Low glycemic index diets and blood lipids: a systematic review and meta-analysis of randomised controlled trials

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Abbreviations: CVD, cardiovascular disease; GI, glycemic index; MetS, metabolic syndrome; RCT, randomised controlled trial; T2DM, type 2 diabetes mellitus.

ABSTRACT

Aims: Low glycemic index (GI) diets are beneficial in the management of hyperglycemia. Cardiovascular diseases are the major cause of mortality in diabetes therefore it is important to understand the effects of GI on blood lipids. The aim was to systematically review randomised controlled trials (RCTs) of low GI diets on blood lipids.

Data Synthesis: We searched OVID Medline, Embase and Cochrane library to March 2012. Random effects meta-analyses were performed on twenty-eight RCTs comparing low- with high GI diets over at least 4 weeks (1272 participants; studies ranged from 6 to 155 participants); one was powered on blood lipids, 3 had adequate allocation concealment. Low GI diets significantly reduced total (-0.13mmol/l, 95%CI -0.22 to -0.04, P=0.004, 27 trials, 1441 participants, I^2=0%) and LDL-cholesterol (-0.16mmol/l, 95%CI -0.24 to -0.08, P<0.0001, 23 trials, 1281 participants, I^2=0%) compared with high GI diets and independently of weight loss. Subgroup analyses suggest that reductions in LDL-C are greatest in studies of shortest duration and greatest magnitude of GI reduction. Furthermore, lipid improvements appear greatest and most reliable when the low GI intervention is accompanied by an increase in dietary fibre. Sensitivity analyses, removing studies without adequate allocation concealment, lost statistical significance but retained suggested mean falls of ~0.10mmol/l in both. There were no effects on HDL-cholesterol (MD -0.03mmol/l, 95%CI -0.06 to 0.00, I^2=0%), or triglycerides (MD 0.01mmol/l, 95%CI -0.06 to 0.08, I^2=0%).

Conclusions: this meta-analysis provides consistent evidence that low GI diets reduce total and LDL-cholesterol and have no effect on HDL-cholesterol or triglycerides.

INTRODUCTION

The glycemic index (GI) is a classification of carbohydrate-containing foods according to the glycemic response that they evoke (1). The relevance of GI to both the prevention and management of diabetes has received much attention; compared to high GI carbohydrates, gram-for-gram, low GI foods stimulate less insulin secretion and reduced incretin levels (2), furthermore they have been shown to limit reductions in insulin sensitivity (3-5). Epidemiological evidence supports a positive relationship between GI and risk of type 2 diabetes (6) whilst the clinical utility of low GI diets in the management of type 2 diabetes has been demonstrated by two systematic reviews demonstrating a 5% reduction in HbA^1c (7;8).

Mortality rates from cardiovascular diseases (CVD) are up to five times higher for patients with diabetes than the non-diabetic population (9) in part due to the atherogenic lipid profile and hypertension which develops (10). An inverse relationship between GI and HDL-cholesterol (HDL-C) has been found in two large cross-sectional studies (11;12). Further epidemiological evidence suggests that there is a positive association between GI and triglycerides (13) but evidence for the effect of GI on total and low-density lipoprotein cholesterol (LDL-C) is less clear (11;14).

The Cochrane meta-analysis which focused on people with, or at high risk of, CVD found small significant reductions in total and LDL-C with low GI diets but no effect on HDL-C or triglycerides however the authors concluded that further ‘well designed, adequately powered, randomised controlled studies’ were needed (15). Since the completion of the Cochrane review there have been a number of larger studies published which may help to elucidate the effects of low GI diets on blood lipids.

We performed a systematic review with the aim to assess the effects of low GI diets on blood lipids. In contrast to the Cochrane review, our review includes healthy participants as well as those who have CVD. We aimed to explore the relationship between GI and blood lipids by performing sub-group analyses to determine dose-response effects, study duration and study participant effects, including whether effect size relates to baseline lipid levels. Furthermore we explored the impact of nutrient changes alongside GI changes on lipid outcomes.

METHODS

Study identification and selection

The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1948 to March 2012) and EMBASE (1980 to March 2012) were searched using text and indexing terms. When possible, the systematic review and meta-analyses were undertaken in line with the relevant criteria of the PRISMA statement (*Supplementary Information* Figure 1 Search strategies). The inclusion and exclusion criteria were developed prior to searching using a PICOS structure (Patient, Intervention, Comparators, Outcome, Study design) and were modelled on those of Kelly et al.(15). Included studies had to be RCTs (crossover or parallel), include non-pregnant and non-institutionalised adults with any baseline lipid levels, compare a low GI diet (with a significant decrease in GI between baseline and the end of the intervention) with a high GI diet (with a significantly higher GI) for at least 4 weeks. Studies were included if at least one meal per day was substituted within the intervention period, the paper was reported in English, and at least one serum lipid outcome (total, LDL, HDL cholesterol or triglycerides) was reported. Studies were excluded if they clearly stated that macronutrient differences were intended between the low and high GI interventions, although dietary fibre differences were included. The intervention and control diets had to be assessed during the study via interaction with a health care worker, and were excluded if no explicit information regarding assessment of compliance was given. Participants who were acutely ill e.g. chronic renal failure, cancer, HIV-positive or AIDS, were excluded.

Located titles, abstracts and full texts were screened by one researcher (DEC) and rejected where they did not meet all the inclusion criteria. A second researcher (LMG) reviewed the eligibility of full text articles against the inclusion criteria.

