycaemic load achieved. Observations are grouped by the category of control over food intake (where total is all categories combined). Each study is represented by a bubble proportional to inverse (Tau^2+SE^2). To facilitate comparison the curves in each graph show the same bold random effects regression curve for all categories combined as well as the category random effects regression curves.

Annex 24(2)

TABLE 10: Macronutrient Intakes: Difference in protein intakes in intervention studies related to difference in glycaemic load achieved, by food intake control category.

	All studies combined	Control	Limited control	Ad libitum
k (df)	37 (35)	14 (12)	18 (16)	5 (3)
Slope (g/ g. eq)	0.07	-0.04	0.2	0.24
SEE	0.05	0.04	0.08	0.12
P>|kh-t|	0.13	0.38	0.024	0.15
3P		>0.99	0.072	0.45
Constant (g eq./d)	6.2	0.1	14	4.9
SEE	2.3	2.3	4	5.0
P>|kh-t|	0.009	0.99	0.002	0.399
3P	-	2.97	0.006	1.197
I^2 (g eq.^{2}/g eq.^{2})	0.99	0.99	0.99	0.99
Tau (g eq./d)	8.6	5.5	8.4	9.1
P>Q	0.001	0.001	0.001	0.001
P>X	0.001	0.001	0.001	0.001

1 Model: difference in protein intake = slope (SEE) x difference in GI + constant (SEE) + Tau + SE.

2 Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 25(1)

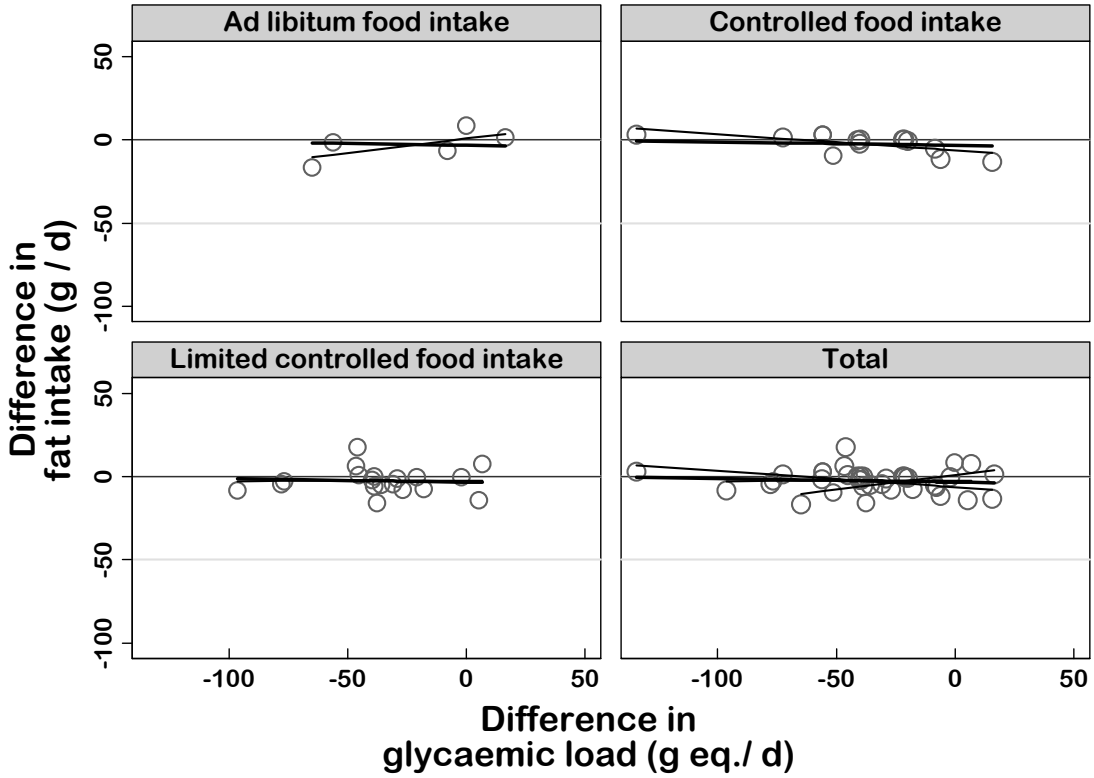

Fig 14: Macronutrient intakes: Difference in fat intake associated with difference in glycaemic load achieved. Observations are grouped by the category of control over food intake (where total is all categories combined). Each study is represented by a bubble proportional to inverse (Tau^2+SE^2). To facilitate comparison the curves in each graph show the same bold random effects regression curve for all categories combined as well as the category random effects regression curves.

Annex 25(2)

TABLE 11: Macronutrient Intakes: Difference in fat intakes in intervention studies related to difference in glycaemic load achieved, by food intake control category.

	All studies combined	Control	Limited control	Ad libitum
k (df)	38 (36)	14 (12)	19 (17)	5 (3)
Slope (g/ g. eq)	-0.02	-0.09	0.01	0.17
SEE	0.04	0.03	0.07	0.11
P>|kh-t|	0.58	0.013	0.958	0.22
3P	-	0.039	>0.99	0.66
Constant (g eq./d)	-3.3	-6.3	-2.3	0.9
SEE	1.7	1.7	3.1	4.3
P>|kh-t|	0.07	0.004	0.465	0.86
3P	-	0.012	>0.99	>0.99
I^2 (g eq.^{2}/g eq.$_2$)	0.99	0.95	0.99	0.97
Tau (g eq./d)	6.9	9.8	7.7	7.9
P>Q	0.001	0.001	0.001	0.001
P>X	0.001	0.001	0.001	0.001

1 Model: difference in fat intake = slope (SEE) x difference in GI + constant (SEE) + Tau + SE.

2 Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 26(1)

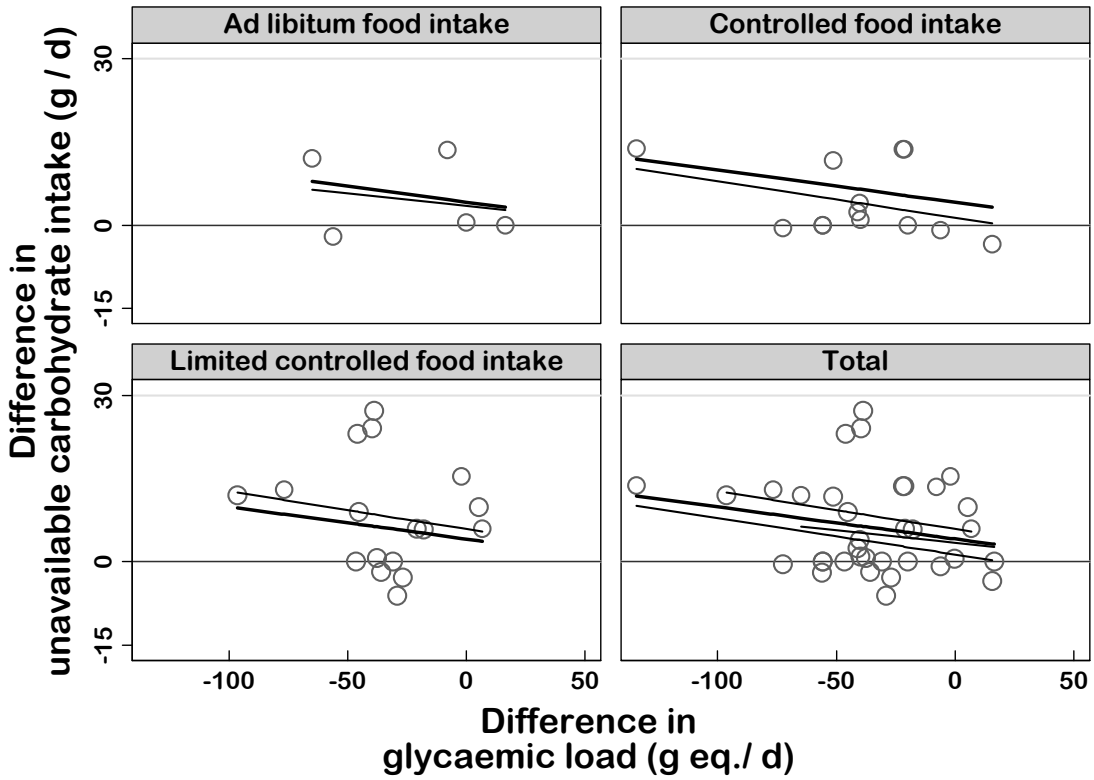

Fig 15: Macronutrient intakes: Difference in unavailable carbohydrate intake associated with difference in glycaemic load achieved. Observations are grouped by the category of control over food intake (where total is all categories combined). Each study is represented by a bubble proportional to inverse (Tau^2+SE^2). To facilitate comparison the curves in each graph show the same bold random effects regression curve for all categories combined as well as the category random effects regression curves.

Annex 26(2)

TABLE 12: Macronutrient Intakes: Difference in unavailable carbohydrate intakes in intervention studies related to difference in glycaemic load achieved, by category of food intake control.

	All studies combined	Control	Limited control	Ad libitum
k (df)	35 (33)	13 (11)	17 (15)	5 (3)
Slope (g/ g. eq)	-0.06	-0.07	-0.07	-0.04
SEE	0.05	0.05	0.09	0.11
P>|kh-t|	0.22	0.22	0.5	0.73
3P	-	0.66	>0.99	>0.99
Constant (g eq./d)	4.1	1.3	5.9	3.4
SEE	2.2	2.6	4.1	4.4
P>|kh-t|	0.07	0.63	0.17	0.49
3P	-	>0.99	0.51	>0.99
I^2 (g eq.^{2}/g eq.^{2})	0.99	0.87	0.99	0.91
Tau (g eq./d)	8.1	5.7	9.9	7.7
P>Q	0.001	0.001	0.001	0.001
P>X	0.001	0.001	0.001	0.001

[1] Model: difference in unavailable carbohydrate intake = slope (SEE) x difference in GI + constant (SEE) + Tau + SE.

[2] Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 27

TABLE 13: Macronutrient Intakes: Difference in available carbohydrate intakes in intervention studies related to difference in glycaemic load achieved, by difference in food intake category.

	All studies combined	Control	Limited control	Ad libitum
k (df)	38 (36)	14 (12)	19 (17)	5 (3)
Slope (g/ g. eq)	0.54	0.28	0.8	0.86
SEE	0.09	0.08	0.15	0.17
P>|kh-t|	0.001	0.005	0.001	0.02
3P	-	0.015	0.001	0.048
Constant (g eq./d)	21	15	28	22
SEE	4	4	7	7
P>|kh-t|	0.001	0.004	0.001	0.047
3P	-	0.012	0.003	0.141
I^2 (g eq.^{2}/g eq.^{2})	0.99	0.99	0.99	0.99
Tau (g eq./d)	16.4	10.6	16.6	12.3
P>Q	0.001	0.001	0.001	0.001
P>X	0.001	0.001	0.001	0.001

1 Model: difference in available carbohydrate intake = slope (SEE) x difference in GI + constant (SEE) + Tau + SE.

2 Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 28(1)

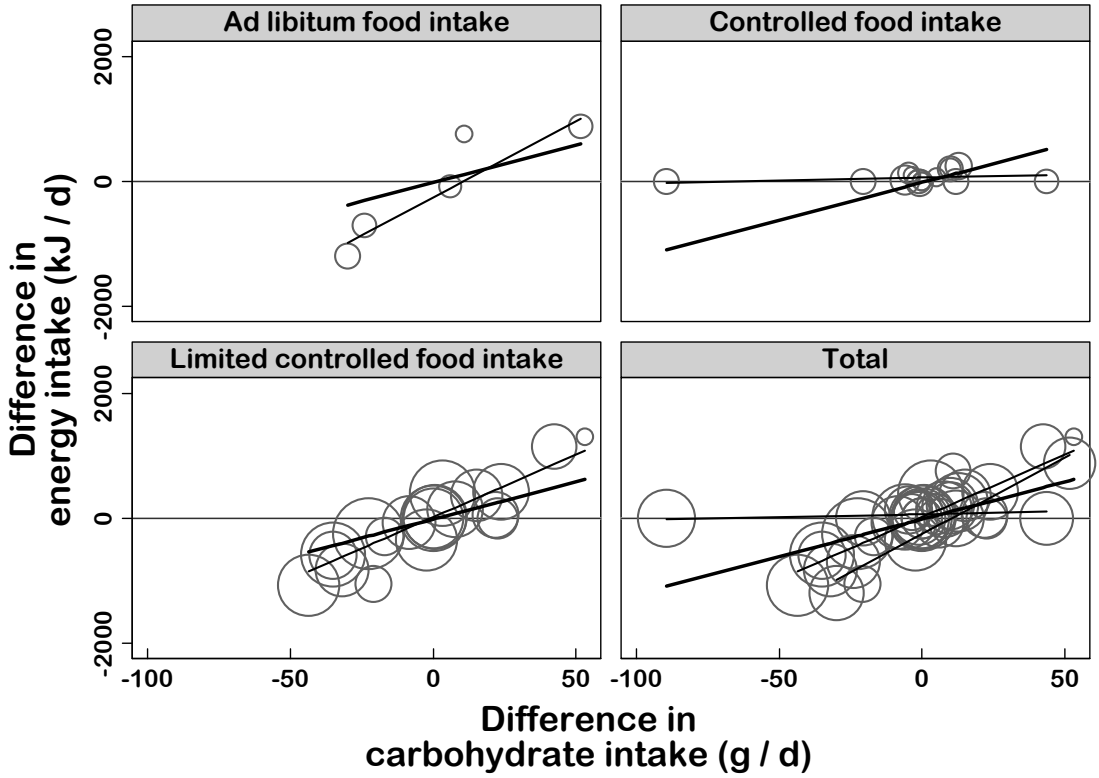

Fig 17: Macronutrient intakes: Difference in metabolisable energy intake associated with difference in available carbohydrate intake achieved. Observations are grouped by the category of control over food intake (where total is all categories combined). Each study is represented by a bubble proportional to inverse (Tau^2+SE^2). To facilitate comparison the curves in each graph show the same bold random effects regression curve for all categories combined as well as the category random effects regression curves.

Annex 28(2)

TABLE 15: Macronutrient Intakes: Difference in metabolisable energy intakes in intervention studies related to difference in carbohydrate intake achieved, by food intake control.

