British Journal of Nutrition (2004), **92**, 367–381
DOI: 10.1079/BJN20041203

Review article

Meta-analysis of the health effects of using the glycaemic index in meal-planning

A. Maretha Opperman[1]*, Christina S. Venter[1], Welma Oosthuizen[1], Rachel L. Thompson[2] and Hester H. Vorster[1]

[1]*School for Physiology, Nutrition and Consumer Sciences, North-West University, Potchefstroom, South Africa*
[2]*Public Health Nutrition, Institute of Human Nutrition, University of Southampton, UK*

(Received 2 December 2003 – Revised 8 April 2004 – Accepted 20 April 2004)

Diabetes mellitus and CVD are some of the leading causes of mortality and morbidity. Accumulating data indicate that a diet characterised by low-glycaemic index (GI) foods may improve the management of diabetes or lipid profiles. The objective of the present meta-analysis was to critically analyse the scientific evidence that low-GI diets have beneficial effects on carbohydrate and lipid metabolism compared with high-GI diets. We searched for randomised controlled trials with a crossover or parallel design published in English between 1981 and 2003, investigating the effect of low-GI *v.* high-GI diets on markers for carbohydrate and lipid metabolism. Unstandardised differences in mean values were examined using the random effects model. The main outcomes were fructosamine, glycated Hb (HbA_{1c}), HDL-cholesterol, LDL-cholesterol, total cholesterol and triacylglycerol. Literature searches identified sixteen studies that met the strict inclusion criteria. Low-GI diets significantly reduced fructosamine by −0·1 (95 % CI −0·20, 0·00) mmol/l ($P=0·05$), HbA_{1c} by 0·27 (95 % CI −0·5, −0·03) % ($P=0·03$), total cholesterol by −0·33 (95 % CI −0·47, −0·18) mmol/l ($P<0·0001$) and tended to reduce LDL-cholesterol in type 2 diabetic subjects by −0·15 (95 % CI −0·31, −0·00) mmol/l ($P=0·06$) compared with high-GI diets. No changes were observed in HDL-cholesterol and triacylglycerol concentrations. No substantial heterogeneity was detected, suggesting that the effects of low-GI diets in these studies were uniform. Results of the present meta-analysis support the use of the GI as a scientifically based tool to enable selection of carbohydrate-containing foods to reduce total cholesterol and to improve overall metabolic control of diabetes.

Glycaemic index: Fructosamine: Glycated haemoglobin: High-density lipoprotein-cholesterol: Low-density lipoprotein-cholesterol: Total cholesterol: Triacylglycerol

Until recently carbohydrates in foods have been classified as 'simple' and 'complex', based on the degree of polymerisation of the carbohydrate. However, the effects of carbohydrate on health may be better described on the basis of their physiological effects (e.g. the ability to raise blood glucose levels), which depend on the type of constituent sugars (glucose, fructose and galactose), the physical form of the carbohydrate (particle size and degree of hydration), nature of the starch (amylose, amylopectin) and other food components (dietary fibre, fat, organic acids) (Augustin *et al.* 2002). This classification is referred to as the glycaemic index (GI) of a food and was introduced by Jenkins *et al.* (1981) as a quantitative assessment of foods based on postprandial blood glucose response (Jenkins *et al.* 1981, 1984), expressed as a percentage of the response to an equivalent carbohydrate portion of a reference food, such as white bread or glucose (Wolever *et al.* 1991).

A high-GI food with an equivalent carbohydrate content as a low-GI food induces a larger area under the glucose curve over the postprandial period. As a consequence of the induced insulin response, intake of a high-GI food may result in lower blood glucose concentrations over the late (2–3 h) postprandial period than that of a low-GI food (Brand-Miller *et al.* 2001). Reducing the rate of carbohydrate absorption by lowering the GI of the diet may have several health benefits, such as a reduced insulin demand, improved blood glucose control and reduced blood lipid concentrations (Augustin *et al.* 2002). These are all factors that play important roles in preventing the onset of CVD and diabetes mellitus (DM).

Despite advances in the prevention and treatment in the second half of the 20th century (Liu, 2002), CVD and DM are still some of the leading causes of mortality and morbidity. CVD is a multi-factorial disease, but its prevalence can also be attributed to a diet high in fat and low in fibre,

Abbreviations: DM, diabetes mellitus; GI, glycaemic index; HbA_{1c}, glycated Hb; TC, total cholesterol; TG, triacylglycerol.

* **Corresponding author:** Ms Maretha Opperman, fax +27 18 299 2464, email vgeamo@puknet.puk.ac.za

with inadequate micronutrient intakes (Vorster *et al.* 1997). Worldwide, the number of people with type 2 DM is expected to rise from 135 million in 1995 to 300 million in 2025 (King *et al.* 1998). Insulin resistance and progressive pancreatic β-cell dysfunction are well-established fundamental steps in the pathogenesis of type 2 DM (Defronzo *et al.* 1992; Kahn 1994). Accumulating metabolic and epidemiological data also indicate that impaired insulin action and compensatory hyperinsulinaemia often result in abnormal blood lipid patterns (elevations of triacylglycerol (TG) and low concentrations of HDL-cholesterol, as well as hypertension, which in turn increase the risk for CHD (Liu, 2002)).

CVD and type 2 DM are common consequences of changing lifestyles (increasing sedentary lifestyles and increased energy density of diets). The conditions mentioned earlier are preventable through lifestyle modifications (Seidell, 2000). But where does the GI fit in? According to Brand-Miller *et al.* (2002), standard dietary advice to reduce fat intake while increasing carbohydrate intake generally increases the glycaemic effect of the diet. The type and amount of carbohydrate consumed influences postprandial glucose levels, and the interaction between the two may be synergistic. A diet high in refined carbohydrates and high-GI foods, such as white bread and potatoes, is rapidly digested and absorbed and results in a high glycaemic load and increased demand for insulin secretion (Holt *et al.* 1997). When insulin resistance is prevalent and high-GI foods are consumed, postprandial hyperglycaemia and insulinaemia are magnified (Salmeron *et al.* 1997*a*,*b*). On the other hand, low-GI, high-carbohydrate foods may maintain insulin sensitivity and increase the weight-loss potential of *ad libitum* low-fat diets (Ludwig, 2002). Low-GI foods may also benefit weight control by promoting satiety and by promoting fat oxidation at the expense of carbohydrate oxidation. These qualities of low-GI foods can be attributed to the slower rates at which they are digested and absorbed and the corresponding effects on postprandial glycaemia and hyperinsulinaemia (Brand-Miller *et al.* 2002).

However, there is no consensus on the importance of the GI to human health and nutrition (Ludwig & Eckel, 2002). Many clinicians and researchers, especially in the USA, have questioned the relevance and practicality of the GI (Coulston & Reaven, 1997). Presently, neither the American Diabetes Association (2001), the American Heart Association (Krauss *et al.* 2000), nor the American Dietetic Association (1999) recognise a role for GI in disease prevention or treatment. In contrast, the Joint Food and Agriculture Organization/World Health Organization Expert Consultation on Carbohydrates (Food and Agriculture Organization/World Health Organization, 1997), the European Association for the Study of Diabetes (Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD) 2000), the Canadian Diabetes Association (2000), Diabetes UK (2003) and the Dietitians Association of Australia (1997) encourage the application of the GI when choosing carbohydrate-containing foods.

This has led to a constructive debate internationally within the academic field, industry, health practitioners and regulatory authorities. It seems, therefore, imperative that a meta-analysis on the long-term physiological effects and health benefits of using the GI to construct diets should be done. A meta-analysis is the structured result of a literature review in which results from several independent but related or comparable studies are systematically and statistically combined or integrated in order to increase power and precision (Vorster *et al.* 2003). We report the results of a meta-analysis to evaluate and integrate a number of studies conducted on the GI and its effects on health. The present meta-analysis summarises results and should further motivate and direct further research; it could form a firm, evidence-based platform for the use or not of the GI in planning diets.

Methods

Randomised controlled trials with a crossover or parallel design that were published between January 1981 and April 2003 were selected through a computer-assisted literature search. EbscoHost Web was used as a gateway to the databases Medline and Academic Search Premier. The Science Direct and PubMed (1981–2003) databases were also used to expand our search. Medical subject headings (MeSH) such as 'glycaemic index' or 'glycemic index' combined with key words (metabolic control, cardiovascular disease, diabetes mellitus, obesity, weight, body mass index, blood lipids, cholesterol, high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, total cholesterol, triacylglycerol, glycated (glycosylated) haemoglobin (hemoglobin), fructosamine, insulin, blood glucose) were used to search for papers. Low-GI diets were defined as those containing most carbohydrate from low-GI sources, such as peas, lentils, beans, pasta, barley, parboiled rice, oats and cereals, known to have a low GI. High-GI diets were those that contained potato, wheatmeal and white bread and high-GI varieties of breakfast cereals such as cornflakes and rice. Reference lists of all available published trials and relevant reviews were cross-checked manually to ensure that all applicable papers were included. Where data were incomplete, authors of the identified trials were contacted to supply comprehensive information. The search was restricted to human studies and only studies that were published in English were considered. Accepted interventions included a high-GI *v.* low-GI diet, investigating the effect of the diet on carbohydrate or lipid metabolism. The participants were patients with type 2 DM, type 1 DM or CVD, or healthy adults. Only studies with good quality methodology were considered. Quality criteria were adapted from the Effective Practice and Organization of Care Cochrane Group, and included methods of randomisation, blinded assessment of variables with regard to blood samples and determination of whether an intention-to-treat analysis was possible on all patients from the published data.

In addition, feeding periods had to be sufficiently long (≥ 14 d) to allow the achievement of new steady-state concentrations of serum lipids and lipoproteins (Brussaard *et al.* 1982) as well as fructosamine (10–14 d) and glycated Hb (HbA_{1c}; 90 d) (Lindsey *et al.* 2002), food intake had to be controlled (either advice given, key foods provided or

all foods provided) and described (low-GI *v*. high-GI diets), the GI of the diet had to be indicated, the subject population had to be homogenous (at least for the main risk factor), and the inclusion and exclusion criteria for subjects had to be clearly defined.