Data extraction and quality assessment

Data extraction was conducted by a single reviewer (DEC) onto a data extraction sheet modelled on Kelly *et al*., 2008 (15) and included: reference details; trial design characteristics; details of intervention and comparator; duration; method of calculating the GI; participant characteristics; baseline and endpoint plasma lipid concentrations. Lipid measurements were converted to mmol/L, and variance data to standard deviations. For GI values, those which were expressed against a bread reference were transformed to the glucose scale using a factor of *0.71. Where the GI scale was not explicitly stated authors were contacted for clarification (n=5). A second researcher (LMG) checked and validated the data extraction. Authors were contacted (n=8) where there were insufficient or missing data.

Two independent researchers (DEC, LMG) assessed the risk of bias using the criteria specified by Jadad (16) and Schulz (17); validity characteristics assessed included randomisation method, allocation concealment, blinding of outcome assessors, number of withdrawals and dropouts. Agreement between assessors was calculated using the Kappa statistic (κ). Inconsistent assessments were discussed and agreed.

Data synthesis

Meta-analysis was performed using Review Manager™ (version 5.1; Nordic Cochrane Centre, Oxford, England) to determine the effects of low GI dietary

interventions on lipid concentrations. The generic inverse variance (IV) method was used. The treatment effect of each trial was estimated as the mean difference between post-intervention measurements for the intervention and control arms (calculated as data for participants ingesting low GI – data for those ingesting high GI). The point estimate of mean difference for a crossover paired analysis is the same as for a parallel-group analysis (the mean of the differences is equal to the difference in means). I^2 was used to assess between study heterogeneity (18) and funnel plots to assess small study bias. A random effects model was used to calculate mean differences (MDs), 95% confidence intervals (CI) for each comparison, a combined overall effect with p-value, and the p-value for testing heterogeneity. Sensitivity analyses were performed on studies of high validity, assessed as low risk of bias relating to randomisation, allocation concealment and reporting; blinding bias was not included in the validity assessment as it is often not feasible to blind dietary interventions.

Subgroup analyses were performed to investigate possible factors that might relate to the effects across included trials:

- Dose-response: on the basis of the scale of absolute difference in GI between the intervention and control groups (up to 10% points, 10.1 to 20% points and over 20% points)
- Study duration: on the basis of tertiles of study duration (0-8wks, 9-20wks and >20wks)
- Study participants: according to whether the study involved participants with or without diabetes

- Baseline lipid status: according to whether the participants had optimal or sub-optimal lipid status at baseline (using the NCEP III guidelines (19)).
- Effects of dietary fibre: according to whether the low GI intervention included a statistically significant change (increase) in dietary fibre compared to the high GI arm.
- Effects of saturated fat changes: analyses were performed to assess whether saturated fat is reduced in low GI diets.

RESULTS

Our searches identified 4464 potential titles and abstracts after de-duplication, of which 109 were potentially relevant and collected in full text. Studies were not eligible for inclusion for a variety of reasons (*Supplementary Information* Figure 2 Review flow diagram). 29 studies fulfilled all inclusion criteria; one study with insufficient variance data was excluded following attempted contact with the authors (20).

Twenty-eight studies, 18 of parallel-group (total participants, n=1073) (21-38) and 10 of crossover design (total participants, n=199) (39-48), were included in the analysis; details of the studies and participants are seen in *Supplementary Information* Table 1.

Twenty-two studies compared a low GI diet with a high GI diet, six studies compared a low GI diet with a 'normal' or 'healthy eating' diet (including a high-cereal fibre diet (27) and a conventional carbohydrate exchange diet (35)) of significantly higher GI.

The validity of the included studies was variable and often difficult to assess due to studies providing insufficient information to assess risk of bias (*Supplementary Information* Table 2). Thirteen studies reported what the study was powered towards, only one (24) was powered towards a change in blood lipids.

Lipid outcomes

Random effects meta-analysis of the 27 trials (1441 participants) revealed that low GI diets significantly reduce total cholesterol by -0.13mmol/l (95%CI -0.22 to -0.04, p=0.004), with non-significant heterogeneity (I^2=0%) and LDL-C by -0.16mmol/l (95%CI -0.24 to -0.08, p<0.0001, 23 trials, 1281 participants, I^2=0%) compared with

high GI diets (Figure 1 & 2). The 24 included studies (1331 participants) that reported HDL-C concentrations did not suggest any effect of GI on HDL-C (MD -0.03mmol/l, 95%CI -0.06 to 0.00, p=0.06, I^2=0%) (*Supplementary Information* Figure 3). Similarly, there were no clear effects of GI on triglycerides (MD 0.01mmol/l, 95%CI -0.06 to 0.08, p=0.69, I^2=0%, 27 RCTs, 1412 participants) (*Supplementary Information* Figure 4).

To investigate the impact of GI on lipid levels independently of weight loss we performed post-hoc analyses removing the nine studies with the stated objective of weight loss. The resultant reductions in total cholesterol (-0.15mmol/l, 95%CI -0.25 to -0.04, p=0.005) and LDL-C (-0.18mmol/l (95%CI -0.27 to -0.09, p<0.001) remained significant.