	All studies combined	Control	Limited control	Ad libitum
k (df)	40 (38)	15 (13)	20 (18)	5 (3)
Slope (kJ/g)	12	1	20	24
SEE	2	2	3	4
P>|kh-t|	0.001	0.67	0.001	0.012
3P		>0.99	0.003	0.036
Constant (kJ/d)	-15	64	18	-252
SEE	58	62	59	140
P>|kh-t|	0.79	0.32	0.76	0.17
3P		0.96	>0.99	0.51
I^2 (J^2/J^2)	0.56	0.00	0.27	0.22
Tau (kJ/d)	259	0	130	0
P>Q	0.001	1.00	0.13	0.28
P>X	0.001	1.00	0.02	1.00

1 Model: difference in metabolisable energy intake = slope (SEE) x difference in available carbohydrate + constant (SEE) + Tau + SE.

2 Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). P>Q probability of significant heterogeneity. P>X likelihood-ratio test of probability that Tau is >0.

Annex 29

Fat intake related to combined glycaemic aspects

In all categories without tight control over food intake, there is no significant association of GI_{ac}, GL or available carbohydrate intake and fat intake when these are combined in a single meta-regression analysis (**Table 16**). This agrees with previous analyses for glycaemic index of available carbohydrate alone (**Fig 6; Table 4**) and glycaemic load alone (**Fig 14**; **Table 11**).

TABLE 16: Macronutrient intakes: Difference in fat intakes related to difference in the glycaemic aspects achieved in all intervention studies combined excluding studies categories with controlled food intake [1,2].

	k (df)	Available carbohydrate	Glycaemic index	Glycaemic Load	Constant	I^2 (J^2/J^2) [3]	Tau (kJ/d) [4]
Slope (kJ/ g)	24 (20)	0.5	3	1	10	0.0	0.0
SEE		6.4	22	10	106		
P>|kh-t|		0.94	0.89	0.92	0.93		

1 Model: Δ fat intake = $slope_{AC}$(SEE) x ΔAC + $slope_{GI}$ (SEE) x ΔGI + $slope_{GL}$ (SEE) x ΔGL + constant (SEE) + Tau + SE.

2 Abbreviations: k, number of studies; df, degrees of freedom; P>|kh-t| statistical significance based on knapphartung t; Tau, standard error among studies, and I^2 variation among studies (Tau^2) as a proportion of total variation (Tau^2+SE^2). Δ difference between treatments, AC available carbohydrate, GI glycaemic index of available carbohydrate, GL glycaemic load.

Sources:

Included studies: As in Table in 14.

Excluded studies: As in Table in 14.

Annex 30:

Sources used in Fig 18

Included studies: see figure.

Excluded studies: Those with good control over food intake (k = 12; Brand et al 1991, Calle-Pascual 1988 (exp1_T2) , Calle-Pascual 1988 (exp2_T2), Carels et al 2005, Fontvieille et al 1992 ('exp1'), Fontvieille et al 1992 ('exp2'), Heilbronn 2002 (d2), Jarvi et al 1999, Jenkins et al 1987a (d2), Kiens et al 1996 (d4), Wolever et al 1992a (d3), Wolever et al 1992b (d2)) and those for which dietary information on glycaemic load was either unavailable or not calculable (k = 4, Agus et al 2000, Price (unpublished), Slabber et al 1994 (exp2), and Spieth et al 2000). Ten studies in the database were without information on the body weight response to treatment [Herrmann et al 2001 (expt2), Lafrance et al 1998, Kurup 1992 (raggi vs rice), Kurup 1992 (expt2 raggi vs tapioca), Frost et al 1998 (exp1), Frost et al 1998 (exp2), Kabir et al 2002, Collier et al 1988 (d2), Yin-fa (2003), and Gilbertson et al 2001.

Annex 31(1)

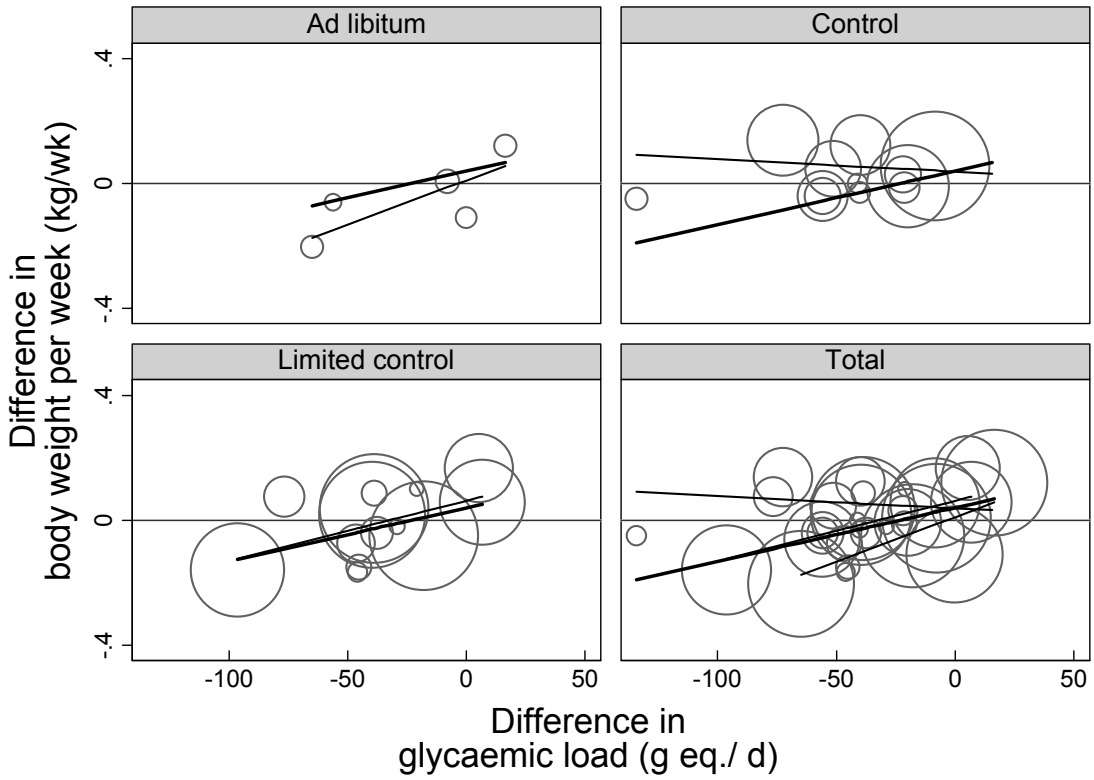

FIG 19: Body Weight: Difference in rate of change in body weight associated with the difference in glycaemic load. Observations are grouped by the category of control over food intake (where total is all categories combined). Each study is represented by a bubble proportional to inverse (Tau^2+SE^2). To facilitate comparison the curves in each graph show the same bold random effects regression curve for all categories combined as well as the category random effects regression curve. Details of the analyses are given in Table wt 2.

Sources:

Included studies: Those with good control over food intake [Agus et al 2000, Brand et al 1991, Calle-Pascual 1988 (exp1_T2), Calle-Pascual 1988 (exp2_T2), Carels et al 2005, Fontvieille et al 1992 ('exp1'), Fontvieille et al 1992 ('exp2'), Heilbronn 2002 (d2), Jarvi et al (1999), Jenkins et al 1987a (d2), Kiens et al 1996 (d4), Wolever et al 1992a (d3), Wolever et al 1992b (d2)]; and those with limited control over food intake [Bouche et al 2002, Fontvieille et al 1988, Frost et al 1994, Frost et al 1996, Frost et al 2004, Giacco et al 2000, Jenkins et al 1987b (all), Jenkins et al 1988, Jimenez-Cruz et al 2003, Komindr et al 2001, Luscombe et al 1999, Price (unpublished), Rizkalla et al 2004, Slabber et al 1994 (exp2)C, and Tsihlias et al 2000 (d2)]; and ad libitum control [Brynes et al 2003 (Su), Brynes et al 2003 (st), Ebbeling et al 2003 (d2), Sloth et al 2004 (d5), Spieth et al 2000, and Wolever & Mehling 2002a (d4)].

Excluded studies: Those without information on body weight response (k = 10), see legend to Fig wt 1.

Annex 31(2)

TABLE 18: Body Weight: The influence of glycaemic load on the average rate of change in body weight with time, by food intake control category. [1]

Food intake category	k (df)	Slope ($g.\ wk^{-1}$ per $g\ eq.d^{-1}$)	SEE	P>|kh-t|	2P [2]	Tau (kg/wk)	I^2 $(kg/wk)^2$
Control	12 (10)	-0.4	1.4	0.8	'-	0.000	0.00
Limited control	14 (12)	1.9	0.9	0.052	0.104	0.052	0.27
Ad-libitum	5 (3)	2.8	1.3	0.11	0.222	0.081	0.83
Ad-libitum + limited control combined	19 (17)	2.1	0.7	0.011	-	0.071	0.75
All categories combined	31 (29)[3]	1.7	0.7	0.017	-	0.071	0.64

1 Abbreviations: k, number of studies; df degrees of freedom; SEE, standard error of estimation; P>|kh-t|, level of significance based on Knapp-Hartung-t; Tau, among studies error; I^2, proportion of variance due to among study variance.

2 Bonferroni adjusted P value, multiplication by 2 to account for the division of studies with freedom to two categories.

3 Presented as if the control category had representative degrees of freedom.

Annex 32

Sources used in Fig 20

Included studies are prior to 2005 and are those designed as weight control studies, which are Price et al, unpublished; Slabber et al 1994 (exp2), Sloth et al 2004 (d5), Spieth et al 2000, Ebbeling et al 2003 (d2), and those with either ad-libitum intake or limited control intake in which the reduction of glycaemic load is by more than 50 g eq. per day achieved by carbohydrate (available or total) exchange, and which are Brynes et al 2003 (st), Rizkalla et al 2004, Luscombe et al 1999, Bouche et al 2002, Jimenez-Cruz et al 2003.

Excluded studies are those for which there is either good control over food intake [Brand et al 1991, Calle-Pascual 1988 (exp1_T2), Calle-Pascual 1988 (exp2_T2), Carels et al 2005, Fontvieille et al 1992 ('exp1'), Fontvieille et al 1992 ('exp2'), Heilbronn 2002 (d2), Jarvi et al 1999, Jenkins et al 1987a (d2), Kiens et al 1996 (d4), Wolever et al 1992a (d3)], or in which glycaemic load reduction is by no more than 50 g equivalents [Jenkins et al 1988, Fontvieille et al 1988, Brynes et al 2003 (Su), Frost et al 1996, Komindr et al 2001, Jenkins et al 1987b (all), Frost et al 1994, Frost et al 2004, Wolever & Mehling 2002a (d4), Giacco et al 2000, Tsihlias et al 2000 (d2).] or studies without information on body weight response, as give in Fig. 18.

Annex 33

TABLE 20: Fasting Glucose: Treatment fractional correction of fasting blood glucose.

		All studies including sub-maintenance intakes with fasting blood glucose >5mmol/L	All studies at maintenance intakes with fasting blood glucose >5mmol/L
Number of studies		22	18
Degrees of freedom		20	16
Fractional correction ($-\Delta$ mmol.L^{-1} per mmol.L^{-1})		0.30	0.30
REML-z	SEE[1]	0.10	0.12
REML-kh-t	SEE	0.10	0.12
Moments-z	SEE	0.11	0.11
REML-z	P>|z|	0.002	0.010
REML-kht	P>|kht|	0.010	0.026
Moments-z	P>|z|	0.002	0.009
Moment-mcp	P>|mcp|	0.005	0.014
Proportion of variance due to heterogeneity (I^2) [2]		0.71	0.66
Likelihood ratio-test for heterogeneity differing from zero (Tau^2=0) [3],	P>|Chibar|	0.000	0.000

1. SEE, standard error of estimation
2. I^2 is the ratio of among-study variation / sum of among-study variation and within study variation.
3. Tau^2 is the among-study variation.

Annex 34

TABLE 21: Fasting Glucose: Correction of fasting blood glucose by low glycaemic carbohydrate diets for fasting blood glucose >5mmol/L.

	Fractional correction	lower 95	upper 95	P>|kht|	k, df
Unlimited	-0.30	-0.51	-0.08	0.01	22,20
Limited to column a.	-0.25	-0.59	0.10	0.14	12,10
Limited to column b.	-0.27	-0.72	0.18	0.20	10,8

	a	b
Energy	± 1000kJ	± 500kJ
Av. carb	± 100 g	± 50 g
Fat	± 20 g	± 10 g
Protein	± 20 g	± 10 g
Unavailable carb.	± 20 g	± 10 g

Annex 35

TABLE 22: Fasting Glucose: Correction of fasting blood glucose by low glycaemic (variable unavailable carbohydrate) diets, before and after adjustment for changes in potential covariates[1].

		Fractional correction	SEE	P>|kh-t|	k. df
Before adjustment		-0.30	0.12	0.026	18,16
Adjusted for:	P>|kh-t| covariate				
Carbohydrate (g)	0.99	-0.34	0.13	0.021	16,13
Energy (kJ)	0.93	-0.33	0.13	0.027	16,13
GL (g glu eq.)	0.81	-0.34	0.12	0.017	16,13
Fat (g)	0.44	-0.32	0.12	0.024	16,13
GI (%G, as is)	0.38	-0.30	0.12	0.029	18,15
Protein (g)	0.34	-0.32	0.13	0.03	15,12
Unavailable carb (g)	0.21	-0.26	0.14	0.09	15,12

1. Fasting glucose > 5mmol/l at maintenance intakes

Annex 36

TABLE 23: Fasting Glucose: Influence of the resulting change in regular dietary parameters on the parameter significance and the among-study variance estimate for reduction in fasting glucose.

