Special Article

Should glycemic index and glycemic load be considered in dietary recommendations?

Helle Hare-Bruun, Birgit M Nielsen, Katrine Grau, Anne L Oxlund, and Berit L Heitmann

High glycemic index (GI) and glycemic load (GL) have been proposed to be associated with increased risk of lifestyle diseases. Since protein intake varies little in humans, adherence to the common recommendation to reduce fat intake probably leads to increases in carbohydrate intake, which emphasizes the need to investigate the effects of carbohydrate on diet-related conditions and diseases. This review examines the epidemiological literature linking GI and GL to heart disease, insulin sensitivity, type 2 diabetes, dyslipidemia, and obesity among initially healthy people. The evidence for associations between GI and particularly GL and health among free-living populations is mixed. Only the positive association between GI and development of type 2 diabetes was consistent across cross-sectional and longitudinal studies for both sexes. Low GI/GL may protect against heart disease in women, and cross-sectional studies indicate low GI/GL may reduce high-density-lipoprotein cholesterol and triacylglycerol levels in both sexes. Based on the evidence found in this review, it seems premature to include GI/GL in dietary recommendations.

INTRODUCTION

The official nutritional recommendations in most high-income countries advise a reduced intake of dietary fat.[1] Since protein intake tends to vary very little in humans, adherence to these recommendations could lead to an increase in the intake of carbohydrate-rich foods. This highlights the importance of exploring the effects of different types of carbohydrate on diet-related conditions and diseases.

Since the concept of the glycemic index (GI) was introduced by Jenkins et al.[2] in 1981, GI has been related to a variety of conditions and diseases such as abnormal blood lipid profiles, heart disease, obesity, type 2 diabetes,[3] and even age-related vision loss.[4] The GI describes the ability of specific carbohydrate-rich foods to increase the concentration of glucose in the blood. The GI of a food is calculated as the incremental area under the blood glucose response curve for the food relative to the incremental area under the blood glucose response curve for a reference food (glucose or white bread is recommended), which is set to be 100. The glycemic load (GL) describes the overall glycemic effect of a specified amount of a food item. It is calculated as the product of the GI and the carbohydrate amount (in grams) of the food item divided by 100.[3]

It has been proposed that eating high-GI carbohydrates is associated with increased risk of cardiovascular disease (CVD), type 2 diabetes, and obesity because of postprandial hyperglycemia and hyperinsulinemia related to eating high-GI carbohydrates.[3] Postprandial hyperglycemia may activate inflammation and lead to oxidation of membrane lipids, proteins, lipoproteins, and DNA. In addition, hyperinsulinemia may increase the risk of cardiovascular disease by affecting blood pressure, serum lipids, coagulation factors, inflammatory mediators, and endothelial function, even in the absence of insulin resistance syndrome.[3] Hyperinsulinemia may also, over time, lead to insulin resistance via increases in the blood glucose concentration[2] and thereby also increase the risk of type 2 diabetes and obesity.[3,5–8]

Affiliations: *H Hare-Bruun*, *BM Nielsen*, *K Grau*, *AL Oxlund*, and *BL Heitmann* are with the Research Unit for Dietary Studies, Institute of Preventive Medicine, Copenhagen University Hospital, Centre for Health and Society, DK 1357 Copenhagen K, Denmark.

Correspondence: *H Hare-Bruun*, Research Unit for Dietary Studies, Institute of Preventive Medicine, Centre for Health and Society, Øster Søgade 18, DK-1357 Copenhagen, Denmark. E-mail: hh2@ipm.regionh.dk, Phone: +45-3338-3777, Fax: +45-3332-4240.

