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Glycaemic index and glycaemic load in relation to blood lipids – 6 years of follow-up in adult Danish men and women

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Abstract

Background: Cross-sectional studies have suggested an association between glycaemic index (GI) or glycaemic load (GL) and serum lipids. However, no prospective studies have been performed.
Objective: To examine whether GI or GL was associated with subsequent changes in serum lipids.
Design: Prospective study with 6 years of follow-up. Overall dietary GI and GL of each participant were assessed from diet history interviews.
Setting: Population-based study.
Subjects: Three hundred and thirty-five healthy men and women aged 35–65 years selected randomly from a larger sample of Danish adults.
Results: In men GI was directly related to changes in total cholesterol (ΔTC), regression coefficient (β) = 0.0044 (95% confidence interval (CI): 0.0008–0.0081) and GL was positively related to changes in low-density lipoprotein cholesterol (ΔLDL), $\beta = 0.1554$ (95% CI: 0.0127–0.2982). Furthermore, the relationship between GL and ΔTC was modified by age, being particularly strong for the younger men ($P = 0.02$). In women the relationship between GI and ΔLDL was modified by age and was stronger for younger rather than older women ($P = 0.01$). A tendency for a similar interaction was seen for GI and ΔTC ($P = 0.09$). Associations between GL and ΔLDL and GL and ΔTC were inverse for women with body mass index $\geq 30\,kg\,m^{-2}$ ($P = 0.03$ and 0.04, respectively).
Conclusions: This is the first study to demonstrate that dietary GI and GL are related to 6-year changes in serum lipid levels. However, associations were weak and generally confined to subgroups.

Keywords
Diet history interview
Cholesterol
Prospective population study
Prevention
Public health

Cardiovascular diseases (CVD), including coronary heart disease (CHD) and cerebrovascular disease, are the most common causes of death in Western societies[1]. There is substantial evidence documenting a relationship between increased serum total cholesterol (TC)/triglycerides (TG) and the risk of developing CVD, where the mediating factor is arteriosclerosis[2,3].

A diet high in saturated fat raises serum lipid levels[4] and low-fat diets are recommended for preventing CVD[5]. However, diets that are low in fat usually are high in carbohydrates, and studies of inpatients in metabolic wards, of short-term outpatients and in different populations[6] have shown that a high intake of carbohydrates is associated with reduced concentrations of high-density lipoprotein cholesterol (HDL). Others have found that increased intake of carbohydrates may even raise fasting TG[6,7].

In this context, Jenkins *et al.* introduced the glycaemic index (GI), a classification index of carbohydrate foods based on their effects on blood glucose response[5]. The GI represents the quality of overall carbohydrate intake, and is a weighted average of the GI values of all carbohydrate-containing foods eaten by a subject over one day. The total glycaemic effect of the diet is calculated as the product of the glycaemic index (GI) and total dietary carbohydrate, and is termed the glycaemic load (GL)[8].

In recent meta-analysis of randomised controlled trials between 1981 and 2003 performed by Opperman *et al.*[9], it was concluded that GI may be used as a tool to enable selection of carbohydrate-containing foods to reduce TC and to improve overall metabolic control of diabetics. On the other hand, later experimental studies published from 2004 onwards have suggested that diets with high GI or GL may raise TC[10], TG[11] and low-density lipoprotein cholesterol (LDL)[12,13] levels among subjects with metabolic disturbances, such as obese, diabetic and cardiac patients. However, results based on healthy subjects[14] are limited. Therefore, the present

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study was conducted with the aim of examining the influence of GI/GL on changes in blood lipids in a healthy population of Danish adults.

All previous observational studies have been cross-sectional and hence have not had the potential for examining the directional relationships between GI/GL and subsequent changes in blood lipids. These cross-sectional studies generally showed that GI/GL is inversely related to HDL and positively related to TG (Table 1 [15–21]). In this first prospective study we chose to observe changes in the lipids HDL, LDL, TC and TG, rather than limit our outcome to HDL and TG, because the previous observational studies, trials and experimental studies have found relationships between GI/GL and all of these four outcomes.