Interactive parameter [1]	P>|kh-t|	Tau^2	n, df
Severity, S (mmolL^{-1} per mmolL^{-1})	0.000	0.36	17, 16
S x Sugar (exchange category) [2]	0.001	0.44	14, 13
S x Δ protein (g/d)	0.05	0.94	14, 13
S x Δ energy (kJ/d)	0.64	1.40	15, 14
S x Δ available carbohydrate (g/d)	0.59	1.42	15, 14
S x Δ fat (g/d)	0.94	1.49	15, 14

1. Alone, i.e. without constant during random effects REML regression.
2. Two diets versus twelve.

Annex 37

TABLE 24: Fasting Glucose: Influence of the resulting change in key dietary parameters on the parameter significance and the among-study variance estimate for reduction in fasting glucose [1]: single parameter

Interactive parameter [2]		P>|kh-t|	Tau^2	k, df
Severity, S alone		0.000	0.36 [3]	17,16
S x Δ GL as is	glycaemic load	0.002	0.54	15, 14
S x Δ GL/'AC'	glycaemic index (per AC)	0.000	0.32	17, 16
S x Δ (GL+F)/('AC'+UC+P+F)	'glycation' index (per OM)	0.000	0.32	13, 12
S x Δ unavailable carbohydrate		0.001	0.35	14,13

1. Abbreviations: GL, glycaemic load; AC, available carbohydrate; F, fat; UC, unavailable Carbohydrate; P, protein, OM organic mass; Δ, change.
2. Alone, i.e. without constant during random effects REML regression
3. Remains 0.36 after dropping studies where the glycation parameter was not calculable Resulting in k = 13, df = 12.

Annex 38

TABLE 25: Fasting Glucose: Influence of the resulting change in key dietary parameters on the parameter significance and the among-study variance estimate for reduction in fasting glucose[1] (k =14, df=12): two parameter models with inclusion of studies with fasting glucose >5mmol/l, studies at maintenance, and studies with a rise in UC and fall in GI.

Interactive parameters [2]	Parameter interacting with S	P>|kh-t|	Tau[2]
Severity, S (n=14, df=12)			0.32
S x ΔGL	glycaemic load	0.060	0.23
+ S x Δ UC	unavailable carbohydrate	0.009	
S x Δ(GL/AC)	glycaemic index (per AC)	0.021	0.23
+ S x Δ (UC/AC)	unavailable carbohydrate index (per AC)	0.014	
S x (Δ(GL/AC) - Δ(UC/AC))	glycaemic index inclusive of UC	0.026	0.17
+ S x (Δ UC)	unavailable carbohydrate	0.052	
S x Δ(GL/AC)	glycaemic index (per AC)	0.024	0.16
+ S x Δ UC	unavailable carbohydrate	0.008	
S x Δ(GL/TC)	glycaemic index (per TC)	0.026	0.16
+ S x Δ UC	unavailable carbohydrate	0.022	
S x Δ(AC-GL) +	aglycaemic carbohydrate 1	0.037	0.14 [3]
+ S x Δ UC	unavailable carbohydrate	0.008	
S x Δ(TC-GL) +	aglycaemic carbohydrate 2	0.037	0.14 [3]
+ S x Δ UC	unavailable carbohydrate	0.046	

1. Abbreviations: S, severity, GL, glycaemic load; UC, unavailable carbohydrate; AC, available carbohydrate; TC, total carbohydrate; Δ, change.
2. Two parameters (where shown) without constant during random effects REML regression
3. Significant reduction in Tau^2 at P<0.1 (F-ratio) when ignoring multiple equations and model parameter additions, otherwise no one model is a significant improvement on any other.

Annex 39

TABLE 26: Fasting Glucose: The influence of study characteristic (inclusion/exclusion) on the parameter estimates relating the change in fasting glucose to change in the glycaemic and unavailable carbohydrate character of diets

		Glycaemic character		Unavailable character				
k[1]	Parameter	SEE	P>|kh-t|	Parameter	SEE	P>|kh-t|	Tau^2	I^2
	S x ΔGL			S x Δ UC				
31	0.0023	0.0009	0.02	-0.011	0.004	0.01	0.02	0.65
25	0.0024	0.0010	0.04	-0.014	0.005	0.01	0.02	0.67
19	0.0031	0.0014	0.04	-0.010	0.005	0.04	0.28	0.64
15	0.0034	0.0016	0.05	-0.013	0.005	0.04	0.32	0.64
14	0.0028	0.0014	0.06	-0.015	0.005	0.01	0.24	0.59
	S x Δ(GL/AC)			S x Δ UC				
31	0.0067	0.0022	0.00	-0.011	0.004	0.01	0.01	0.60
25	0.0068	0.0025	0.01	-0.014	0.004	0.01	0.01	0.62
19	0.0080	0.0029	0.01	-0.014	0.004	0.03	0.21	0.59
15	0.0088	0.0033	0.02	-0.012	0.005	0.03	0.22	0.59
14	0.0074	0.0029	0.02	-0.014	0.004	0.01	0.16	0.52
	S x Δ(AC-GL)			S x Δ UC				
31	-0.0030	0.0009	0.00	-0.011	0.003	0.00	0.01	0.54
24	-0.0028	0.0010	0.01	-0.014	0.004	0.00	0.01	0.57
19	-0.0033	0.0012	0.01	-0.011	0.004	0.02	0.17	0.58
15	-0.0034	0.0014	0.03	-0.013	0.006	0.03	0.20	0.59
14	-0.0028	0.0012	0.04	-0.015	0.005	0.01	0.14	0.52

1 All studies with AC, GI, and UC included (k = 31), retaining only those at maintenance (k = 25) or with fasting glucose >5 mmol/L (k = 19) or both (k=15), and retaining all studies with no fall in UC and no rise in GI (k=14)

2 Abbreviations: n, number of studies; SEE, standard error of estimation; P, level of significance based on Knapp-Hartung-t, Tau2, between study variance; I2, proportion of variance due to between study variance; S, severity of abnormality in fasting glycaemia; GL, glycaemic load, AC, available carbohydrate.

Annex 40

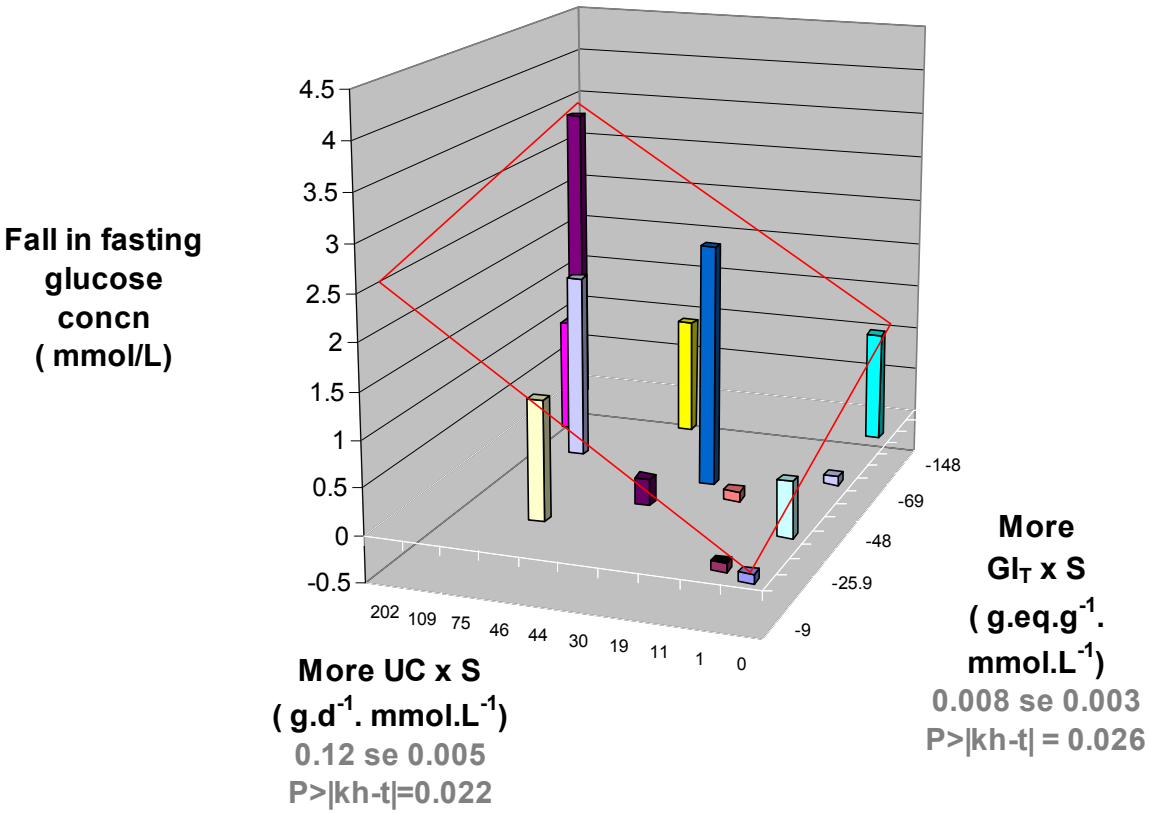

Fig 24: Fasting Glucose: A second trivariate set of determinants of the effect size for reduction in fasting glycaemia.

Here the severity of abnormality in fasting glucose (S = FBG – 5 mmol/L), unavailable carbohydrate (UC) and glycaemic index, calculated on the basis of total carbohydrate, (GI_T) are the explanatory variables. NB axes rise discontinuously. Each vertical bar is an individual study. The tilted quadrangle joins predicted points at each corner with straight lines

Annex 41

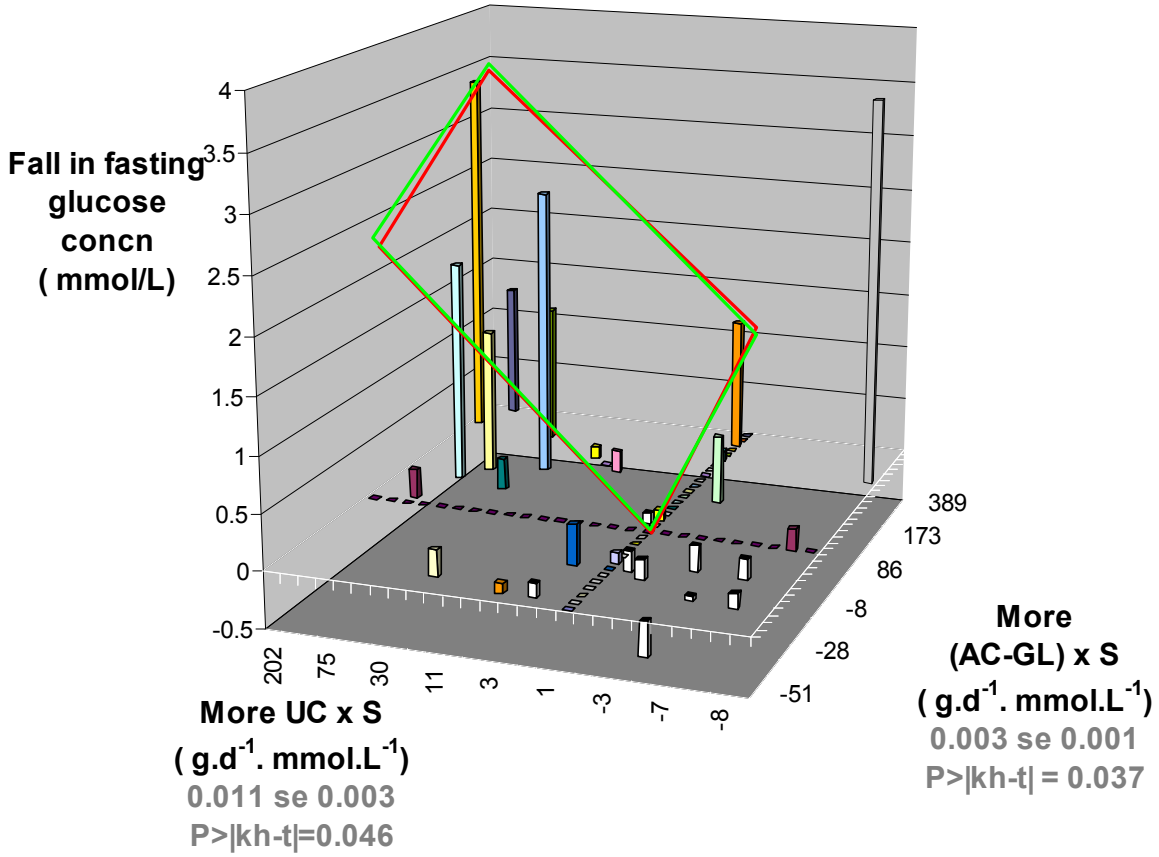

Fig 25: Fasting Glucose: A third trivariate set of determinants of the effect size for reduction in fasting glycaemia.

Here severity of abnormality in fasting glucose (S = FBG - 5), unavailable carbohydrate (UC) and aglycaemic carbohydrate (AC-GL) are the explanatory variables. The tilted quadrangle joins predicted points at each corner ($x \geq 0$, $z \geq 0$) with straight lines, red for all 31 studies and green for 30 studies when excluding the outlying datum (grey rightmost column) for the purpose of assessing influence only. This study was 4.2 residual standard errors from its predicted value, however, being a study of low power, and not yielding a result significantly different from zero, its influence statistic $\Delta\hat{\beta}ij = 0.22$ was less than 1, indicating a small influence, as apparent from the red and green quadrangles. NB axis rise discontinuously. Each vertical bar is an individual study.

Annex 42

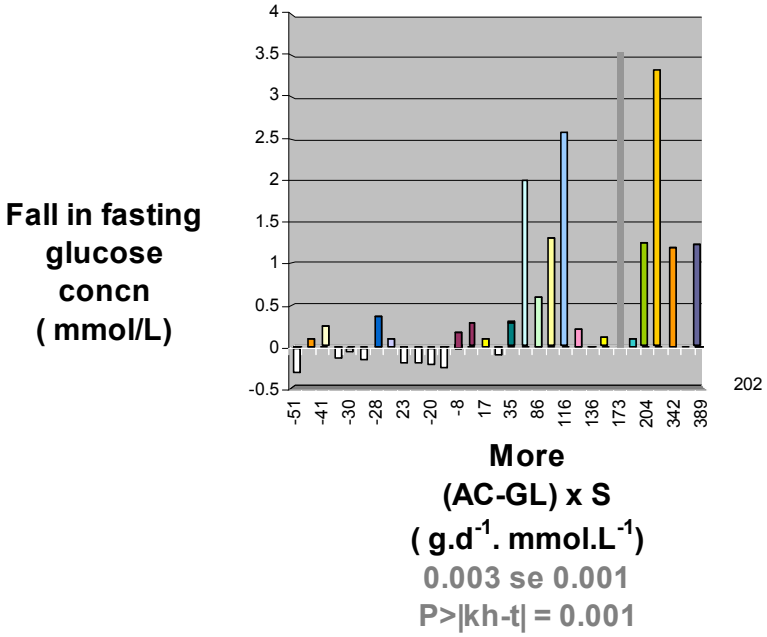

Fig 26: Fasting Glucose: View facing the right-hand side of prior Fig. 25.