Key words: blood lipids, carbohydrates, heart disease, obesity, type 2 diabetes

doi:10.1111/j.1753-4887.2008.00108.x

The relationships between GI/GL and lifestyle diseases and conditions has been studied in clinical intervention studies, observational studies, and even primary prevention studies. Several reviews and meta-analyses[9–14] of the evidence from intervention studies have been published previously. A positive effect of low GI/GL diets on weight loss in obese subjects was observed in the Cochrane Review by Thomas et al.,[13] and Brand-Miller et al.[9] found positive effects of low GI on fructosamine and hemoglobin A1c (HbA1c) in subjects with type 2 diabetes. Four other meta-analyses all found small protective effects of low GI on some or all measures of insulin sensitivity and blood lipids.[10–12,14] However, results from studies performed on subjects with diabetes, hyperlipidemia, or obesity and a consequently disturbed metabolism have limited relevance for primary prevention and general public health recommendations. In contrast to randomized controlled trials, which are primarily used to study shorter-term clinical effects, as they are often very demanding on the study subjects in terms of daily life restrictions, prospective observational studies are able to assess the long-term changes in disease endpoints such as heart disease, type 2 diabetes, or obesity related to differences in habitual dietary practices and other lifestyle factors. One recent meta-analysis examined the association between GI and GL and chronic disease risk in prospective cohort studies and found significantly increased risks of type 2 diabetes, heart disease, colorectal cancer, endometrial cancer, and gallbladder disease on high GI and/or GL diets compared to low GI/GL diets.[15] However, risk factors for chronic disease such as measures of insulin sensitivity, dyslipidemia, and obesity were not considered.

The aim of the present review is to establish whether there is sufficient evidence to support a general recommendation for lowering dietary GI and/or GL at this point in time and to evaluate the long-term effects of GI and GL on the development of lifestyle disease. The review evaluates the available evidence from observational studies on the effect of GI and GL in the development and prevention of lifestyle diseases and obesity among initially healthy subjects. The effects of GI and GL among clinical populations with disturbed metabolism are not included.

SEARCH METHODOLOGY

Observational studies were identified through a literature search in PubMed. The search terms glyc(a)emic index or glyc(a)emic load and epidemiolog* were combined with heart disease, coronary heart disease (CHD), diabetes, fasting insulin, HbA1c, homeostasis model assessment of insulin resistance (HOMA-IR), insulin sensitivity, serum insulin, acute insulin response, insulin disposition index, blood lipid*, high-density-lipoprotein (HDL), low-density-lipoprotein (LDL), triacylglycerol (TAG), triglyceride*, cholesterol, total cholesterol (TC), obesity, body weight, BMI, waist circumference, hip circumference, body fat, body composition, and fat distribution, respectively. Studies on humans published in English before March 2008 were considered. Reference lists in identified papers were cross-checked manually to ensure that all relevant papers were identified. Studies presenting an adjusted cross-sectional or longitudinal association, significant or non-significant, between either GI or GL and at least one of the outcomes in a healthy population were included. Only studies using a measure of the habitual dietary GI or GL were included.

HEART DISEASE

Six observational studies on the effect of GI and/or GL on the risk of heart disease were identified[16–21] (Table 1). Two studies conducted in male populations found no association between either GI or GL and heart disease.[16,17] Among women, both GI and GL were positively associated with the risk of heart disease. Two of the three studies identified were based on data from the Nurses' Health Study (NHS)[18,21] and reported similar risk estimates for both GI (relative risk [RR] 1.31, 95% confidence interval [CI] 1.02–1.68[18] and RR 1.19, 95% CI 0.91–1.55[21]) and GL (RR 1.98, 95% CI 1.41–2.77[18] and RR 1.90, 95% CI 1.15–3.15[21]) in the fifth compared to the first quintile of GL. The major differences between the two studies were the number of participants and the length of follow-up. Liu et al.[18] included 75,521 women with a follow-up of 10 years, whereas Halton et al.[21] included 82,802 women and followed them for 20 years. The results by Beulens et al.[19] support these results with a higher risk of CVD in the 4th compared to the 1st quartile of GI (hazards ratio [HR] 1.33, 95% CI 1.07–1.67) and a higher risk of CVD in the 4th compared to the 1st quartile of GL (HR 1.47, 95% CI 1.04–2.09) among 15,714 women in the Dutch EPIC-cohort.[19]

Tavani et al.[20] observed no association between either GI or GL and the risk of acute myocardial infarction (AMI) in a case-control design including non-diabetic men and women; stratification by sex did not alter any conclusions. However, in subjects older than 60 years of age, the risk of AMI was significantly increased in the second (RR 1.72, 95% CI 1.01–2.94) and third tertile of GI (RR 1.81, 95% CI 1.07–3.07), and in subjects with a BMI above 25, the risk of AMI was increased in the third tertile of GI (RR 2.02, 95% CI, 1.21–3.34).