Data extraction

Each potentially relevant study was assessed for inclusion independently by at least two reviewers. Two investigators (A. M. O. and C. S. V.), by means of an agreed standardised data collection form, independently extracted the relevant data. Co-investigators adjudicated areas of disagreement or uncertainty and resolved it by discussion. The κ statistic for the agreement between the reviewers was 0·6 (a good agreement). Information about the outcome variables that was extracted for the randomised controlled trials included: authors, publication date, number of subjects, study design (crossover or parallel), duration of the study, wash-out period (if applicable), subject characteristics, the diet setting, reduction in GI, age, BMI and weight (maintenance or loss), provision of test meals, compliance, baseline and end values, mean change (end value – baseline value), and the *P* value and SD for both low-GI and high-GI groups. If SD were not presented, data on SEM or 95 % CI were extracted. Measured variables included in the meta-analysis were: risk markers of carbohydrate metabolism e.g. blood glucose, insulin, insulin resistance, glycated plasma protein (HbA_{1c} and fructosamine); risk markers for lipid metabolism e.g. TG, total cholesterol (TC), HDL-cholesterol, LDL-cholesterol and weight.

Data analysis

We used the Cochrane software package (Review manager 4.2; Cochrane, Copenhagen, Denmark) to process results. The mean difference over time for the high-GI diet was subtracted from the mean difference of the low-GI diet over time to get an overall difference between the two treatments. For each trial, we estimated the SD of the treatment effect for the outcome measures by using the SEM or paired differences (end values – baseline values) for low-GI and high-GI groups. If SD were not reported, they were estimated using the methods described by Follmann *et al.* (1992). The net changes in TC, LDL-cholesterol, HDL-cholesterol, TG and blood glucose are presented in mmol/l. Where variables were reported in mg/dl, converting factors were used (for TC, HDL-cholesterol and LDL-cholesterol, values in mg/dl were multiplied by 0·0259; for TG, values in mg/dl were multiplied by 0·0113 (Van Horn & Ernst, 2001)). The variables blood glucose and insulin were not included in the meta-analysis, due to units that were not comparable, different time intervals of measurement, only insulin or glucose responses reported, incomplete and/or missing data, and only graphs and/or response curves given to report data. Unstandardised differences in mean values were examined using the random effects model. Weighted mean differences in mean values were also performed, because outcomes were measured in a standard way across studies. Differences between the results of the trials were checked for heterogeneity by visual inspection of the graphs and by statistical test (χ^2).

Results

The literature search yielded 413 references (titles and abstracts, original research and review papers). Of these, ninety-six original research papers were identified as possible studies to include in the meta-analysis. Two investigators examined the full-text publications, of which sixteen studies met the inclusion criteria. The main reason for exclusion was incomplete or missing data, response curves only for some of the variables (actual data not reported), and incompatible units. Details of the studies included in the meta-analysis are shown in Table 1.

There were two studies conducted in healthy subjects (Jenkins *et al.* 1987*a*; Bouche *et al.* 2002), two in CHD (Frost *et al.* 1996, 1998), nine in type 2 diabetic subjects (Jenkins *et al.* 1988; Brand *et al.* 1991; Wolever *et al.* 1992*a*; Frost *et al.* 1994; Heilbronn *et al.* 2002; Jarvi *et al.* 1999; Luscombe *et al.* 1999; Tsihlias *et al.* 2000; Kabir *et al.* 2002) and three studies in type 1 diabetics (Collier *et al.* 1998; Lafrance *et al.* 1998; Gilbertson *et al.* 2001). Studies were carried out under free-living conditions except for that of Frost *et al.* (1996), who studied subjects who were hospitalised. Ten studies had a crossover and six a parallel design. A total of 396 subjects were studied (type 1 DM *n* 105, type 2 DM *n* 228, healthy *n* 17, CHD *n* 46). Intervention periods varied from 12 d to 6 months, wash-out periods from none to 7 weeks in crossover studies and a GI reduction of between 5 and 35 units was achieved. Studies that were excluded from the meta-analysis were those of Jenkins *et al.* (1985, 1987*b*), Wolever *et al.* (1992*b*), Calle-Pascual *et al.* (1988), Fontvielle *et al.* (1988, 1992), Brynes *et al.* (2003), Gilbertson *et al.* (2003) and Wolever & Mehling (2003), due to incomplete data for the purpose of the present meta-analysis. The reason for exclusion of such high profile studies was that baseline and end values of variables were not included, and therefore, SD could not be calculated. Twelve of the included studies assessed markers for carbohydrate metabolism, while fourteen studies assessed markers for lipid metabolism.

Table 2 shows the nutrient composition of high-GI and low-GI intervention diets. The aim was to maintain the same proportions of macronutrients and fibre in both diets, but in some cases this was not achieved. Some high-GI diets were higher in fat and lower in fibre, complicating the interpretation of results.

Explanation of forest plots

The type of graphical display in the present meta-analysis used to report results is called a forest plot. The mean results of each computed study and the 95 % CI are reported. The midpoint of the square in the middle of the forest plot represents the effect size (the mean difference in the measure between low-GI and high-GI diets) and the horizontal line the 95 % CI of the individual studies. The size of the square relates to the weight each study

Table 1. Study design, number and characteristics of subjects, duration of study, wash-out period, settings and reduction in the glycaemic index*

Study	Design†	Subjects (*n*)	Duration of study	Wash-out period (weeks)	Subject characteristics	Setting	GI reduction (units)	Outcomes reported
Bouche *et al.* (2002)	X	11	2 × 5 weeks	5 weeks	Healthy	Free-living	35	Fructosamine, HDL-c, LDL-c, TC and TG
Brand *et al.* (1991)	X	16	2 × 12 weeks	3 weeks	Type 2 DM (well controlled)	Free-living	13	HbA_{1c}, LDL-c, TC and TG
Collier *et al.* (1988)	X	7	2 × 6 weeks	4 weeks	Type 1 DM (children)	Free-living	12	HDL-c and TG
Frost *et al.* (1994)	‖	25/26‡	12 weeks	NA	Type 2 DM (newly diagnosed)	Free-living	5	Fructosamine, HDL-c, LDL-c, TC and TG
Frost *et al.* (1996)	‖	15/15‡	4 weeks	NA	CHD	Hospital	12	HDL-c, LDL-c, TC and TG
Frost *et al.* (1998)	‖	8/8	3 weeks	NA	CHD	Free-living	14	TC and TG
Gilbertson *et al.* (2001)	‖	38/51‡	12 months	NA	Type 1 DM (children)	Free-living	1	HbA_{1c}
Heilbronn *et al.* (2002)	‖	24/21‡	8 weeks	NA	Type 2 DM (overweight)	Free-living	32	HbA_{1c}, HDL-c, LDL-c, TC and TG
Jarvi *et al.* (1999)	X	20	2 × 24 d	None	Type 2 DM (borderline control)	Free-living	19	Fructosamine, HbA_{1c}, HDL-c, LDL-c, TC and TG
Jenkins *et al.* (1987*a*)	X	6	2 × 2 weeks	3–4 weeks	Healthy	Free-living	29	Fructosamine, HDL-c, LDL-c, TC and TG
Jenkins *et al.* (1988)	X	8	2 × 2 weeks	4–7 weeks	Type 2 DM (overweight)	Free-living	23	Fructosamine, HbA_{1c}, HDL-c, LDL-c, TC and TG
Kabir *et al.* (2002)	X	13	2 × 4 weeks	15 d	Type 2 DM (poorly controlled)	Free-living	24	HbA_{1c}, HDL-c, TC and TG
Lafrance *et al.* (1998)	X	9	3 × 12 d	None	Type 1 DM (well controlled)	Free-living	27	Fructosamine, HbA_{1c}
Luscombe *et al.* (1999)	X	21	2 × 4 weeks	None	Type 2 DM (obese)	Free-living	20	TG, TC
Tsihlias *et al.* (2000)	‖	26/22‡	3 × 6 months	NA	Type 2 DM (borderline control, hyperlipidaemic)	Free-living	11	HbA_{1c}, HDL-c, LDL-c, TC and TG
Wolever *et al.* (1992*a*)	X	6	2 × 6 weeks	4-6 weeks	Type 2 DM (obese)	Free-living	28	Fructosamine, HDL-c, LDL-c, TC and TG

GI, glycaemic index, c, cholesterol; HbA_{1c} glycated Hb; TC, total cholesterol; TG, triacylglycerol; DM, diabetes mellitus, NA not applicable.
* For details of selection of studies, see p. 368.
† X, crossover; ‖, parallel.
‡ Increased GI, decreased GI.

Table 2. Nutrient composition of high- and low-glycaemic-index diets*
(Mean values and standard deviations)

	Carbohydrate (% TE)				Protein (% TE)				Fat (% TE)				Fibre (g)			
	Low GI		High GI		Low GI		High GI		Low GI		High GI		Low GI		High GI	
Studies	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Bouche *et al.* (2002)	39	1	42	1	20	1	18	1	38	1	37	1	NR		NR	
Brand *et al.* (1991)	44	2	46	2	22	1	19	1	30	2	31	2	26	2	26	2
Collier *et al.* (1988)	49	2	47	1	18	1	16	1	33	2	37	2	39	3	24	3
Frost *et al.* (1994)	49	2	44	1	23	2	22	1	25	1	32†	2	21	1	14†	1
Frost *et al.* (1996)	45	3	45	2	18	1	17	1	24	3	25	2	14	1	13	1
Frost *et al.* (1998)	53		51		15		12		32		37		19		21	
Gilbertson *et al.* (2001)	49		49		17		17		34		34		21		21	
Heilbronn *et al.* (2002)	59		59		22		22		19		19		NR		NR	
Jarvi *et al.* (1999)	55		54		18		18		27		28		38		34	
Jenkins *et al.*(1987*a*)	61		61		19		19		20		20		26 g/4200 kJ		21 g/4200 kJ‡	
Jenkins *et al.* (1988)	54	1	53	1	22	1	21	0·5	24	1	21	0·5	34	2	28	1
Kabir *et al.* (2002)	57		60		15		15		28		25		10		9	
Lafrance *et al.* (1998)	57	4	53	6	17	2	18	2	26	4	29	7	15	6	17	7
Luscombe *et al.* (1999)	51		53		22		23		23		21		30	2	30	2
Tsihlias *et al.* (2000)	50	1	54	1	20	1	17	1	28	1	29	1	50	1	23	1§
Wolever *et al.* (1992*a*)	57		57		20		20		23		23		34		33	

GI, glycaemic index; NR, not reported; TE, total energy.
* For a summary of the studies, see Table 1.
† Low-GI diet contained less fat (25 *v.* 32 %) and more fibre (21 *v.* 14 g).
‡ Low-GI diet contained more fibre (26 g/4200 kJ (1000 kcal) *v.* 21 g/4200 kJ (1000 kcal)).
§ Low-GI diet contained more fibre (50 *v.* 23 g).

contributes to the meta-analysis (presented as a weighted mean difference). The weights are usually in inverse proportion to their variance, a method that gives more weight to larger studies and to studies with less variation in results. The diamond at the bottom of the graph gives a summary of the included studies statistics, which represents the mean difference (between low-GI and high-GI diets) and the 95 % CI (Vorster *et al.* 2003). When the diamond does not touch the vertical line (the line of no effect) in the middle of the plot, it indicates that the overall effect is statistically significant. A random effects model was implemented to present the results. This model assumes that the studies used are a random sample from a hypothetical population of studies and consider both between-study and within-study variation. Random effects models, however, are more conservative, generate wider 95 % CI and are less likely to show a significant treatment effect than the fixed effects model when significant heterogeneity exists between studies (Clarke & Oxman, 2001). When homogeneity dominates (as in the present meta-analysis) both models give similar results.