Dose-response analysis

The LDL-C effect in studies with a greater difference in GI between the intervention and control groups appeared larger and more reliable (MD -0.21, 95%CI -0.33, -0.09, p=0.0005) than in those with smaller GI differences (MD -0.10, 95%CI -0.21, 0.01, p=0.08) but was not statistically different (p=0.36) (*Supplementary Information* Figure 5). Table 1 shows a summary of the sub-group analyses: there was no indication of a dose-response effect on other lipids (*Supplementary Information* Figure 6).

Study duration analysis

The LDL-C lowering effect appeared to be inversely related to the study duration, with the greatest, most reliable reductions in LDL-C being evident in studies of the shortest duration (MD -0.21, 95%CI -0.33, -0.10, p=0.0004) however the overall subgroup effect was not significant (p=0.43) (Figure 3). The impact of study duration

on total cholesterol was less clear, studies of 20 weeks or shorter appeared to more reliably reduce total cholesterol than the studies of longer duration however there was no significant difference between subgroups (*p*=0.70), Table 1 (*Supplementary Information* Figure 7).

Study participant analysis

The total and LDL-C reductions appear to be greatest and most reliable in participants without diabetes (total-C MD -0.20, 95%CI -0.32, -0.07, *p*=0.002; LDL-C MD -0.19, 95%CI -0.29, -0.08, *p*=0.0004) however there was no significant difference between subgroups (*p*=0.22 and *p*=0.55, respectively), Table 1 (*Supplementary Information* Figure 8 & 9).

Baseline lipid status analysis

Few studies had above optimal total cholesterol and LDL-C concentrations at baseline and there were no clear differences in effects between above optimal and optimal total cholesterol and LDL-C studies (Table 1).

Dietary fibre analysis

In 13 studies, the low GI intervention was accompanied by significant increases in dietary fibre and significantly higher endpoint fibre intakes compared to the high GI intervention (*Supplementary Information* Table 3 Dietary data). There were no significant changes in dietary fibre in the remaining 15 studies. Subgroup analysis based on whether there was an increase in dietary fibre showed that total cholesterol and LDL-C reduced significantly only when the low GI intervention was accompanied by increased fibre intake, Table 1 (figure 4 and *Supplementary Information* Figure 10).

Saturated fat analysis

Eleven studies reported saturated fat and two studies reported significantly lower saturated fat intakes in the low GI intervention compared to the high GI arm (*Supplementary Information* Table 3). We further explored the saturated fat data by performing a meta-analysis to assess mean difference between endpoint saturated fat intakes in low GI and high GI groups and found a statistically significant effect of lower saturated fat in the low GI arms (MD -0.55%, 95%CI -1.02 to -0.08, *p*=0.02, I^2=28%) (*Supplementary Information* Figure 11). A sensitivity analysis, removing all studies which reported a significantly lower saturated fat intake or which did not report saturated fat continued to identify significant effects of low GI interventions on total cholesterol (MD -0.20mmol/l 95%CI -0.33 to -0.07, *p*=0.0003, n=640) and LDL-C (MD -0.21mmol/l, 95%CI -0.31 to -0.10, *p*=0.0001, n=552).

There was no clear evidence of small trial effects in funnel plots of total and LDL-C data, but as there were no very large studies the funnel plot was underpowered to detect any such effects (*Supplementary Information* Figure 12). Analyses separating parallel (n=18) and crossover (n=10) studies revealed significant lipid lowering effects in both groups (total cholesterol: parallel MD -0.11mmol/l, 95%CI -0.22, -0.00, p=0.04, I^2=0%; crossover MD -0.16mmol/l, 95%CI -0.31, -0.01, p=0.04, I^2=0%. LDL-C: parallel MD -0.11mmol/l, 95%CI -0.21, -0.01, p=0.02, I^2=0%; crossover MD -0.24mmol/l, 95%CI -0.36, -0.11, p=0.0002, I^2=0%). Sensitivity analyses, removing studies of moderate or low validity, leaving only three RCTs (27;31;36) resulted in loss of the significant effects of low GI diets on total cholesterol while retaining similar point-estimate mean differences (MD -0.09mmol/l, 95%CI -0.25 to 0.07, *p*=0.28, 3 RCTs, 375 participants, I^2=0%) and LDL-C (MD -0.11mmol/l, 95%CI -0.25 to 0.03, *p*=0.12, 3 RCTs, 365 participants, I^2=0%). The majority of studies were

264 removed from the sensitivity analyses due to a lack of information regarding
265 selection bias (both randomisation procedures and allocation concealment.

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DISCUSSION

We found 28 RCTs that assessed the effects of a low GI diet on serum lipids. These trials provided consistent evidence that a low GI diet reduced total (-0.13mmol/L, 95%CI -0.22 to -0.04) and LDL-C (-0.16mmol/L, 95%CI -0.24 to -0.08), furthermore these lipid lowering effects appear to occur independently of weight loss.

Subgroup analysis aimed at further exploring the relationship between GI and serum lipids recognised that LDL-C reductions were more consistent in studies in which the GI reduction was of greatest magnitude, ideally at least 20 points lower than control. Study duration also appeared to be an important determinant of total and LDL-C changes with studies of 20 weeks or less bringing about more consistent reductions than studies of longer duration which may suggest there is an adaptive response occurring or issues relating to participant compliance in longer studies. Additionally, lipid changes were more consistent in people without diabetes, perhaps because individuals with diabetes are more likely to be receiving pharmaceutical therapy for hyperlipidemia and therefore are resistant to any further changes. We investigated the impact of dietary changes, other than GI, on lipid changes and have shown that low GI diets, which are accompanied by increases in dietary fibre, are more effective at reducing total and LDL-C than low GI interventions alone.