The aim of the present study was therefore to determine the influence of GI and GL on subsequent changes in blood lipids over a 6-year period – i.e. changes in HDL, LDL, TC and TG – among healthy adult men and women.

Materials and methods

Study population and inclusion/exclusion criteria

The present study is based on data from the Danish MONICA surveys (an international study conducted under the auspices of the World Health Organization (WHO) to monitor trends in and determinants of mortality from CVD)[22]. A random sample of 30-, 40-, 50- and 60-year-old men and women ($n = 4807$) was drawn from the Central Personal Register of citizens living in the western part of Copenhagen County in 1982. Subjects not born in Denmark were excluded ($n = 226$). The remaining 4581 subjects were found to be reasonably representative of the total Danish population with respect to sex, age, educational level, occupation and housing[23]. The response rate was 79%, and thus 3608 subjects participated in a health examination. In December 1987 to November 1988, all the participants from 1982 who were active were re-invited to a second health examination and 2987 participated (83%). A random subset of these, 552 subjects, was asked to give a diet history interview. In total 493 (89%) agreed to take part in this diet study. In 1993 to 1994 a second follow-up examination was conducted[24]. Subjects with self-reported cancer, diabetes or CHD, and participants who took medication or were prescribed a strict diet as treatment for raised serum lipid levels, were excluded. The project was approved by the Ethics Committee for Copenhagen County, and is in accordance with the Helsinki II Declaration on human rights. Of the 493 subjects who agreed to take part in the diet study, 64 males and 50 females were excluded because of incomplete data. Furthermore, 44 unhealthy subjects were excluded. Analyses were based on the 335 participants with complete data – 172 males and 163 females.

Table 1 Cross-sectional studies (1999–2005) investigating the relationships between glycaemic index (GI) and glycaemic load (GL) and lipid metabolism in healthy, overweight, diabetic and hyperlipidaemic subjects

Reference	Population and/or mean BMI	Mean age or age range (years)	Number of subjects	Lipids investigated				Comment (determinant)
Frost *et al.* (1999)[15]	25 kg m^{-2}	40	699 M, 721 F	LDL	−HDL	TC		GI as quantitative variable
Van Dam *et al.* (2000)[16]	26 kg m^{-2}	71	394 M		HDL	TC		Quintiles of GI
Buyken *et al.* (2001)[17]	Type 1 diabetics/27 kg m^{-2}	33	2708 HDL, 2746 TC, 1851 LDL, 1851 TG (M + F)		HDL		TG	Quintiles of GI
Ford and Liu (2001)[18]	27 kg m^{-2}	20	6825 M, 7082 F		−HDL			Quintiles of GL
Liu *et al.* (2001)[19]	Postmenopausal women/> 26 kg m^{-2}	43–69	185 F 95 F		−HDL		+TG	Quintiles of GL
					HDL		+TG	Quintiles of GI
McKeown *et al.* (2004)[20]	27 kg m^{-2}	54	1290 M		HDL		TG	Quintiles of GL
			1544 F		HDL		+TG	Quintiles of GI
Slyper *et al.* (2005)[21]	Hyperlipidaemics	11–25	32 (M + F)		−HDL			GL as quantitative variable

BMI – body mass index; LDL – low-density lipoprotein cholesterol; HDL – high-density lipoprotein cholesterol; TC – total cholesterol; TG, triglycerides; M – males; F – females; + indicates a significant positive relationship; − indicates a significant inverse relationship.

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Diet

The same trained dietitian interviewed all subjects about their diet in 1987/88 using a diet history interview. Average daily intakes were calculated from responses describing the previous month. Data on meal patterns, dishes and food items were obtained with a pre-coded interview form. Quantities were assessed with food models, series of photographs, cups and household measures. Calculations of nutrients were carried out with the DANKOST program, which is derived from the Danish food composition tables[25]. Information about cooking and frequency was also collected.