Carbohydrate metabolism

Figs 1 and 2 represent the effects of low-GI *v.* high-GI diets on carbohydrate metabolism. For the present study, fructosamine and HbA_{1c} were investigated. No heterogeneity (Higgins *et al.* 2003) was detected for fructosamine (I^2 0 %; Fig. 1). The random effects analysis demonstrated an overall statistically significant reduction in fructosamine in subjects receiving the low-GI diet compared with the high-GI diet (change −0·1 (95 % CI −0·20, 0·00) mmol/l; $P=0·05$). However, when studies were subgrouped into DM and healthy subjects a non-significant improvement was observed in each group (DM, change −0·11 (95 % CI −0·25, 0·03) mmol/l, $P=0·12$; healthy, change −0·09 (95 % CI −0·24, 0·06) mmol/l, $P=0·25$). The GI reduction for the included studies was 24 (SD 9) units. Frost *et al.* (1994) and Wolever *et al.* (1992*a*), who had the longest intervention periods, found the biggest change in mean fructosamine concentrations.

There was a statistically significant decrease in mean HbA_{1c} concentrations in subjects receiving the low-GI diet (change −0·27 (95 % CI −0·5, −0·03) %; $P=0·03$) (Fig. 2). No heterogeneity was detected (I^2 0 %). All the studies included, except that of Lafrance *et al.* (1998), found an improvement in HbA_{1c} concentrations. The difference in GI between the low-GI and high-GI diets was 21 (SD 7) units. Brand *et al.* (1991) observed the biggest change with an intervention period of 12 weeks. All the included studies that measured HbA_{1c} in the present meta-analysis were performed on DM subjects.

Lipid metabolism

We investigated the effects of low-GI *v.* high-GI diets on markers for lipid metabolism such as HDL-cholesterol, LDL-cholesterol, TC and TG. Moderate heterogeneity (I^2 32·4 %; Higgins *et al.* 2003) was detected for

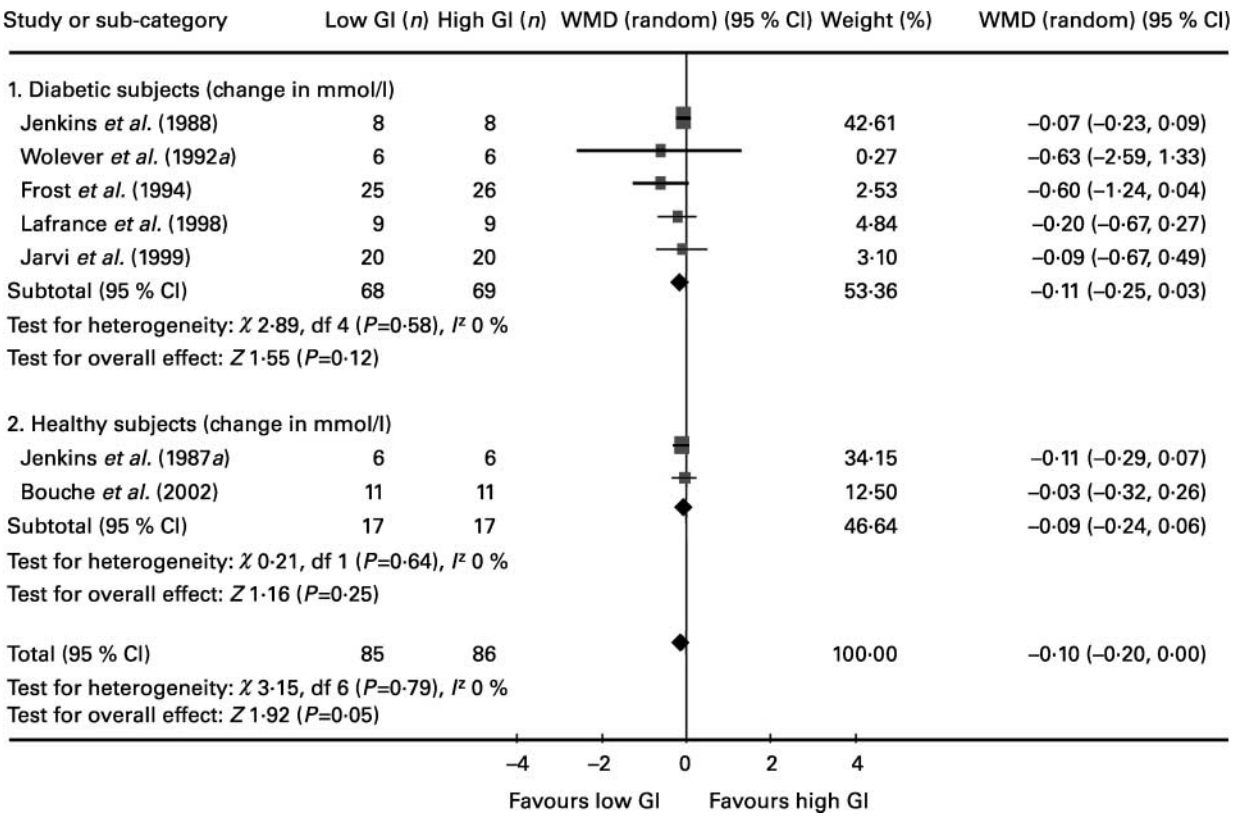

Fig. 1. Net changes in fructosamine (mmol/l). GI, glycaemic index; WMD, weighted mean difference. For an explanation of the forest plot, see p. 369. For details of selection of studies, see Table 1. GI, glycaemic index.

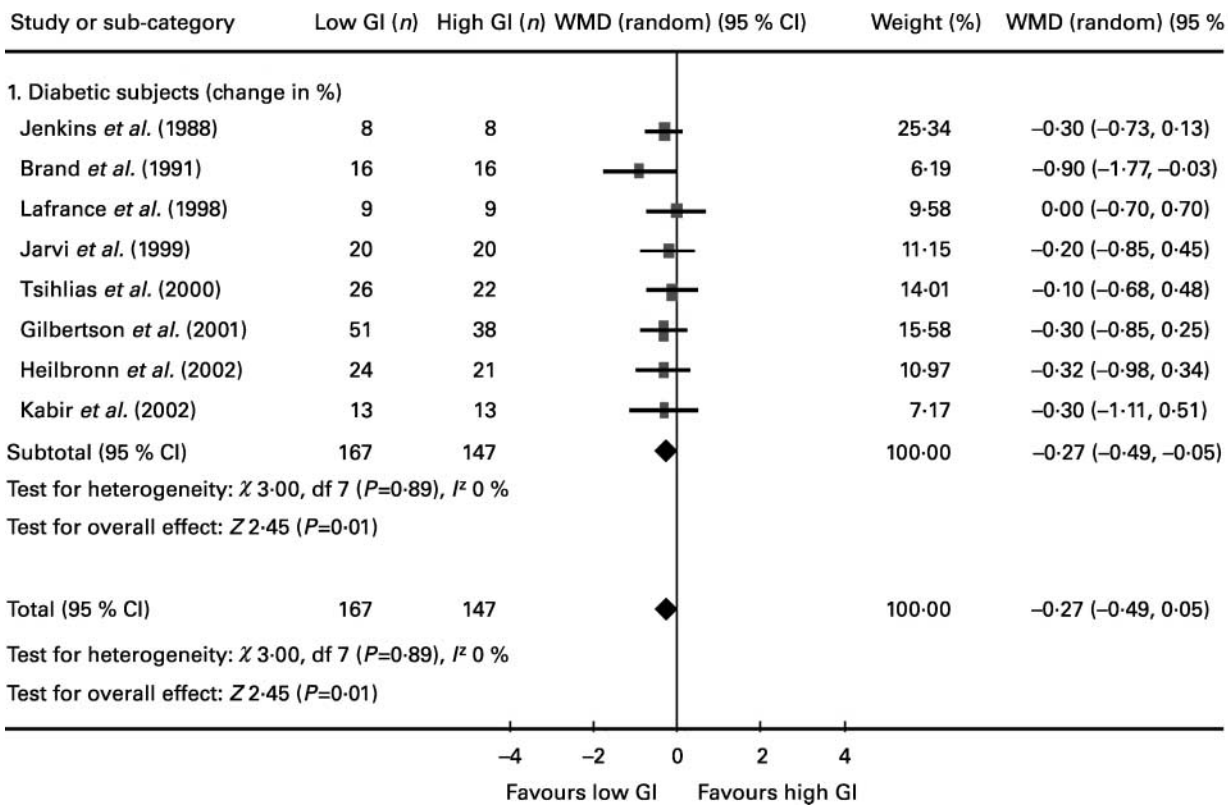

Fig. 2. Net changes in glycated Hb (HbA_{1c}; %). GI, glycaemic index; WMD, weighted mean difference. For an explanation of the forest plot, see p. 369. For details of selection of studies, see Table 1.

HDL-cholesterol. No heterogeneity (I^2 0 %) was observed for LDL-cholesterol, TC and TG.

Lowering the GI of the intervention diets by 22 (SD 9) units did not cause an overall significant change in mean HDL-cholesterol (change −0·03 (95 % CI −0·08, 0·02) mmol/l; $P=0·23$) (Fig. 3). From the forest plot it seems that neither high-GI nor low-GI diets had an effect on mean HDL-cholesterol concentrations in subjects with type 2 DM. Only Frost *et al.* (1996) investigated the effect of low-GI *v.* high-GI diets in subjects with CHD and found no significant difference. Jenkins *et al.* (1987*a*) and Bouche *et al.* (2002) found no statistically significant effect in healthy subjects.