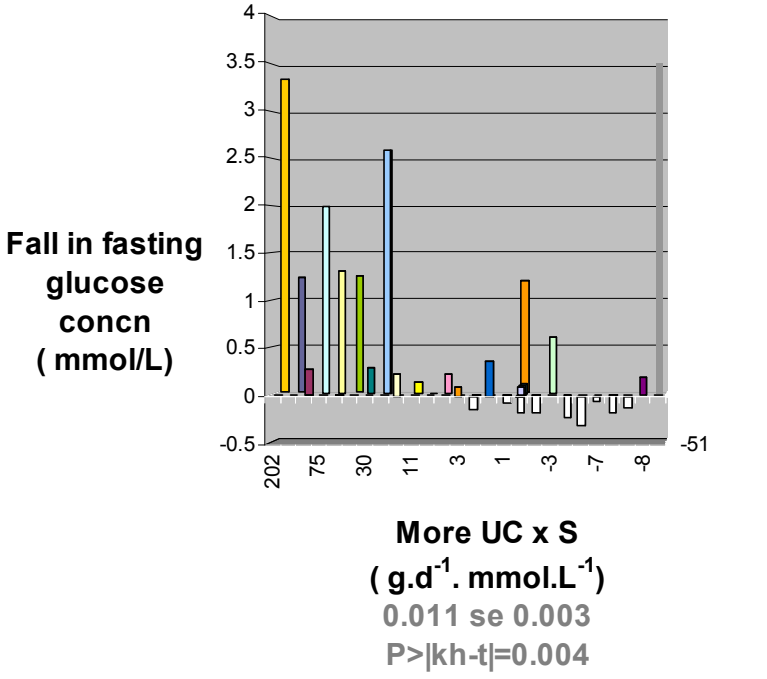

Fig 27: Fasting Glucose: View facing the front side of prior Figure 25.

Annex 43

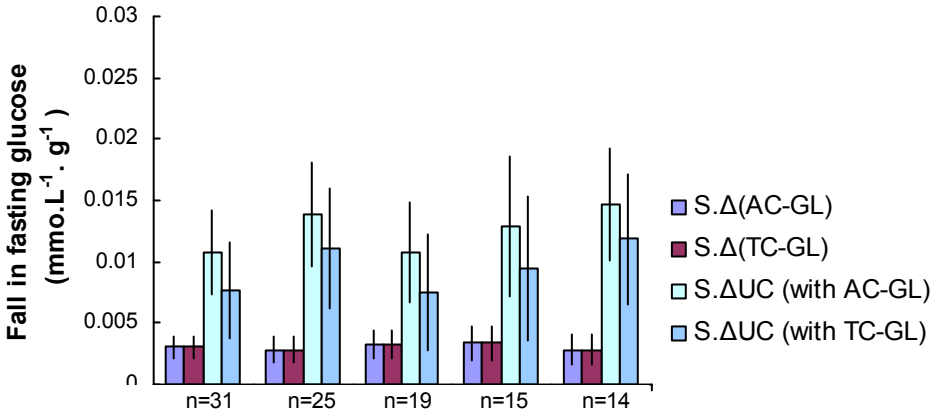

Fig 28: Fasting Glucose: Implications of using total rather than available carbohydrate when attributing determinants of the treatment difference in fasting blood glucose.

Data are parameter estimates and standard errors of estimation for, and are shown for all studies (k = 31), after exclusion of studies at sub-maintenance energy intakes (k remaining = 19), after further exclusion of studies with fasting glucose <5mmol/L (k remaining =15), and after further exclusion of an outlying study (k remaining = 14). Abbreviation: S, severity of abnormity in fasting glucose; TC total carbohydrate, GL glycaemic load. The legend identifies parameter estimates for two meta-regression models including the determinants S x Δ(AC-GL) and S x ΔUC (no constant) in one model and S x Δ(TC-GL) and S x ΔUC (no constant) in another.

Annex 44

TABLE 29: Fasting Glucose: Comparison of outcomes when exchanging glycaemic index, glycaemic load and aglycaemic carbohydrate in diabetics (Degrees of freedom = k-2).

	Glycaemic character			Unavailable character				
k	Coefficient	SEE	P>|kh-t|	Coefficient	SEE	P>|kh-t|	Tau^2	I^2
All type-1 and 2 diabetics together								
	S x Δ(AC-GL)[1]			S x Δ UC[1]				
18	-0.0033	0.0012	0.02	-0.011	0.004	0.02	0.21	0.59
	S x ΔGL[1]			S x Δ UC[1]				
18	0.0032	0.0015	0.04	-0.010	0.005	0.048	0.33	0.65
	S x ΔGI			S x Δ UC[1]				
18	0.0082	0.0030	0.02	-0.010	0.004	0.03	0.25	0.60

Abbreviations: k, number of studies; SEE, standard error of estimation; P, level of significance based on Knapp-Hartung-t, Tau2, between study variance; I2, proportion of variance due to between study variance; S, severity of abnormality in fasting glyca

1. Units: $mmol.L^{1}$ per g change in aglycaemic carbohydrate or unavailable carbohydrate, except in the case of glycaemic index when it is $mmol\text{-}L^{1}$ per $g.100g^{-1}$

Annex 45 (1)

TABLE 30: Fasting Glucose: Estimation and application of prediction factors for fasting glucose. (Degrees of freedom = k – 2.)

Estimated prediction factors

k[1]	Coefficient S x Δ(AC-GL)	SEE	P>|kh-t|	Coefficient S x Δ UC	SEE	P>|kh-t|	Tau^2	I^2
2 to 26 weeks								
31	-0.0030	0.0009	0.001	-0.011	0.003	0.004	0.01	0.54

Application of prediction factors

Meta-regression observed versus predicted

	n [1]	Coefficient	SEE	P>|kh-t|	Tau^2	I^2
to all weeks	31	0.99	0.15	0.000	0.01	0.52
to <12 weeks	25	1.03	0.18	0.000	0.01	0.55
to >12 weeks	6	0.92	0.26	0.016	0.02	0.42

1 Abbreviations: n, number of studies; SEE, standard error of estimation; P, level of significance based on Knapp-Hartung-t, Tau2, between study variance; I2, proportion of variance due to between study variance; S, severity of abnormality in fasting glycaemia; GL, glycaemic load, AC, available carbohydrate.

Here predicted outcomes were based on the severity of abnormality in fasting glucose, and the unavailable and aglycaemic carbohydrate intakes as determinants (cf **Table 27**, n = 31)

More detail is show for the individual studies ≥ 12 weeks in **Fig. 31** (this Annex).

Studies with outcomes showing little effect were as predicted, likewise studies with larger changes in fasting glucose.

The coefficient of equality between observed and predicted changes was 1.03 SEE 0.18 in studies <12 weeks duration and 0.92 SEE 0.26 in those ≥ 12 weeks (**Table 30:** this annex). Thus observed values from studies of >12 weeks duration were neither practically nor significantly different to those

predicted; as such there was no obvious loss of potency of dietary treatment with the studies of longer duration.

Annex 45 (2)

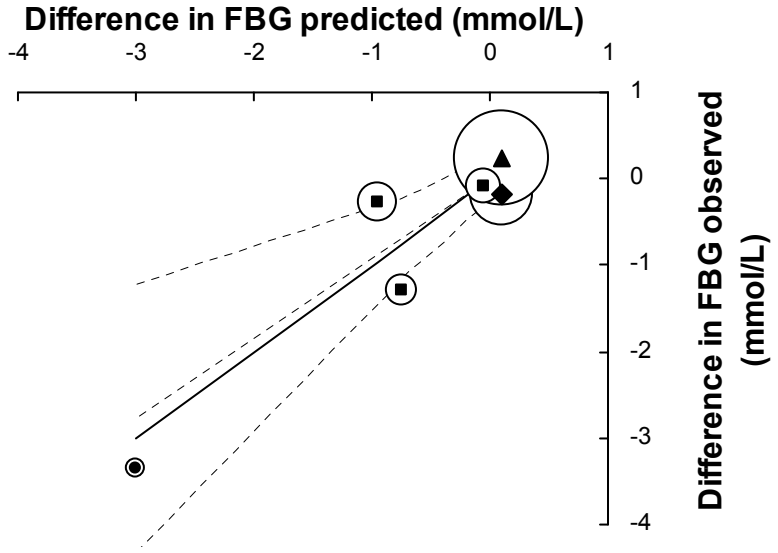

Fig 31 Fasting Glucose: Trend for difference in fasting blood glucose (FGB) comparing model predicted differences with observed differences for studies ≥ 12 weeks duration.
Predictions are based on the severity of abnormality in fasting glycaemia (FFBG-5), and changes in unavailable carbohydrate and aglycaemic carbohydrate (AC-GL) ingestion during treatment (Table 8, k = 31 studies). Data are for individual studies, one in type-1 diabetes (●), three in type-2 diabetes, (■), one study with individuals at increase risk of CHD (▲), and one study in individuals with impaired glucose tolerance (♦). Bubbles show study weights (inverse variance). The random effects regression line and corresponding 95% confidence intervals for the population of studies are shown (--------). Line of identity (——).

Annex 46

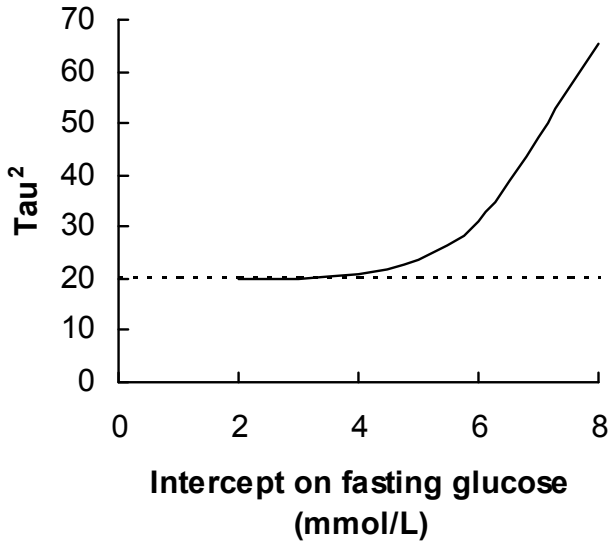

Fig 33: Glycated Proteins: Intercept on the average fasting glucose concentration for the difference in glycated protein.

Tau^2 is variance among studies, and is derived by fitting a no constant inverse variance random effects regression of the 'difference in glycated protein concentration' (k = 28 studies) on the 'average of fasting blood glucose concentration' less an unknown 'trial' intercept'. Tau^2 is evidently minimised at below a clinically relevant 7 mmol/L, approx 5 mmol/L is assumed.

Annex 47

TABLE 31: Glycated Proteins: Random effects meta-regression [1] for treatment differences in glycated proteins according to methods difference.

Measurement	k (df) [2]	Units for slope	Slope (zero effect at 5mmol/L glucose)[3]	SEE	P>|kh-t|	Tau^2 (%.%) [4, 5]	I^2 [5]
Unadjusted							
Fructosamine	12 (11)	(% per mmol glucose/L)	-2.76	0.52	0.001	27	0.85
HbA_{1c}	17 (16)	(% per mmol glucose/L)	-0.98	0.57	0.11	80	0.96
Combined	24 (23)	(% per mmol glucose/L)	-1.88	0.34	0.001	23	0.82
Adjusted for half-lives							
Fructosamine	12 (11)	(% per mmol glucose/L)	-3.8	0.80	0.001	69	0.78
HbA_{1c}	17 (16)	(% per mmol glucose/L)	-1.8	1.30	0.17	416	0.96
Combined	24 (23)	(% per mmol glucose/L)	-2.79	0.62	0.001	98	0.83

1 The model: ΔT (%MT) = slope x (fasting glucose - 5) + Tau^2 + SE (noconstant).

2 Shows k number of studies and df degrees of freedom.

3 No constant forced at a fasting glucose concentration of 5 mmol/L.

4 Likelihood-ratio test of significance for tau^2, P>|Xbar| <0.001 in all cases.

5 Abbreviations: ΔT, difference due to dietary treatment; MT average outcome of dietary treatments; Tau^2, variation among studies; I^2 ,ratio of variation among studies to sum of variation among studies and within studies.

Annex 48

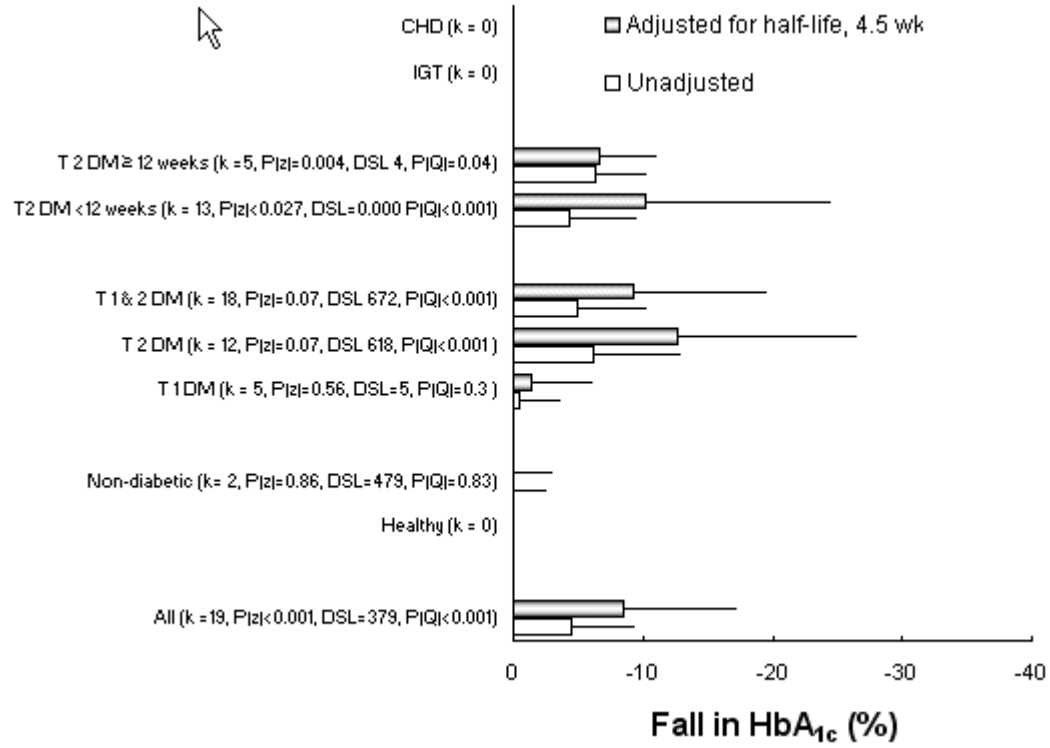

Fig 35: Glycated Proteins: Combined mean and 95% confidence interval for treatment differences in HbA_{1c} concentration, by health type and duration.