GI and GL were determined for foods reported in the diet history interview[26]. The GI values of the individual foods included in the calculations of GI and GL were found in the 'International table of glycemic index and glycemic load values: 2002'[27]. The overall GI for each participant was calculated by dividing the dietary GL (the numerator in the formula below) by the total amount of carbohydrate consumed[18,19]:

$$\text{Overall GI} = \sum(M_i \cdot CHO_i \cdot GI_i)/\sum(CHO_i \cdot M_i),$$

where M_i is the amount of the food i in grams per day, CHO_i is the amount of available or glycaemic carbohydrate per gram of food i and GI_i is the glycaemic index for each food i.

GI values may also depend upon differences in methodology and within-individual variations[27–29]. To minimise such non-food-related variations, the GI values used for estimating overall GI and GL in the present study were based on mean GI values from different studies that had measured the GI of similar foods. The following criteria had to be met by the GI values to be included in the calculation of the overall GI and GL:

- The GI value was measured over 2 h if subjects were healthy or over 3 h if subjects were type I or type II diabetic[28–30].
- The reference food originally used to measure the GI value was either glucose or white bread (when glucose was the reference food, the GI value was multiplied by 1.43 to obtain the GI value with white bread as the reference food).
- The reference food and test food portions used for measurement generally both contained (with some exceptions) 50 g carbohydrate[30].
- The GI value was (with few exceptions) measured on more than five subjects[5].

Most vegetables, apart from root vegetables and legumes, were not included in the calculations of overall GI and GL, as their GI values had not been measured. However, most of the vegetables not included in the calculations of overall GI and GL contain an amount of carbohydrates that is too small to affect overall GI and GL appreciably, whether they have high or low GI[31].

Blood lipids

Blood samples were drawn after a 12 h overnight fast. HDL, TC and TG were measured in serum using commercial enzymatic methods (Boehringer Mannheim GmbH, Mannheim, Germany). LDL concentrations (mmol l^{-1}) were calculated from TG, if the TG level was $< 4.5\ \text{mmol l}^{-1}$, using the Friedewald equation[32].

Anthropometry

All anthropometric measurements were made in accordance with WHO standards[5]. Height was measured to the nearest 0.5 cm without shoes. Body weight was measured to the nearest 0.1 kg using a SECA scale, with subjects wearing light indoor clothes only. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in metres.

Questionnaire information (1987/88)

All participants answered questions about leisure-time physical activity, which was classified as: (1) sitting most of the time; (2) light activity at least 4 h per week; (3) active in sport at least 3 h per week or heavy work during leisure; and (4) active in competitive sport several times a week. For the present analysis we grouped subjects as sedentary (comprising group 1) or active (comprising groups 2, 3 and 4). The subjects were asked whether they were current smokers (light, medium, heavy), ex-smokers or had ever smoked. We grouped subjects as non-smokers (non-smokers and ex-smokers) or current smokers. Furthermore, participants were asked about their educational level (<7, 7–12 and >12 years of schooling).

Statistical analysis

All analyses were performed separately for men and women. Associations between overall GI/GL and 6-year changes in blood lipids were analysed using multiple linear regression analysis (SAS version 8.2; SAS Institute, Cary NC, USA). Differences were considered significant at $P < 0.05$. Both overall GI/GL and the lipid changes were treated as continuous variables. We applied logarithmic transformation to lipid levels and GL values to make residuals homoscedastic, and to better approximate normality. In the following, measures of lipids and GL are referred to without mentioning the logarithmic transformation. Three models were applied.

