Supplemental Materials: Is there a dose-response relation of dietary glycemic load to risk of type-2 diabetes? Meta-analysis of prospective cohort studies[1-5]

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SUPPLEMENTAL MATERIALS

Search strategies

Strategies shown are updates on prior searches conducted in 1999, and March 2012.

*MEDLINE/PROQUEST**/ Royal Society of Medicine, UK; *1997 to week 3 of August 2012*
Yield, 907 records. Hits, 18 records. Identified omissions, 1 record Patel et al (15).

1. MESH.EXPLODE("Cohort Studies")
2. MESH.EXPLODE("Prospective Studies")
3. MESH.EXPLODE("risk")
4. s1 or s2 or s3
5. MESH.EXPLODE("Diabetes Mellitus")
6. ti,ab(Glycemic index)
7. ti,ab(Glycemic load)
8. s6 or s7
9. yr(1997-2012)
10. s4 and s5 and s8 and s9
11. ab(glycemic index OR glycemic load) AND ab(Diabetes)
12. ab(risk OR association)
13. yr(>2010)
14. s11 and s12 and s13
15. s10 or s14

where 's' followed by a number abbreviates for search at line number; MESH , medical subject heading, ti, title; ab, abstract; and yr, year.

EMBASE/ PROQUEST (Dialog™, National Health Service, UK) / Royal Society of Medicine, UK; *1997 to week 3 of August 2012*

Yield, 1474 records. Hits, 18 records. Identified omissions, 1 record van Woudenberg et al (30).

1. EMB.EXACT("cohort analysis")
2. EMB.EXACT("prospective study")
3. EMB.EXACT("risk assessment")
4. EMB.EXACT("risk reduction")
5. EMB.EXACT("risk factor")

6. EMB.EXACT("follow up")
7. EMB.EXACT("hazard ratio")
8. EMB.EXACT("incidence")
9. s1 or s2 or s3 or s4 or s5 or s6 or s7 or s8
10. EMB.EXPLODE("Diabetes Mellitus")
11. EMB("glucose blood")
12. s10 or s11
13. TI,AB("carbohydrat*")
14. TI,AB("glycemic index")
15. TI,AB("glycemic load")
16. s13 or s14 or s15
17. s9 and s12 and s16
18. s17 and yr(1997-2012)
19. TI,AB("glycemic load")
20. TI,AB("glycemic index")
21. s19 or s20
22. TI,AB(diabetes)
23. TI,AB(risk)
24. TI,AB(association)
25. TI,AB(incidence)
26. TI,AB(cohort)
27. TI, AB(prospective)
28. s23 or s24 or s25 or s26 or 27
29. s21 and s22 and s28 and YR(>2010)
30. s18 or s29

where 's' followed by a number abbreviates for search at line number; EMB, the EMBASE equivalent of MESH (both are medical subject headings) in Medline; TI, title, and AB, abstract. 'Glycemic' included the alternative spelling 'Glycaemic'.

WWW/CENTRAL (http://www.thecochranelibrary.com/view/0/index.html) / INLogic Ltd, UK.

All dates to week 3 August 2012.

Yield, 66 records. Hits, 0 records. Identified omissions, 19 records, which is consistent with CENTRAL being focused on interventions.

All text (Glyc*emic load and Diabetes)

WWW/INLOGIC, UK *1997 to week 3 of August 2012.*

Yield, zero additional records identified via the following online sources:

CDC, UK Centre for Reviews and Dissemination (www.york.ac.uk/inst/crd).

PROSPERO Register of Systematic Reviews

(www.york.ac.uk/inst/crd/projects/register.htm).

The Centers for Disease Control and Prevention (www.cdc.gov).

The National Institute of Health (www.nih.gov).

Google Scholar (http://scholar.google.co.uk).

Excluded studies

Articles identified by title and abstract but on examination of the full article did not meet the inclusion/exclusion criteria for the following reasons:

1) Was not an original study (2 reports):

- Pereira 2008 (1) was a commentary on the original study of Sahyoun et al (2) already included.
- Hu et al 2001(3) reviews data from the Nurses Health Study of Salmeron 1997 (4) amongst other lifestyle data.

2) Was not analyzed as a prospective cohort design (1 reports):

- Mohan et al 2009 (5) was a cross-sectional study.

3) Used an ineligible population (2 reports):

- Schulz et al 2006 (6) used a population that did not exclude T2D patients at baseline.
- Mayer-Davies et al 2006 (7) used a population that did not exclude T2D patients at baseline and summarizes their report noted immediately above (6).

4) Did not address the questions asked (2 reports):

- Fung et al 2002 (8) focused on whole grain and T2D in men of the Health Professionals Follow-up Study. Information on GL was not independent of that report earlier by Salmerón et al 1997 (9).
- Barclay et al 2007 (10) provided data on glycemic index only- no data on glycemic load was presented.

5) Dietary or other details were insufficient (1 report):

- Yu et al 2011 (11) provide limited information on glycemic load and T2D among 690 Honk Kong adults in a prospective cohort study with follow up of 9 to 14y, and report for their most adjusted model a non-significant effect of OR of 1.03 (CI 0.78-1.34) per 1 SD intake of GL unadjusted by the residual method for energy (equivalent to an OR of approx. 1.12 for the range of intakes of about 4SD, with potentially for higher value for energy adjusted GL intake. For this small study, a prior publication reported on validity of the FFQ used (12) but neither glycemic load nor any aspect of carbohydrate intake was addressed (CORR was unknown).

6) Reports of misidentified studies:

- Two publications (13, 14) incorrectly cited information about a mixed-sex population study (15). Information was available for the mixed-sex population only and did not report results for men or women separately. Correspondence with the first author of the original study (15), and with the first author in one citing the original study (13), indicates mistaken data extraction and/or misreporting. These errors are not perpetuated further in the present work.

Included studies

These are listed in Tables S1-4 below and in FIGURE 2 of the main article**.**

Table S1. Extracted and calculated data for the included studies [1,2]

Quantile	RR			Glycemic load (g/d reported, adjusted to energy)	Reference food (White bread or glucose)	Study energy intake		Cases	Non-case
	Median	L95CI	U95CI			Median or mean	units	n	n
Salmerón et al 1997 (16) in women, RR based on rate ratios.									
1	1	— [3]	— [3]	111				156	~12879 [4]
2	1.24	0.99	1.55	131				189	~12846 [4]
3	1.22	0.97	1.54	144	WB	7424 [5]	kJ/d	185	~12850 [4]
4	1.25	0.99	1.59	157				179	~12856 [4]
5	1.47	1.16	1.86	178				206	~12829 [4]
Salmerón et al 1997 (9) in men, RR based on odds ratios									
1	1	—	—	119				120	~8432 [6]
2	1.07	0.82	1.41	144				120	~8432 [6]
3	1.04	0.78	1.39	160	WB	1995 [7]	kcal/d	103	~8449 [6]
4	1.13	0.83	1.54	177				93	~8459 [6]
5	1.25	0.90	1.73	203				87	~8465 [6]
Meyer et al 2000 (17), RR based on rate ratios. [8]									
1	1	—	—	94				247	~6951 [9]
2	0.96	0.79	1.15	110				236	~6962 [9]
3	0.86	0.71	1.05	120	WB	7531 [10]	kJ/d	220	~6978 [9]
4	0.92	0.75	1.12	129				214	~6984 [9]
5	0.95	0.78	1.16	145				224	~6974 [9]

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Stevens et al 2002 (18), white participants, RR is based on a rate ratio. Other data used are in footnotes [11]									
1	1	—	—	—				nr [11]	nr [11]
2	—	—	—	—				nr	nr
3	—	—	—	146 [12]	WB	1625 [13]	kcal/d	nr	nr
4	—	—	—	—				nr	nr
5	1.10	0.90	1.39	—				nr	nr
Stevens et al 2002 (18), African Americans, RR is a rate ratios .[14]									
1	1	—	—	—				nr [14]	nr [14]
2	—	—	—	—				nr	nr
3	—	—	—	154 [15]	WB	1602 [16]	kcal/d	nr	nr
4	—	—	—	—				nr	nr
5	0.97	0.73	1.35	—				nr	nr
Schulze et al 2004 (19), RR is based on rate ratios.									
1	1	—	—	139				184	~18066 [17]
2	1.31	1.05	1.64	159				192	~18058 [17]
3	1.20	0.92	1.56	172	WB	1811 [18]	kcal/d	141	~18109 [17]
4	1.14	0.84	1.55	187				115	~18135 [17]
5	1.33	0.92	1.91	211				109	~18141 [17]
Hodge et al 2004 (20), RR is based on odds ratios. [19]									
1	*1*	—	—	*91.8*				*82*	*7828*
2	*0.86*	*0.61*	*1.20*	*101.2*	*G*	*8830* [20]	kJ/d	*70*	*7840*
3	*1.17*	*0.86*	*1.60*	*118.9*				*111*	*7799*
4	*0.92*	*0.65*	*1.30*	*155.7*				*102*	*7809*

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Zhang et al 2006 (21), RR is based on rate ratios.

1	1	—	—	137				210	2045 [21]
2	0.99	0.76	1.28	157				174	~2404 [21]
3	0.89	0.65	1.22	171	WB	1813 [22]	kcal/d	128	2621 [21]
4	1.21	0.84	1.74	186				145	~2660 [21]
5	1.61	1.02	2.53	212				139	2576 [21]

Villegas et al 2007 (22), RR is based on rate ratios.[23]

1	1	—	—	*164*				221	~12624 [24]
2	1.06	0.88	1.27	*181*				256	~12589 [24]
3	0.97	0.81	1.17	*190*	G	1683 [25]	kcal/d	253	~12592 [24]
4	1.23	1.03	1.46	*200*				349	~12496 [24]
5	1.34	1.13	1.58	*235*				526	~12319 [24]

Krishnan et al 2007 (23), RR is based on rate ratios.

1	1	—	—	82				463	~7553 [26]
2	1.00	0.85	1.17	99				368	~7648 [26]
3	1.09	0.92	1.31	109	G	1715 [27]	kcal/d	369	~7647 [26]
4	1.10	0.91	1.33	120				362	~7654 [26]
5	1.22	0.98	1.51	142				376	~7640 [26]

Mosdol et al 2007 (24), RR is based on rate ratios.

1	1	—	—	121 [28]				119	1721 [29]
2	1.05	0.76	1.44	145	G [30]	2095 [31]	kcal/d	117	1755 [29]
3	0.8	0.51	1.26	169				93	1793 [29]

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Patel et al 2007 (15), data is available for a mixed sex population only, RR is based on rate ratios.

1	1	—	—	93 [32]				nr [33]	nr[33]
2	—	—	—					nr	nr
3	—	—	—	129 [32]	WB	*1494* [34]	kcal/d	nr	nr
4	—	—	—					nr	nr
5	1.15	1.06	1.25	163 [32]				nr	nr

Sahyoun et al 2008 (2), RR is based on odds ratios. [35]

1	1	—	—	95				17	362 [36]
2	1.50	0.70	3.00	117				22	359 [36]
3	1.00	0.50	2.20	127	G	1835 [35]	kcal/d	18	360 [36]
4	1.50	0.70	3.20	138				20	361 [36]
5	1.30	0.60	2.70	162				22	357 [36]

Halton et al 2008 (25), RR is based on rate ratios.