Abbreviations are: CHD risk of primary coronary heart disease; IGT, impaired glucose tolerance; T2DM, type-2 diabetes mellitus, T1DM, type-1 diabetes mellitus; k, number of studies (zero when no studies published prior to 2005); P|z|, probability based on the z-score for a statistical significant difference from zero; DSL , Der Simonian and Laird estimate of between studies variance (%.%), and PQ, probability of significant among-studies variation based on the Q-statistic, with degrees of freedom = k-1.

Annex 49

TABLE 32: Glycated Proteins: Random effects meta-regression [1] for treatment differences in fructosamine: influence of the glycaemic character, unavailable carbohydrate and severity of abnormality in fasting blood glucose.

Parameter	Units for slope	Slope (zero effect at 5mmol/L glucose)	SEE	P>|kh-t|	Tau^2 (%.%) [2,3]	I^2 [3]	k (df) [4]
Without dietary characteristics							
S	(% per mmol/L)	-2.75	0.52	0.001	28	0.85	12 (11)
With glycaemic load							
S x GL	(% per g.mmol/L)	0.044	0.018	0.039	72	0.90	12 (10)
S x UC	(% per g.mmol/L)	-0.214	0.103	0.063			
With glycaemic index of available carbohydrate							
S x (GL/AC)	(% per g%.mmol/L)	0.107	0.04	0.016	57	0.89	12 (10)
S x UC	(% per g.mmol/L)	-0.165	0.10	0.123			
With glycaemic index of total carbohydrate							
S x (GL/TC)	(% per g%.mmol/L)	0.121	0.04	0.016	57	0.89	12 (10)
S x UC	(% per g.mmol/L)	-0.149	0.10	0.164			
With aglycaemic carbohydrate							
S x (AC-GL)	(% per g.mmol/L)	-0.044	0.01	0.009	52	0.89	12 (10)
S x UC	(% per g.mmol/L)	-0.103	0.10	0.321			

1 The model: ΔT (%MT) = $slope_1$ x ($parameter_1$) + $slope_2$ x $parameter_2$ + Tau^2 + SE (noconstant).

2 Likelihood-ratio test of significance for Tau^2, P>|Xbar| <0.001 in all cases.

3 Abbreviations: ΔT, difference due to dietary treatment; MT average outcome of dietary treatments; Tau^2, variation among studies; I^2, ratio of variation among studies to sum of variation among studies and within studies.

4 Shows k number of studies and df degrees of freedom.

Annex 50

TABLE 33: Fasting Insulin: Summary of fixed and random effects[1] meta-analysis for treatment differences in fasting insulin

Conditions	k (df) [2]	Combined mean effect [3]	SE	P>|z|	Q [4]	Hetero-geneity P>X [4]	DSL variance [1]
All with insulin < 100 pmol/L	12 (11)	2.7	3	0.32	5.4	0.91	0
All with insulin >100 pmol/L	6 (5)	-12	18 [5]	0.49	10.7	0.06	930
All non-diabetic with insulin >100 pmol/L	2 (1) [6]	-73	23	0.001	0.59	0.44	0
All type 2 diabetics	5 (4)	5.9	6.8	0.38	1.2	0.88	0
All overweight or obese non-diabetic with insulin <100 pmol/L	5(4)	4.6	3.9	0.24	2.6	0.626	0
All overweight or obese non-diabetic with insulin >100 pmol/L	2 (1) [6]	-73	23	0.001	0.59	0.44	0

1 All analyses were conducted with random effects, data report random effects when the Der Simonian and Laird estimate of between studies variance is >0 otherwise data report fixed effects.

2 Shows k number of studies and df degrees of freedom.

3 A normal value for fasting insulin is typically 53 pmol/l.

4 Q-test for heterogeneity and its significance, heterogeneity P greater than chi-square.

5 The 95% confidence intervals for this random effects result are -47 to +22 pmol/l.

6 Below minimal considered acceptable for meta-analysis

Annex 51

TABLE 34: Insulin Sensitivity: Summary of fixed and random effects[1] meta-analysis for treatment differences in fasting insulin.

Conditions	k (df) [2]	Combined mean effect (%rise)	95% CI for the mean	P>|z|	Q [3]	Hetero-geneity [3] P>X	DSL variance (%.%)[1]
All studies	18 (17)	20	6 to 33	0.004	78	0.001	563
All non diabetics (ostensible healthy)	12 (11)	25	5 to 44	0.014	68	0.001	879
Healthy	5 (4)	22	-5 to 49	0.11	20	0.001	724
Impaired glucose tolerance	2 (1) [4]	16	-4 to 36	0.11	-[4]	-	-
Type 2 DM	5 (4)	12	2 to 22	0.014	1.4	0.65	0
Type 1 DM	1 (-) [4]	3	-28 to 33	0.87	-[4]	-	-
1^{o} and 2^{o} CHD risk	5 (4)	29	-3 to 63	0.08	22	0.001	1049

1 All analyses were conducted with random effects, data report random effects when the Der Simonian and Laird estimate of between studies variance is >0 otherwise data report fixed effects.

2 Shows k number of studies and df degrees of freedom.

3 Q-test for heterogeneity and its significance, heterogeneity P greater than chi-square.

4 Too few studies (<3) were undertaken to warrant providing full data from meta-analysis (random effects assumed).

Annex 52

TABLE 35: Insulin Sensitivity: Summary of fixed and random effects[1] meta-analysis for treatment differences in fasting insulin.

Conditions	k (df) [2]	Combined mean effect (%rise)	95% CI	P>|z|	Q [3]	Hetero-geneity P>X [3]	DSL variance [1]
All studies	18 (17)	20	6 to 33	0.004	78	0.001	563
Normal wt [4] (from all studies)	4 (3)	27	-15 to 69	0.21	57	0.001	1706
Overweight [4] (from all studies)	11 (10)	12	4 to 20	0.004	7	0.76	0
Obese [4] (from all studies)	3 (3)	28	7 to 49	0.009	3	0.27	84
Obese + overweight [4] (from all studies)	14 (13)	14	7 to 21	0.001	11	0.59	0

1 All analyses were conducted with random effects, data report random effects when the Der Simonian and Laird estimate of between studies variance is >0 otherwise data report fixed effects.

2 Shows k number of studies and df degrees of freedom.

3 Data and values of k are for the primary measurement method reported (supporting methods were ignored in this analysis)

4 Normal weight, overweight and obese refer to body mass index (BMI,) of <25, 25 to 30, & >30 $kg.m^{-2}$

Annex 53

TABLE 36: Insulin Sensitivity: Summary of fixed and random effects[1] meta-analysis for treatment differences in insulin sensitivity according to study duration.

Conditions	k (df) [2]	Combined mean effect	95% CI for the mean	P>|z|	Q [3]	Hetero-geneity P>X [3]	DSL variance (%.%)[1]
All studies	18 (17)	20	6 to 33	0.004	78	0.001	563
All studies <12 weeks	14 (13)	20	3 to 35	0.015	74	0.001	661
All studies ≥ 12 weeks	4 (3)	16	-4 to 35	0.11	4	0.24	112

1 All analyses were conducted with random effects, data report random effects when the Der Simonian and Laird estimate of between studies variance is >0 otherwise data report fixed effects.

2 Shows k number of studies and df degrees of freedom.

3 Q-test for heterogeneity and its significance, heterogeneity P greater than chi-square.

Annex 54

TABLE 37: Insulin Sensitivity: Summary of fixed and random effects[1] meta-analysis for treatment differences in insulin sensitivity by method

Conditions	k (df) [2]	Combined mean effect (% rise)	95% CI for the mean	P>|z|	Q [3]	Heterogeneity P>X [3]	DSL variance (%.%)[1]
All studies (without 2[ary] measures) [5]	18 (17)	20	5 to 33	0.004	78	0.001	563
Euglycaemic hyperinsulinaemic clamp	3 (2)	7	-5 to 30	0.54	5.7	0.06	237
Homa S	5 (4)	13	-2 to 29	0.10	4.8	0.30	59
Insulin tolerance test	3 (2)	41	4 to 78	0.03	33	0	971
Freq. sample iv. glucose tolerance	1 (-) [6]	20	-38 to 77	0.05	-[6]	-	-
Inverse HOMA PP	8 (7)	30	-9 to 79	0.03	22	0.001	995
Erythrocyte binding	2 (1) [6]	3	-23 to 28	0.84	-[6]	-	-
Adipocyte	3 (2)	35	-20 to 91	0.21	21	0.001	2058

1 All analyses were conducted with random effects, data report random effects when the Der Simonian and Laird estimate of between studies variance is >0 otherwise data report fixed effects.

2 Shows k number of studies and df degrees of freedom.

3 Q-test for heterogeneity and its significance, heterogeneity P greater than chi-square.

5 Where two methods were used to assess insulin sensitivity combining all studies, preference was give to in vivo or primary method reported.

6 Too few studies (<3) were undertaken to warrant providing full data from meta-analysis (random effects assumed).

Annex 55

Sources of Figure 41

Sources (included, from top of the figure):
Ad CHD: Frost et al 1996, *CHD Risk:* Brynes et al 2003 (st), Brynes et al 2003 (Su), Frost et al 1998 (exp1), Frost et al 2004 *Healthy:* Bouche et al 2002, Sloth et al 2004 (d5), Ebbeling et al 2003 (d2), and Frost et al 1998 (exp2), Kiens et al 1996 (d4), *Impaired glucose tolerance (IGT):* Slabber et al 1994 (exp1)P, and Wolever & Mehling 2002a (d4), *Type 1 diabetes:* Fontvieille et al 1992 ('exp1'), *Type 2 diabetes:* Rizkalla et al 2004, Kabir et al 2002, Jarvi et al 1999, Fontvieille et al 1992 ('exp2'), and Komindr et al 2001.

Studies for which no measures of insulin sensitivity were found are automatically excluded: Agus et al 2000, Brand et al 1991, Calle-Pascual 1988 (exp1_T1), Calle-Pascual 1988 (exp2_T2), Carels et al 2005, Collier et al 1988 (d2), Fontvieille et al 1988, Frost et al 1994, Giacco et al 2000, Gilbertson et al 2001, Heilbronn 2002 (d2), Herrmann et al 2001 (expt2), Jenkins et al 1987a (d2), Jenkins et al 1987b (all), Jenkins et al 1988, Jimenez-Cruz et al 2003, Jimenez-Cruz et al 2004, Kurup 1992 (raggi vs rice), Kurup 1992 (expt2 raggi vs tapioca), Lafrance et al 1998, Luscombe et al 1999, Pereira et al 2004, Price (unpublished), Spieth et al 2000, Tsihlias et al 2000 (d2), Wolever et al 1992a (d3),Wolever et al 1992b (d2), andYin-fa (2003)

Annex 56

TABLE 38: Insulin Sensitivity: Summary of inverse variance random effects meta-regression analysis for treatment differences (%) in insulin sensitivity according to dietary treatment.

Conditions[1]	k (df) [2]	Units for mean effect	Combined mean effect	SEE	P>|kh-t|	Tau^2 (%.%) [3]	I^2
AC	18 (17)	(% per g)	0.06	0.31	0.09	679	0.86
UC	19 (15)	(% per g)	1.06	1.13	0.36	761	0.89
TC	15 (14)	(% per g)	0.15	0.34	0.67	705	0.88
GL	16 (15)	(% per g)	-0.30	0.14	0.055	531	0.85
AC-GL	16 (15)	(% per g)	0.37	0.15	0.022	446	0.87
TC-GL	15 (14)	(% per g)	0.33	0.14	0.039	533	0.83
GL/AC (or GI_{AC})	18 (17)	(% per g/g)	-0.89	0.35	0.023	422	0.82
GL/(AC+UC) (or GI_T)	15 (14)	(% per g/g)	-0.92	0.41	0.042	544	0.85
GL/(AC+UC+P)	15 (14)	(% per g/g)	-1.33	0.54	0.027	505	0.84
(GL+F)/(AC+UC+P+F)	15 (14)	(% per g/g)	-1.67	0.63	0.019	473	0.82

1 Abbreviations: AC, available carbohydrate; UC unavailable carbohydrate; TC, total carbohydrate; GL, glycaemic load; GI, Glycaemic index; TC, total carbohydrate; P, protein; F fat.