A number of reports claim that diets low in GI or GL may be protective against heart disease.[22–25] However, the results from this review suggest that the effect of GI and GL on risk of heart disease may differ between men and women. In a hospital-based case-control setting includ-

Table 1 **Associations between glycemic index and glycemic load and heart disease in observational studies.**

Reference	Study	Subjects				Outcome	Follow-up	Diet method	Association	Magnitude
		No.	Age (y)†	Sex	Cases					
Glycemic index										
Van Dam et al. (2000)[16]	Zutphen Elderly Study	646	64–84	M	94	CHD	4527 py	DHI	NS (↑)	–
Levitan et al. (2007)[17]	COSM	36246	45–79	M	2959	CVD	6 y	FFQ	NS (↔)	–
Liu et al. (2000)[18]	NHS	75521	38–63	F	761	CHD	729472 py	FFQ	↑**	RR (95% CI) = 1.31 (1.02;1.68) in GI Q5 vs. Q1
Beulens et al. (2007)[19]	Dutch EPIC	15714	49–70	F	799	CVD	141633 py	FFQ	↑*	HR (95% CI) = 1.33 (1.07;1.67) in GI-Qa4 vs. Qa1
Halton et al. (2006)[21]	NHS	82802	30–55	F	1994	CHD	1584042 py	FFQ	NS (↑)	–
Tavani et al. (2003)[20]	–	881	25–79	M + F	433‡	AMI	–	FFQ	NS (↑)	–
Glycemic load										
Van Dam et al. (2000)[16]	Zutphen Elderly Study	646	64–84	M	94	CHD	4527 py	DHI	NS (↔)	–
Levitan et al. (2007)[17]	COSM	36246	45–79	M	2959	CVD	6 y	FFQ	NS (↔)	–
Liu et al. (2000)[18]	NHS	75521	38–63	F	761	CHD	729472 py	FFQ	↑***	RR (95% CI) = 1.98 (1.41;2.77) in GL-Q5 vs. Q1
Beulens et al. (2007)[19]	Dutch EPIC	15714	49–70	F	799	CVD	141633 py	FFQ	↑*	HR (95% CI) = 1.47 (1.04;2.09) in GL-Qa4 vs. Qa1
Halton et al. (2006) [21]	NHS	82802	30–55	F	1994	CHD	1584042 py	FFQ	↑**	RR (95% CI) = 1.90 (1.15;3.15) in GL-Q5 vs. Q1
Tavani et al. (2003)[20]	–	881	25–79	M + F	433‡	AMI	–	FFQ	NS (↔)	–

† Age at baseline (range).
‡ Case-control study.
* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.
Abbreviations: AMI, acute myocardial infarction; CHD, coronary heart disease; CI, confidence interval; COSM, Cohort of Swedish Men; CVD, cardiovascular disease; DHI; dietary history interview; EPIC, European Prospective Investigation into Cancer and Nutrition; F, female; FFQ, food frequency questionnaire; GI, glycemic index; GL, glycemic load; HR, hazard ratio; M, male; NHS, Nurses' Health Study; NS, no significant association; py, person years; Q, quintile; Qa, quartile; RR, relative risk; y, years; ↑, positive association.

ing men and women, Tavani et al.[20] found no significant association between either dietary GI or GL and risk of AMI. Furthermore, in prospective cohort studies no associations between GI or GL and risk of heart disease were observed in male populations.[16,17] Among women, however, there seems to be a protective effect of both low dietary GI[18,19] with risk estimates around 1.3, and dietary GL[18,19,21] with risk estimates between 1.5 and 2 for high versus low dietary GI or GL, on risk of heart disease. However, since two[26,27] of the three identified studies of women were based on data from the NHS, the results are not independent, even though the sample sizes and follow-up times differed. Nevertheless, the results are supported by a meta-analysis on prospective cohort studies performed by Barclay et al.,[28] who reported a relative risk of heart disease of 1.25 (95% CI 1.00–1.56) on high-GI diets compared to low-GI diets. Most of the participants in the included studies were women, so the finding remains to be confirmed in men. Furthermore, it may be speculated that a potential difference in the effect of GI on heart disease risk between men and women may be related to diet composition. Low- and/or high-GI diets may be composed very differently in men and women and may consequently affect heart disease risk in different ways. Increased TAG levels, which may be related to high GI/GL diets, may additionally be a stronger risk factor for heart disease in women than men.[29]