In the first model, crude associations were studied. The second model included analyses that were adjusted for age and baseline serum lipids, BMI, total energy intake and fat intake as a percentage of total energy – all treated as continuous variables – and smoking habits, level of education and physical activity – all treated as categorical variables. In the third model, confounders were added to model II if they changed the estimate by more than 10% in one gender[33]. The potential confounders included were intakes of protein, carbohydrate and alcohol as a percentage of total energy, coffee (cups), fibre (g),

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added sugar (g), meal frequency and systolic blood pressure (mmHg) – all treated as continuous variables. Fat, protein and carbohydrate as a percentage of total energy were not included in models describing the effects of GL, since these models assume that carbohydrate intake is held constant. Since GL was highly correlated with energy, the residuals from the regression of GL versus energy were used when controlling for this confounder[34].

A standard *F*-test was used to examine if age, BMI and physical activity (sedentary vs. active) modified the associations between overall GI/GL and changes in blood lipids. Product terms between the exposures and the continuous covariates BMI and age were added in turn to the models. In the enlarged models, the associations between exposure and changes in lipid levels depend on BMI (respectively age), and the dependence is given as a linear function of BMI (respectively age).

To study possible differences in food intake between subgroups of participants, food group variables were constructed for vegetables, fruits, milk products, bread & cereals, sweets and soft drinks[35]. It was calculated how much the carbohydrate energy from each food group variable contributed to overall intake of carbohydrate energy. The carbohydrate content of each food item was assessed using the Danish food composition tables[25]. Only food items assigned a GI value were included in a food group variable. It was then possible to compare how much each food group contributed to overall GI in the different subgroups of sex and age. One-way analysis of variance was used to examine correlations between overall GI and food intake.

Power analysis was based on data from a cross-sectional study by Frost *et al.*[15], who investigated the relationship between GI and HDL and demonstrated a significant inverse relationship (0.013) for women. Standard error was 0.0016, choosing the level of significance $\alpha = 5\%$ we obtain a power of 98% for the women in this study regarding HDL. The estimated power is based on weak relationships between GI and HDL; hence the chance of detecting significant differences, provided they exist, for the other variables should be good.

Results

The baseline characteristics of the male and female subjects are given in Table 2. The mean age was 49 years for both sexes, and the mean BMI was 26 kg m^{-2} for men and 24 kg m^{-2} for women.

Glycaemic index

In men, the linear regression analyses showed significant positive relationships between overall GI and ΔTC in both adjusted models (II and III) (Table 3); however, a significant relationship was not observed in the crude model (I). The predictive value of model III did not differ much from that of model II, but the estimate in model III was 100% higher compared with the crude model (I).

Table 2 Baseline characteristics of male and female subjects after exclusion of unhealthy subjects

Variable	Men	Women
n	172	163
Glycaemic index	82 (5)	80 (5)
Glycaemic load (units)†	167 (6)	128 (5)
Age (years)	49 (11)	49 (11)
BMI (kg m^{-2})	26 (3)	24 (4)
Systolic blood pressure (mmHg)	127 (16)	123 (16)
Baseline TC (mmol l^{-1})	6.05 (1.11)	5.96 (1.12)
Baseline LDL (mmol l^{-1})	4.1 (1.02)	3.75 (1.05)
Baseline HDL (mmol l^{-1})	1.33 (0.34)	1.69 (0.49)
Baseline TG (mmol l^{-1})	1.33 (0.63)	1.11 (0.55)
Current smoker (%)	50	39
Sedentary at leisure time (%)	22	22
Schooling 0–7 years (%)	29	33
Schooling >12 years (%)	25	11
Energy intake (MJ)	10.3 (2.7)	7.3 (1.8)
Fibre intake (g)	25 (10)	20 (7)
% Energy from carbohydrate	39 (7)	42 (6)
% Energy from protein	14 (2)	15 (3)
% Energy from fat	39 (6)	40 (6)
% Energy from alcohol	6 (6)	4 (5)
Added sugar (g)	36 (32)	27 (29)
Coffee (cups)	6 (4)	5 (4)

BMI, body mass index; TC – total cholesterol; LDL – low-density lipoprotein cholesterol; HDL – high-density lipoprotein cholesterol; TG, triglycerides.
Values are means (standard deviation) unless stated otherwise.
† Each unit of glycaemic load resembles 1 g available carbohydrate from white bread.