1	1	—	—	62 [37]				~279 [38]	~8227 [39]
3	1.23	1.00	1.49	79 [37]				~348	~8158 [39]
5	1.56	1.24	1.97	89 [37]	G	1560 [40]	kcal/d	~436	~8070 [39]
7	1.88	1.45	2.45	99 [37]				~525	~7981 [39]
10	2.47	1.75	3.47	122 [37]				~690	~7816 [39]

Hopping et al 2010 (26), European American (Caucasian) men, RR is based on rate ratios. [41]

1	1	—	—	*84* [41]				257	2766 [42]
2	1.08	0.89	1.31	*120*				236	2788 [42]
3	1.09	0.87	1.36	150	G	9045	kJ/d	202	2821 [42]
4	1.31	1.01	1.68	*186*				207	2816 [42]
5	1.54	1.12	2.10	*256*				178	2845 [42]

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Hopping et al 2010 (26), European American (Caucasian) women, RR is based on rate ratios.									
1	1	—	—	*71*				141	2787 [42]
2	1.34	1.04	1.73	*100*				158	2771 [42]
3	1.48	1.10	1.99	125	G	7144	kJ/d	152	2777 [42]
4	1.47	1.03	2.08	*155*				131	2798 [42]
5	2.13	1.37	3.31	*211*				133	2795 [42]
Hopping et al 2010 (26), Japanese American men, RR is based on rate ratios.									
1	1	—	—	*103*				369	2945 [42]
2	1.06	0.92	1.23	*141*				527	2788 [42]
3	1.08	0.92	1.26	173	G	9052	kJ/d	574	2740 [42]
4	1.09	0.91	1.29	*213*				647	2668 [42]
5	1.05	0.85	1.31	*281*				560	2754 [42]
Hopping et al 2010 (26), Japanese American women, RR is based on rate ratios.									
1	1	—	—	*86*				284	3450 [42]
2	1.17	0.99	1.38	*117*				475	3260 [42]
3	1.24	1.02	1.50	144	G	7150	kJ/d	542	3192 [42]
4	1.23	0.98	1.54	*175*				569	3166 [42]
5	1.18	0.88	1.58	*235*				504	3230 [42]
Hopping et al 2010 (26), Native Hawaiian men, RR is based on rate ratios.									
1	1	—	—	101				119	795 [42]
2	0.89	0.67	1.17	147				110	804 [42]
3	0.98	0.73	1.32	193	G	10628	kJ/d	122	792 [42]
4	0.93	0.68	1.27	247				154	760 [42]
5	1.10	0.76	1.61	335				293	620 [42]

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Hopping et al 2010 (26), Native Hawaiian women, RR is based on rate ratios.

1	1	—	—	*84*				110	1078 [42]
2	0.97	0.73	1.28	*126*				111	1077 [42]
3	1.13	0.84	1.51	163	G	8625	kJ/d	145	1044 [42]
4	1.32	0.97	1.81	*212*				204	984 [42]
5	1.44	0.98	2.12	*329*				373	815 [42]

Sluijs et al 2010 (27), RR is a rate ratio, based on other data in footnotes [43-45]

1	1	—	—	—				nr [43]	nr [43]
2	—	—	—	—				nr	nr
3	—	—	—	118	G	2053	kcal/d	nr	nr
4	—	—	—	—				nr	nr
5	~1.83[44]	~1.30[44]	~2.53[44]	~141[45]				nr	nr

Simila et al 2011 (28), RR is based on rate ratios

1	1	—	—	144				280	~ 4909 [46]
2	0.95	0.79	1.14	162				241	~4948 [46]
3	0.88	0.71	1.09	175	G	10800 [47]	kJ/d	203	~4986 [46]
4	0.88	0.69	1.11	188				195	~4994 [46]
5	0.88	0.65	1.17	208				179	~5010 [46]

Sakurai et al 2012 (29), RR is based on rate ratios. Published GL has units of g/1000kcal [48]

1	1	—	—	62.7				23	377
2	1.16	0.66	2.06	78.0				26	375
3	1.56	0.89	2.71	87.2	G	2198 [49]	kcal/d	34	364
4	1.07	0.57	1.99	97.1				23	377
5	1.24	0.65	2.24	114.4				27	369

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Van Woudenbergh et al 2011 (30), RR is based on rate ratio									
1	1	—	—	107				173	~1282 [50]
2	0.91	0.71	1.16	126	*G* [51]	1981 [52]	kcal/d	149	~1306 [50]
3	1	0.74	1.36	146				134	~1321 [50]
Mekary et al 2011 (31) (32), RR is based on rate ratio									
1	1	—	—	58				1239	14173 [53]
2	1.02	0.94	1.11	80 [54]				1283	~12820 [53]
3	1.13	1.03	1.23	99	G [55]	*1743*[56]	kcal/d	1390	14450 [53]
4	1.22	1.10	1.35	118 [54]				1466	~12637 [53]
5	1.32	1.16	1.51	153				1572	14491 [53]

Footnotes:

[1] Values in normal font without superscripts are data published the citation tabulated.
Values in italics were supplied on correspondence with authors of the citation—see corresponding footnotes.
Values in normal font with superscripts are calculated and regard as exact as a published value unless preceded by a tilda (~) when the values are approximate. The approximations were made to enable the meta-analytical procedures where small errors are of little consequence to the assessment of dose response—see corresponding footnotes.

[2] Other extracted data and author supplied information are given in subsequent footnotes.

[3] All such in this column in rows for Q1, authors of the original reports provide 95CI values for relative risks from Q_1 to Q_n defining the relative risk at Q1 as one with zero degrees of freedom, hence no 95CI values are given for Q_1.

[4] Calculated: Number of participants (65173) divided by the number of quantiles (5), less the number of cases tabulated (16).

[5] Calculated: Mean of quintile values (7253+7636+7594+7531+7106)÷5 (16).

[6] Calculated: Number of participants (42759) divided by the number of quantiles (5), then less the number of cases tabulated (9)

[7] Calculated: Mean of quintile values (1960+2010+2016+2016+1971)÷5 from reference (9).

[8] Author response confirmed further information was not available or not readily accessible (17).

[9] Calculated. Number of participants (35988) divided by the number of quantiles (5), then less the number of cases tabulated (17).

[10] Calculated: Mean of ten energy intake values (6879+6879+7297+7945+8577+8368+7075+7046+7226+8021)÷10 (kJ/d) (17).

[11] Other extracted data for European Americans: incremental RR per 1sd of energy adjusted GL (mean and 95%CI) 1.13 (1.0 to 1.276) meant that case and control data were not needed to obtain rates of change in RR with GL in the first step of two-step analysis. 1SD of energy adjusted GL was calculated at 62g for the mean energy intake shown and is the combined SD values obtained on pooling means and SDs for quantiles of energy adjusted GL in Tables 1 and 2 of the original publication (18).

[12] Calculated: The range of GL from quantile 1 to quantile 5 was obtained assuming a normal distribution calculated from study mean and SD for energy adjusted GL intakes in Tables 1 and 2 of the original publication. The study average of glycemic load was derived from the mean of two sets of ten quintiles values (18), thus (144+130+136+148+172+122+141+150+159+160) ÷10. A value for 1SD of energy adjusted GL was calculated at 62g by combining the SD values for each quantile, and accounting for the SD between quantiles. This complex arrangement was used because information on GL intakes by quantile was available not for GL quantiles directly but was available for fiber and glycemic index quantiles, while correspondence with authors was not able to provide answers.

[13] Calculated: Mean of ten energy intake values (1796+1531+1528+1562+1708+ 1566+1647+1658+1673+1581)÷10 (18).

[14] Hazard ratio for slope (mean and 95%CI) 0.999 (0.966-1.002) for African-Americans (18) was extracted, which meant that case and control data were not needed to obtain rates of change in RR with GL in the first step of two-step analysis.

[15] Calculated: Study average of glycemic load was derived from the mean of two sets of 5 quintiles values (165+135+141+151+177+136+156+164+161+151) ÷10 (18).

[16] Calculated: Mean of ten energy intake values (1606+1654+1674+1587+1483 +1780+1456+1485+1551+1740)÷10 (18).

[17] Calculated: Total number of participants (91249) divided by the number of quantiles (5), then less the number of cases tabulated.

[18] Calculated: Using glycemic load (g/d) and glycemic index to calculate carbohydrate intake (g/d), followed by use of carbohydrate intake per unit energy intake (kcal/100kcal energy) to calculate energy intake (19).

[19] Data provided by correspondence with the first author of the original report (20), who kindly re-analyzed their data with GL adjusted for energy intake by the residual method.

[20] Calculated: Mean of four energy intake values (8803+8038+8559+9919)÷4.

[21] Calculated: Total number of participants in the quantile less the number of cases shown. Participant numbers were 2255, 2749, and 2718 in the 1^{st}, 3^{rd}, and 5^{th} quantiles and interpolated for the 2^{nd} and 4^{th} quantiles with adjustments to ensure the correct total number of participants (21).

[22] Calculated: Mean of six energy intake values reported (1822+1833+1792+1790+1856+1783)÷6 (21).

[23] Values for GL were obtained by correspondence with the first author of the original report (22) and were: Q_1 = 164.4, Q_2 = 180.5, Q_3 = 190.0, Q_4 = 200.2 and Q_5 = 234.7 g GL/d.

[24] Calculated: Total number of participants (64227) divided by the number of quantiles (5), then less the number of cases

tabulated (22).

[25] Calculated: Mean of energy intakes by quintile (1773.2 + 1643.9 + 1609.5 +1602.6 +1784.1)÷5 (22).

[26] Calculated: Total number of participants (40078) divided by the number of quantiles (5), then less the number of cases tabulated (23) .

[27] Calculated: Mean for study energy intakes reported for quantiles (1966+1429+1882+1582+1697+1638+1946+1516+1779)÷9 (23).

[28] Calculated: GL for the mixed population is calculated from the reported GL values for men (127, 152 & 176 g/d for Q_1 to Q_3) and women (108, 129 & 152 g/d for Q_1 to Q_3) and the fraction of the population that were men (0.71) (24).

[29] Calculated: Number of persons per quantile reported in the original report (24) less the number of cases tabulated.

[30] Based on very low reported central-quantile GI values of 56 and 54.5 for men and women (24), a glucose reference standard was assumed. This appears corroborated by a value of 86 for the same community at a time when white bread was usually a standard (33). Two corresponding authors were not available to report differently.

[31] Calculated: Based on the reported fat and carbohydrate intakes (24), calorie conversion factors of 9 and 3.75 kcal/g for fat and carbohydrate as monosaccharide respectively, and 14.8% energy as protein average across sexes and tertiles for this population (34).

[32] Calculated: Based on reported values of GL (g/d) (15) of 145 sd 32 for men, and 114 sd 23 in women, a normal distribution and the fraction of men in the population of 0.46 being applied to all quantiles.