TYPE 2 DIABETES

One study reported an unadjusted positive association between GI and serum insulin among 8-year-old children ($P = 0.03$, data not shown).[30] Adjusted associations between GI or GL and different insulin measures have been reported in nine cross-sectional studies[16,31–38] (Table 2). One study found a positive association between GI and HOMA-IR,[33] one found a positive association between GI and HbA1c,[32] and two studies found positive associations between GI and fasting insulin in either the whole[38] or part of the study population.[31] Five studies found no associations between GI and insulin measures.[16,34–37]

The association between GI and subsequent development of type 2 diabetes was examined in 11 identified studies. Six of these found that high dietary GI increased the risk of incident type 2 diabetes with risk estimates ranging from 1.21 to 1.59,[26,39–43] whereas four found no significant risk difference for different levels of dietary GI[38,44–46] (Table 2). Barclay et al.[47] found that high dietary GI increased the risk of type 2 diabetes in men and women younger than 70 years of age (HR 1.75, 95% CI 1.05–2.92), whereas no association was present in persons aged 70 years or older.

GL was positively associated with HOMA-IR in one adjusted cross-sectional analysis.[33] In all other published cross-sectional studies, associations between GL and insulin measures were not significant.[31,32,34–38] Three longitudinal studies observed significantly increased risks of type 2 diabetes in the fifth compared to the first quintile of GL with RRs ranging from 1.34 to 1.47,[26,27,42] and one study found a borderline significant increased risk in the fifth compared to the first quintile of GL (RR 1.22, 95% CI, 0.98–1.51),[41] whereas GL was unrelated to the development of type 2 diabetes in seven other studies[38–40,43–46] (Table 2).

The associations between GI and measures of type 2 diabetes were fairly consistent, with generally positive associations in both cross-sectional and longitudinal studies. The picture is less clear regarding GL and development of type 2 diabetes. Most studies relating GL to either insulin measures or type 2 diabetes were nonsignificant. Only 4 of 19 studies observed significant associations.[26,27,33,42] Again, two studies were based on data from the NHS[26,27] so the results are not independent, despite differences in sample size and follow-up time. Our findings are partly supported by Barclay et al.,[48] who found positive associations between both GI and GL and risk of type 2 diabetes in prospective cohort studies (GI: RR 1.40, 95% CI 1.23–1.59; GL: RR 1.27, 95% CI 1.12–1.45). Our observations are also partly supported by different meta-analyses of intervention studies. Positive effects of low-GI diets on HbA1c and fructosamine were reported by four[9–11,14] and three[9,11,14] meta-analyses, respectively. However, one meta-analysis found no evidence of a difference between low- and high-GI diets in relation to changes in fructosamine and HbA1c.[12] Livesey et al.[14] found that insulin sensitivity was improved by low-GI diets in subjects without diabetes, and evidence of a positive effect of low-GI diets compared to high-GI diets was observed for fasting plasma glucose in two meta-analyses.[12,14] However, the Cochrane collaboration[10] did not find evidence to support an effect of GI on fasting glucose.

BLOOD LIPIDS

Associations between GI and GL and various blood lipids among healthy individuals have been reported in 11[16,32,38,49–56] and 10[32,38,50,51,53–58] observational studies, respectively, most of which were cross-sectional.

Total cholesterol (TC) was not associated with GI in cross-sectional analyses in either men[16,49] or women.[32,49–53] One longitudinal study found a positive association between GI and change in TC among men (mmol/L: $\beta = 0.0044$, 95% CI 0.0008–0.008), but not among women,[54] whereas another[53] failed to show a significant association in a mixed population (Table 3).