Sensitivity analysis, removing studies of lower validity, suggested a loss of the significant effects of low GI dietary interventions on total and LDL-C. Larger studies and studies with high validity (for example robust randomisation methods, concealed allocation, blinding) are needed to confirm the findings of effects on total and LDL-C. The sensitivity analyses emphasize the need to publish full methodological details regarding randomisation and allocation concealment as the majority of studies were deemed ‘unclear’ for these sources of bias.

We acknowledge the limitations of our review. We intended to investigate whether the magnitude of lipid changes were related to baseline lipid concentrations however baseline lipid concentrations were too narrow to assess such an effect. Furthermore, it should be considered that only one of the studies included in our review was powered on serum lipids; the majority of studies were powered on an index of insulin action or glycaemia. The risk of publication bias should also be considered; as the majority of the studies were not primarily focused on lipids there is a risk that these outcomes were only reported when there were 'positive' findings. We have only reviewed manuscripts published in English and acknowledge the possibility of selection bias. Furthermore, whilst we were guided, wherever possible, by the recommendations of the Cochrane library for undertaking a systematic review, it was not feasible for us to adhere strictly to these recommendations at all stages.

It is important to consider whether dietary alterations other than to GI could have contributed to the significant reductions in total and LDL-C as dietary intervention studies focused on manipulating single dietary components are inherently difficult to perform. Our meta-analyses are the first to investigate the impact of weight loss, saturated fat and dietary fibre changes alongside low GI interventions on lipid outcomes thus helping to recognise aspects of study design which impact on lipid changes and may explain some of the variability in the published outcomes. Unfortunately only a small number of studies published full dietary information, including saturated fat, and therefore some of our analyses may not be conclusive. Further investigation of all types of fat intakes for the studies in this review is warranted in order to better understand the impact of saturated and unsaturated fats. Our review is limited to investigating GI effects however glycemic load (GL) is

another important consideration, which captures the effect of carbohydrate quantity as well as quality and may be more effective at altering blood triglycerides (49).

The variation in the average GI of both the low and the high GI groups between the studies is remarkable (21 to 57 for the low GI diets, and 51 to 75 for the high GI diets, indexed to glucose) and makes it difficult to translate the findings of this review in to a health promotion message as an optimal GI is unclear. A further issue when comparing these studies is the varying scale upon which the GI has been calculated and expressed; although there is expert agreement that GI should be measured in relation to a glucose standard (50), older studies often used a bread standard and a number of studies did not publish the reference standard. In the present review clarification was sought from authors and the data have been transformed to the glucose scale, thus allowing for a robust comparison.

Large cross-sectional studies have suggested that low GI diets are associated with higher HDL-C (11;12) and lower fasting triglyceride concentrations (13) however the results of our meta-analysis and others (15) do not support this epidemiological evidence. There is often a divergence between epidemiological and clinical trial findings; the former being limited by confounding effects and the later often underpowered to detect significant changes. Our meta-analysis supports the prospective epidemiological findings of Liu et al (2000) who found dietary GI (and load) are significantly associated with CHD risk (51), and is in complete agreement with the Cochrane meta-analysis which reports a total and LDL-C lowering effect of low GI diets (15).

Our analyses have shown importantly that low GI interventions are more effective at lowering serum lipids when there is a concurrent increase in dietary fibre intake,

suggesting that GI and fibre are working in combination to affect lipid absorption or synthesis. The effects of high fibre diets on lipid concentrations have been previously investigated; cereal sources, rich in insoluble fibre, appear to have little effect on serum lipids (27;52) but soluble fibre sources are effective at lowering lipids (53). The mechanisms by which low GI diets reduce total cholesterol and LDL-C are not fully understood; it may be that low GI interventions lead to increased intakes of soluble fibre which cannot be assessed in the current review. It has been proposed that increased dietary fibre will bring about reductions in bile acid and cholesterol reabsorption from the ileum, which may inhibit hepatic cholesterol synthesis (54). A further theory is that low GI diets have their effects through reducing insulin secretion thus reducing insulin-stimulated activity of 5-hydroxy-3-methylglutaryl-CoA reductase, the rate-limiting enzyme involved in cholesterol synthesis (54).

While the reductions in total cholesterol and LDL-C are only small and do not compare to the reductions that are brought about by pharmacological therapies, they are comparable with other dietary interventions which have been used to reduce cardiovascular risk. In the Cochrane review (55) of dietary advice for reducing cardiovascular risk, Brunner et al (2007) found total cholesterol reduced by 0.16mmol/L and LDL-C by 0.18mmol/L using a variety of dietary interventions including fat quantity and type, and increased fruit and vegetable consumption.

Diabetes management guidelines have recognised for some time the potential benefits of low GI carbohydrates for the management of blood glucose levels (56;57). Patients with type 2 diabetes are usually also characterised by dyslipidemia, often present at diagnosis, and reduction of LDL-C and triglycerides is a management priority in order to reduce cardiovascular risk (58). The results of our review provide evidence that the promotion of low GI carbohydrates will bring about

beneficial reductions in serum total and LDL-C in addition to the benefits to glycemic control (8).