[33] Case and control data were not needed when obtaining the rate of change in RR with GL in the first step of two-step analysis because the rate estimate is based on only one quantile versus referent. Case and control data were only needed when there was multiple data within the study when the case and control data help account for non-independence of observations from the same study (27).

[34] Calculated from values for each quantile in men and women separately and the fraction of the population that were men, (0.46x(1723+1732+1726+1727+1690)÷5) +(1-0.46)x(1288+1336+1326+1291+1268)÷5

[35] By correspondence, the first author of the original report (2) indicates that GL was adjusted for energy intake in men and women separately, with means of 2016.7 kcal/d in men and 1608.4 kcal/d in women, with a combined sex mean of 1835 kcal/d. Correspondence confirms GL values were based on the glucose standard, and that all non-European American participants were African-American.

[36] Calculated: Number of persons per quantile (379, 381, 378, 381, 379) less the number of cases per quantile tabulated (2).

[37] By analysis, assuming a normal distribution, a mean GL from the original report (25) and a range of 60 given between lowest and highest deciles by Lui & Chou (13).

[38] Calculated from the total number of cases distributed according to the relative risks in each quantile.

[39] Calculated: Total number of participants (85059) divided by the number of quantiles (10), then less the number of cases

tabulated.

[40] Calculated: Mean of nine reported energy values (1553+1559+1559+1550+1555+1551+1565+1552+1591)÷9 (25) .

[41] Authors explained by correspondence that the published and author provided values of GL for this study (shown above) had not been energy adjusted. Prior to meta-analysis, a factor of 1.62 was applied to approximate this adjustment, which is the ratio of energy adjusted variance in GL for the similar whole multiethnic cohort in Howarth et al (35) to the variance in GL in the multiethnic cohort in the Hopping et al study (26) after adjustments for differences in energy intakes reported.

[42] Calculated: Number participants less the number of cases, by quantile, data supplied by authors. Values agrees to 1 in 3000 with values calculated as the total number of participants divided by the number of quantiles, then less the number of cases by quantile for the published data (26).

[43] Case and non-case data was not used because the authors supplied rate information: RR was reported to increase by 1.27 (95%CI: 1.11,1.44) per 1SD rise in reported GL (g/2053kcal) of 21.2 g (27). This information was re-expressed per 100g GL in 2000kcal. Operationally this was via lnRR per 1SD rise in glycemic load

[44] Data not used in the two-step analysis, but approximated for the meta-analysis of rise in lnRR from the lowest to highest quantile (Fig S1 in the Supplemental Materials online). Data was calculated from information in footnotes 43 & 45.

[45] The median glycemic load for quantile 5 was approximated using the reported glycemic load of 117.9g and its SD 21.2 g (27). Using these values a normal distribution was simulated for 100000 observations, divided into quintiles, and the median for the fifth quintile obtained. A normal distribution was indicated by the authors reporting an SD value for glycemic load among other data showing interquartile ranges when the normality assumption was not justified.

[46] Calculated: Total number of participants (25943) divided by the number of quantiles (5), then less the number of cases tabulated.

[47] Calculated as the mean of six values expressed in MJ (10.8 +11+10.7+10.8+11+10.5)÷6

[48] Values for GL were reported in g per 1000 kcal (29).

[49] Calculated as the mean of five values (2394 + 2299 +2183 +2104 + 2011)÷5

[50] Calculated: Total number of participants (4366) divided by the number of quantiles (3), then less the number of cases tabulated.

[51] Correspondence with the first author of the original study confirms.

[52] Calculated as the mean of three quntile values (1967 +2005 +1971)÷3

[53] Calculated approximately: Total number of participants less the number of participants in Q1, Q3 and Q4, this remainder divided between Q2 and Q4, each less the published number of cases in Q2 and Q4 respectively.

[54] Values at Q2 and Q4 were not published. We used mid-range values for these quantiles.

[55] Based on very low reported GI values and published correspondence comparing values in this and the prior study of Halton et al (25), a glucose reference standard was evident, as in the prior study from this group at 20y follow-up.

56 Reported in published correspondence (32).

Table S2 Study identities, region, ethnicities, outcome ascertainment, population sample size, and number of cases accumulated [1]

	First author, date and (citation)	Region	Ethnicity	Ascertainment [2] of outcome	Number of quantiles	Years of follow-up	Population sample (n)	No. Cases (n)
1	Salmerón 1997 (f) (16)	USA	EA	Clinical report	5	6	65173	915
2	Salmerón 1997 (m)(9)	USA	95% EA	Clinical report	5	6	42759	523
3	Meyer 2000 (17)	USA	EA	Self report	5	6	35988	1141
4	Stevens 2002 (18)	USA	EA	Clinical report	5	9	9529	971
5	Stevens 2002 (18)	USA	AA	Clinical report	5	9	2722	478
6	Schulze 2004 (19)	USA	EA	Clinical report	5	8	91249	741
7	Hodge 2004 (20)	Australia	EAu	Self report	4	4	31641	365
8	Zhang 2006 (21)	USA	EA	Self report GDM	5	8	13110	796
9	Villegas 2007 (22)	China	CH	Mixed reports [3]	5	4.6	64227	1605
10	Krishnan 2007 (23)	USA	AA	Self report	5	8	40078	1938
11	Patel 2007 (15)	USA	mixed	Self report	5	9	124907	~2700
12	Mosdol 2007 (24)	Europe	Eu	Clinical report	3	13	5598	329
13	Sahyoun 2008 (2)	USA	67% EA	Clinical report	5	4	1898	99
14	Halton 2008 (25)	USA	EA	Clinical report	10	20	85059	4670
15	Hopping 2010 (26)	Hawaii- men	EA	Clinical report	5	14	15116	1080
16	Hopping 2010 (26)	Hawaii- women	EA	Clinical report	5	14	14643	715
17	Hopping 2010 (26)	Hawaii- men	JA	Clinical report	5	14	16572	2677
18	Hopping 2010 (26)	Hawaii- women	JA	Clinical report	5	14	18672	2364
19	Hopping 2010 (26)	Hawaii- men	NH	Clinical report	5	14	4568	798
20	Hopping 2010 (26)	Hawaii- women	NH	Clinical report	5	14	5941	943
21	Sluijs 2010 (27)	Europe	Eu	Clinical report	5	10.1	37846	915
22	Simila 2011 (28)	Europe	Eu	Clinical report	5	12	25943	1098
23	Sakurai 2011 (29)	Japan	Jp	Clinical report	5	6	1995	133
24	Van Woudenbergh	Europe	Eu	Clinical report	3	12.4	4366	456

	2011 (30)							
25	Mekary 2011 (31)	USA	EA	Clinical report	5	26	81827	6950

[1] *Abbreviation:* USA, United States of America; EA, European-American; AA, African-American; EAu European-Australian; CH, Chinese; mix, mixed ethnicities; JA, Japanese-American; NH, Native Hawiian; Eu, European; Jp, Japanese; T2D, Type 2 diabetes; GDM, gestational diabetes.

[2] Medical reports include hospital or medical doctor's records or biochemical tests.

[3] Of 1608 self-reported cases, 896 were confirmed by medical record.

Table S3. Characteristics of the dietary instrument used [1]

	First author, date and (citation)	Instrument used for dietary assessment	Number of food items in the instrument	Instrument correlation with food records [2]	Whether correlation was deattenuated	Validity of instrument for cohorts analyzed	No. of assessments made with instrument(s)
1	Salmerón 1997 (f) (16)	FFQ	134	0.64	yes	yes	1
2	Salmerón 1997 (m) (9)	FFQ	131	0.73	yes	yes	1
3	Meyer 2000 (17)	FFQ	127	0.45	yes	yes	1
4	Stevens 2002 (18)	FFQ	66	0.45	yes	no	1
5	Stevens 2002 (18)	FFQ	66	0.45	yes	no	1
6	Schulze 2004 (19)	FFQ	133	0.64	yes	yes	2
7	Hodge 2004 (20)	FFQ	121	0.41 (0.56) [3]	no (~yes) [3]	no (~yes) [3]	1
8	Zhang 2006 (21)	FFQ	133	0.64	yes	yes	2
9	Villegas 2007 (22)	FFQ	77	0.66 (0.71) [4]	no (yes) [4]	yes	2
10	Krishnan 2007 (23)	FFQ	68	0.43	yes	yes	1
11	Patel 2007 (15)	FFQ	68	0.62[5]	yes	yes	1
12	Mosdol 2007 (24)	FFQ	127	0.50	yes	yes	1
13	Sahyoun 2008 (2)	FFQ	108	0.65	yes	yes	1
14	Halton 2008 (25)	FFQ	61,116,134 [6]	0.45,0.61,0.64 [7]	yes	yes	6
15	Hopping 2010 (26) mEA	FFQ	125	0.68	yes	yes	1
16	Hopping 2010 (26) fEA	FFQ	125	0.80	yes	yes	1
17	Hopping 2010 (26) mJA	FFQ	125	0.56	yes	yes	1
18	Hopping 2010 (26) fJA	FFQ	125	0.54	yes	yes	1
19	Hopping 2010 (26) mNH	FFQ	125	0.62 [8]	yes	no [8]	1
20	Hopping 2010 (26) fNH	FFQ	125	0.67 [8]	yes	no [8]	1

21	Sluijs	2010 (27)	FFQ	178	0.75	yes	yes	1
22	Simila	2011 (28)	DHQ	276	0.55 (0.71) [9]	no (yes) [9]	yes	1
23	Sakurai	2011 (29)	DHQ	147	0.62	yes	yes	1
24	van Woudenbergh 2011 (30)		FFQ	170	0.79	yes	yes	1
25	Mekary 2011 (31)		FFQ	61,116,134 [10]	0.45,0.61,0.64 [11]	yes	yes	7

[1] *Abbreviations*: FFQ, food frequency questionnaire; DHQ, diet history questionnaire.

[2] Correlations were for carbohydrate intake, and are reproduced either from the citation or from its referenced validation study. Values are after adjustment for energy intake (unless specified differently) and de-attenuation (unless also accompanied by bracketed values, when values in brackets indicated approximate deattenduated values obtained as described in the main article. The correlation shown is for validation of one application of the instrument. To aid comparability between studies, correlations obtained by repeated measures were not used.

[3] As discussed in the citation (20), a discrepancy appears between the published validation of the instrument, which was on a population external to the population sampled for the cohort study, and the reproducibility of the instrument in a sample of the cohort studied. Within the study the FFQ showed only "fair" to "moderate" agreement—interpretable from tables of kappa as 0.21-0.4 and 0.41 to 0.60 respectively, for which the mid-range of 0.41 was used as a crude estimate. Adjustments to approximate an energy-adjusted deattenuated value suggest a value of approx. 0.56 compared with the questionnaires validation, which gave 0.78 for in a different population.

[4] Crude value as reported in the validation publication, in which the authors claim an energy adjustment did not change the result appreciably. Value in parenthesis is after approximate adjustment at present for de-attenuation.

[5] A value for the mixed sex population was the average of values for men (0.73) and women (0.51).

[6] Mean number of foods for the three FFQ used 116=(61x4/20 + 116x2/20 + 134x14/20) weighted by years of use (4, 2 ,20) over the 20 year follow-up.