Seven of the ten studies found an improvement in mean LDL-cholesterol concentrations on a low-GI diet (Fig. 4). Overall, low-GI diets tended to decrease LDL-cholesterol concentrations; however, it was not statistically significant (change −0·15 (95 % CI −0·31, 0·00) mmol/l; $P=0·06$). The GI of the diets was decreased by 21 (SD 10) units. In type 2 DM subjects, it seems that mean LDL-cholesterol concentrations were decreased to a greater extent than in subjects with CHD and healthy subjects. Larger decreases in LDL-cholesterol were reported for longer studies in well-controlled type 2 DM subjects (Brand *et al.* 1991; Frost *et al.* 1994) except for an unexpected non-significant increase in mean LDL-cholesterol concentrations after 6 months, as reported by Tsihlias *et al.* (2000).

The random effects analysis demonstrated an overall statistically significant improvement in TC in subjects receiving low-GI diets compared with high-GI diets (change −0·33 (95 % CI −0·47, −0·18) mmol/l; $P<0·001$). This improvement was achieved by lowering the GI of the intervention diet by 22 (SD 8) units. Larger decreases in TC concentrations were observed in patients with elevated TC baseline concentrations (>5·2 mmol/l) (Jenkins *et al.* 1988; Brand *et al.* 1991; Wolever *et al.* 1992*a*; Frost *et al.* 1994, 1996; Jarvi *et al.* 1999; Luscombe *et al.* 1999; Bouche *et al.* 2002; Heilbronn *et al.* 2002; Kabir *et al.* 2002). Two studies showed that mean TC concentrations of healthy subjects significantly improved on low-GI diets (Jenkins *et al.* 1988; Bouche *et al.* 2002), while the studies of Frost *et al.* (1996, 1998) found no change in patients with CHD (Fig. 5).

Only six of the thirteen studies showed an improvement in TG concentrations with a low-GI diet. Furthermore, the overall change was not statistically significant (change 0·03 (95 % CI −0·12, 0·17); $P=0·73$). No improvement was observed by lowering the GI of the intervention diet by 20 (SD 9) units. When divided into subgroups no difference was found within type 2 DM, CHD or healthy subjects (Fig. 6). No effect was observed when only subjects with elevated TG concentrations were included.

Discussion

Carbohydrate metabolism

Seven and eight of the sixteen randomised controlled trials measured fructosamine and HbA_{1c} respectively and indicated that low-GI diets overall decreased the markers

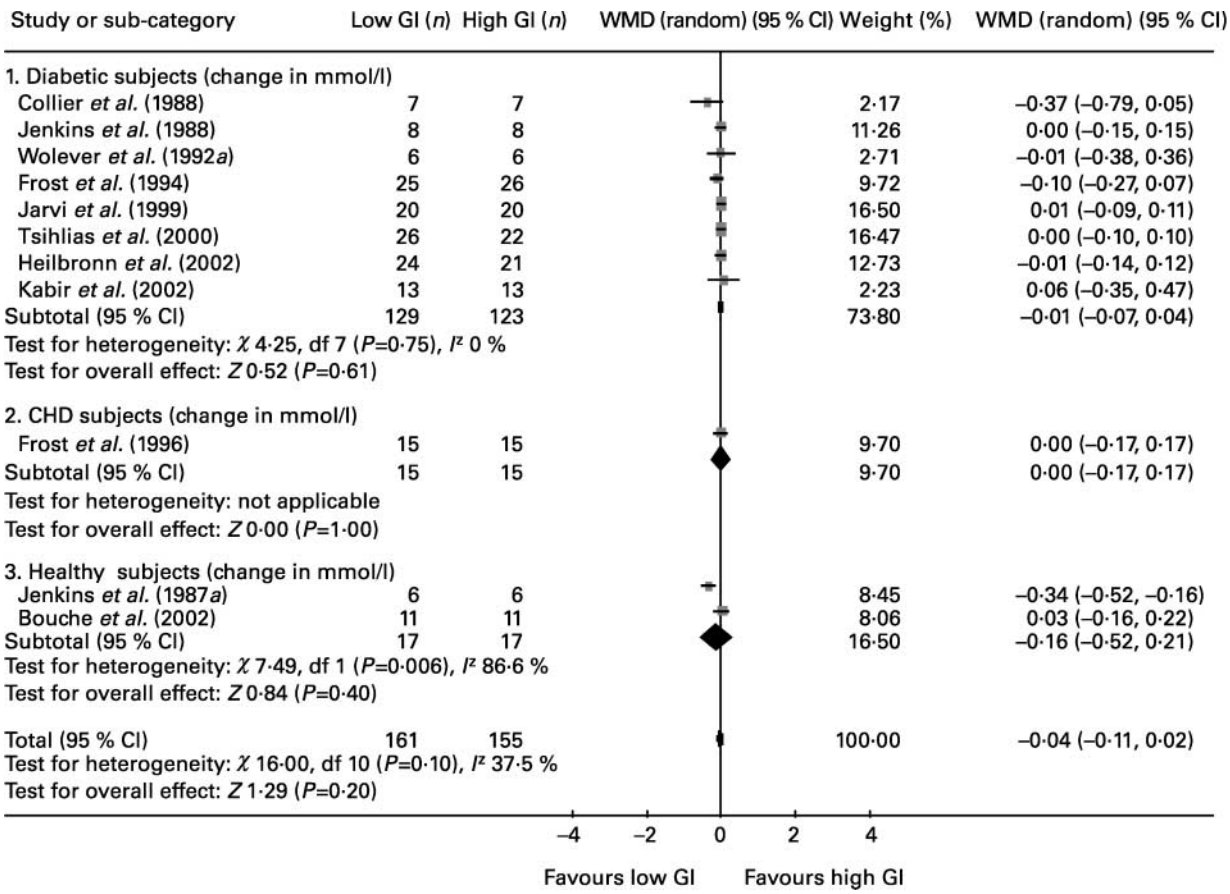

Fig. 3. Net changes in HDL-cholesterol (mmol/l). GI, glycaemic index; WMD, weighted mean difference. For an explanation of the forest plot, see p. 369. For details of selection of studies, see Table 1.

of blood glucose control statistically significantly. When dividing studies into subgroups of DM (type 1 and type 2) and healthy subjects, a non-significant decrease was reported for fructosamine in each group. However, the overall decrease was significant. HbA_{1c} was reported only in DM subjects and a statistically significant decrease was observed. Decreases in fructosamine and HbA_{1c} observed in the present meta-analysis are generally consistent with individual published reports. There was no heterogeneity among individual studies, suggesting that effects of low-GI diets on blood glucose control are uniform. Although studies included were of relatively short duration and small numbers of subjects participated, these results indicate that beneficial effects exist when using low-GI diets instead of high-GI diets in planning diets for DM subjects as well as healthy subjects. These findings are in accordance with meta-analyses conducted by Brand-Miller (1994), Brand-Miller *et al.* (2003) and Wolever (2003), who looked mainly at the influence of the GI on markers for carbohydrate metabolism. However, Brand-Miller *et al.* (2003) found a slightly larger reduction in glycated proteins, probably because of different statistical methods, a combination of the measurements of HbA_{1c} and fructosamine, and access to a larger number of studies. Our present meta-analysis is the first to investigate the effects of low-GI diets on markers for lipid as well as carbohydrate metabolism.

Fructosamine

Fructosamine is measured as a short-term (2 weeks) index of glycaemic control. Glycated albumin is the main constituent of fructosamine and has a half-life of only 12 d, explaining the usefulness of fructosamine as a short-term marker (Kumar & Clarke, 1998). The studies of Jenkins *et al.* (1987*a*, 1988) contributed the most weight to the meta-analysis, irrespective of the fact that only six and eight subjects participated in the studies and intervention periods were only 2 weeks long. This could be attributed to the small CI of the studies. Frost *et al.* (1994) and Wolever *et al.* (1992*a*) found the biggest improvement in mean fructosamine concentrations. These two studies had the longest intervention periods. Although fructosamine is a shorter-term marker for blood glucose control than HbA_{1c}, it seems that the longer low-GI diets are followed, the larger the decreases in fructosamine concentrations that are observed. According to Jones *et al.* (1983), maximum changes in fructosamine take 4–6 weeks to occur. More profound decreases were documented in DM subjects than in healthy subjects. Results would probably be more representative if all available studies conducted on fructosamine and the GI could be included, but due to a lack of complete data (mean values and SD of baseline and end values) this was not possible. However, the combined meta-analysis suggests that low-GI diets will reduce