2 Shows k number of studies and df degrees of freedom.

3 Likelihood-ratio test of significance for Tau^2, P>|Xbar| = 0.000 in all cases.

Annex 57

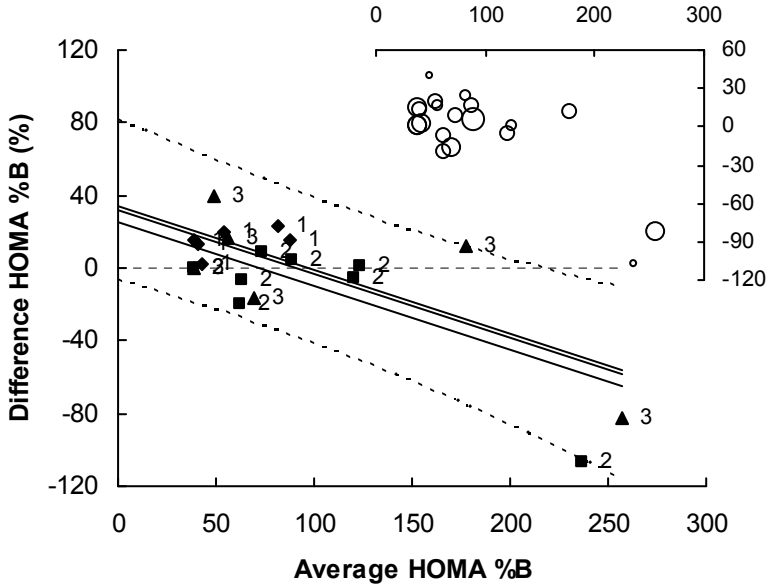

Fig 45 HOMA scores: Dietary methods difference plot for HOMA %B after treatment with variably lower glycaemic, variably high unavailable carbohydrate diets.

Observations are for all health types categorised by HOMA %D 1, 2 and 3 (cf Fig ho 1). Common regression slopes are fitted to each HOMA %D category (——) with dummy variables to force separate constants on the y-axis. The 95% confidence interval is shown (- - - -). Bubbles show weights (inverse variance) for the same observations by separate graph.

Annex 58

TABLE 39: HOMA Scores: A random effects meta-regression of the HOMA %B response to variably lower glycaemic variably higher unavailable carbohydrate diets, common slope, and constant by HOMA %D category[1.]

Parameter	k (df)	Units for mean effect	Parameter estimate	SEE	P>|kh-t|	Tau^2 (%.%)[2.]	I^2[3.]
Slope on HOMA %B	18 (1)	ΔT% per unit MT	-0.35	0.01	0.004	322	0.75
Constant HOMA %D cat 1	6 (1)	ΔT% at MT=0	34	10	0.005		
Constant HOMA %D cat 2	7 (1)	ΔT% at MT=0	26	13	0.061		
Constant HOMA %D cat 3	5 (1)	ΔT% at MT=0	32	17	0.080		
Error	- (14)						

Comment: sparse data above HOMA %B = 100, high leverage from HOMA D cat 1 (k = 1) and HOMA %D cat 2 (k = 1)

1 Abbreviations: k, number of studies; df, degrees of freedom; SEE, standard error of estimation; P>|kh-t|, level of significance based on the Knapp-Hartung t test; $Tau^{2,}$ REML estimate of between study variance; I^2, contribution of between study variation to total variation; ΔT%, difference between treatment outcomes expressed as a percentage of MT ; MT, mean of treatment outcomes. HOMA, homeostatic model assessment; cat, disposition category for HOMA D.

2 Likelihood-ratio test of significance for tau^2, P>|Xbar| = 0.000.

3 Q-test for heterogeneity, Q = 18(14)=57, P>Q=0.000.

Annex 59

TABLE 40: HOMA scores: Dietary methods comparison for retrospective HOMA %B , influence of HOMA %D and HOMA %S[1,2,3].

Model	k (df)		Slope			Intercept	Tau^2	I^2
			HOMA B	HOMA D	HOMA S			
1	18 (15)	Slope or intercept	-0.38	0.05	-	30	312	0.75
		SEE	0.11	0.14	-	10		
		P>|kh-t|	0.003	0.72	-	0.009		
2	18 (16)	Slope or intercept	-0.27	0.24	-	-	523	0.84
		SEE	0.12	0.17	-	-		
		P>|kh-t|	0.04	0.16	-	-		
3	18 (15)	Slope or intercept	-0.36	-	-0.045	34	294	0.74
		SEE	0.08	-	0.100	12		
		P>|kh-t|	0.001	-	0.660	0.014		
4	18 (16)	Slope or intercept	-0.21	-	0.160	-	483	0.83
		SEE	0.07	-	0.088	-		
		P>|kh-t|	0.012	-	0.096	-		
5	18 (16)	Slope or intercept	-0.36	-	-	31	282	0.73
		SEE	0.08	-	-	9		
		P>|kh-t|	0.001	-	-	0.003		

1 Treatment difference in HOMA %B (ΔT, %MT) = intercept (±SEE) + $slope_1$ (±SEE) x treatment mean HOMA %B (MT) + $slope_2$ (± SEE) HOMA %D + $slope_3$ (± SEE) x HOMA %S ± Tau ± SE
where $Tau^2 / (Tau^2 + SE^2) = I^2$

2 There is an occurrence of high influence in these regressions due to uneven distribution of data.

3 Abbreviations: k, number of studies; df, degrees of freedom; SEE, standard error of estimation; P, level of significance based on Knapp-Hartung-t; Tau^2, between study variance; I^2, proportion of variance due to between study variance.

Annex 60

TABLE 41: HOMA Scores: Dietary methods comparison for retrospective HOMA %B, by diagnosis [1,2,3].

k (df) [2,4]	Intercept			Slope			Tau^2	I^2
	Coefficient	SEE	P>|kh-t|	Coefficient	SEE	P>|kh-t|		
	%ΔT			*%ΔT per MT HOMA %B*				
All studies								
18 (16)	31	9	0.003	-0.36	0.081	0.001	282	0.73
All non-diabetics								
12 (10)	30	14	0.06	-0.37	0.11	0.007	443	0.80
All metabolic disease (below) bar diabetes								
6 (4)	51 [5]	7	0.002	-0.51 [5]	0.050	0.002	0	0
Healthy groups								
6 (4)	18	29	0.6	-0.28	0.25	0.320	1000	0.76
1^0 CHD risk								
4 (2)	27	25	0.39	-0.25	0.26	0.430	0	0
IGT								
2 (0)	46 [5]	- [6]	-	-0.49 [5]	-	-	-	-
Type 2 diabetes								
5 (4)	-4	16	0.82	0.34	0.33	0.397	0	0

.

1 Treatment difference in HOMA %B (ΔT, %MT) =
intercept (±SEE) + slope (±SEE) x treatment mean HOMA %B (MT) ± Tau ± SE
where $Tau^2 / (Tau^2 + SE^2) = I^2$

2 A value for df of approx 10 is recommended before placing reliance on outcomes in the absence of other information (e.g. similar regressions from other health groups).

3 There is an occurrence of highly influential studies in these regressions even with df ≥10 due to uneven distribution of data.

4 Abbreviations: k, number of studies; df, degrees of freedom; SEE, standard error of estimation; P, level of significance based on Knapp-Hartung-t; Tau^2, between study variance; I^2, proportion of variance due to between study variance.

5 Some nearby numerical values are missing, so values are approximate.

6 Insufficient number of studies (df = 0).

Annex 61

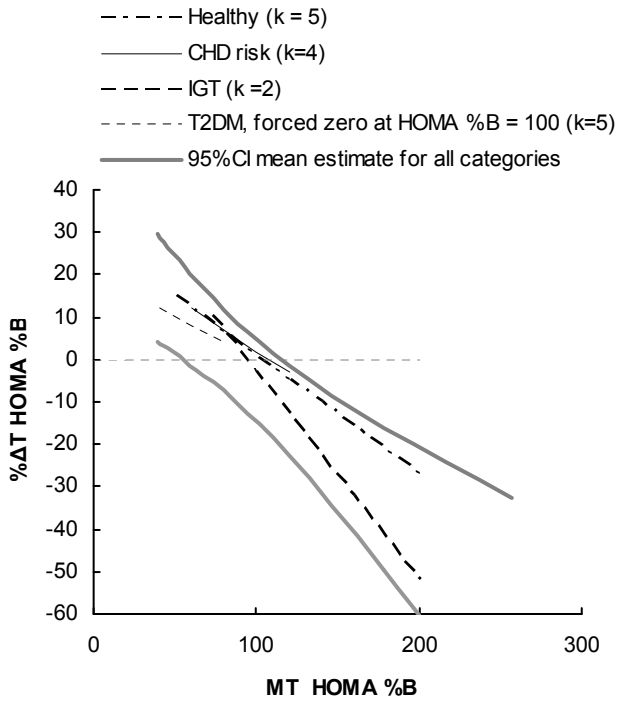

FIG 46: HOMA scores: Normalisation of HOMA %B in various health categories. Departure from zero effect arises from the consumption of low glycaemic high unavailable carbohydrate diets. Lines represent the meta-regression coefficients for each category as detailed in Table homa 4. Data for each regression are present as dietary methods difference in treatments (%ΔT) and dietary methods mean treatment (MT). k shows the number of studies per dietary category. In the case of type 2 diabetes, %ΔT was forced to zero at HOMA %B=100 (approximately as found in other categories). The all category combined 95% confidence intervals surround an intercept 30 SEE 9 (P>|kh-t|=0.003) and slope -0.36 SEE 0.08 (P>|kh-t|=0.001).

Annex 62

TABLE 42: HOMA scores: Summary of fixed and random effects meta-analysis for treatment differences in retrospective HOMA %B by health type [1.]

Health group	k (df) [2]	Expression of mean effect	Combined mean	SEE	P>|z|	Q [3]	Hetero-geneity P>X [3]	DSL variance (%.%) [2.]
Type 2 diabetes, all studies up to including 4weeks duration	5 (4)	ΔT%	12	4	0.004	3.2	0.52	0
Type 2 diabetes, studies of 4 weeks duration	4 (3)	ΔT%	17	5	0.001	0.5	0.92	0
CHD risk	4 (3)	ΔT%	4	4	0.41	1.1	0.77	0
Healthy people	6 (5)	ΔT%	-8	9	0.34	17	0.004	307
IGT, HOMA %B <100	1 (0)	ΔT%	9	10	0.38	-	-	-
IGT, HOMA %B >100	1 (0)	ΔT%	-82	7	0.001	-	-	-

1 Data are for fixed effects except where the DSL variance is >0 when they are random effects

2 Abbreviations: k, number of studies; df, degrees of freedom; SEE, standard error of estimation; P>|z|, level of significance; Q test for heterogeneity and P>X its level of significance; DSL, Der Simonian and Laird estimate of between studies variance; ΔT%, difference between treatment outcomes expressed as a percentage of the mean of treatment outcomes. HOMA, homeostatic model assessment;

3 Q-test for heterogeneity, Q = 18(14)=57, P>Q=0.000.

Annex 63

Sources for Fig 47 HOMA scores:

Included studies (in order of appearance from the top): Jarvi et al 1999, Kabir et al 2002, Komindr et al 2001. Luscombe et al 1999, and Rizkalla et al 2004.

All studies in type 2 diabetics not reporting fasting insulin values at the end of the study are automatically excluded from retrospective calculation of HOMA scores: Brand et al 1991, Calle-Pascual 1988 (exp2_T2), Fontvieille et al 1992 ('exp2'), Frost et al 1994, Heilbronn 2002 (d2), Jenkins et al 1988, Jimenez-Cruz et al 2003, Jimenez-Cruz et al 2004, Tsihlias et al 2000 (d2), Wolever et al 1992a (d3), Wolever et al 1992b (d2), Yin-fa (2003).

Annex 64

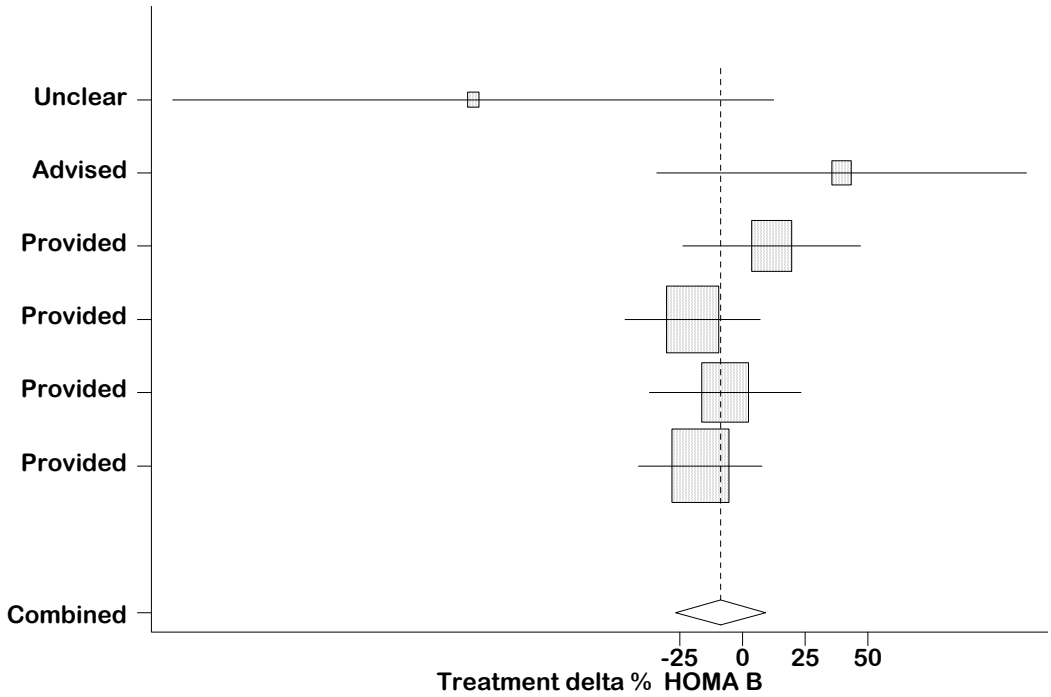

FIG 48: HOMA Scores: Meta-analysis of the retrospective HOMA %B response to variably lower glycaemic variably higher unavailable carbohydrate diets in studies of healthy people.

Studies are prior to 2005. The y-axis shows the method by which diets were administered, either some or all foods were provided or participants where advised about the foods they should consumed; in one case the study report was unclear (ambiguous) about how the food was provided. The Der Simonian and Laird estimate of between studies variance is 307 (%.%) and the Q-test indicates significant heterogeneity (Q = 17, P = 0.004). The combined mean effect did not differ from zero (P>|z| = 0.34).

Source:

Included studies (in order of appearance from the top): Bouche et al 2002, Frost et al 1998 (exp2), Herrmann et al 2001 (expt2), Jenkins et al 1987a (d2), Kiens et al 1996 (d4), and Sloth et al 2004 (d5).