[7] Mean correlation for the three FFQ used 0.60=(0.45x4/20 + 0.61x2/20 + 0.64x14/20) weighted by years of use (4, 2 ,20) over the 20 year follow-up. Note, for comparison with other studies this corresponds to a single representative FFQ validation weighted by the years of use as opposed to a higher correlation obtainable by repeated measures.

[8] An average was used for men and another average for women, obtained from among the population of non-native Hawaiians. (26)

[9] Energy adjusted deattenuated value (0.71) from validation paper.

[10] Mean number of foods for the three FFQ used, 119=(61x4/26 + 116x2/26 + 134x20/26) weighted by years of use (4, 2 ,20) over the 26-year follow-up.

[11] Mean correlation for the three FFQ used, 0.61=(0.45x4/26 + 0.61x2/26 + 0.64x20/26) weighted by years of use (4, 2 ,20) over the 26-year follow-up. Note that, for comparison with other studies, this corresponds to a single representative FFQ validation weighted by the years of use as opposed to a higher correlation such as obtainable by repeated measures.

Table S4. Characteristics of the study participants, duration of study, number of quantiles, and study baseline exclusions. [1]

	First author, date and (citation)	Sample population as male (fraction)	Mean BMI of sample population (kg/m^2)	Mean age of sample population at baseline (y)	Mean energy intake (kcal)	Range of GL intake Q_1 to Q_{max} (g per 2000kcal)[2]	Reasons for excluding participants at baseline [1]	Newcastle Ottawa quality scale [3]	Conflict of interest declared
1	Salmerón 1997(f) (16)	0	25	53	1774	88 - 140	dm,ca,cvd,iei,mis	8	nr
2	Salmerón 1997(m) (9)	1	25	58	1995	83 - 142	dm,ca,cvd,iei,mis	8	nr
3	Meyer 2000 (17)	0	27	62	1800	73 - 113	dm,iei, mis	6	nr
4	Stevens 2002 EA (18)	0.46	27	54	1625	62 - 189	dm,iei,mis,ipc,eth	8	nr
5	Stevens 2002 AA (18)	0.37	29	53	1602	63 - 206	dm,iei, mis,ipc,eth	8	nr
6	Schulze 2004 (19)	0	25	36	1811	107 - 163	dm,ca,cvd,iei,mis	8	nr
7	Hodge 2004 (20)	0.5	26	55	2110	87 - 148	dm,chd,preg,iei,mis	6	none
8	Zhang 2006 (21)	0	23	32	1813	106 - 164	dm,mg,cvd,ca,iei,mis	7	nr
9	Villegas 2007 (22)	0	<30 [4]	51	1683	195 - 279	dm,cvd,cam	8	nr
10	Krishnan 2007 (23)	0	<31 [5]	38	1715	96 - 166	dm,ca,iei,igl,mis [6]	6	none
11	Patel 2007 (15)	0.46	26	63	1494	88 - 154	dm,1yd,ca,iei,mis	7	none
12	Mosdol 2007 (24)	0.71	25	49	2095	116 - 161	dm, em, mis, iei	7	none
13	Sahyoun 2008 (2)	0.45	27	75	1835	104 - 177	dm,iei,mis	8	none
14	Halton 2008 (25)	0	24	46	1560	79 - 156	dm,ca,cvd,iei,mis	8	none
15	Hopping 2010 (26) mEA	1	26	57	2162	101 - 199	dm,oe,mis,sr	8	none
16	Hopping 2010 (26) fEA	0	26	58	1707	108 - 208	dm,oe,mis,sr	8	none
17	Hopping 2010 (26) mJA	1	25	59	2163	120 - 222	dm,oe,mis,sr	8	none
18	Hopping 2010 (26) fJA	0	24	59	1709	126 - 234	dm,oe,mis,sr	8	none
19	Hopping 2010 (26) mNH	1	28	56	2540	107 - 221	dm,oe,mis,sr	8	none
20	Hopping 2010 (26) fNH	0	27	56	2061	111 - 257	dm,oe,mis,sr	8	none

21	Sluijs 2010 (27)	0.26	26	51	2053	89 - 141	dm,iei,mis	8	none
22	Simila 2011 (28)	1	26	57	2629	110 - 158	dm,ns	8	none
23	Sakurai 2011 (29)	1	23	46	2000	125 - 229	dm, mis,iei	7	none
24	van Woudenbergh 2011 (30)	0.4	26	67	1981	108 - 147	dm,mis,hcrp,ini	8	nr
25	Mekary 2011 (31)	0	26	46	1743	66-176	dm,cvd,ca,mis,iei,	7	none

[1] *Abbreviations*: BMI, body mass index (kg/m^2); f, female; m, male; nr, not reported; dm, diabetes mellitus; ca, cancer; cvd, cardiovascular disease; chd, coronary heart disease; iei, implausible energy intakes; mis, missing or inadequately compete information; ipc, inadequate number of participants within a field centre; eth, ethnicity; preg, pregnancy; igl, implausible glycemic load; mg, multiple gestations; 1yd, one year deaths to minimize undiagnosed disease at baseline; oe, other ethnicities; ns non-smokers; hcrp, high C-reactive protein; ini, implausible nutrient intakes.

[2] Calculated values, energy adjusted for glycemic load.

[3] The Newcastle-Ottawa observational study quality scale ranges from 0 to 9 representing a minimum to maximum quality (37).

[4] An approximate estimate made using the percentage persons in categories of BMI was ~26 kg/m^2.

[5] An approximate estimate made using the percentage persons in categories values of BMI ~26 kg/m^2.

[6] Other exclusions: pregnancy, age less than 30y.

Table S5. Assessment of assumptions about accuracy of data used in the two-stage meta-analysis with covariates applied to all 24 studies (model 5 as reported in Tables 2 & 3 of the main article). Observations and comments apply to the current application and dataset only.

	Potential weakness in data	Studies affected	Assumption made	Approach or new assumption	Overall outcome for the fully adjusted RR for T2D (cf Table 2 main article)	Comment 1	Comment 2
1	Assumes all data collated in Table S1 are accurate	All	Hypothetically, none	No new assumption	1.45 (1.31, 1.61)	—	—
2	**Case numbers** in each quantile were not available, and so were approximated when needed.	Halton et al (25)	Approximation of these values based on both the total case numbers and value for RR in each quantile has negligible effect on the overall outcome	Case numbers approximated for all studies, not just the one study affected.	1.45 (1.31, 1.61)	Agrees with line 1	Assumption justified
3	**Person-years** in each quantile were not available for all studies, and so were approximated consistently for all studies based on the number of participants per	Salmeron et al f (16) Schulze et al (19) Stevens et al EA (18) Stevens et al AA (18) Sahyoun et al (2) Hodge et al (20) Patel et al (15) Zhang et al (21) Hopping et al (both	Approximation of these values based on the number of participants per quantile and the number of years has negligible effect on the	Person-years by quantile reported for the unaffected studies were used, only approximating these values when not available. (May introduce	1.45 (1.31, 1.61)	Agrees with line 1	Assumption justified

	quantile and the number of follow-up years. In some studies also the no of participants in each quantile was assumed to equal the total number of participants in the study divided by the number of quantiles.	sexes and all ethnicities) (26) Halton et al (25) Sluijs et al (27) Simila et al (28)	overall outcome	bias between those that report person-years and those that don't)			
4	**Study average energy intake** was calculated from reported diet compositions and food energy conversion factors	Mosdol et al (24) Schulze et al (19)	Errors in calculations are ≤10% so have negligible effects the outcome	Energy assumed 10% too low for Mosdol et al (24) Energy assumed 10% too high for Mosdol et al (24) Energy assumed 10% too low for Schultz et al (19) Energy assumed 10% too high for Schultz et al	1.45 (1.31,1.61) 1.45 (1.31,1.61) 1.46 (1.31,1.61)	Agrees with line 1 Agrees with line 1 Assumption used is conservative	Assumption justified
5	**Glycemic load values** were not reported directly but were approximated assuming a normal distribution from values for mean and SD of GL in the population	Stevens et al (18) EA Stevens et al (18) AA Patel et al (15) Halton et al (25)	Errors in calculations are ≤10% so have negligible effects the outcome	GL assumed 10% too high for Stevens et al (18) EA . GL assumed 10% too low for Stevens et al (18) EA. GL assumed 10% too high for Stevens et al (18) AA.	1.45 (1.31,1.61) 1.45 (1.31,1.61) 1.45 (1.31,1.61)	Agrees with line 1 Agrees with line 1 Agrees with line 1	Assumption justified

				GL assumed 10% too low for Stevens et al (18) AA. GL assumed 10% too high for Patel et al (15) GL assumed 10% too low for Patel et al (15) GL assumed 10% too high for Halton et al (26) GL 10% too low for Halton et al	1.45 (1.31,1.61) 1.45 (1.31,1.60) 1.45 (1.31,1.62) 1.45 (1.31,1.61) 1.45 (1.31,1.61)	Agrees with line 1 Agrees with line 1 Agrees with line 1 Agrees with line 1 Agrees with line 1	
6	**Standard for GI as bread or as glucose** was clearly rational assumption, but unconfirmed via correspondence.	Mosdol et al (24)	Standard used was glucose	Standard used was bread	1.45 (1.31-1.61)	Agrees with line 1	Assumption leads to no appreciable error overall
7	**Analytical values for all glycemic load values are imprecise for foods and diets**.	Potentially, all studies reviewed	Errors are random leading to random errors among studies, and if excessive would both underestimate the outcome for RR and elevate I^2	Effect of additional random error in GL causing deviation in RR per unit GL was examined (error of mean 0 and SD 10% of the study range of GL was applied)	1.42 (1.28, 1.58)	RR was significantly lower (t= -9.5 for 10 reps) indicating random error among GL intakes leads to a conservative estimate	Assumption reasonable and conservative …continued

					I^2 was elevated from 2% to 13% (average of 10 reps)	Confirms that this random error elevates I^2, so that the I^2 of 2% indicates random error in analytical values for GL appear of limited concern	…continued