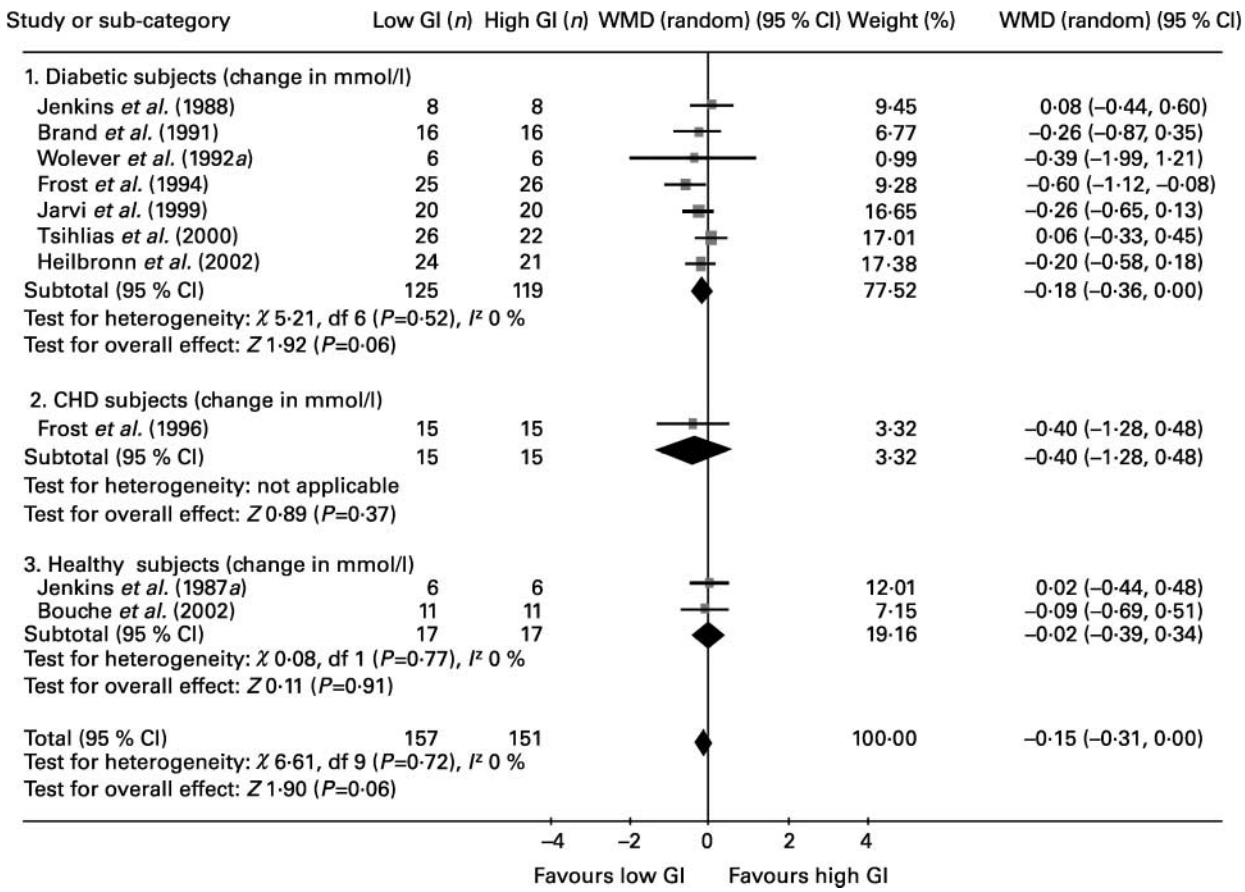

Fig. 4. Net changes in LDL-cholesterol (mmol/l). GI, glycaemic index; WMD, weighted mean difference. For an explanation of the forest plot, see p. 369. For details of selection of studies, see Table 1.

mean fructosamine concentrations by 0·1 mmol/l above that seen with high-GI diets over a period of 4·6 (SD 3) weeks. GI reductions of 24 (SD 9) units were achieved.

Glycated Hb

HbA_{1c} is a longer-term marker for carbohydrate metabolism than fructosamine. This test provides an index of the average blood glucose concentration over the half-life of the Hb molecule (approximately 6 weeks) (Kumar & Clarke, 1998). Studies that lasted longer than 4 weeks showed greater improvements in HbA_{1c} concentrations than in shorter studies. However, the study of Tsihlias *et al.* (2000) lasted 6 months, but no improvement in HbA_{1c} concentration was seen. This may be attributed to the fact that only a small GI reduction of 11 units was observed, the GI of only one meal (breakfast) was lowered and the possibility of poorer compliance with longer studies exists. Brand *et al.* (1991) attained the biggest reduction over a period of 12 weeks, although the GI reduction was only 13 units. They studied well-controlled DM subjects and reduced the GI of the whole diet and not just a single meal. Nonetheless, from these results one may conclude that low-GI diets beneficially influenced long-term glycaemic control. A significant reduction of 0·27 % in HbA_{1c} concentrations may be expected over a period of 8 (SD 8) weeks with a GI reduction of 21(SD 7) units. In addition, more than one type of low-GI food may need to be incorporated into the diet to achieve measurable long-term improvements in glycaemic control. Differences in fructosamine and HbA_{1c} might be confounded by differences in energy intake or weight loss. In most studies body weight, energy intake, fat, protein and carbohydrate and fibre intake were held constant.

Poor blood glucose control has been associated with a greater incidence of long-term macrovascular complications in both type 1 and type 2 DM patients (Balkau *et al.* 1998; UK Prospective Diabetes Study Group, 1998; Couthinho *et al.* 1999; Stratton *et al.* 2000). The UK Prospective Diabetes Study Group found that each 1 % reduction in mean HbA_{1c} concentration was associated with reductions in risk of 21 % for deaths related to diabetes, 14 % for myocardial infarction and 37 % for microvascular complications. It is not clear precisely how low-GI diets improve the markers of carbohydrate metabolism and prevent the onset of type 2 DM. Several mechanisms have been proposed. Briefly, high-GI diets have been associated with high postprandial blood glucose concentrations and increased insulin demands (Ludwig, 2002; Willet *et al.* 2002). Primary hyperinsulinaemia may cause insulin resistance, which reduces insulin sensitivity. In addition, habitual consumption of high-GI meals in the long-term initiates a cycle of hyperinsulinaemia and insulin resistance, leading to a loss of pancreatic β-cell function (Ludwig, 2002); this can result in glucose intolerance and an irreversible state of DM (Willet *et al.* 2002).

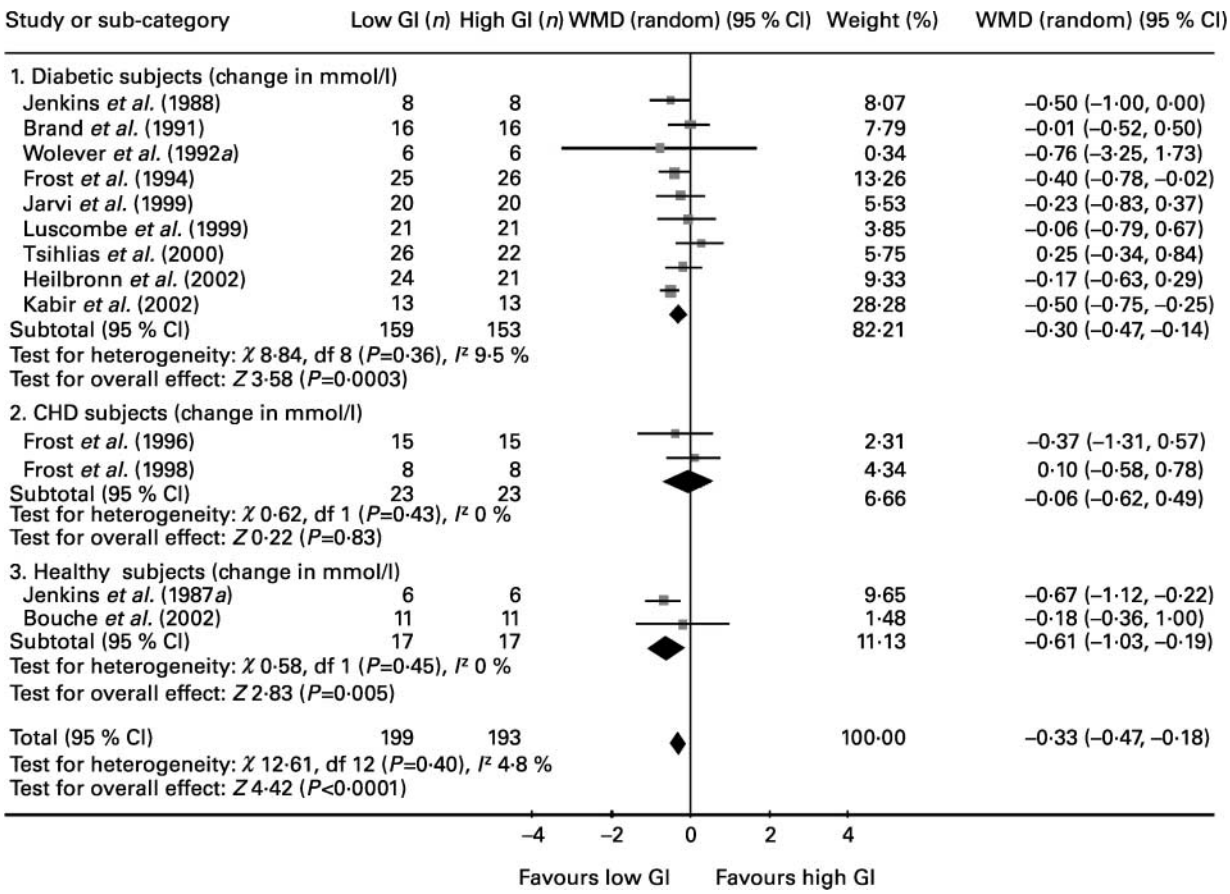

Fig. 5. Net changes in total cholesterol (mmol/l). GI, glycaemic index; WMD, weighted mean difference. For an explanation of the forest plot, see p. 369. For details of selection of studies, see Table 1.

Hyperglycaemia also causes deleterious effects on counter-regulatory hormone secretion, increased late postprandial serum NEFA concentrations (Ludwig, 2002) and leads to the occurrence of oxidative stress (Augustin *et al.* 2002). Low-GI diets, on the other hand, tend to delay glucose absorption, thereby resulting in reduced peak insulin concentrations and overall insulin demand (Augustin *et al.* 2002).

Considering epidemiological evidence, the cross-sectional EURODIAB Complications Study (*n* 2054) reported that the lower GI diet of European outpatients with type 1 DM was associated with significantly lower HbA_{1c} concentrations. Compared with the highest GI quartile, adjusted HbA_{1c} in the lowest quartile was 11 % lower in patients from southern European centres and 6 % lower in patients from the rest of the European centres (Buyken *et al.* 2001). Furthermore, the Framingham Heart Study showed a strong positive association between prevalence of CHD and increased HbA_{1c} concentrations, suggesting the importance of hyperglycaemia in the development of CHD (Singer *et al.* 1992).

Lipid metabolism

The present meta-analysis pooled the results of fourteen randomised controlled trials studying low-GI *v.* high-GI diets and their effects on markers for lipid metabolism. In the studies reviewed, low-GI diets caused a statistically significant improvement in TC concentrations, while non-significant improvements were observed in LDL-cholesterol. No significant change was found in TG and HDL-cholesterol with low-GI diets. The unchanged HDL-cholesterol concentrations were somewhat unexpected, since cross-sectional studies, such as the Survey of British Adults (1986–1987; Frost *et al.* 1999) and the Third National Health and Nutrition Examination Survey (1988–1994; Ford & Liu, 2001), found an increase in HDL-cholesterol concentrations with low-GI diets in the long term. It should also be noted that differences in lipids might be confounded by differences in energy intake or weight loss. In most studies body weight, energy intake, fat, protein and carbohydrate and fibre intake were held constant.

HDL-cholesterol

A possible explanation for the unchanged HDL-cholesterol concentrations is the length of studies. Intervention periods differed from 2 weeks to 6 months. Although the study of Tsihlias *et al.* (2000) was the longest (6 months), they also observed no effect. However, in that study the GI of only one meal (breakfast) was lowered.