In conclusion, the results of our meta-analysis of low GI diets on blood lipids show that there is consistent evidence that low GI diets significantly reduce total and LDL-C without affecting HDL-C or triglycerides; this finding supports previous systematic reviews. However, our analyses did not demonstrate a lowering of triglycerides or an increase in HDL-C by the low GI studies which is at odds with epidemiological findings. Our sub-analysis recognised the important role of increasing dietary fibre alongside reduced GI in effectively lowering serum lipids. Other components of study design, such as duration and magnitude of change, may be responsible for the variability seen in the effects of low GI interventions on serum lipid changes. Overall we found that the strength of the evidence is moderate and sufficiently powered investigations are needed. Further investigations are warranted to understand the mechanisms by which low GI alter blood lipids, and whether such an effect is secondary to changes in other dietary components, for example fibre, saturated or unsaturated fat.

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Table 1 Summary of subgroup meta-analyses investigating effects of dose response, study duration, study participant status, baseline lipid status and increasing dietary fibre on lipid outcomes

Subgroup analysis	Total cholesterol mean difference (95% CI) (mmol/l)	LDL-cholesterol mean difference (95% CI) (mmol/l)	HDL-cholesterol mean difference (95% CI) (mmol/l)	Triglycerides mean difference (95% CI) (mmol/l)
Dose response effect				
GI difference 0-10 points	-0.08 (-0.21, 0.05)	-0.10 (-0.21, 0.01)	-0.04 (-0.08, 0.00)	0.02 (-0.11, 0.16)
GI difference 10.1-20 points	-0.21 (-0.42, 0.01)	-0.21 (-0.43, 0.01)	0.00 (-0.07, 0.07)	0.03 (-0.11, 0.17)
GI difference >20 points	-0.12 (-0.30, 0.05)	**-0.21 (-0.33, -0.09)***	-0.03 (-0.08, 0.02)	-0.04 (-0.16, 0.08)
Subgroup differences (*p*)	0.60	0.36	0.65	0.73
Study duration effect				
0-8wks	**-0.14 (-0.28, 0.00)***	**-0.21 (-0.33, -0.10)***	-0.02 (-0.07, 0.03)	0.00 (-0.13, 0.13)
9-20wks	**-0.20 (-0.40, -0.00)***	-0.18 (-0.36, 0.00)	-0.01 (-0.08, 0.06)	-0.06 (-0.25, 0.13)
>20wks	-0.09 (-0.24, 0.05)	-0.10 (-0.23, 0.03)	-0.04 (-0.08, 0.01)	0.04 (-0.06, 0.14)
Subgroup differences (*p*)	0.70	0.43	0.83	0.67
Study participant effect				
Participants with diabetes	-0.08 (-0.21, 0.04)	**-0.14 (-0.26, -0.01)***	0.00 (-0.04, 0.05)	0.04 (-0.09, 0.16)
Participants without diabetes	**-0.20 (-0.32, -0.07)***	**-0.19 (-0.29, -0.08)***	**-0.05 (-0.09, -0.01)***	-0.04 (-0.13, 0.06)
Subgroup differences (*p*)	0.22	0.55	0.10	0.37
Baseline lipid status effect				
Optimal lipids at baseline	**-0.11 (-0.23, 0.00)***	**-0.14 (-0.25, -0.04)***	-0.03 (-0.06, 0.00)	-0.03 (-0.10, 0.05)
Sub-optimal lipids at baseline	**-0.14 (-0.21, -0.04)***	**-0.17 (-0.28, -0.06)***	-0.05 (-0.14, 0.05)	**0.17 (0.03, 0.31)***
Subgroup differences (*p*)	0.79	0.72	0.67	**0.01**
Increasing dietary fibre effects				
Studies with increased fibre in low GI arm	**-0.17 (-0.28, -0.06)***	**-0.18 (-0.27, -0.09)***	**-0.04 (-0.07, -0.00)***	0.03 (-0.06, 0.11)
Studies with no change in fibre	-0.06 (-0.20, 0.09)	-0.10 (-0.26, 0.05)	-0.00 (-0.06, 0.05)	-0.01 (-0.13, 0.10)
Subgroup differences (*p*)	0.23	0.39	0.26	0.57