8	**Glycemic load** values were reported **without adjustment for energy intake**	Hopping et al for both sexes and all three ethnicities (26). This although the corresponding validation study for the dietary instrument used energy-adjusted carbohydrate intakes	The adjustment is imputable from the ratio of variance for the multiethnic study of Hopping et al (26) and the related multiethnic study of Howarth et al (35), who report GL with energy adjustments .	Error from this assumption would contribute towards elevation of I^2. The alternative assumption was to apply an energy adjustment than minimized I^2, which is made viable because of the multiple observations by sex and ethnicity.	I^2 decreased to a minimum and increased again as the adjustment was raised from below to above that indicated by the imputation from the study of Howarth et al (35). At the minimum (I^2 = 0.14%) RR was: 1.49 (1.33,1.67)	I^2 behaved as expected. With the imputation I^2 was already low at 2% implying the assumption was reasonable. The imputed information indicated a conservative estimate for RR was reached at line 1	Assumption made (Column 4) was reasonable, and on balance conservative.
9	**Values for CORR are imprecise**	Potentially, all studies reviewed	Values for CORR are accurate other than for random error	Effect of additional random error in CORR was simulated to examine deviation in RR and the β-	I^2 was raised from 2 to 8% RR per unit GL was marginally higher, but not	There was no evidence of significant error in RR per unit GL due to this	Assumption made (column 4) was reasonable

				coefficient for CORR. (Error of mean 0 and SD 10% of the study range of CORR was applied.)	significantly so (t=0.66 for 10 repeats) to: 1.47 (1.30, 1.65) The β-coefficient for CORR fell from 2.05 to 1.89 (P=0.05, t-test, 10 repeats)	level of random error in CORR	
10	**Adjustments were made towards deattenuated values for CORR when non-deattenuated values were reported, or a deattenuated CORR within a study was estimable only approximately.**	Villegas et al (22) reported CORR of 0.66, which became 0.71 following our adjustment towards a deattenuated value	An energy adjusted and deattenuated value for CORR is preferred.	No adjustment is made, and the non-deattenuated value 0.66 would have been preferred.	1.47 (1.30,1.67)	Little different from line 1	Assumption (Column 4) was reasonable, and on balance conservative.
		Simila et al (28) reported CORR of 0.55. However, the validation study (36) reports a value of 0.71 after adjustment for energy and deattenuation (Table S3 footnote 9).	An energy adjusted and deattenuated value for CORR is preferred.	The non-adjusted value 0.55 (28) should have been used rather than the deattenuated energy adjusted value reported in the validation study	1.48 (1.31,1.67)	Little different from line 1	Assumption (Column 4) was reasonable, and on balance conservative.
		Hodge et al (20) describe agreement categorically between repeated FFQs, consistent with a CORR unadjusted for energy and deattenuation of 0.41,	An energy adjusted and deattenuated value for CORR is preferred and that estimated is reasonable	No adjustment is made, and the non-adjusted value of 0.41 would have been preferred	1.46 (1.31,1.61)	Little different from line 1	Assumption (Column 4) was reasonable, and on balance conservative.

		and which became 0.57 following our adjustment towards a deattenuated and energy adjusted value (see Table S3 footnote 3).					
	Assumption investigated	Covariates (cf Table 3 in the main article)				Comments	
		SEX	CORR	FUY (per 10 y)	ETH		
1 *	Model 5	0.22 (0.02,0.46)	2.05 (0.6,4.7)	0.00 (-0.19.0.20)	0.22(0.05,0.41)		
2-6	Highest value	0.24 (0.03,0.50)	2.21 (0.7,5.0)	0.04 (-0.16,0.24)	0.22(0.05,0.41)	Alternative assumptions lead to relatively small differences from model 5 (line 1 immediately left)	
2-6	Lowest value	0.19 (0.01, 0.41)	1.87 (0.6, 4.3)	-0.03(-0.21,0.16)	0.20 (0.04,0.39)		
7	Added random error to GL (see above at 7)	0.22 (0.01,0.47)	1.78 (0.5, 4.3)	-0.01(-0.18,0.16)	0.20 (0.06,0.38)		
8	Alternative energy adjustment for obs. from Hopping et al (26)	0.28 (0.04,0.56)	2.42 (0.8,5.5)	0.01(-0.13,0.30)	0.23(0.05,0.44)	Adjustments based on imputations from Howarth et al (35) appear conservative compared with a best fitting solution.	
9	Added random error to CORR (see above at 9)	0.22 (0.06, 0.62)	1.89 (0.50, 4.59)	-0.01(-0.14, 0.59)	0.21 (0.03, 0.42)	Random error in CORR leads to an underestimation of the β coefficient for CORR	
10	Adjustments to CORR. Highest values	0.26 (0.04,0.53)	2.29 (0.52,0.61)	-0.02(-0.22,0.29)	0.21(0.04,0.41)	Alternative assumptions lead to relatively small differences compared with our preferred assumptions leading to coefficients at line 1 immediately left	
10	Adjustments to CORR. Lowest values	0.21(0.01,0.45)	2.02 (0.052, 6.14)	-0.07(-0.28,0.15)	0.18(0.01,0.39)		

Abbreviations: CORR, the energy adjusted and deattenuated dietary instrument correlation for carbohydrate; FUY, the duration of follow-up in years; ETH, European American ethnicity versus all other ethnicities examined combined; f, female; I^2, percentage of total variance due to among-

studies variance. SEX, the proportion of study participants that are male (reported as RR for females > RR for males); RR, relative risk for T2D of 100g GL increment in 2000kcal diets.

* The number and all such below in this column refer to the corresponding assumptions and simulations noted in rows for corresponding numbers in this column above.

Table S6. Parameter estimates according the two-step meta-analysis approaches used aside a one-step approach, each on the full dataset of 24 studies

Parameter	Steps	Method [1]	RR or ΔRR [2]	95%CI [2]	P
Adjusted RR	Two-step	GLST then metareg	1.45	(1.31,1.61)	<0.001
	One-step	Pooled GLST [3]	1.46	(1.31,1.61)	<0.001
SEX (ΔRR per 100g GL; F>M)	Two-step	GLST then metareg	0.22	(0.02,0.46)	0.031
	One-step	Pooled GLST	0.22	(0.03,0.45)	0.024
CORR (ΔRR per 100g GL; over CORR to 1)	Two-step	GLST then metareg	2.05	(0.6, 4.7)	<0.001
	One-step	Pooled GLST	1.98	(0.5, 4.8)	0.001
FUY (ΔRR per 100g GL; over 10y)	Two-step	GLST then metareg	0.00	(-0.19,0.20)	0.96
	One-step	Pooled GLST	0.01	(-0.18,0.19)	0.94
ETH (ΔRR per 100g GL; EA>Other)	Two-step	GLST then metareg	0.22	(0.05,0.41)	0.011
	One-step	Pooled GLST	0.22	(0.03,0.43)	0.018

			R^2	I^2	P for I^2 [4]
Statistics	Two-step	GLST then metareg	97	2	0.43
	One-step	Pooled GLST	100	0	0.78

1. All models here assume relationships are linear.
2. Analyses conducted in log form and displayed here in unlogged form.
3. One step analysis of lnRR in pooled GLST meta-regression was versus 5 determinants: increment in GL dose (GL from Q_1 to $Q_{>1}$); and increments in four dose-covariate interactions (dose-x-SEX, dose-x-CORR, dose-x-FUY, dose-x-ETH, where SEX, CORR, FUY and ETH were centered).
4. The P-values: Two-step, Q-test for among-studies variance or model deviance from linearity; One step, chi^2 test for goodness-of-fit.

Table S7. Influence of study factors on incremental RR values and β-coefficients for the covariates SEX, CORR, FUY and ETH (n=24 studies) [1].

Characteristic or influence factor [2]	Units or subjective score	Z-score [3]	IRR	Hypothesized covariate			
				SEX	CORR	FUY	ETH
			Percentage change in IRR or β coefficient due to addition of the potentially influential study characteristic as a 5th covariate [1]				
Dietary factor							
Study mean glycemic load	(g/2000 kcal)	-0.11	<0.1	4	2	- [4]	-2*
Study mean energy intake	(kcal/d)	-0.03	0.4	-15*	6	-	-1
Glucose or bread reference	(Glucose=1, bread=0)	0.38	-0.5	1	-5	-	5*
No. of dietary assessments	(n)	0.08	-0.8	1	-1	-	0
No. foods in the dietary instruments	(n)	-1.40	-3.7	-10	19*	-	9
Dietary instrument (CORR) [5]	(Fractional)			(Included in model 5)			
,, applicability within population	(Yes=1, doubtful=0)	0.45	-3.0	5	-10	-	8
,, used energy-adjusted intakes	(Yes=1, no=0)	1.75	-4.0	-23	4	-	-9
Fibre excluded as confounder	(Yes=1, no=0)	0.08	0.1	3	1	-	-1
Population factor							
T2D excluded at baseline [6]	(Yes=1, no=0)	0.00	0	0	0	-	0
Population sample analysed (n)	(n)	0.47	-3.1	2	-5	-	4
European American versus other (ETH) [5]	(ETH=1, others = 0)			(Included in model 5)			
Gender (SEX) [5]	(Male=1, Female=0)			(Included in model 5)			
Body mass index	(kg/m^2)	-0.40	-1.0	2	-5	-	-1
Age at baseline	(y)	-1.44	9.7	-23	11	-	-9
Progress factor							
Person-years	(ny)	0.51	-2.3	3	-4	-	4
Total incidents (cases) in study	(n)	0.86	-2.4	1	-1	-	12
Follow-up years (FUY) [5]	(years)			(Included in model 5)			
Outcome ascertainment (method of diagnosis)	(Clinical =1, self =0)	-0.37	-0.1	2	1	-	3

Study quality factors							
Selection criteria:							
Truly or somewhat representative of population	(Yes=1, no=0)	-0.45	3.5	0	1	-	-5
Cohorts selected from the same population [6]	(Yes=1, no=0)	0.00	0.0	0	0	-	0
Ascertainment of exposure (CORR >0.5)	(Yes=1, no=0)	-[7]	-[7]	-[7]	-[7]	-[7]	-[7]
Outcome of interest not present at start of study [6]	(Yes=1, no=0)	0.00	0.0	0	0	-	0
Total score for selection criteria	(Calc. range 0 to 4)	-0.23	-3.0	0	6	-	-5
Outcome criteria:							
Secure assessment (clinical or self-report)	(Yes=1, no=0)	-0.37	-0.1	2	1	-	3
Follow-up period sufficient long (>4 y) [6]	(Yes=1, no=0)	0.00	0	0	0	-	0
Few subjects lost or lost explained [6]	(Yes=1, no=0)	0.00	0	0	0	-	0
Total score for outcome criteria	(Calc. range 0 to 3)	-0.37	-0.1	2	1	-	3
Comparability criteria:							
Study control for non-nutrient risk factors	(Yes=1, no=0)	1.01	3.5	1	5	-	-2
Study control for nutrient risk factors	(Yes=1, no=0)	-0.04	-0.9	2	-1	-	0
Total score for comparability criteria	(Calc. range 0 to 2)	0.24	2.7	0	6	-	-6
Sum for all quality criteria	(Calc. range 0 to 9)	-0.33	1.1	1	3	-	2

Abbreviations: IRR, incremental relative risk for energy-adjusted GL increment of 100g after adjustment for centred covariates; SEX, of adult males or females ; CORR, dietary instrument correlation with food intake record for carbohydrate; FUY, number of follow-up years; EA, European American ethnicity versus other ethnicities; Calc., calculated as sum of the immediate above.

* Indicates factors that correlate or potentially correlate (monovariate P<0.05) with the covariate as found in Table 1 in the main article.

[1] Influence values are shown as positive when the influence is to increase the absolute value of a coefficient and negative when lowering the absolute value. Thus the influence of each j^{th} coefficient by each v^{th} factor in the studies was expressed as $100*(\Delta\beta)/\beta$ were β is the coefficient in meta-regression model 5 and $\Delta\beta$ is the change in β due to addition to the model of the v^{th} among-study variable.

[2] Influence factors were centered before assessing influence on model 5 coefficients.