Excluded studies: All studies in healthy subjects not reporting fasting insulin values at the end of the study are automatically excluded from retrospective calculation of HOMA scores: Agus et al 2000, Carels et al 2005, Ebbeling et al 2003 (d2), Kurup 1992 (raggi vs rice), Kurup 1992 (expt2 Raggi vs tapioca), Price (unpublished) & Spieth et al 2000.

Annex 65

Additional information on HOMA B in relation to diet composition in type-2 diabetes.

Nevertheless, according to these limited data, B-cell function in type 2 diabetics is morel likely than not sensitive to unavailable carbohydrate intake in the context of a low-glycaemic diet. Thus HOMA B improvement occurs at a rate of 1.38 % per g increase in daily unavailable carbohydrate intake over approx 4 weeks of treatment. However, this evidence lacks strength with an SE 0.96% that is relatively wide (cv = 0.69) such that the possibility of an effect of unavailable carbohydrate from these data alone is refutable ($P > |kh-t| = 0.22$; $k = 3$).

Sensitivity of HOMA B to change in the glycaemic character of the diet may be less than to change in unavailable carbohydrate intake. Thus in the type-2 diabetics HOMA B rises by 0.23% per g AC-GL eaten each day. Again the possibility of such an effect is refutable as the evidence is weak ($P> |kh-t| = 0.1$, $k = 3$) In other terms, HOMA B was inversely associated with glycaemic load, improving by 0.24% per g decrease in GL/d ($P> |kh-t |= 0.07$, $k = 4$). Improvement in HOMA B was less sensitive to unit change (%) in GI than to unit change (g/d) in UC, though comparison is obscured by the differing units. Thus HOMA B appears to improve by 0.59% for each 1% fall in GI; the possibility of no effect is refutable ($P > |kh-t| = 0.05$, $k = 5$) in this univariate association. However, it cannot be excluded that the additional studies (k = 5 studies reporting the diets GI, verses k = 3 reporting the diets UC) is not the result of undisclosed co-linearity between UC and GI among this small number of studies.

Annex 66

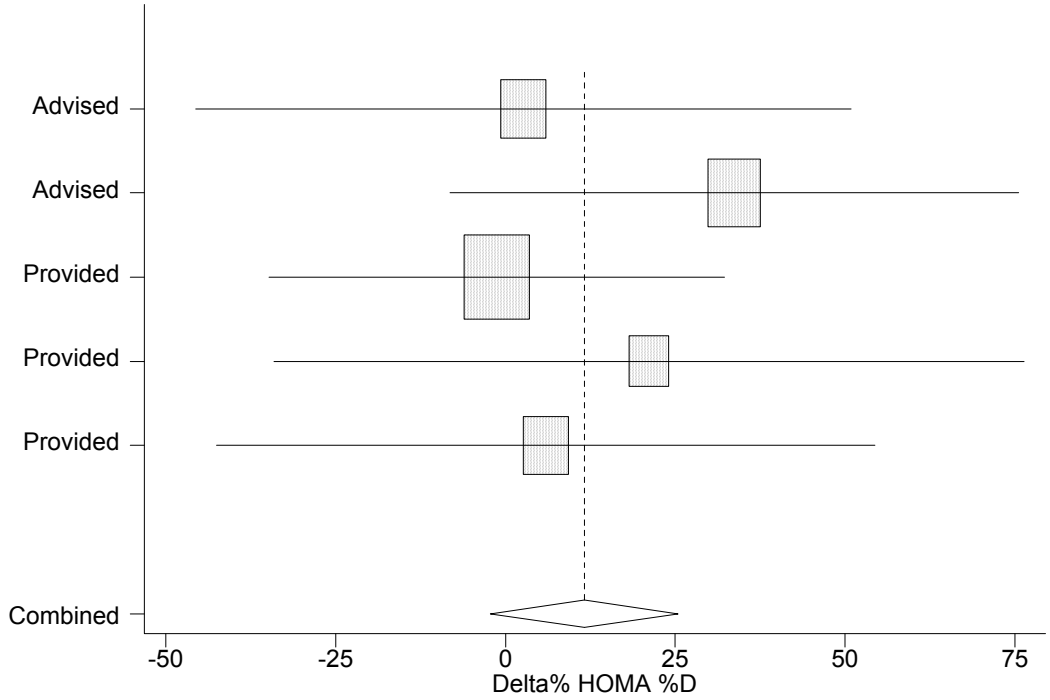

FIG 49: HOMA Scores: Meta-analysis of the retrospective HOMA %D response to variably lower glycaemic (variably higher unavailable carbohydrate) diets in studies of type 2 diabetes

Studies are prior to 2005. The y-axis shows the method of diet administration, either some or all foods were provided or participants where advised about the foods they should consume.

Annex 67

TABLE 43: HOMA Scores: Dietary methods difference for HOMA %D assessed by random effects meta-regression [1.]

Condition	k (df)	Constant	SEE	P>|kh-t|	Slope	SEE	P>|kh-t|	Tau^2 (%.%) [2.]	I^2 [3.]
All studies	18 (16)	9.2	7.8	0.26	-0.13	0.1	0.22	218	0.62
All studies, HOMA %D<150 [4]	17 (15)	15.3	6.9	0.04	-0.28	0.1	0.013	117	0.55

Comment: The influence statistic [4] B_{ij} for k = 1 removed is >1 indicating appreciable influence on the overall outcome and so leaving it in the analysed dataset to influence the outcome may distort the truer relation indicated by the remaining studies.

1 Abbreviations: k, number of studies; df, degrees of freedom; SEE, standard error of estimation; P>|kh-t|, level of significance based on the Knapp-Hartung t test; Tau^2, REML estimate of between study variance; I^2, contribution of between study variation to total variation; ΔT%, difference between treatment outcomes expressed as a percentage of MT ; MT, mean of treatment outcomes. HOMA, homeostatic model assessment.

2 Likelihood-ratio test of significance for Tau^2, P>|Xbar| = 0.001.

3 Q-test for heterogeneity, Q = 18(14) =57, P>Q=0.001.

4 The influence statistic for the study removed by truncation, Bij = 1.5 > 1, indicates appreciable influence.

Annex 68

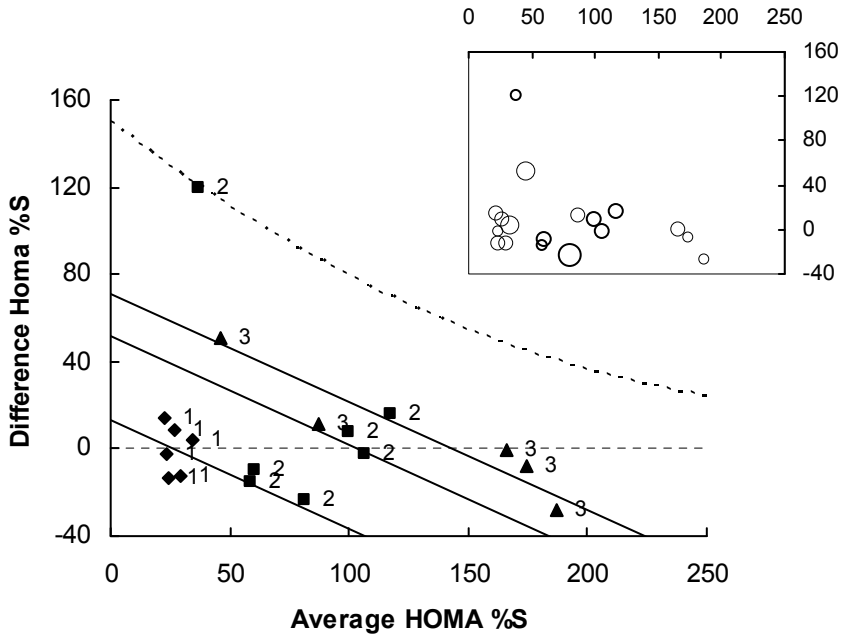

FIG 51: HOMA Scores: Dietary methods difference for HOMA %S response to variably lower glycaemic variably higher unavailable carbohydrate diets in all health types combined.

Bubble areas shows the relative weights of each study (inverse variance) the data (k = 18 studies) are labelled by HOMA %D category (cf Fig. ha 1). Curves show the combined study meta-regression slopes (——) forced to be common for each category with potential for differing constants permitted by using dummy variables. The upper 95% confidence interval for the population of studies is shown (-----) (The lower 95% CI is off scale). Given the outlying observation further studies are needed to establish or refute a significant relationship.

Annex 69

TABLE 44: HOMA Scores: Dietary methods difference for HOMA %S (v. HOMA %S and HOMA %B) assessed by random effects meta-regression [1.]

k (df)		Parameter estimate	SEE	P>|kh-t|	Tau^2 (%.%) [2.]	I^2
18 (14)	Model: ΔT %MT (HOMA %S) = slope x (MT HOMA %S) + category specific constant					
	Slope vs. MT HOMA %S	-0.50	0.21	0.031	655	0.85 [3]
	Constant, category 1	13	13	0.34		
	Constant, category 2	51	20	0.023		
	Constant, category 3	71	29	0.029		
18 (14)	Model: ΔT %MT (HOMA %S) = slope x (MT HOMA %B) + category specific constant					
	Slope vs. MT HOMA %B	0.39	0.09	0.001	395	0.78 [4]
	Constant, category 1	-23	11	0.046		
	Constant, category 2	-32	13	0.027		
	Constant, category 3	-43	17	0.021		

1 Abbreviations: k, number of studies; df, degrees of freedom; SEE, standard error of estimation; P>|kh-t|, level of significance based on the Knapp-Hartung t test; Tau^2, REML estimate of between study variance; I^2, contribution of between study variation to total variation; ΔT difference in treatment outcomes ; MT, mean of treatment outcomes. HOMA, homeostatic model assessment; cat, disposition category for HOMA %D.

2 Likelihood-ratio test of significance for Tau^2, P>|Xbar| = 0.001.

3 Q-test for heterogeneity, Q = 90, P > Q = 0.001

4 Q-test for heterogeneity, Q = 63, P > Q = 0.001

Annex 70

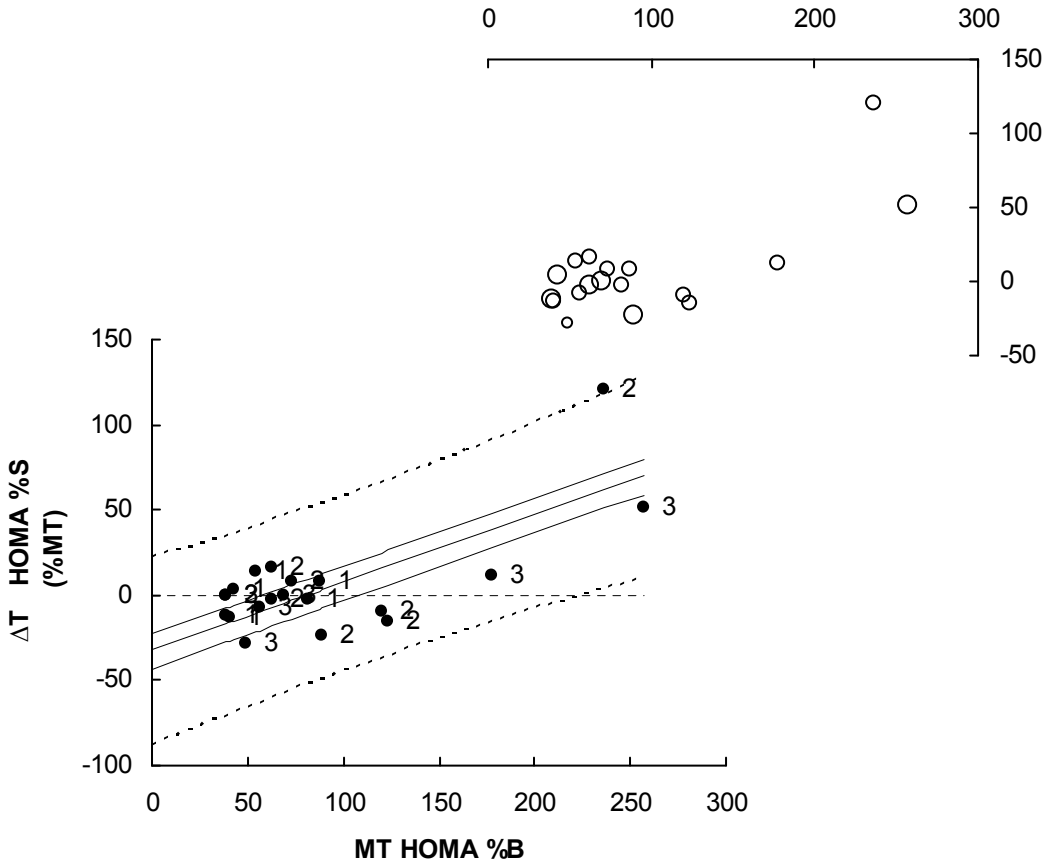

FIG 52: HOMA Scores: Dietary methods difference for HOMA %S related to HOMA %B in response to variably lower glycaemic variably higher unavailable carbohydrate diets in all health types combined.

Curves show a common regression coefficient (——, result: 0.398 SEE 0.09) originating from each category intercept permitted by introduction of dummy variables (result: 1, -23 SE 1; 2, -32 SE 13; 3, -43 SE 17) and the 95% confidence interval for the population of studies (-----). Bubble areas in the separate graph show for the same observations the relative weights (inverse variance).