A low HDL-cholesterol concentration is a strong independent predictor of CHD and has several causes, many

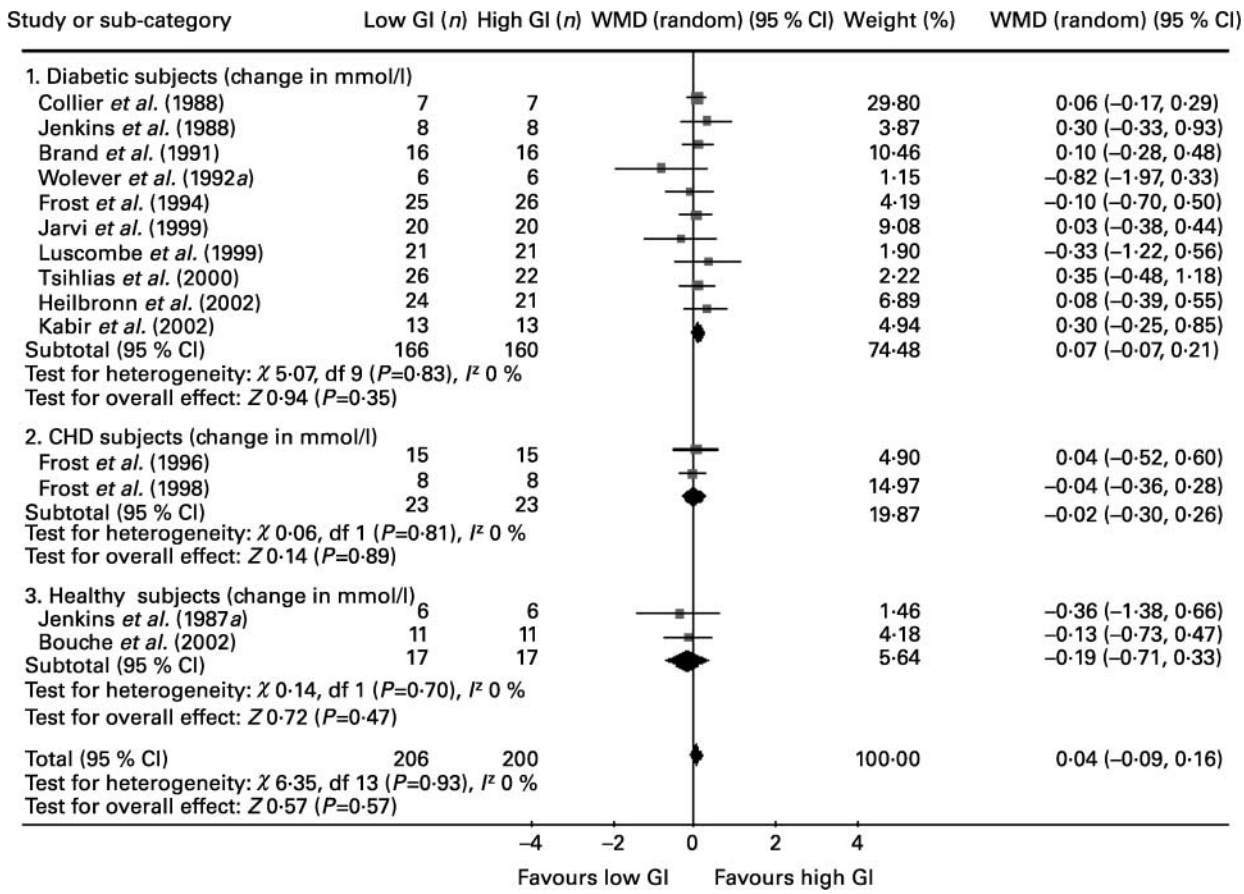

Fig. 6. Net changes in triacylglycerol (mmol/l). GI, glycaemic index; WMD, weighted mean difference. For an explanation of the forest plot, see p. 369. For details of selection of studies, see Table 1.

of which are associated with insulin resistance, elevated TG, overweight and obesity, physical inactivity and type 2 DM (Adult Treatment Panel III, 2001). While we found no significant change for HDL-cholesterol in randomised controlled trials, some cross-sectional epidemiological studies found improvements. In the Third National Health and Nutrition Examination Survey (1988–1994) an inverse relationship was found between the GI and HDL-cholesterol concentrations (n 13 907). Ford & Liu (2001) reported a statistically significant change in HDL-cholesterol concentrations of $-0{\cdot}06$ mmol/l per 15 unit increase in the GI, after adjusting for covariates such as gender, BMI, smoking status, alcohol intake, physical activity, energy intake derived from fat and carbohydrate, etc. HDL-cholesterol concentrations for the lowest and the highest GI quintiles were 1·36 and 1·28 mmol/l respectively.

Frost *et al.* (1999), who reported data from the Survey of British Adults (1986–1987), found a significant negative relationship between serum HDL-cholesterol concentration and the GI of the diet for both men ($P=0{\cdot}02$) and women ($P<0{\cdot}0001$). For women the improvement in HDL-cholesterol concentrations between the lowest and the highest quintile of the GI was 0·25 mmol/l, representing a possible 29 % reduction in CHD morbidity. In men the potential decrease in CHD morbidity was found to be 7 %, reflecting a 0·09 mmol/l difference in HDL-cholesterol concentration between the lowest and the highest quintiles of the GI.

In the EURODIAB Complications Study, higher HDL-cholesterol concentrations were observed in patients from the northern, eastern and western European centres who consumed low-GI diets. The observed relationships of the dietary GI with HDL-cholesterol concentrations were independent of dietary fibre intake (Buyken *et al.* 2001). However, in the Zutphen Elderly Study, conducted on elderly male subjects, no associations were found between the GI and HDL-cholesterol concentrations. These differences in findings between the epidemiological studies could be attributed to the age and gender differences between study populations (Van Dam *et al.* 2000).

Although no overall improvement in HDL-cholesterol was found in the present meta-analysis such an improvement was expected, because low-GI foods are associated with reduced hepatic gluconeogenesis, suppression of NEFA release and therefore increases in the HDL-cholesterol fraction (Wolever 2000; Rizkalla *et al.* 2002). Furthermore, Augustin *et al.* (2002) suggested that lower postprandial blood glucose concentrations after low-GI meals might reduce acute and chronic inflammatory responses and raise HDL-cholesterol concentrations when compared with high-GI diets. These discrepancies in results between randomised controlled trials and

epidemiological studies could be due to the difference in the length of intervention periods. Therefore, long-term intervention studies are needed to assess the effects of low-GI diets on HDL-cholesterol concentrations (Frost *et al.* 1999).

LDL-cholesterol

Frost *et al.* (1994) and Wolever *et al.* (1992*a*) reported the most profound improvement in LDL-cholesterol concentrations. In the study of Frost *et al.* (1994) the GI of the whole diet was lowered by only 5 units over a 12-week period, while Wolever *et al.* (1992*a*) reduced the GI of the diet by 28 units over a 6-week period. Jarvi *et al.* (1999) and Brand *et al.* (1991) also found notable decreases in LDL-cholesterol concentrations after periods of 24 d and 12 weeks respectively, and with GI reductions of 19 and 13 units. Nutrient compositions within the studies of Wolever *et al.* (1992*a*), Jarvi *et al.* (1999) and Brand *et al.* (1991), as well as between the high-GI and low-GI groups, remained the same. Therefore, the tendency for LDL-cholesterol to decrease can be attributed to the effect of the low-GI diets. The most substantial effects were observed in type 2 DM subjects. The GI reduction of only 5 units in the study of Frost *et al.* (1994) is small. They concluded that the effect of the change in LDL-cholesterol could be caused by changes in dietary constituents due to a significant drop in fat intake and a significant increase in fibre intake in the group that followed the low-GI diet (Frost *et al.* 1994). The low-GI group also had higher baseline LDL-cholesterol concentrations than the control group.

Not all available studies conducted on the GI and LDL-cholesterol could be included. The randomised controlled trials of Jenkins *et al.* (1985, 1987*b*) showed promising results on low-GI diets and LDL-cholesterol, but did not report mean values and SD for the change. Both these studies found significant improvements in LDL-cholesterol concentrations with low-GI diets. However, epidemiological studies, such as the Zutphen Elderly Study (Van Dam *et al.* 2000) and the EURODIAB Complications Study (Buyken *et al.* 2001), failed to prove a relationship between LDL-cholesterol concentrations and low-GI diets.

When comparing corresponding studies that measured markers for carbohydrate metabolism and LDL-cholesterol (Brand *et al.* 1991; Jarvi *et al.* 1999; Heilbronn *et al.* 2002), improvements in LDL-cholesterol concentrations were observed where decreases in fructosamine and HbA_{1c} were perceived. But how can low-GI diets contribute to lower LDL-cholesterol concentrations? A possible mechanism may be that insulin resistance may occur with consumption of a high-GI meal because of the direct effects of hyperglycaemia (Ludwig, 2002). Insulin resistance impairs normal suppression of NEFA release from adipose tissue in the postprandial state (Granberry & Fonseca, 1999). According to Timar *et al.* (2000), increased NEFA released from abdominal adipose tissue, delivered to the liver, offers an efficient substrate for enhanced synthesis of TG and VLDL-cholesterol, resulting in elevated cholesterol concentrations.

Furthermore, with the prevalence of insulin resistance as seen in type 2 DM subjects, LDL-receptor activity is reduced, resulting in less LDL-cholesterol removal from the blood, thereby contributing to higher LDL-cholesterol concentrations (Garg, 1996). Barakat *et al.* (1996) explained that reduced receptor activity may be attributed to glycation of the LDL-particle in the presence of hyperglycaemia. Glycated LDL-cholesterol cannot bind as efficiently as non-glycated LDL because of impairment in the binding of the LDL particles to LDL-receptors; therefore, glycated LDL particles will remain in the circulation longer.

From these results it seems that low-GI diets have favourable effects on LDL-cholesterol concentrations in type 2 DM subjects. A reduction of 0·15 mmol/l in LDL-cholesterol concentrations with low-GI diets can be expected over a period of 10 (SD 7) weeks with a reduction of 28 (SD 8) units in the GI of the diet. It is also recommended that more long-term studies should be performed to investigate the relationship between low-GI diets and LDL-cholesterol.

