nutrients

1. Table S1. Observations in single-sex studies by duration (time, years) of exposure.

Table S1. Observations from the USA in single-sex studies by duration (time, years) of exposure.

Substrate	Study	Follow-up	Risk ratio [a]			Risk relation [b]	
			Mean	(95%CI)	Ref.	Mean	(95%CI)
		(*years*)	(*Per extreme quintiles*)			(*Per 10 units GI*)	
GI	Women	6	1.37	(1.09-1.17)	[1]	1.27	(1.08-1.45)
GI	(NHS I)	24	1.44	(1.33-1.57)	[2]	1.65	(1.48-1.83)
GI		26	1.46	(1.34-1.58)	[3]	1.47	(1.35-1.60)
GI	Women	8	1.59	(1.21-2.10)	[4]	1.50	(1.18-1.90)
GI	(NHS II)	18	1.20	(1.08-1.34)	[2]	1.26	1.10-1.44)
GI	Men	6	1.37	(1.02-1.83)	[5]	1.23	(1.01-1.51)
GI	(HPFS)	22	1.30	(1.15-1.47)	[2]	1.41	(1.20-1.65)
			(*Per extreme quintile*)			(*Per 80 g GLin 2000 kcal diet*)	
GL	Women	6	1.47	(1.16-1.86)	[1]	1.66	(1.18-2.13)
GL	(NHS I)	24	-[c]	-	[2]	-	-
GL		26	1.32	(1.16-1.51)	[3]	1.84	(0.85-4.00)
GL	Women	8	1.33	(0.92-1.91)	[4]	1.28	(0.78-2.09)
GL	(NHS II)	18	-	-	[2]	-	-
GL	men	6	1.25	(1.09-1.73)	[5]	1.33	(0.88-2.03)
GL	HPFS)	22	-	-	[2]	-	-

a. Risk ratios (point estimates) were from published studies. b. Risk relations (rates) were estimated at present using dose-response meta-analysis. c. All such, fully adjusted model was not presented in the original publication by individual study.

2. Normalisation of fasting blood glucose when lowering the dietary glycemic index in recent medium to long term intervention studies

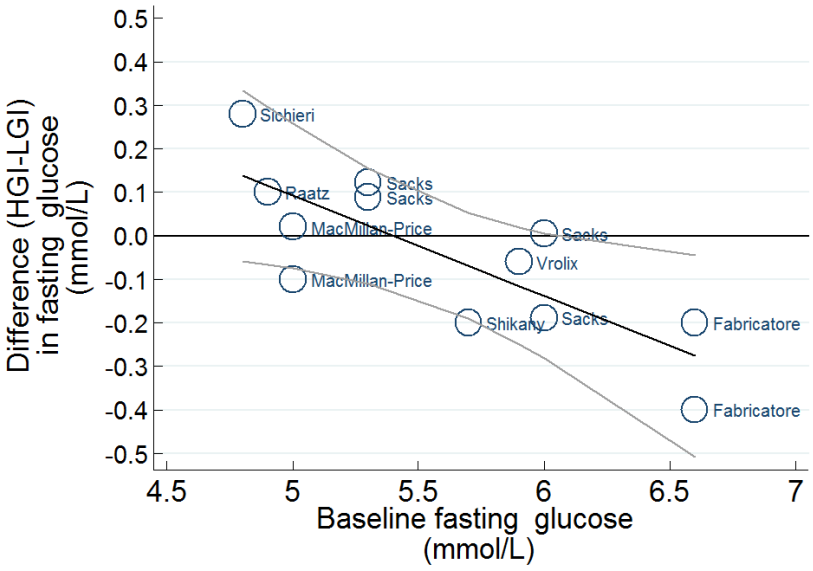

Figure 1. Differences in fasting blood glucose in participants consuming diets of higher and lower glycemic index. Meta-regression curves (grey lines) are 95% confidence intervals. Shown also are the

first author names associated with the studies extracted. Simply throwing these into a forest plot suggest no significant effects but meta-regression shows a significant relation to baseline fasting glucose, considered together with earlier observations [6], there is evidence of lower GI carbohydrate diets reducing both hypoglycaemia and hyperglycaemia among the otherwise random effects.

Following observations in a meta-analyses of human intervention studies published by us elsewhere in 2008 [6] indicating a transition point on the fasting blood glucose concentration for the direction of effect, which was at approx. 5 to 6 mmol/L, the present meta-regression analysis of subsequent findings from randomised control studies in humans (n = 615) from 0.25 to 1.5 years treatment duration [7–13] are confirmatory of the existence of a transition (Figure S1). The slope is the meta-regression relationship based on studies having equal weights with a median effect size SE value of 3.9 mmol/L. The slope was -0.23 mmol/L per mmol/L basal fasting glucose, was significant ($P > t = 0.03$), and intersected the Y-axis (at y = 0) at a fasting value of 5.4 mmol/L (the transition point) at which the direction effect on fasting glucose changes with baseline fasting blood glucose, and where no effect is expected to be observed.

A weakness of the present meta-regression analysis is the small number of study effects (n = 12), the use of findings from 4 studies at more than one duration of treatment ([12,13], [7,13]), the use of equal weights to alleviate excessive leverage from two studies and heterogeneities in disease states related to blood glucose control and treatment modalities for body weight maintenance and body weight reduction. A strength of the analysis is the agreement with the prior meta-analysis on 50 similar observations [6] over a shorter duration and which showed also a continued greater fall in fasting blood glucose with increasing severity of T2D when lower GI diets were eaten.

Together these analyses indicate both the effect size and direction of effect can be dependent on the effectiveness of blood glucose control in the study groups, and with a transition at about 5.4 mmol/L fasting blood glucose, which otherwise explains heterogeneity in the treatment effect of lower versus higher glycemic index diets. In the present analysis heterogeneity (I^2) was zero after taking account of the status of baseline glucose control. Together with a lack of effect on fasting insulin concentrations by lower versus higher GI diets at below 100 pmol/L [1] these analyses imply a similar implication for the assessment of insulin sensitivity, which is often approximated in models (HOMA IR) by the product of fasting glucose and insulin concentrations and which need robust analytical data [14,15].

A further implication of the meta-analysis (Figure S1 above and in [6]) is that low glycemic diets help to normalise the fasting blood glucose whether it is below a value close to normal or too high. Too few observations are available to verify this at fasting glucose values below 4.5 mmol/L and above 13 mmol/L). Delay in the short term gluco-regulatory mechanisms such as the glucose-fatty-acid cycle [16] and the Staub-Traugott effect likely explain the blood glucose raising potential of lower GI diets at below the transition point.

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