FIGURES

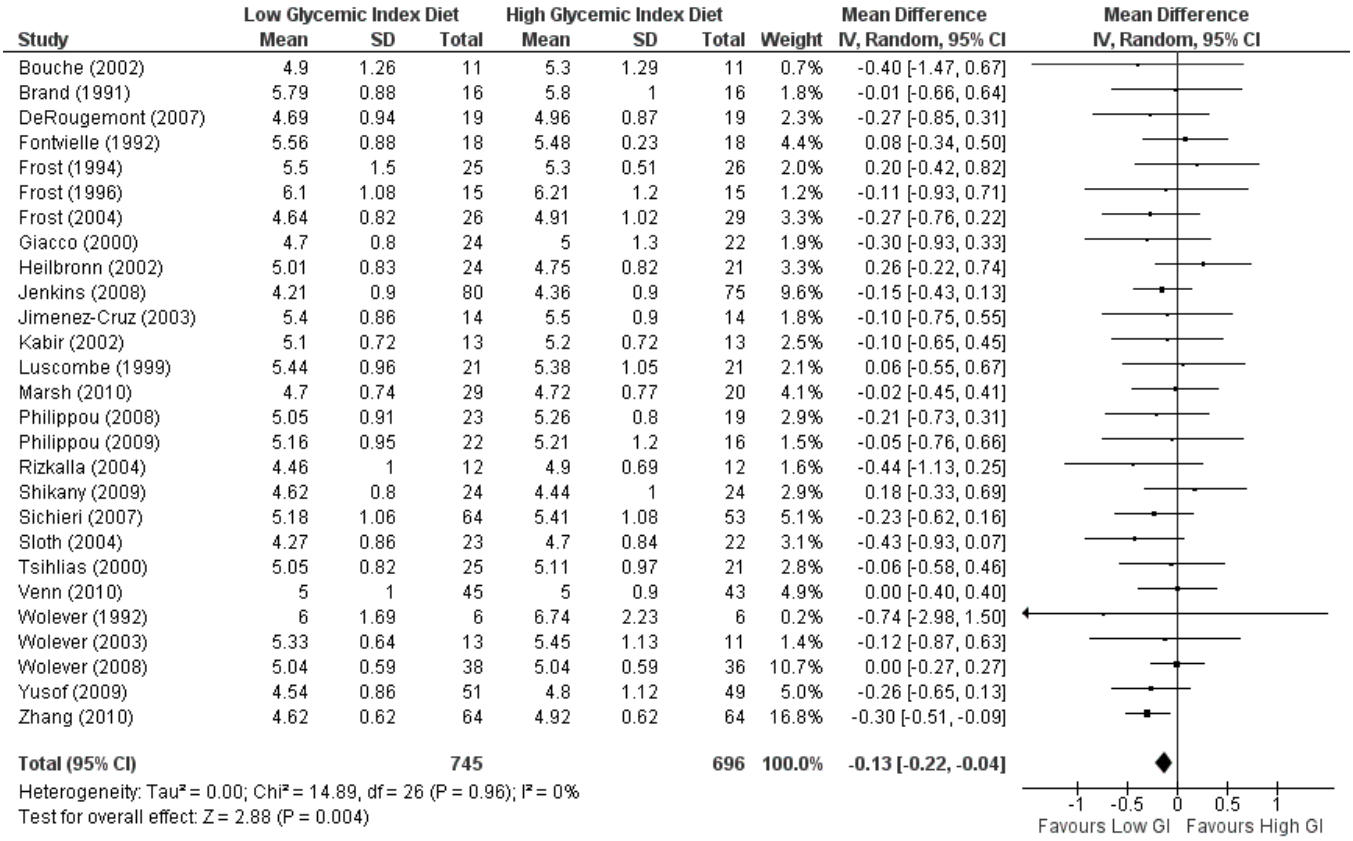

Figure 1 Effects of low and high glycemic index dietary interventions on total cholesterol concentrations (mmol/l). Analysis includes all studies which assessed total cholesterol. ▪, effect estimate of each study, horizontal line denote the 95%CI; ♦, combined overall effect; CI, confidence interval; GI, glycemic index; random, random effects model; mean difference, mean of difference in post-intervention cholesterol/LDL-C concentrations between low GI and high GI groups; SD, standard deviation.