In women, there was no relationship between overall GI and ΔTC, and overall GI was not found to be associated with changes in the other lipids. The relationship between overall GI and ΔLDL differed by age category in women ($P = 0.01$ for interaction) (Table 4), and was significant and positive for the 35-year-old women only. However, there was a tendency for a similar interaction between overall GI and ΔTC ($P = 0.09$ for interaction) (data not shown).

Physical activity (sedentary vs. active) did not seem to modify the relationship between overall GI and changes in lipids in men or women ($P > 0.11$) (data not shown).

Glycaemic load

In men the linear regression analysis showed a significant positive relationship between GL and ΔLDL in the fully adjusted model (III) (Table 5), but not in models II and I.

Overall, GL was not associated with change in the other lipids in men and women. However, in men, the relationship between GL and ΔTC differed by age category ($P = 0.05$ for interaction), being strongest and positive in the youngest men ($P = 0.02$) and insignificant in men >35 years old (Table 6).

In women (Table 7), associations between GL and ΔLDL, and between GL and ΔTC, differed by BMI, and in both relationships the associations were inverse ($P = 0.03$ and 0.04, respectively) for the more obese. Further

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Table 3 Results of raw and multiple linear regression analyses of serum lipids. Estimated regression coefficients (β) in associations between baseline GI and ΔTC, ΔLDL, ΔHDL and ΔTG (1987/88 to 1993/94), in 172 men and 163 women

	Men			Women		
	β			β		
	Model I†	Model II‡	Model III	Model I†	Model II‡	Model III
GI → ΔTC§	0.0018	0.0035*	0.0044*	−0.0025	−0.0009	0.0009
GI → ΔLDL¶	0.0012	0.0033	0.0038	−0.0032	−0.0012	0.0005
GI → ΔTG‖	0.0030	0.0028	0.0055	−0.0006	0.0018	0.0030
GI → ΔHDL††	0.0022	0.0034	0.0038	−0.0020	−0.0014	0.0007

GI – glycaemic index; Δ – change in; TC – total cholesterol; LDL – low-density lipoprotein cholesterol; HDL – high-density lipoprotein cholesterol; TG, triglycerides.
* $P < 0.05$.
† Crude.
‡ Adjusted for age, education, body mass index (BMI), smoking status, physical activity, serum lipids (TC, LDL, TG and HDL, respectively) at baseline, total energy intake and intake of fat.
§ In model III adjusted for age, education, BMI, smoking status, physical activity, serum TC at baseline, alcohol, added sugar, total energy intake and intakes of fat, carbohydrate and protein.
¶ In model III adjusted for age, education, BMI, smoking status, physical activity, serum LDL at baseline, meal frequency, added sugar, fibre, systolic blood pressure (SBP), coffee, total energy intake and intakes of fat, carbohydrate and protein.
‖ In model III adjusted for age, education, BMI, smoking status, physical activity, serum TG at baseline, coffee, added sugar, fibre, total energy intake and intakes of fat, carbohydrate and protein.
†† In model III adjusted for age, education, BMI, smoking status, physical activity, serum HDL at baseline, added sugar, fibre, SBP, coffee, meal frequency, total energy intake and intakes of fat carbohydrate and protein.

adjustment for body weight change at follow-up gave virtually similar results (data not shown).

Physical activity (sedentary vs. active) did not modify the relationship between GL and change in lipids in men or women (all $P > 0.22$) (data not shown).