[3] Z-score for the β-coefficient accompanying this factor alongside the hypothesized covariates SEX, CORR, FUY and ETH.

[4] Over all studies the β-coefficient for FUY was non-significant and near zero.

[5] Factor included in the model.

[6] These factors scored equally for all studies, so that zero effects on the β coefficients shown have zero degrees of freedom.

[7] The full range of CORR is accounted in fully adjusted model 5.

FIGURE S1 (right)**. Meta-analysis of incremented RR with increase in GL from lowest to highest quantile, by sex group.** Data points (■) for each study vary in size— larger points for studies of greatest weight in the meta-analysis. The associated horizontal lines indicate the corresponding 95% confidence interval for a study— arrow heads indicating truncations. Diamond show the combined study means (upper and lower tips) and the corresponding 95% confidence intervals (left and right tips). Note that the scale for ΔRR is logarithmic with values showing the means for studies and untransformed combined means for subtotals and overall total. *Abbreviations*: Correlation, 100 x the correlation for carbohydrate intake (dietary instrument versus objective measure); RR, relative risk; LCI and UCI, lower and upper 95% confidence intervals; %WT, percentage weight based on random effects; P, level of statistical significance (z-test for RR, Q-test for I^2); I^2, heterogeneity = $100 \cdot \tau^2 / (\tau^2 + se^2)$ where τ^2 is the among-studies variance; HaltMeka 08-11, data from Halton et al 2008 (25) and Mekary et al 2011 (31) are from the same study differing in the duration of follow-up (20 and 26y) and so were combined prior to the meta-analysis.

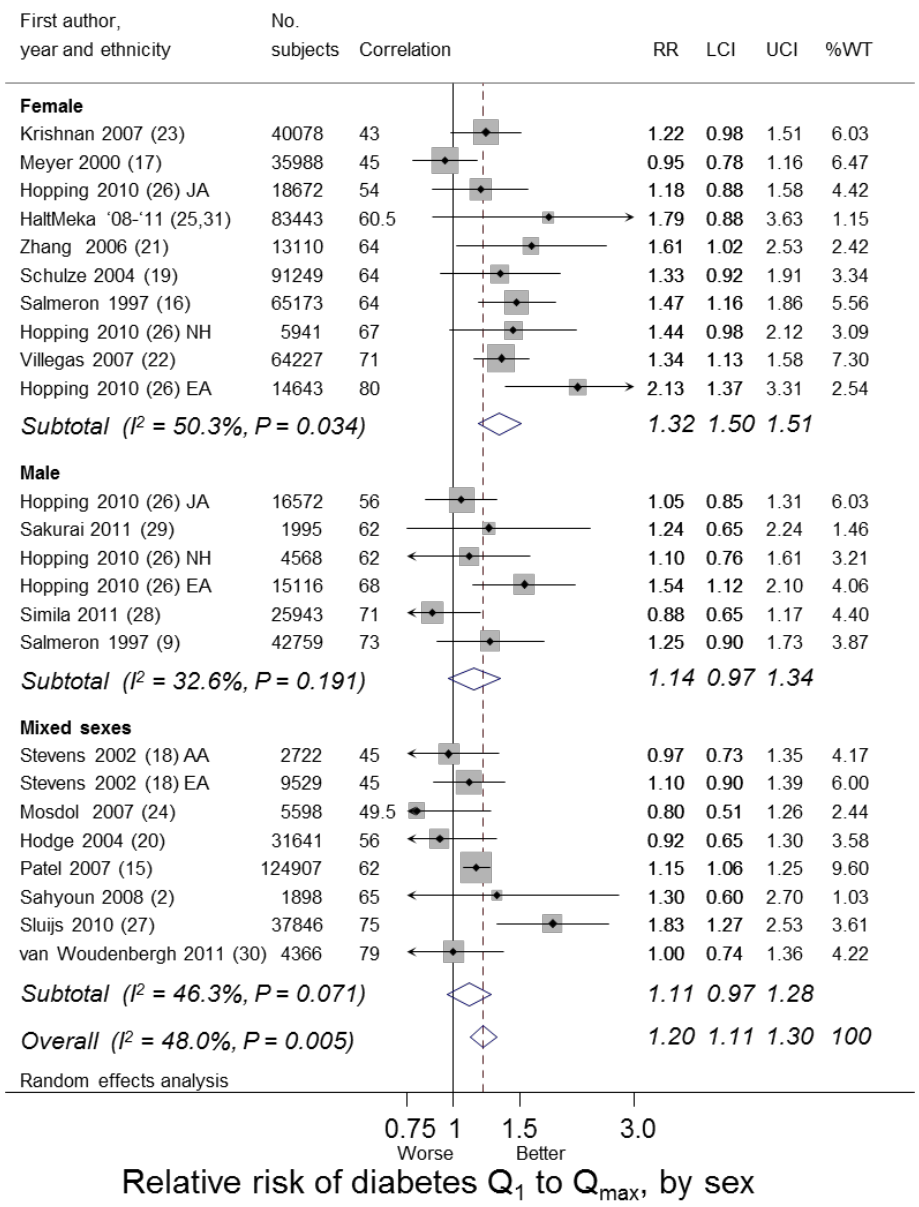


FIGURE S2 (right)**. Funnel plot of residuals (B) for model 5 obtained by the two-step approach to meta-analysis** (cf Tables 2 and 3 in the main article)**.** Points (●) represent individual studies. Triangular sides represent 95%CIs which ideally bound 95% of studies. Trim-and-fill analysis indicated no hypothetical points were required to eliminate bias if it were present.

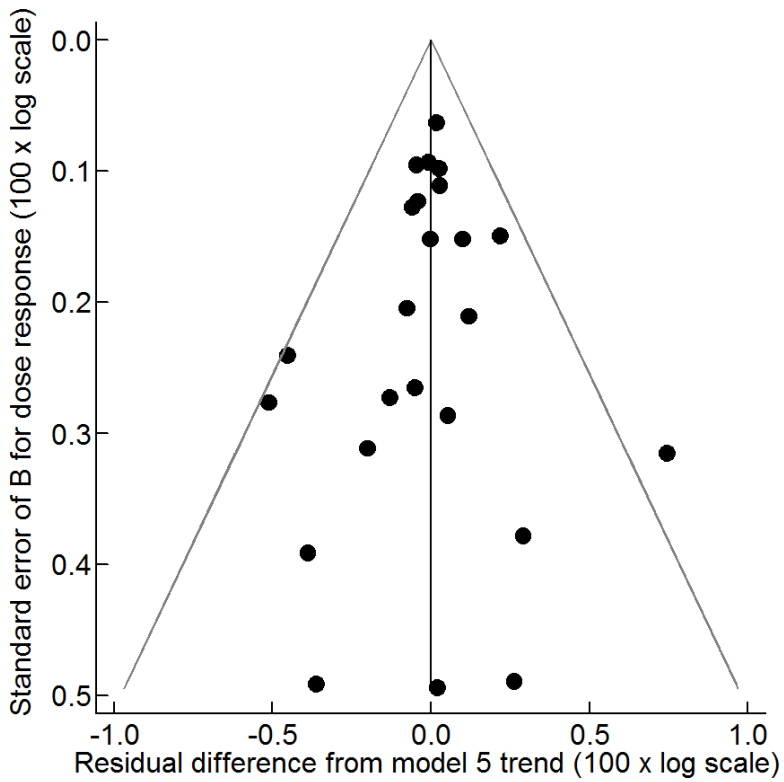


FIGURE S3 (right)**. Factors hypothesized to affecting the size of the relative risk for T2D per 100g glycemic load.** Panels A, the proportion of males in the sampled population (SEX). Panel; B, the validity of the dietary instrument (CORR). Panel; C, the number of follow-up y (FUY). Panel; D, European American participation (EA) versus all other ethnicities. Study means (O) with larger bubbles have greater weight. Lines are combined trends or means and their 95% CIs for 24 studies summarized in Table 3 of the min article by the fully adjusted model 5.

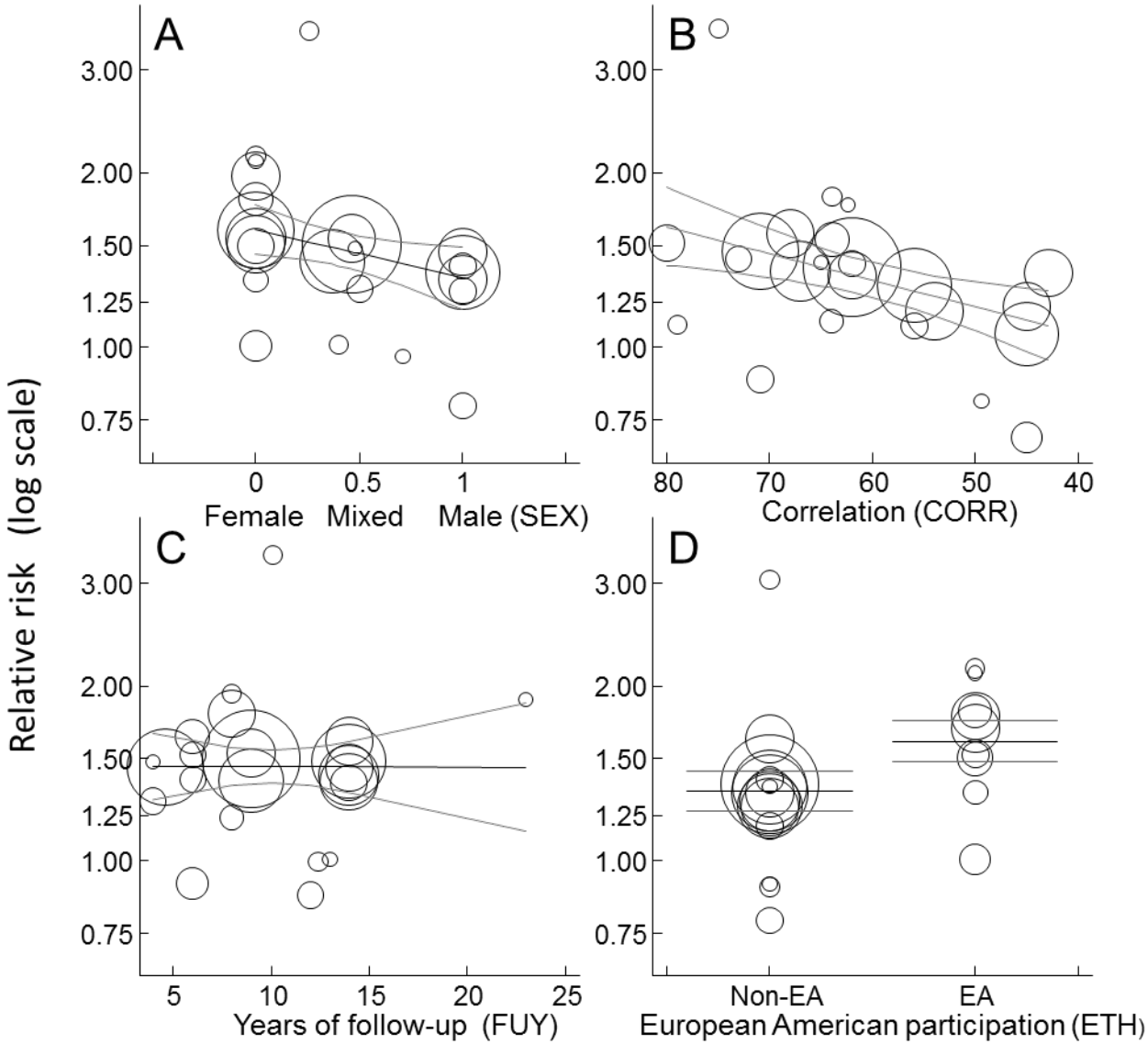


FIGURE S4 (right)**. Sensitivity of covariates to study deletions.** With the 24 studies no more than 2-3 studies were expected to fall outside the box shown. To ±1 study this was evident for each β-coefficient. Another feature, except for FUY, each box height was small relative to the z-score for the corresponding β-coefficient (indicated by positive and negative values on the y-scale).