Total cholesterol

There was no substantial heterogeneity (Higgins *et al.* 2003) among included studies, suggesting that the effects of low-GI diets on TC are uniform. Considering type 2 DM subjects, all the included studies, except that of Tsihlias *et al.* (2000), reported elevated ($>5{\cdot}2$ mmol/l) baseline TC concentrations. After receiving low-GI intervention diets all the studies showed an improvement in TC to some extent. Only the study of Tsihlias *et al.* (2000) found a slight increase in TC with low-GI diets. No significant improvements were observed in the two studies conducted on CHD patients, while a significant reduction was observed in the two studies performed on healthy subjects. From these findings it can be concluded that by lowering the GI by 19 (SD 8) units over 8 (SD 6) weeks, a significant decrease of 0·3 mmol/l can be expected in TC concentrations of type 2 DM subjects. However, epidemiological evidence from the EURODIAB Complications Study (Buyken *et al.* 2001), the Zutphen Elderly Study (Van Dam *et al.* 2000) and the Survey of British Adults (Frost *et al.* 1999) failed to show any inverse relationship between low-GI diets and TC.

The mechanisms by which low-GI diets may reduce TC concentrations remain unclear. Speculatively, these mechanisms involve: lower insulin-stimulated 2-hydroxy-2-methylglutaryl-CoA reductase activity as a result of a reduced rate of carbohydrate absorption; impaired bile acid and cholesterol reabsorption from the ileum due to the high fibre content of low-GI foods; inhibition of hepatic cholesterol synthesis by SCFA, such as propionate (Augustin *et al.* 2002).

Triacylglycerol

We could not find notable effects on TG concentrations with low-GI or high-GI diets. It also seems that the type of subjects did not influence results. Only Wolever *et al.* (1992*a*) and Luscombe *et al.* (1999) found decreases

with low-GI diets. In both studies baseline TG concentrations were elevated (>1·69 mmol/l; Kratz & Lewandrowski, 1998). No relationship was found between low-GI diets and TG when investigating epidemiological data (Van Dam *et al.* 2000; Buyken *et al.* 2001).

Contrary to the general belief, an inverse relationship between low-GI diets and TG was found. According to Wolever *et al.* (1992*b*), insulin regulates both cholesterol and TG synthesis. One would therefore expect an improvement in TG concentrations, because markers for carbohydrate metabolism (HbA_{1c}) in the present meta-analysis significantly improved. Furthermore, it appears obvious that improved blood glucose control would reduce insulin resistance accompanied by an improvement in TG concentrations. Nevertheless, intra-individual biological variation in TG concentrations has been well documented (Nazir *et al.* 1999; Castro Cabezas *et al.* 2001). According to Nazir *et al.* (1999) and Castro Cabezas *et al.* (2001), several factors contribute to the variation of TG, such as intervention diet (amount of fat and carbohydrate), exercise, alcohol consumption, diurnal and seasonal variation and smoking, and could possibly explain the lack of effects on TG concentrations.

Conclusion

From the present meta-analysis on randomised controlled trials, it is clear that implementing the GI concept in choosing carbohydrate-containing foods beneficially influenced carbohydrate and lipid metabolism. These results are supported by experimental evidence from the last 20 years.

The low-GI diets significantly improved blood glucose control in type 2 DM subjects. These findings were in accordance with other meta-analyses conducted on markers of carbohydrate metabolism (Brand-Miller, 1994; Brand-Miller *et al.* 2003; Wolever, 2003). Regarding lipid metabolism, a significant improvement in LDL-cholesterol and TC was observed for type 2 DM subjects, while TG and HDL-cholesterol concentrations were not influenced. Only two randomised controlled trials were performed: CHD patients and healthy subjects. No notable effects of a low-GI diet on lipid and carbohydrate metabolism were observed in these patients. It is therefore difficult to draw a final conclusion. More studies should therefore be conducted in non-DM subjects to investigate the effect of low-GI diets on HDL-cholesterol, LDL-cholesterol and TC concentrations. Furthermore, many of the studies included in the present meta-analysis involved only small numbers of subjects and were of short duration: it is recommended that more long-term studies should be conducted.

Nonetheless, results from the present meta-analysis support the use of the GI as a scientifically based tool in selecting carbohydrate-containing foods. It appears that a low-GI diet has independent effects contributing to a healthy diet. When incorporating these benefits with other dietary interventions such as a high-fibre and low-saturated-fat diet, and adequate amounts of micronutrients, the influence of low-GI diets will probably be magnified and clinically significant effects may be expected.

Acknowledgement

We gratefully acknowledge the financial assistance of the South African Sugar Association (SASA) in conducting this research project.

References

Adult Treatment Panel III (2001) Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. *J Am Med Assoc* **285**, 2486–2498.

American Diabetes Association (2001) Nutrition recommendations and principles for people with diabetes mellitus. *Diabetes Care* **24**, Suppl. S44–S47.

American Dietetic Association (1999) Medical nutrition therapy and pharmacotherapy – position of the ADA. *J Am Diet Assoc* **99**, 227–230.

Augustin LS, Franceschi S, Jenkins DJA, Kendall CWC & La Vecchia C (2002) Glycemic index and chronic disease: a review. *Eur J Clin Nutr* **56**, 1049–1071.

Balkau B, Shipley M, Jarret RJ, Pyorala K, Forhan A & Eschwege E (1998) High blood glucose concentration is a risk factor for mortality in middle-aged nondiabetic men. 20-year follow-up in the Whitehall Study, the Paris Prospective Study, and the Helsinki Policemen Study. *Diabetes Care* **21**, 360–367.

Barakat HA, Vadlamudi S, Maclean P, Macdonald K & Pories WJ (1996) Lipoprotein metabolism in non-insulin dependent diabetes mellitus. *J Nutr Biochem* **7**, 586–598.

Bouche C, Rizkalla SW, Luo J, Vidal H, Veronese A, Pacher N, Fouquet C, Lang V & Slama G (2002) Five week, low-glycemic index diets decreases total fat mass and improves plasma lipid profile in moderately overweight nondiabetic men. *Diabetes Care* **25**, 822–828.

Brand JC, Colagiuri S, Crossman S, Allen A, Roberts DCK & Truswell AS (1991) Low-glycemic index foods improve long-term glycemic control in NIDDM. *Diabetes Care* **14**, 95–101.

Brand-Miller J, Hayne S, Petocz P & Colagiuri S (2003) Low-glycemic index diets in the management of diabetes. A meta-analysis of randomized controlled trials. *Diabetes Care* **26**, 2261–2267.

Brand-Miller J, Nantel G, Slama G & Lang V (2001) *Glycemic index and health: the quality of the evidence*. Paris: John Libbey Eurotext.

Brand-Miller JC (1994) Importance of glycemic index in diabetes. *Am J Clin Nutr* **59**, Suppl., 747S–752S.

Brand-Miller JC, Holt SHA, Pawlak DB & McMillan J (2002) Glycaemic index and obesity. *Am J Clin Nutr* **76**, Suppl., 281S–285S.

Brussaard JH, Katan MB, Groot PHE, Havekes LM & Hautvast JGAJ (1982) Serum lipoproteins of healthy persons fed a low-fat diet or a polyunsaturated fat diet for three months. *Atherosclerosis* **42**, 205–219.

Brynes AE, Edwards CM, Ghatei MA, Dornhorst A, Morgan LM, Bloom SR & Frost GR (2003) A randomised four-intervention crossover study investigating the effect of carbohydrates on daytime profiles of insulin, glucose, non-esterified fatty acids and triacylglycerols in middle-aged men. *Br J Nutr* **89**, 207–218.

Buyken AE, Toeller M, Heitkamp G, Karamaros B, Rottiers R, Muggeo M, Fuller J & The EURODIAB IDDM Complications Study Group (2001) Glycemic index in the diet of European outpatients with type 1 diabetes: relations to glycated hemoglobin and serum lipids. *Am J Clin Nutr* **73**, 574–581.

Calle-Pascual A, Gomez V, Leon E & Bordiu E (1988) Foods with a low glycemic index do not improve glycemic control of both type 1 and type 2 diabetic patients after one month of therapy. *Diabete Metab* **14**, 629–633.