Discussion

This is the first prospective study to examine whether GI and GL are associated with subsequent changes in serum lipids. Our results suggest that associations are present but are weak, gender-specific and occur particularly in subgroups; whereas main findings of overall effects are virtually absent. Our data showed positive relationships, particularly for GI and change in TC and GL and change in LDL for men ($P < 0.05$). In contrast, no overall relationships were found for women, and neither GI nor GL seemed to influence change in HDL or change in TG.

In the present study, age was identified as a modifying variable on the relationships between GI and change in LDL for women, with a tendency for stronger positive associations among the younger. Regarding GL, associations were present particularly for the young men (changes in TC) and the more obese women (changes in TC and LDL). However, in women, the associations between GL and these lipids were inverse. The finding of inverse associations between GL and change in TC or GL and change in LDL for women with BMI $\geq 30\,kg\,m^{-2}$ was unexpected and suggests that dietary effects on serum cholesterol may, in fact, behave differentially among those with metabolic disturbances, e.g. obese versus non-obese.

A dilution effect may explain the generally stronger association among the younger rather than the older subjects. Rothman[36] has argued that if risk factors are few and rare (as in young subjects) rather than many and common (as in elderly subjects), the strength of an association will decrease in the elderly. Another explanation for the age differences may be differences in the food intake that determines the GI of young and older subjects. For instance, the older women had a higher

Table 4 Subgroup analysis. Regression coefficients (β) and 95% confidence intervals (CI) in associations between baseline GI × age and ΔLDL (1987/88 to 1993/94), in 172 men and 163 women

	Men		Women	
Model†	β	95% CI	β	95% CI
GI × age → ΔLDL	0.0001	−0.0003, 0.0005	−0.0006	−0.0010, −0.0001
35 years	0.0026	−0.0051, 0.0104	0.0091	0.0005, 0.0176
45 years	0.0034	−0.0018, 0.0087	0.0033	−0.0023, 0.0090
55 years	0.0042	−0.0011, 0.0096	−0.0024	−0.0080, 0.0033
65 years	0.0050	−0.0028, 0.0128	−0.0080	−0.0165, 0.0004

GI – glycaemic index; Δ – change in; LDL – low-density lipoprotein cholesterol.
† Adjusted for age, education, body mass index, smoking status, physical activity, serum LDL at baseline, added sugar, fibre, systolic blood pressure, coffee, total energy intake and intakes of fat, carbohydrate and protein.

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Table 5 Results of raw and multiple linear regression analyses of serum lipids. Estimated regression coefficients (β) in associations between baseline GL and ΔTC, ΔLDL, ΔHDL and ΔTG (1987/88 to1993/94), in 172 men and 163 women

	Men			Women		
	β			β		
	Model I†	Model II‡	Model III	Model I†	Model II‡	Model III
GL → ΔTC§	0.0282	0.0114	0.0729	−0.0860	−0.0835	−0.0645
GL → ΔLDL¶	0.0755	0.0836	0.1554*	−0.1454	−0.0915	−0.0915
GL → ΔTG‖	−0.0714	−0.2040	−0.1809	−0.1345	−0.1134	−0.0840
GL → ΔHDL††	−0.0343	−0.0120	0.0131	0.0041	−0.0514	−0.0433

GL – glycaemic load; Δ – change in; TC – total cholesterol; LDL – low-density lipoprotein cholesterol; HDL – high-density lipoprotein cholesterol; TG, triglycerides.
* $P < 0.05$.
† Crude.
‡ Adjusted for age, education, body mass index (BMI), smoking status, physical activity, serum lipids (TC, LDL, TG and HDL respectively) at baseline, total energy intake and alcohol.
§ In model III adjusted for age, education, BMI, smoking status, physical activity, TC at baseline, alcohol, added sugar, total energy intake and fibre.
¶ In model III adjusted for age, education, BMI, smoking status, physical activity, LDL at baseline, alcohol, added sugar, fibre, systolic blood pressure (SBP), total energy intake and coffee.
‖ In model III adjusted for age, education, BMI, smoking status, physical activity, TG at baseline, alcohol, added sugar, fibre, total energy intake and meal frequency.
†† In model III adjusted for age, education, BMI, smoking status, physical activity, HDL at baseline, alcohol, added sugar, fibre, SBP, coffee, total energy intake and meal frequency.