Annex 71

TABLE 45: HOMA scores: Random effects meta-regressions of the response of insulin sensitivity (HOMA %S) on response of B-cell function (HOMA %B) to variably lower glycaemic variably higher unavailable carbohydrate diets [1.]

k (df)		Slope	SEE	P>|kh-t|	Constant	SEE	P>|kh-t|	Tau^2 (%.%)	I^2
	Model: ∆T HOMA %S (%MT) = slope x ∆T HOMA %B (%MT) + constant + Tau + SE								
18 (16)	All studies	-0.73	0.13	0.001	2.13	4.1	0.61	183 [2]	0.67
12 (10)	All non-diabetic	-0.83	0.15	0.001	2.9	5.7	0.62	222 [2]	0.69
5 (3)	HOMA %D cat 3	-0.56	0.15	0.035	2.1	7.5	0.79	91 [3]	0.33
7 (5)	HOMA %D cat 2	-1.12	0.21	0.003	-7.4	7.3	0.36	213 [4]	0.72
6 (4)	HOMA %D cat 1 (diabetic)	-0.02	0.75	0.978	-1	11.5	0.94	68 [4]	0.38
4 (2)	CHD risk	-0.12	0.92	0.907	-18	5.9	0.089	10 [5]	0
2 (-)	Impaired glucose tolerance	-0.47 [7]	-	-	12 [7]	-	-	-	-
6 (4)	Healthy	-0.96	0.22	0.012	1.5	9.6	0.88	329 [6]	0.76

1 Abbreviations: k, number of studies; df, degrees of freedom; SEE, standard error of estimation; P>|kh-t|, level of significance based on the Knapp-Hartung t test; Tau^2, REML estimate of between study variance; I^2, contribution of between study variation to total variation; ∆T difference in treatment outcomes ; MT, mean of treatment outcomes. HOMA, homeostatic model assessment; cat, disposition category for HOMA %D.

2 Likelihood-ratio test of significance for Tau^2, P>|Xbar| = 0.001.

3 Likelihood-ratio test of significance for Tau^2, P>|Xbar| = 0.18.

4 Likelihood-ratio test of significance for Tau^2, P>|Xbar| = 0.004.

5 Likelihood-ratio test of significance for Tau^2, P>|Xbar| = 0.45.

6 Likelihood-ratio test of significance for Tau^2, P>|Xbar| = 0.004.

7 Two point calculation of slope and intercept (for comparative purposes only).

Annex 72

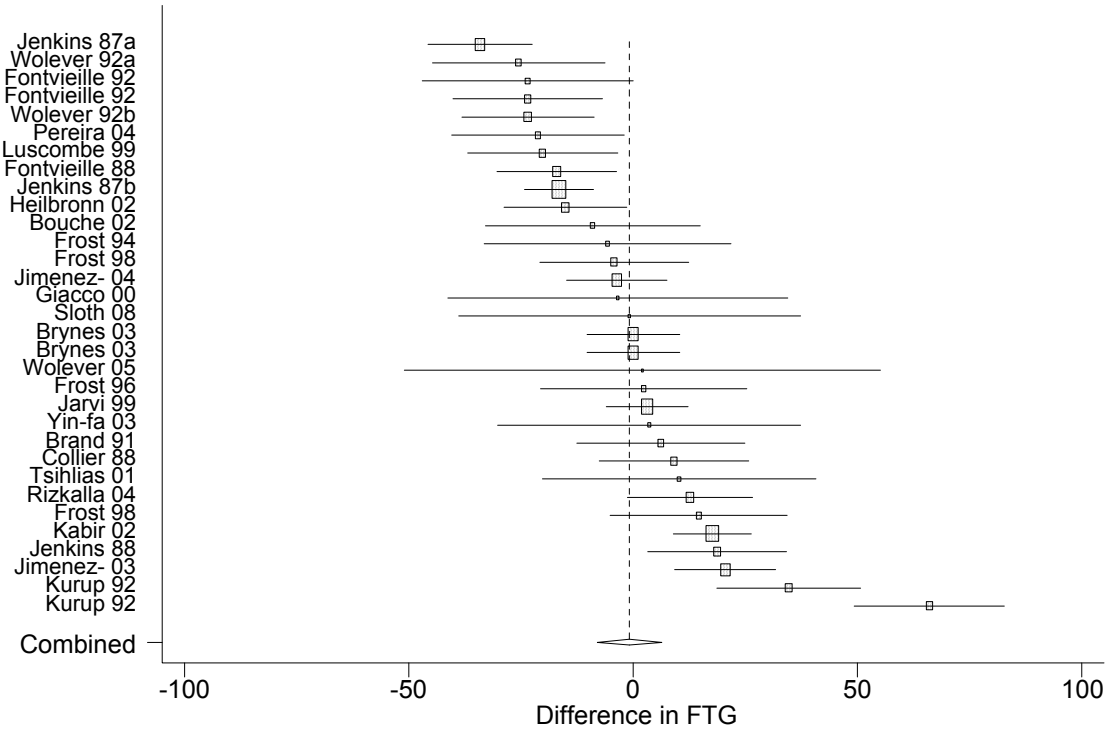

FIG 55: Fasting Triglycerides: Random effects meta-analysis of the fasting triglyceride (FTG) response to variably lower glycaemic (variably higher unavailable carbohydrate) diets in all health categories combined (ΔT as %MT).

Observation are from studies in mixed hyperlipidaemic (k = 1), primary and secondary CHD risk (k = 4), type-1 diabetes (k = 4), type-2 diabetes (k = 15), impaired glucose tolerance (k = 1), and healthy (k =7) groups of participants. Effect sizes (means and 95% confidence intervals) are presented in order of effect size. Studies are identified by first author and abbreviated date. Data point sizes show the relative weight (inverse variance) for each study.

Annex 73

TABLE 46: Fasting Triglycerides: Summary of fixed and random effects meta-analysis for treatment differences in fasting triglycerides according to body weight group, heath group and duration of study [1].

Health group	k (df) [2]	Units for mean effect	Combined mean	SEE	P>|z|	Q [3]	Hetero-geneity P>X [3]	DSL variance (mmol/L)[2] [2.]
All	31 (30)	ΔT mmol/L	0.0	0.1	0.72	319	0.000	0.078
All <12 weeks	26 (25)	ΔT mmol/L	0.0	0.1	0.78	317	0.000	0.083
All ≥ 12 weeks	5 (4)	ΔT mmol/L	0.0	0.1	0.95	1.4	0.92	0.000
Obese	5 (4)	ΔT mmol/L	-0.2	0.1	0.105	26	0.000	0.061
Overweight	15 (14)	ΔT mmol/L	0.0	0.1	0.88	68	0.77	0.000
Normal weight	10 (9)	ΔT mmol/L	0.1	0.1	0.43	214	0.000	0.133
Type 2 diabetes	15 (14)	ΔT mmol/L	0.0	0.1	0.63	96	0.000	0.061
Type 1 diabetes	4 (3)	ΔT mmol/L	-0.1	0.1	0.68	19	0.000	0.033
Impaired glucose tolerance	1 (-)	ΔT mmol/L	0.0	-	-	-	-	-
CHD risk	4 (3)	ΔT mmol/L	0.0	0.0	0.76	0.3	0.95	0.000
Healthy	6 (5)	ΔT mmol/L	0.2	0.1	0.266	167	0.000	0.168

…continued

Table tg 1 continued…

1 Data are for fixed effects except where the DSL variance is >0 when they are random effects

2 Abbreviations: k, number of studies; df, degrees of freedom; SEE, standard error of estimation; P>|z|, level of significance; Q test for heterogeneity and P>X its level of significance ; DSL, Der Simonian and Laird estimate of between studies variance ; ΔT, difference between treatment outcomes.

3 Q-test for heterogeneity.

Annex 74

TABLE 47: Fasting Triglycerides: Summary of random effects meta-regression analysis [1] for treatment differences in fasting triglycerides according to dietary variables differing during treatment with variably lower glycaemic variably higher unavailable carbohydrate diets.

Parameter [2]	k (df) [3]	Units for covariance effect	Combined covariance effect	SEE	P>|kh-t|	Tau^2 (%.%) [4]	I^2
Protein	29 (27)	(% per g)	-0.19	0.36	0.61	416	0.91
Energy	30 (28)	(% per kJ)	-0.001	0.007	0.87	407	0.90
UC	30 (28)	(% per g)	-0.1	0.48	0.84	405	0.90
AC	30 (28)	(% per g)	0.21	0.13	0.13	368	0.90
Fat	30 (28)	(% per g)	-1.08	0.43	0.019	325	0.89
GL	30 (28)	(% per g eq.)	0.34	0.102	0.003	277	0.88

1 The model used was ΔT (%MT) = combined covariance effect x parameter + B_1 x MT + constant + Tau^2 + SE. the parameter B_1 (slope on MT) and the constant not shown.

2 Abbreviations: ΔT, difference due to dietary treatment; MT average outcome of dietary treatments; Tau^2, variation among studies; I^2 ,ratio of variation among studies to sum of variation among studies and within studies; AC, available carbohydrate; UC unavailable carbohydrate; TC, total carbohydrate; GL, glycaemic load;

3 Shows k number of studies and df degrees of freedom.

4 Likelihood-ratio test of significance for Tau^2, P>|Xbar| <0.001 in all cases.

Annex 75

TABLE 48: Fasting Triglycerides: Covariates by mode of carbohydrate and glycaemic expressions in random effects meta-regression [1] of differences in fasting triglycerides, after adjustments for change in fat intake.

Parameter [2]	k (df) [3]	Units for covariance effect	Combined covariance effect	SEE	P>|kh-t|	Tau^2 (%.%) [4]	I^2
UC	30 (28)	(% per g)	-0.14	0.36	0.71	336	0.89
TC	30 (28)	(% per g)	0.16	0.14	0.29	322	0.89
AC	30 (28)	(% per g)	0.15	0.13	0.26	321	0.89
GL/(AC+UC+P)	29 (27)	(% per g eq./g)	0.48	0.26	0.07	297	0.90
(GL+F)/(AC+UC+P+F)	29 (27)	(% per g eq./g)	0.55	0.30	0.08	299	0.90
TC-GL	30 (28)	(% per g)	-0.13	0.07	0.07	296	0.88
GL/(AC+UC) (or GI_T)	30 (28)	(% per g eq./g)	0.39	0.20	0.06	294	0.89
AC-GL	30 (28)	(% per g)	-0.15	0.08	0.05	289	0.88
GL/AC (or GI_{AC})	32 (30)	(% per g eq./g)	0.39	0.19	0.05	289	0.88
GL	30 (28)	(% per g)	0.16	0.06	0.02	270	0.88

1 The model used was ΔT (%MT) = combined mean effect x parameter + B_1 x change in fat intake + Tau^2 + SE. Parameter estimates B_1 (effect of change in fat intake)are shown in Table tg 4.

2 Abbreviations: ΔT, difference due to dietary treatment; MT average outcome of dietary treatments; Tau^2, variation among studies; I^2 ,ratio of variation among studies to sum of variation among studies and within studies; AC, available carbohydrate; UC unavailable carbohydrate; TC, total carbohydrate; GL, glycaemic load; GI, Glycaemic index; TC total carbohydrate; P, protein; F fat.

3 Shows k number of studies and df degrees of freedom.

4 Likelihood-ratio test of significance for Tau^2, P>|Xbar| <0.001 in all cases.

Annex 76

TABLE 49: Fasting Triglycerides: Co-variance of fasting triglycerides and fat intake, assessed by random effects meta-regression, after adjustments for co-variation with various carbohydrate and glycaemic expressions that differ between treatment diets [1].

Covariate adjusted [2]	k (df) [3]	Units for mean effect	Combined mean effect of ∆fat intake	SEE	P>|kh-t|	Tau^2 (%.%) [4]	I^2
UC	30 (27)	(% per g fat)	-0.97	0.43	0.03	336	0.89
TC	30 (28)	(% per g fat)	-0.85	0.44	0.06	322	0.89
AC	30 (28)	(% per g fat)	-0.84	0.43	0.06	321	0.89
GL/(AC+UC+P)	29 (27)	(% per g fat)	-1.08	0.43	0.017	297	0.90
(GL+F)/(AC+UC+P+F)	29 (27)	(% per g fat)	-1.13	0.43	0.013	299	0.90
TC-GL	30 (28)	(% per g fat)	-1.07	0.41	0.015	296	0.88
GL/(AC+UC) (= GI_T)	30 (28)	(% per g fat)	-1.02	0.41	0.018	294	0.89
AC-GL	30 (28)	(% per g fat)	-1.09	0.41	0.012	289	0.88
GL/AC (= GI_{AC})	32 (30)	(% per g fat)	-1.04	0.40	0.016	289	0.88
GL	30 (28)	(% per g fat)	-0.96	0.39	0.022	270	0.88

…

1 The model used was ∆T (%MT) = combined covariance effect x ∆fat + B_1 x adjusting covariate + Tau^2 + SE. Parameters estimates for B_1 (adjusting covariates) are shown in Table tg 3.

2 Abbreviations: ∆T, difference due to dietary treatment; MT average outcome of dietary treatments; Tau^2, variation among studies; I^2, ratio of variation among studies to sum of variation among studies and within studies; AC, available carbohydrate; UC, unavailable carbohydrate; TC, total carbohydrate; GL, glycaemic load; GI, Glycaemic index; TC total carbohydrate; P, protein; F fat.

3 Shows k number of studies and df degrees of freedom.

4 Likelihood-ratio test of significance for Tau^2, P>|Xbar| <0.001 in all cases.

Annex 77

TABLE 50: Fasting Triglycerides: Interaction of fasting triglyceride concentration (severity of abnormality) [1] with both glycaemic load and fat intake in trivariate determination of the response of fasting triglycerides to variably low glycaemic (variably higher unavailable carbohydrate) diets: an assessment by meta-regression [2]

Model	k (df) [3]	Parameters	Combined mean effect	SEE	P>|kh-t|	Tau^2 (%.%) [4]	I^2
	30 (28)						
ΔT (%MT) = B_1 x ΔGL + B_2 x Δfat + Tau + SE							
		ΔT (%MT) per g ΔGL	0.16	0.06	0.021	270	0.88
		ΔT (%MT) per g Δfat	-0.96	0.39	0.022		
ΔT (%MT) = B_1 x (ΔGL x S) + B_2 x (Δfat x S) + Tau + SE							
		ΔT (%MT) per ΔGL x S (g.g)	0.12	0.04	0.010	261	0.88
		ΔT (%MT) per Δfat x S (g.g)	-0.58	0.22	0.013		

1 Severity of abnormality in fasting triglycerides (S) is left equal to the end of study treatment average fasting triglyceride concentration since no intercept was found on the triglyceride-axis.

2 Abbreviations: ΔT, difference due to dietary treatment; MT average outcome of dietary treatments; S, severity of abnormality (here = MT); Tau^2, variation among studies; I^2 ,ratio of variation among studies to sum of variation among studies and within studies; GL, glycaemic load.

3 Shows k number of studies and df degrees of freedom.

4 Likelihood-ratio test of significance for Tau^2, P>|Xbar| <0.001 in all cases.