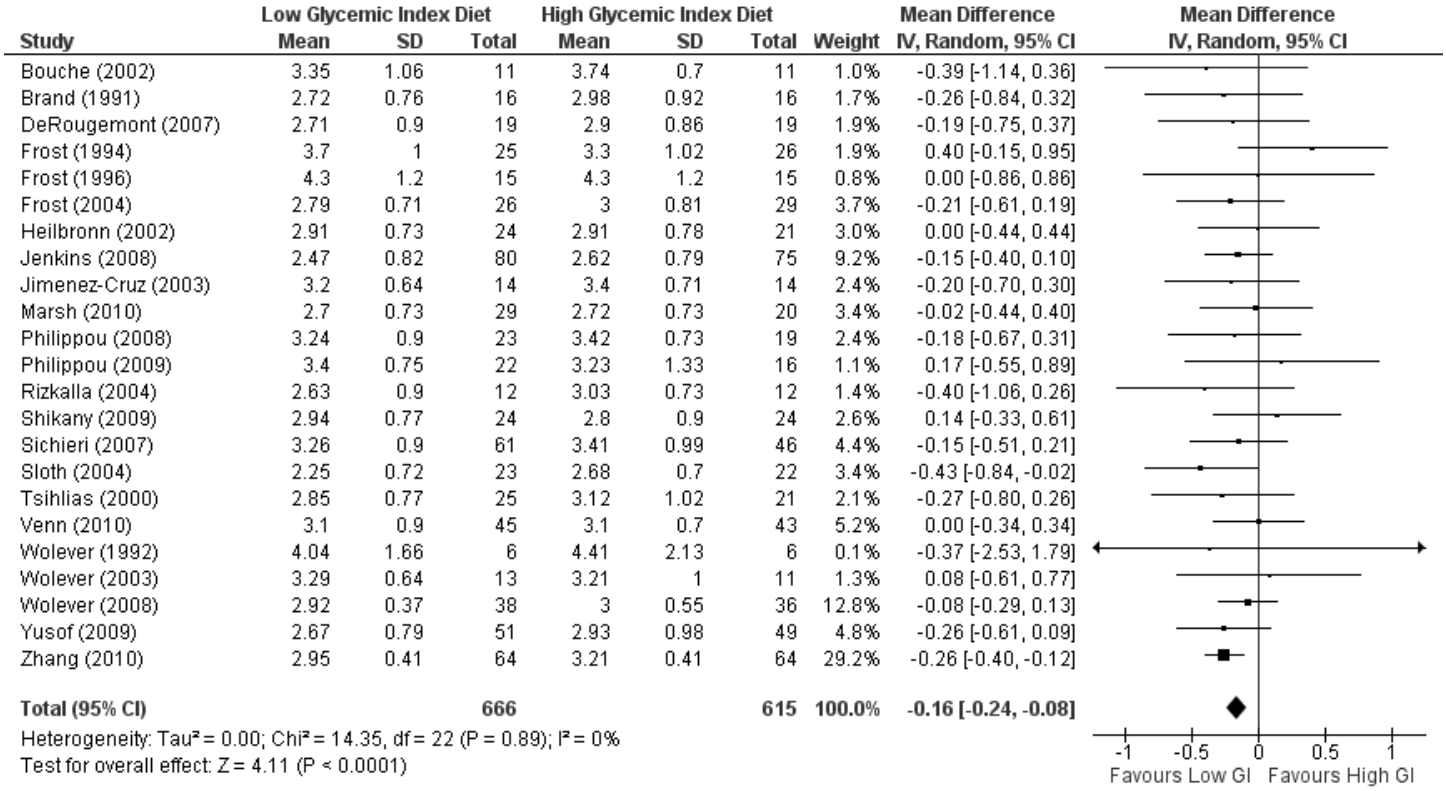

Figure 2 Effects of low and high glycemic index dietary interventions LDL-cholesterol (mmol/l). Analysis includes all studies which assessed LDL-cholesterol. ▪, effect estimate of each study, horizontal line denote the 95%CI; ♦, combined overall effect; CI, confidence interval; GI, glycemic index; random, random effects model; mean difference, mean of difference in post-intervention cholesterol/LDL-C concentrations between low GI and high GI groups; SD, standard deviation.