Table 6 Subgroup analysis. Regression coefficients (β) and 95% confidence intervals (CI) in associations between baseline GL × age and ΔTC (1987/88 to 1993/94), in 172 men and 163 women

	Men		Women	
Model†	β	95% CI	β	95% CI
GL × age → ΔTC	−0.0071	−0.0140, −0.0001	−0.0032	−0.0117, 0.0052
35 years	0.1636	0.0232, 0.3040	−0.0264	−0.1748, 0.1221
45 years	0.0927	−0.0175, 0.2030	−0.0587	−0.1699, 0.0526
55 years	0.0219	−0.0976, 0.1414	−0.0909	−0.2209, 0.0390
65 years	−0.0489	−0.2104, 0.1126	−0.1232	−0.3119, 0.0655

GL – glycaemic load; Δ – change in; TC – total cholesterol.
† Adjusted for age, education, body mass index, smoking status, physical activity, TC at baseline, alcohol, added sugar, total energy intake and fibre.

Table 7 Subgroup analysis. Regression coefficients (β) and 95% confidence intervals (CI) in associations between baseline GL × BMI and ΔTC and baseline GL × BMI and ΔLDL (1987/88 to 1993/94), in 163 women

	Women				
Model†	β	95% CI	Model‡	β	95% CI
GL × BMI → ΔTC	−0.0164	−0.0316, −0.010	GL × BMI → ΔLDL§	−0.0243	−0.0463, −0.0023
BMI = 20 kg m^{-2}	0.0264	−0.1118, 0.1647	BMI = 20 kg m^{-2}	0.0467	−0.1560, 0.2494
BMI = 25 kg m^{-2}	−0.0554	−0.1646, 0.0537	BMI = 25 kg m^{-2}	−0.0750	−0.1809, 0.0853
BMI = 30 kg m^{-2}	−0.1374	−0.2658, −0.0089	BMI = 30 kg m^{-2}	−0.1966	−0.3836, −0.0100

GL – glycaemic load; BMI – body mass index; Δ – change in; TC – total cholesterol; LDL – low-density lipoprotein cholesterol.
† Adjusted for age, education, BMI, smoking status, physical activity, TC at baseline, alcohol, added sugar, total energy intake and fibre.
‡ Adjusted for age, education, BMI, smoking status, physical activity, LDL at baseline, alcohol, added sugar, fibre, systolic blood pressure, total energy intake and coffee.
§ Tables examples of the BMI-modified association between GL and ΔLDL – point-wise estimates of the association between GL and change in LDL level for BMI = 20, 25 and 30 kg m^{-2}.

intake of fruit and vegetables in spite of a habitually high-GI diet. This may have offered some protection in relation to the subsequent lipid changes.

Differences in the food intake patterns that determine GI could also offer an explanation for the different findings among men and women. Indeed, in men, higher intakes of soft drinks, potatoes and cereals were associated with high GI, whereas women with high GI consumed a higher intake of fruit and vegetables. Similarly, different dietary practices determined GL in men and women;

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e.g. higher GL for men was determined by a higher intake of carbohydrates, whereas a higher GI determined higher GL for women. This could also account for some of the inconsistencies between the results of the analyses with GI and GL. Additionally, it should be mentioned that others have also found different results for the effect of GI and GL on changes in blood lipids[37].