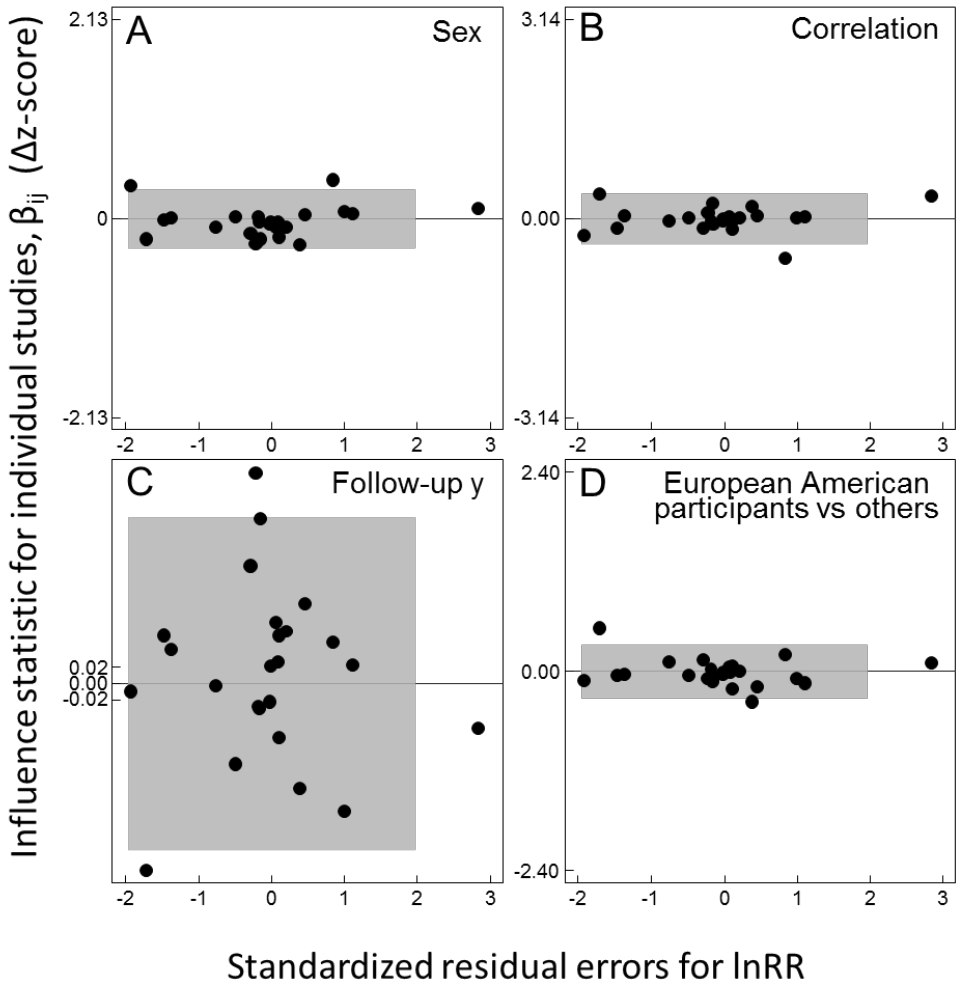
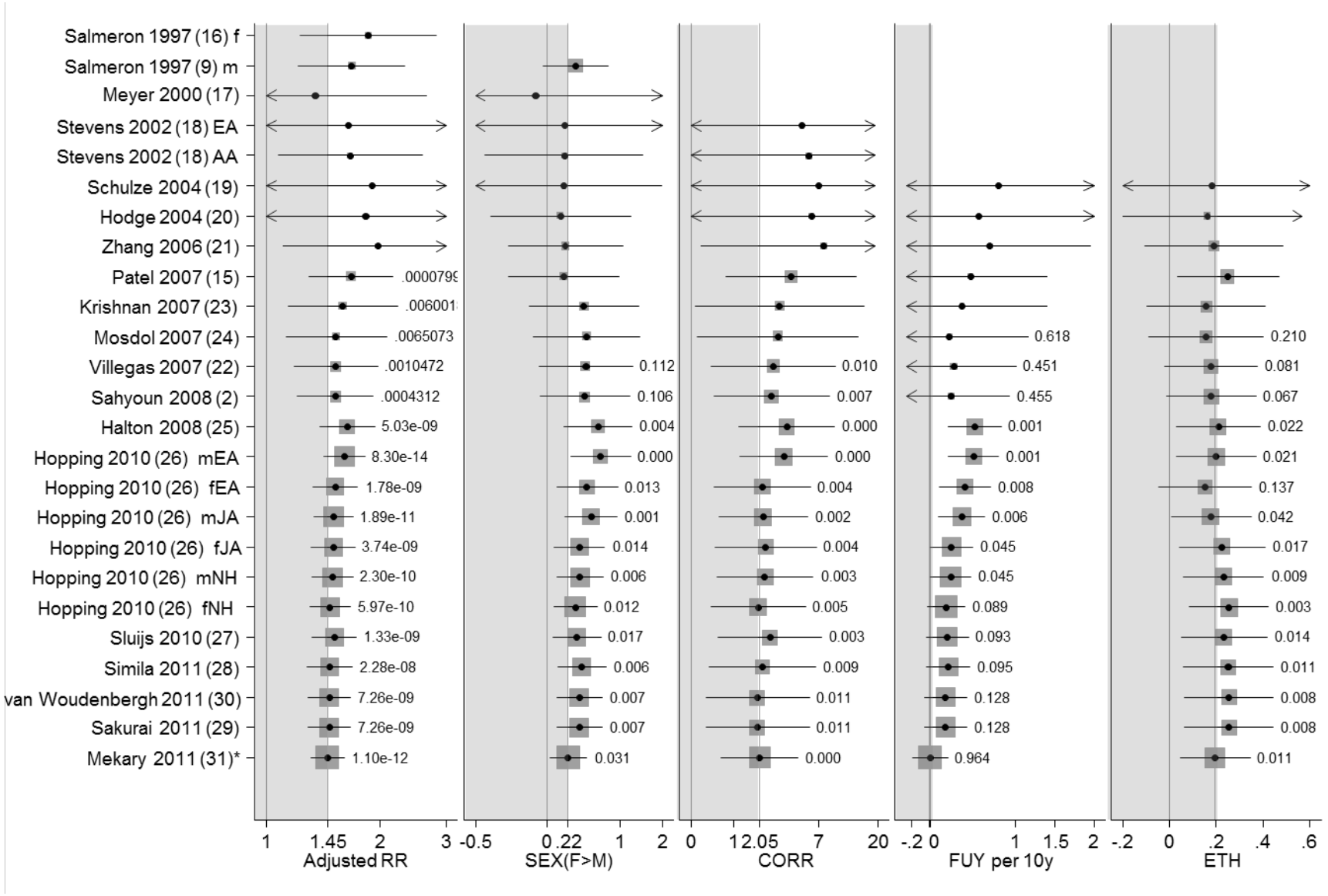


FIGURE S5 (below)**. Cumulative meta-regression analysis**. Data show relative risk for type-2 diabetes associated with an increase in energy-adjusted glycemic load of 100g/2000kcal and the adjustment coefficients of covariance as they occur with each additional study (n=24) or update (n=25). *Note the number for updates exceeds number of studies by one as information from Mekary et al 2011 (31) for 26y follow-up updates that from Halton et al 2008 (25) at 20y follow-up in the present analysis. Points (■) show values reached after study inclusion based on the multivariate model 5 (Tables 2 and 3 in the main article). Horizontals are 95%CIs. Arrow heads truncate. Shaded areas represent the size of relation finally reached. Natural log scales are used and labels are unlogged. P-vales are shown right of points (z-test for RR and covariates). Units are as described in Tables 2 & 3 in the main article. Studies are identified by first author, date and other marks. *Abbreviations*: RR, relative risk; F or f, females; M or m, males; CORR, correlation for dietary instrument validity; FUY, follow-up y; AA, African-American; EA, European-American; ETH, European-American ethnicities versus other ethnicities combined; JA, Japanese-American; NH, Native Hawaiian.


Salmeron 1997 (16) f
Salmeron 1997 (9) m
Meyer 2000 (17)
Stevens 2002 (18) EA
Stevens 2002 (18) AA
Schulze 2004 (19)
Hodge 2004 (20)
Zhang 2006 (21)
Patel 2007 (15)
Krishnan 2007 (23)
Mosdol 2007 (24)
Villegas 2007 (22)
Sahyoun 2008 (2)
Halton 2008 (25)
Hopping 2010 (26) mEA
Hopping 2010 (26) fEA
Hopping 2010 (26) mJA
Hopping 2010 (26) fJA
Hopping 2010 (26) mNH
Hopping 2010 (26) fNH
Sluijs 2010 (27)
Simila 2011 (28)
van Woudenbergh 2011 (30)
Sakurai 2011 (29)
Mekary 2011 (31)*
.0000799
.006001
.0065073
.0010472
.0004312
5.03e-09
8.30e-14
1.78e-09
1.89e-11
3.74e-09
2.30e-10
5.97e-10
1.33e-09
2.28e-08
7.26e-09
7.26e-09
1.10e-12
0.112
0.106
0.004
0.000
0.013
0.001
0.014
0.006
0.012
0.017
0.006
0.007
0.007
0.031
0.010
0.007
0.000
0.000
0.004
0.002
0.004
0.003
0.005
0.003
0.009
0.011
0.011
0.000
0.618
0.451
0.455
0.001
0.001
0.008
0.006
0.045
0.045
0.089
0.093
0.095
0.128
0.128
0.964
0.210
0.081
0.067
0.022
0.021
0.137
0.042
0.017
0.009
0.003
0.014
0.011
0.008
0.008
0.011
1 1.45 2 3
Adjusted RR
-0.5 0 .22 1 2
SEX(F>M)
0 1 2.05 7 20
CORR
-.2 0 1 1.5 2
FUY per 10y
-.2 0 .2 .4 .6
ETH

Newcastle-Ottawa score of study quality (NOS) as used in the present study

While generally accepted that individual study quality should be assessed and reported when conducting systematic reviews, no method has been validated for non-randomized studies such as prospective cohort studies. The value of study quantity assessment remains for the present primarily in providing a measure to which a study has been conducted and reported according to generally recognized practices for studies deemed of high quality. Individual quality items and groups of quality items are generally recognized as potential determinants of a successful study and may correlate with study outcomes, but this should not be expected automatically and there is increasing recognition that study quality score should not be used as if a determinant of a study outcome.