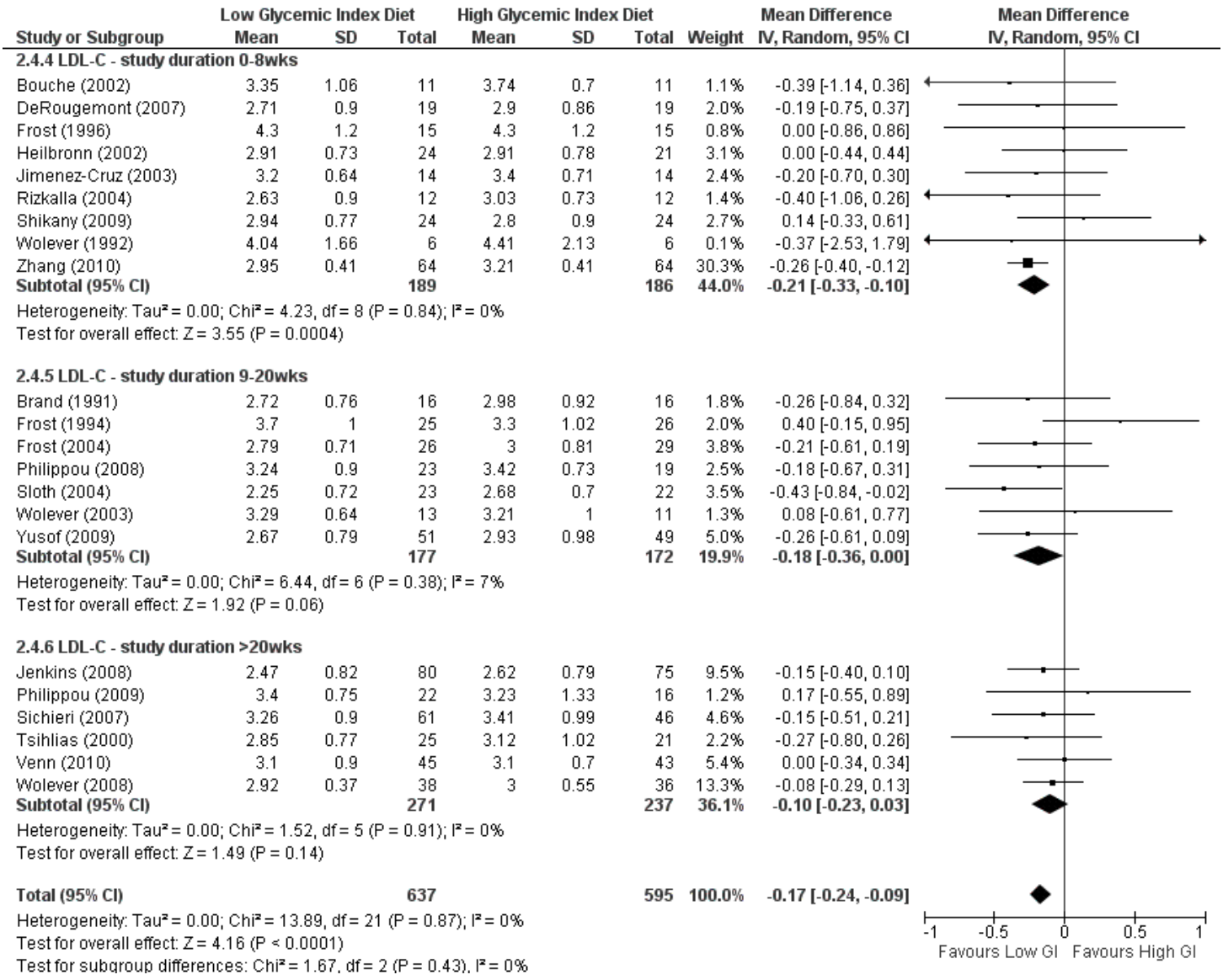

Figure 3 Effects of low and high glycemic index dietary interventions on LDL-cholesterol concentrations (mmol/l). Studies sub-grouped according to tertiles of study duration (Marsh et al., 2010 excluded from analysis due to varying study duration). ▪, effect estimate of each study, horizontal line denote the 95%CI; ♦, combined overall effect; CI, confidence interval; GI, glycemic index; LDL-C, LDL-cholesterol; random, random effects model; mean difference, mean of difference in post-intervention LDL-cholesterol concentrations between low GI and high GI groups; SD, standard deviation.

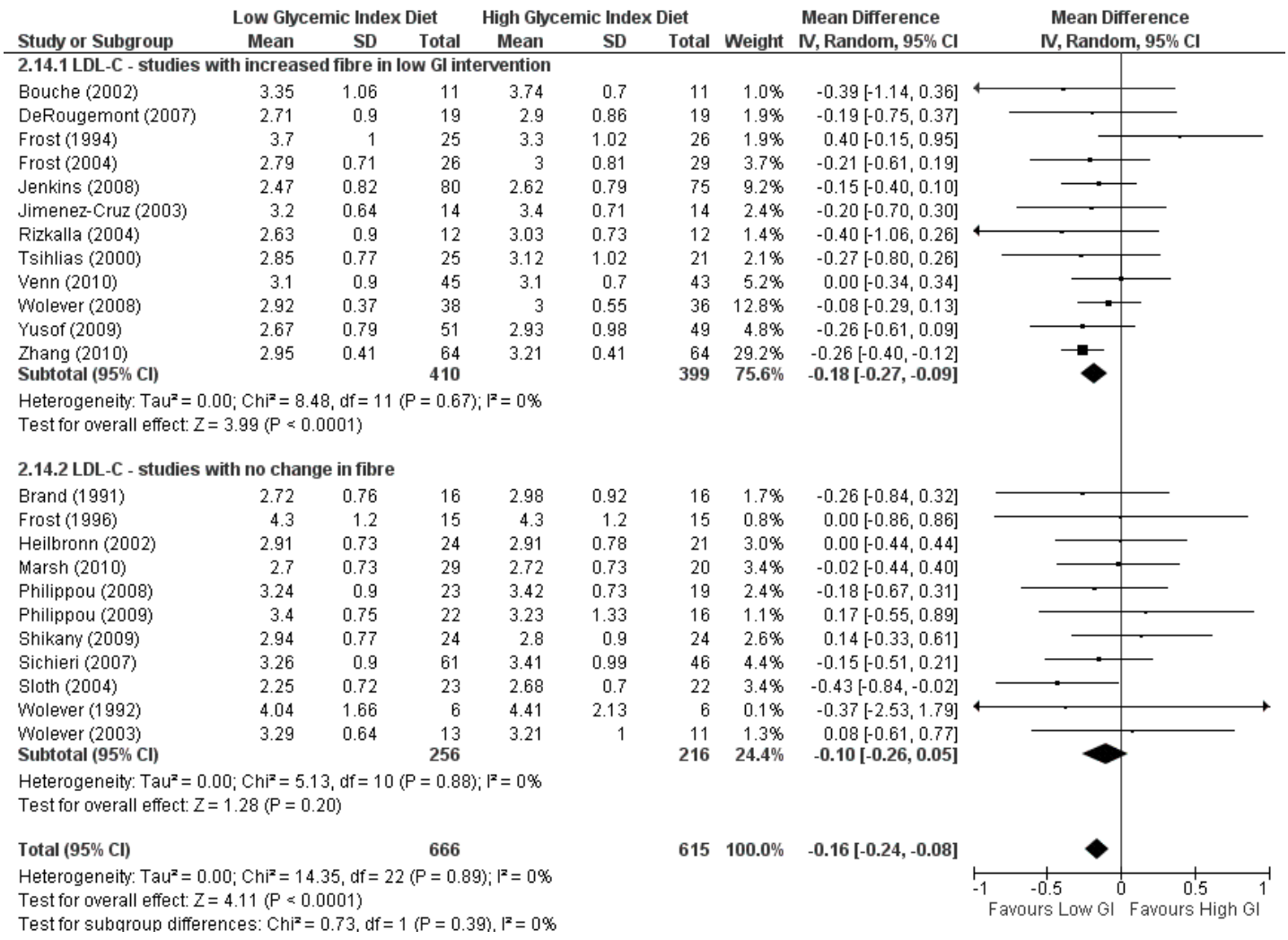

Figure 4 Effects of low and high glycemic index dietary interventions on LDL-cholesterol concentrations (mmol/l). Studies sub-grouped according to whether the low GI intervention included a significant increase in dietary fibre. ▪, effect estimate of each study, horizontal line denote the 95%CI; ♦, combined overall effect; CI, confidence interval; GI, glycemic index; LDL-C, LDL-cholesterol; random, random effects model; mean difference, mean of difference in post-intervention LDL-cholesterol concentrations between low GI and high GI groups; SD, standard deviation.