To date, there are no other prospective studies that have examined associations between GI, GL and changes in lipids; hence we cannot compare our findings with other results from the literature. Findings from some cross-sectional studies have demonstrated that diets high in GI or GL seem negatively related to HDL for both normal and overweight subjects[18,15,19,21] (Table 1), and one study reported a positive relationship between GL and TG for overweight postmenopausal women[19]. Our data do not support these findings and hence our results emphasise that it may be premature to make recommendations from cross-sectional data about dietary GI and GL in relation to serum lipids among healthy subjects. In Australia, labelling GI of foods is on the agenda already, which may be helpful for subjects with diabetes but would seem inappropriate for healthy people.

Numerous intervention studies have compared effects of high- and low-GI or -GL diets on changes in lipids, and found that the overall GI of the diet particularly affects TC, LDL and TG. However, the participants in these studies often had metabolic disturbances, such as diabetics, obesity or hyperlipidaemia[12–14,38–50]. Furthermore, these studies were all short-term in nature, and hence their results may not easily be compared with ours from a general healthy population, even if it appears that the findings in the present study were indeed consistent with the data from metabolic studies of diabetics, hyperlipidaemics and overweight subjects[12,13,38–41,44–48]. The strengths of the associations between GI and change in TC, and GL and change in LDL, were weaker in the present study than in the mentioned intervention studies. However, the difference may be explained by: (1) the metabolic differences between the healthy and disturbed subgroups; (2) the difference between groups of high- and low-GI diets in the intervention studies were 20–40 GI units[12,38,41–45,48,51], whereas we were studying differences of approximately 14 units; or (3) the fact that the intervention studies often replaced high-GI foods with low-GI foods, such as wholegrain bread and pulses, whereas in the present study low GI was not associated with these kinds of foods because the GI of the subject was based on the habitual diet.

These explanations may also explain why previous cross-sectional[19] and intervention studies[42,44–46,48,49] found that high GI or GL influences TG levels.

A few limitations should be noted. First, bias in dietary reporting of energy and protein intakes has previously been assessed for the cohort[52,53] by comparing reported intake with intake estimated from 24-hour nitrogen output and estimated 24-hour energy expenditure. This analysis showed that total energy was underreported more than energy from protein, indicating that energy from fat and/or carbohydrate must have been underreported, too. Furthermore, it was demonstrated that particularly the obese seem to underreport their intake of foods high in energy from sugar and fat. The consequence of such a reporting bias may be the appearance of spurious, rather than attenuated results[54]. Indeed, the puzzling inverse associations observed for the overweight women between GL and change in either LDL or TC in the present study could be a consequence of such bias.

Second, underestimation of total energy intake is strongly dependent on dietary methodology. In this regard, Black *et al.*[55] have shown that, compared to the 24-hour diet recall or diet records, the diet history interview – as used in the present study – gives the most valid total energy estimates, and hence may be the most valid dietary assessment method. Based on the Danish food composition tables we calculate that on average 95% (standard deviation: 3%) of the total carbohydrate intake was covered when coding dietary GI from the 'International table of glycemic index and glycemic load values: 2002'[27]. On the other hand, since the data used in the present study were collected to assess macronutrient intake, rather than to assess GI and GL, this may have added to the diet variability.

Third, it has been questioned whether GI tables can be used to predict the GI of mixed meals[56]. Recently Flint *et al.*[56] showed that the GI calculated by table values did not seem to be in agreement with the measured GI, and furthermore that the GI of mixed meals was more strongly correlated with both the fat and protein content of the diet than with carbohydrate content alone. Such lack of agreement would tend to attenuate our results.

In conclusion, this is the first prospective study examining whether dietary GI and GL influence changes in serum lipids among healthy adult men and women. Our findings show that GI/GL seems to influence change in both TC and LDL. However, associations were weak, not consistent for men and women, and generally confined to subgroups. Hence, our results do not provide sufficient support for using GI as a tool for reducing the level of blood lipids in general. The results from the present study would suggest that it is premature to educate the general public about how to understand and use the GI. Future prospective studies or primary intervention studies of healthy subjects are needed.

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