The following reproduces the protocol as encountered (36) with insert in bold italics to adapt it to the present study.

Note: A study can be awarded a maximum of one star ***(point)*** for each numbered item within the Selection and Outcome categories. A maximum of two stars ***(points)*** can be given for Comparability

Selection ***for healthy persons representative of a community aiming for national (and eventually global) representation.***

1) Representativeness of the exposed cohort

a) truly representative of the average ***__adult mixed gender or male or female*** __ in the community ? *

b) somewhat representative of the average __ ***adult mixed gender or male or female***_ in the community ?* ***For example not full age range of the community for which type-2 diabetes is incident.***

c) selected group of users eg nurses, volunteers

d) no description of the derivation of the cohort

2) Selection of the non exposed cohort

a) drawn from the same community as the exposed cohort ? *

b) drawn from a different source

c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure

a) secure record (e.g. surgical records) ?* ***Dietary instrument used and reported to be validated***

b) structured interview ?*

c) written self report

d) no description

4) Demonstration that outcome of interest ***(type-2 diabetes)*** was not present at start of study

a) yes ?*

b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis

a) study controls for ___***exposure to known non-nutrient risk factors*** ____***age, BMI, smoking, physical activity.*** *

b) study controls for any additional factor ? ***Exposure to suspected macronutritional risk factors, at least two from intakes of dietary fiber (or cereal fiber) intake, energy intake, fat intake, and alcohol intake.****

Outcome

1) Assessment of outcome *

a) independent blind assessment ?

b) record linkage ? ***Clinical report*** *

c) self report

d) no description

2) Was follow-up long enough for outcomes to occur.

a) yes? ***Select yes if four or more years of follow-up (low to allow duration of follow up to be assessed as a covariate)*** *

b) no

3) Adequacy of follow up of cohorts

a) complete follow up - all subjects accounted for ? *

b) subjects lost to follow up unlikely to introduce bias - small number lost - _***<20%***___ or description provided of those lost ?*

c) follow up rate _***>20%***__lost and no description of those lost.

d) no statement.

Registration of protocol.

Date of registration: 6 Dec 2011

Registration no. CRD42011001810 at http://www.crd.york.ac.uk/PROSPERO.

SUPPLEMENTAL MATERIALS REFERENCES

1. Pereira MA. Dietary glycemic index and glycemic load in diabetes prevention--what can we learn from observational studies? Nat Clin Pract Endocrinol Metab 2008;4:430-1.
2. Sahyoun NR, Anderson AL, Tylavsky FA, Lee JS, Sellmeyer DE, Harris TB, ; Health A, and Body Composition Study. Dietary glycemic index and glycemic load and the risk of type 2 diabetes in older adults. Am J Clin Nutr 2008;87:126-31.
3. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med 2001;345:790-7.
4. Salmeron J, Hu FB, Manson JE, Stampfer MJ, Colditz GA, Rimm EB, Willett WC. Dietary fat intake and risk of type 2 diabetes in women. Am J Clin Nutr 2001;73:1019-26.
5. Mohan V, Radhika G, Sathya RM, Tamil SR, Ganesan A, Sudha V. Dietary carbohydrates, glycaemic load, food groups and newly detected type 2 diabetes among urban Asian Indian population in Chennai, India (Chennai Urban Rural Epidemiology Study 59). Br J Nutr 2009;102:1498-506.
6. Schulz M, Liese AD, Fang F, Gilliard TS, Karter AJ. Is the association between dietary glycemic index and type 2 diabetes modified by waist circumference? Diabetes Care 2006;29:1102-4.
7. Mayer-Davis EJ, Dhawan A, Liese AD, Teff K, Schulz M. Towards understanding of glycaemic index and glycaemic load in habitual diet: associations with measures of glycaemia in the Insulin Resistance Atherosclerosis Study. Br J Nutr 2006;95:397-405.
8. Fung TT, Hu FB, Pereira MA, Liu S, Stampfer MJ, Colditz GA, Willett WC. Whole-grain intake and the risk of type 2 diabetes: a prospective study in men. Am J Clin Nutr 2002;76:535-40.

9. Salmerón J, Ascherio A, Rimm EB, Colditz GA, Spiegelman D, Jenkins DJ, Stampfer MJ, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of NIDDM in men. Diabetes Care 1997;20:545-50.
10. Barclay AW, Flood VM, Rochtchina E, Mitchell P, Brand-Miller JC. Glycemic index, dietary fiber, and risk of type 2 diabetes in a cohort of older Australians. Diabetes Care 2007;30:2811-3.
11. Yu R, Woo J, Chan R, Sham A, Ho S, Tso A, Cheung B, Lam TH, Lam K. Relationship between dietary intake and the development of type 2 diabetes in a Chinese population: the Hong Kong Dietary Survey. Public Health Nutr 2011;14:1133-41.
12. Woo J, Leung SSF, Ho SC, Lam TH, Janus ED. A food frequency questionnaire for use in the Chinese population in Hong Kong : description and examination of validity. Nutrition Research 1977;17:1633-41.
13. Liu S, Chou EL. Dietary glycemic load and type 2 diabetes: modeling the glucose-raising potential of carbohydrates for prevention. Am J Clin Nutr 2010;92:675-7.
14. Barclay AW, Petocz P, McMillan-Price J, Flood VM, Prvan T, Mitchell P, Brand-Miller JC. Glycemic index, glycemic load, and chronic disease risk--a meta-analysis of observational studies. Am J Clin Nutr 2008;87:627-37.
15. Patel AV, McCullough ML, Pavluck AL, Jacobs EJ, Thun MJ, Calle EE. Glycemic load, glycemic index, and carbohydrate intake in relation to pancreatic cancer risk in a large US cohort. Cancer Causes Control 2007;18:287-94.
16. Salmerón J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. JAMA 1997;277:472-7.
17. Meyer KA, Kushi LH, Jacobs DRJ, Slavin J, Sellers TA, Folsom AR. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. Am J Clin Nutr 2000;71:921-30.
18. Stevens J, Ahn K, Juhaeri, Houston D, Steffan L, Couper D. Dietary fiber intake and glycemic index and incidence of diabetes in African-American and white adults: the ARIC study. Diabetes Care 2002;25:1715-21.

19. Schulze MB, Liu S, Rimm EB, Manson JE, Willett WC, Hu FB. Glycemic index, glycemic load, and dietary fiber intake and incidence of type 2 diabetes in younger and middle-aged women. Am J Clin Nutr 2004;80:348-56.
20. Hodge AM, English DR, O'Dea K, Giles GG. Glycemic index and dietary fiber and the risk of type 2 diabetes. Diabetes Care 2004;27:2701-6.
21. Zhang C, Liu S, Solomon CG, Hu FB. Dietary fiber intake, dietary glycemic load, and the risk for gestational diabetes mellitus. Diabetes Care 2006;29:2223-30.
22. Villegas R, Liu S, Gao YT, Yang G, Li H, Zheng W, Shu XO. Prospective study of dietary carbohydrates, glycemic index, glycemic load, and incidence of type 2 diabetes mellitus in middle-aged Chinese women. Arch Intern Med 2007;167:2310-6.
23. Krishnan S, Rosenberg L, Singer M, Hu FB, Djousse L, Cupples LA, Palmer JR. Glycemic index, glycemic load, and cereal fiber intake and risk of type 2 diabetes in US black women. Arch Intern Med 2007;167:2304-9.
24. Mosdol A, Witte DR, Frost G, Marmot MG, Brunner EJ. Dietary glycemic index and glycemic load are associated with high-density-lipoprotein cholesterol at baseline but not with increased risk of diabetes in the Whitehall II study. Am J Clin Nutr 2007;86:988-94.
25. Halton TL, Liu S, Manson JE, Hu FB. Low-carbohydrate-diet score and risk of type 2 diabetes in women. Am J Clin Nutr 2008;87:339-46.
26. Hopping BN, Erber E, Grandinetti A, Verheus M, Kolonel LN, Maskarinec G. Dietary fiber, magnesium, and glycemic load alter risk of type 2 diabetes in a multiethnic cohort in Hawaii. J Nutr 2010;140:68-74.
27. Sluijs I, van der Schouw YT, van der AD, Spijkerman AM, Hu FB, Grobbee DE, Beulens JW. Carbohydrate quantity and quality and risk of type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition-Netherlands (EPIC-NL) study. Am J Clin Nutr 2010;92:905-11.
28. Simila ME, Valsta LM, Kontto JP, Albanes D, Virtamo J. Low-, medium- and high-glycaemic index carbohydrates and risk of type 2 diabetes in men. Br J Nutr 2011;105:1258-64.

29. Sakurai M, Nakamura K, Miura K, Takamura T, Yoshita K, Morikawa Y, Ishizaki M, Kido T, Naruse Y, Suwazono Y, et al. Dietary glycemic index and risk of type 2 diabetes mellitus in middle-aged Japanese men. Metabolism 2011.
30. van Woudenbergh GJ, Kuijsten A, Sijbrands EJ, Hofman A, Witteman JC, Feskens EJ. Glycemic index and glycemic load and their association with C-reactive protein and incident type 2 diabetes. J Nutr Metab 2011;2011:623076.
31. Mekary RA, Rimm EB, Giovannucci E, Stampfer MJ, Willett WC, Ludwig DS, Hu FB. Joint association of glycemic load and alcohol intake with type 2 diabetes incidence in women. Am J Clin Nutr 2011;94:1525-32.
32. Livesey G. Joint association of glycemic load and alcohol intake with type 2 diabetes incidence in women. Am J Clin Nutr 2012;95:983.
33. Frost G, Leeds AA, Dore CJ, Madeiros S, Brading S, Dornhorst A. Glycaemic index as a determinant of serum HDL-cholesterol concentration. Lancet 1999;353:1045-8.
34. Brunner E, Stallone D, Juneja M, Bingham S, Marmot M. Dietary assessment in Whitehall II: comparison of 7 d diet diary and food-frequency questionnaire and validity against biomarkers. Br J Nutr 2001;86:405-14.
35. Howarth NC, Murphy SP, Wilkens LR, Henderson BE, Kolonel LN. The association of glycemic load and carbohydrate intake with colorectal cancer risk in the Multiethnic Cohort Study. Am J Clin Nutr 2008;88:1074-82.
36. Pietinen P, Hartman AM, Haapa E, Rasanen L, Haapakoski J, Palmgren J, Albanes D, Virtamo J, Huttunen JK. Reproducibility and validity of dietary assessment instruments. I. A self-administered food use questionnaire with a portion size picture booklet. Am J Epidemiol 1988;128:655-66.
37. Wells G, Shea S, O'Connell D, Robertson J, Peterson P, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. URL http://www.evidencebasedpublichealth.de/download/Newcastle_Ottowa_Scale_Pope_Bruce.pdf. Accessed 28th August 2009.