Canadian Diabetes Association (2000) Guidelines for the nutritional management of diabetes mellitus in the new millennium. A position statement by the Canadian Diabetes Association. *Can J Diabetes Care* **23**, 56–69.
Castro Cabezas M, Halkes CJM, Meijssen S, Van Oostrom AJHHM & Erkelens DW (2001) Diurnal triglyceride profiles: a novel approach to study triglyceride changes. *Atherosclerosis* **155**, 219–228.
Clarke M & Oxman AD (2001) Analysing and presenting the results. In *Cochrane Reviewers Handbook 4.1.4* (updated October 2001), section 8, pp. 59–78. The Cochrane Library, Oxford: Update Software.
Collier G, Giudici S, Kalmusky J, Wolever T, Helman G, Wesson V, Ehrlich R & Jenkins D (1988) Low glycaemic index starchy foods improve glucose control and lower serum cholesterol in diabetic children. *Diabetes Nutr Metab* **1**, 11–19.
Coulston AM & Reaven GM (1997) Much ado about (almost) nothing. *Diabetes Care* **20**, 241–243.
Coutinho M, Gerstein HC, Wang Y & Yusuf S (1999) The relationship between glucose and incident cardiovascular events. A meta-regression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. *Diabetes Care* **22**, 233–240.
Defronzo RA, Bonadonna RC & Ferrannini E (1992) Pathogenesis of NIDDM: a balanced overview. *Diabetes Care* **13**, 610–630.
Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD) (2000) Recommendations for the nutritional management of patients with diabetes mellitus. *Eur J Clin Nutr* **54**, 353–355.
Diabetes UK (2003) Diabetes in Practice. New Nutritional Guidelines. http://www.diabetes.org.uk
Dietitians Association of Australia (1997) Glycaemic index in diabetes management. *Aust J Nutr Diet* **54**, 57–63.
Follmann D, Elliott P, Suh I & Cutler J (1992) Variance imputation for overviews of clinical trials with continuous response. *J Clin Epidemiol* **45**, 769–773.
Fontvielle A, Acosta M, Rizkalla S, Bornet F, David P, Letanoux M, Tchobroutsky G & Slama G (1988) A moderate switch from high to low glycaemic-index foods for 3 weeks improves the metabolic control of type I (IDDM) diabetic subjects. *Diabetes Nutr Metab* **1**, 139–143.
Fontvielle A, Rizkalla S, Penfornis A, Acosta M, Bornet F & Slama G (1992) The use of low glycaemic index foods improves metabolic control of diabetic patients over five weeks. *Diabetic Med* **9**, 444–450.
Food and Agricultural Organization/World Health Organization (1997) Carbohydrates in Human Nutrition – A Summary of the Joint FAO/WHO Expert Consultation. http://www.fao.org/docrep/w8079e/w8079e00.htm
Ford ES & Liu S (2001) Glycemic index and serum high-density lipoprotein cholesterol concentration among US adults. *Arch Intern Med* **161**, 572–576.
Frost G, Keogh B, Smith B, Smith D, Akinsanya K & Leeds A (1996) The effect of low-glycemic carbohydrate on insulin and glucose response in vivo and in vitro in patients with coronary heart disease. *Metabolism* **46**, 669–672.
Frost G, Leeds A, Trew G, Margara R & Dornhorst A (1998) Insulin sensitivity in women at risk of coronary heart disease and the effect of a low glycemic diet. *Metabolism* **47**, 1245–1251.
Frost G, Leeds AA, Dore CJ, Madeiros S, Brading S & Dornhorst A (1999) Glycaemic index as determinant of serum HDL-cholesterol concentration. *Lancet* **353**, 1029–1030.
Frost G, Wilding J & Beecham J (1994) Dietary advice based on the glycaemic index improves dietary profile and metabolic control in type 2 diabetic patients. *Diabet Med* **11**, 397–401.
Garg A (1996) Insulin resistance in the pathogenesis of dyslipidemia. *Diabetes Care* **19**, 387–389.
Gilbertson H, Brand-Miller J, Thorburn A, Evans S, Chondros P & Werhter G (2001) The effect of flexible low glycemic index dietary advice versus measured carbohydrate exchange diets on glycemic control in children with type 1 diabetes. *Diabetes Care* **24**, 1137–1143.
Gilbertson H, Thorburn A, Brand-Miller J, Chandros P & Werhter G (2003) Effect of low-glycemic-index dietary advice on dietary quality and food choice in children with type 1 diabetes. *Am J Clin Nutr* **77**, 83–90.
Granberry MC & Fonseca VA (1999) Insulin resistance syndrome: options for treatment. *South Med J* **92**, 2–14.
Heilbronn L, Noakes M & Clifton P (2002) The effect of high- and low-glycemic index energy restricted diets on plasma lipid and glucose profiles in type 2 diabetic subjects with varying glycemic control. *J Am Coll Nutr* **21**, 120–127.
Higgins PT, Thompson SG, Deeks JJ & Altman DG (2003) Measuring inconsistency in meta-analyses. *Br Med J* **327**, 557–560.
Holt SH, Brand-Miller JC & Petocz P (1997) An insulin index of common foods: the insulin demand generated by 1000 kJ portions of common foods. *Am J Clin Nutr* **66**, 1264–1276.
Jarvi A, Karlstrom B, Granfelt Y, Bjork I, Asp N & Vessby B (1999) Improved glycaemic control and lipid profile and normalized fibrinolytic activity on a low-glycaemic index diet in type 2 diabetic patients. *Diabetes Care* **22**, 10–18.
Jenkins D, Wolever T, Buckley G, *et al.* (1988) Low-glycemic-index starchy foods in the diabetic diet. *Am J Clin Nutr* **48**, 248–254.
Jenkins D, Wolever T, Collier G, Ocana A, Venketeshwer A, Buckley G, Lam Y, Mayer A & Thompson L (1987*a*) Metabolic effects of a low-glycemic-index diet. *Am J Clin Nutr* **46**, 968–975.
Jenkins D, Wolever T, Kalmusky H, *et al.* (1985) Low glycemic index carbohydrate foods in the management of hyperlipidemia. *Am J Clin Nutr* **42**, 604–617.
Jenkins D, Wolever T, Kalmusky H, *et al.* (1987*b*) Low-glycemic index diet in hyperlipidemia: use of traditional starchy foods. *Am J Clin Nutr* **46**, 66–71.
Jenkins DJ, Wolever TM, Taylor RH, Barker H, Fielden H, Baldwin JM, Bowling AC, Newman HC, Jenkins AL & Goff DV (1981) Glycemic index of foods: a physiological basis for carbohydrate exchange. *Am J Clin Nutr* **34**, 362–366.
Jenkins DJA, Wolever TMS, Jenkins AL, Josse RG & Wong GS (1984) The glycaemic response to carbohydrate foods. *Lancet* **2**, 388–391.
Jones IR, Owens DR, Williams S, Ryder RE, Birtwell AJ, Jones MK, Gicheru K & Hayes TM (1983) Glycosylated serum albumin: an intermediate index of diabetic control. *Diabetes Care* **6**, 501–503.
Kabir M, Oppert J-M, Vidal H, Bruzzo F, Fiquet C, Wursch P, Slama G & Rizkalla S (2002) Four-week low-glycemic index breakfast with a modest amount of soluble fibres in type 2 diabetic men. *Metabolism* **51**, 819–826.
Kahn CR (1994) Insulin action, diabetogenes, and the cause of type II diabetes. *Diabetes* **43**, 1066–1084.
King H, Aubert RE & Herman WH (1998) Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. *Diabetes Care* **21**, 1414–1431.
Kratz A & Lewandrowski KB (1998) Normal reference laboratory values. Case records of the Massachusetts General Hospital. *N Engl J Med* **339**, 1063–1072.
Krauss RM, Eckel RH, Howard B, *et al.* (2000) AHA dietary guidelines: revision: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association. *Circulation* **102**, 2284–2299.

Kumar P & Clark M (1998) *Clinical Medicine*. London: W.B. Saunders.

Lafrance L, Rahasa-Lohret R, Poisson D, Ducros F & Chiasson J-L (1998) Effects of different glycaemic index foods and dietary fibre intake on glycaemic control in type 1 diabetic patients on intensive insulin therapy. *Diabet Med* **15**, 972–978.

Lindsey CC, Carter AW, Mangum S, Greene D, Richardson A & Brown S (2002) A prospective, randomized, multi-centered controlled trial to compare the annual outcomes of patients with diabetes mellitus monitored with weekly fructosamine testing versus usual care: a 3-month interim analysis. *Diabetes Technol Ther* **4**, 637–642.

Liu S (2002) Intake of refined carbohydrates and whole grain foods in relation to risk of type 2 diabetes mellitus and coronary heart disease. *J Am Coll Nutr* **21**, 298–306.

Ludwig DS (2002) The glycemic index. Physiological mechanisms relating to obesity, diabetes and cardiovascular disease. *J Am Med Assoc* **287**, 2414–2423.

Ludwig DS & Eckel RH (2002) The glycemic index at 20 y. *Am J Clin Nutr* **76**, Suppl., 264S–265S.

Luscombe N, Noakes M & Clifton P (1999) Diets high and low in glycemic index versus high monounsaturated fat diets: effects on glucose and lipid metabolism in NIDDM. *Eur J Clin Nutr* **53**, 473–478.

Nazir DJ, Roberts RS, Hill SA & McQueen MJ (1999) Monthly intra-individual variation in lipids over a 1-year period in 22 normal subjects. *Clin Biochem* **5**, 381–389.

Rizkalla SW, Bellisle F & Slama G (2002) Health benefits of low glycaemic index foods, such as pulses, in diabetic patients and healthy individuals. *Br J Nutr* **88**, Suppl., S255–S262.

Salmeron J, Manson J, Stampfer M, Colditz G, Wing A & Willet W (1997*a*) Dietary fibre, glycemic load and risk of non-insulin-dependent diabetes mellitus in women. *J Am Med Assoc* **277**, 472–477.

Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL & Willet WC (1997*b*) Dietary fibre, glycemic load and risk of NIDDM in men. *Diabetes Care* **20**, 545–550.

Seidell JC (2000) Obesity, insulin resistance and diabetes – a worldwide epidemic. *Br J Nutr* **83**, 5–8.

Singer DE, Nathan DM, Anderson KM, Wilson PW & Evans JC (1992) Association of HbA_{1c} with prevalent cardiovascular disease in the original cohort of the Framingham Heart Study. *Diabetes* **41**, 202–208.

Stratton IM, Adler AI, Andrew H, Neil W, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC & Holman RR (2000) Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *Br Med J* **321**, 405–412.

Timar O, Sestier F & Levy E (2000) Metabolic syndrome X: a review. *Can J Cardiol* **16**, 779–789.

Tsihlias EB, Gibbs AL, McBurney I & Wolever T (2000) Comparison of high- and low-glycemic-index breakfast cereals with monounsaturated fat in the long-term dietary management of type 2 diabetes. *Am J Clin Nutr* **72**, 439–449.

UK Prospective Diabetes Study Group (1998) Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* **352**, 837–853.

Van Dam RM, Visscher AWJ, Feskens EJM, Verhoef P & Kromhout D (2000) Dietary glycemic index in relation to metabolic risk factors and incidence of coronary heart disease: the Zutphen Elderly Study. *Eur J Clin Nutr* **54**, 729–731.

Van Horn L & Ernst N (2001) A summary of the science supporting the new National Cholesterol Education Program dietary recommendations: what dietitians should know. *J Am Diet Assoc* **10**, 1148–1154.

Vorster HH, Oosthuizen W, Jerling JC, Veldman FJ & Burger HM (1997) *The Nutritional Status of South Africans. A Review of the Literature from 1975–1996*. Part 1. Durban: Health Systems Trust.

Vorster HH, Venter CS, Thompson RL & Margetts BM (2003) Evidence-based nutrition – using a meta-analysis to review the literature. *S Afr J Clin Nutr* **16**, 43–48.

Willet W, Manson J & Liu S (2002) Glycemic index, glycemic load, and risk of type 2 diabetes. *Am J Clin Nutr* **76**, Suppl., 274S–280S.

Wolever T, Jenkins D, Vuksan V, Jenkins A, Buckley G, Wong G & Josse R (1992*a*) Beneficial effect of a low glycemic index diet in type 2 diabetes. *Diabet Med* **9**, 451–458.

Wolever T, Jenkins D, Vuksan V, Jenkins A, Wong G & Josse R (1992*b*) Beneficial effect of low-glycemic index diet in overweight NIDDM subjects. *Diabetes Care* **15**, 562–564.

Wolever T & Mehling C (2003) Long-term effect of varying the source or amount of dietary carbohydrate on postprandial plasma glucose, insulin, triacylglycerol, and free fatty acid concentrations in subjects with impaired glucose tolerance. *Am J Clin Nutr* **77**, 612–621.

Wolever TMS (2000) Dietary carbohydrates and insulin action in humans. *Br J Nutr* **83**, Suppl., S97–S102.

Wolever TMS (2003) Carbohydrate and the regulation of blood glucose and metabolism. *Nutr Rev* **61**, Suppl., S40–S48.

Wolever TMS, Jenkins DJA, Jenkins AL & Josse RG (1991) The glycemic index: methodology and clinical implications. *Am J Clin Nutr* **54**, 846–854.