Table 2 **Associations between glycemic index and glycemic load and measures of insulin sensitivity or type 2 diabetes in observational studies.**

Reference	Study	Subjects				Outcome	Follow-up	Diet method	Association	Magnitude
		No.	Age (y)†	Sex	Cases					
Glycemic index										
Cross-sectional studies										
Van Dam et al. (2000)[16]	Zutphen Elderly Study	332	64–84	M	–	Fasting ins.	–	DHI	NS (↔)	–
Sahyoun et al. (2005)[31]	Health ABC	1079	70–79	M	–	HbA1c	–	FFQ	NS (↔)	–
					–	Fasting ins.	–		↑**	Fasting ins. (mean (SE)): GI-Q1: 6.1 (0.2), GI-Q5: 7.2 (0.3) μU/mL
Sahyoun et al. (2005)[31]	Health ABC	1169	70–79	F	–	HbA1c	–	FFQ	NS (↔)	–
					–	Fasting ins.	–		NS (↔)	–
Murakami et al. (2006)[32]	JMETS	845	20–78	F	–	HbA1c	–	DHQ	↑*	HbA1c (mean (SE)): GI-Q1: 5.0 (0.1), GI-Q5: 5.2 (0.1) %
McKeown et al. (2004)[33]	Framingham Offspring	2834	26–82	M + F	–	HOMA-IR	–	FFQ	↑***	HOMA-IR (mean (95% CI)): GI-Q1: 6.4 (6.2;6.7), GI-Q5: 7.0 (6.7;7.2)
Lau et al. (2005)[34]	Inter99	5675	30–60	M + F	–	HOMA-IR	–	FFQ	NS (↑)	–
Liese et al. (2005)[35]	IRAS	979	40–69	M + F	–	S_I	–	FFQ	NS (↓)	–
					–	Fasting ins.	–		NS (↑)	–
					–	AIR	–		NS (↑)	–
					–	Disp. index	–		NS (↓)	–
Mayer-Davis et al. (2006)[36]	IRAS	775	40–69	M + F	–	HbA1c	–	FFQ	NS (↔)	–
Davis et al. (2007)[37]	SOLAR	120	10–17	M + F	–	SI	–	2 × 24-h recall	NS (↔)	–
					–	AIR	–	2 × 24-h recall	NS (↔)	–
					–	Disp. index	–	2 × 24-h recall	NS (↔)	–
Mosdøl et al. (2007)[38]	Whitehall II	5832	39–63	M + F	–	Fasting ins.	–	FFQ	↑*	β (SE) = 0.054 (0.023) IU
Longitudinal studies										
Salmeron et al. (1997)[39]	HPFS	42759	40–75	M	523	T2D	6 y	FFQ	↑*	RR (95% CI) = 1.37 (1.02;1.83) in GI-Q5 vs. Q1
Salmeron et al. (1997)[26]	NHS	65173	40–65	F	915	T2D	6 y	FFQ	↑**	RR (95% CI) = 1.37 (1.09;1.71) in GI-Q5 vs. Q1
Meyer et al. (2000)[44]	IWHS	35988	55–69	F	1141	T2D	202654 py	FFQ	NS (↓)	–

Table 2 **Continued**

Reference	Study	Subjects				Outcome	Follow-up	Diet method	Association	Magnitude
		No.	Age (y)†	Sex	Cases					
Schulze et al. (2004)[40]	NHS II	91249	26–46	F	741	T2D	716300 py	FFQ	↑***	RR (95% CI) = 1.59 (1.21;2.10) in GI-Q5 vs. Q1
Krishnan et al. (2007)[41]	BWHS	40078	21–69	F	1938	T2D	123466 py	FFQ	↑***	RR (95% CI) = 1.23 (1.05;1.44) in GI-Q5 vs. Q1
Villegas et al. (2007)[42]	SWHS	64227	40–70	F	1605	T2D	297942 py	FFQ	↑*‡	RR (95% CI) = 1.21 (1.03;1.43) in GI-Q5 vs. Q1
Stevens et al. (2002)[45]	ARIC	9529	45–64	M + F (Wh)	10.2% of 9529	T2D	9 y	FFQ	NS (↔)	–
		2722	45–64	M + F (AA)	17.5% of 2722	T2D	9 y	FFQ	NS (↔)	–
Hodge et al. (2004)[43]	Melbourne Collaborative Cohort Study	31641	40–69	M + F	365	T2D	4 y	FFQ	↑*	OR (95% CI) = 1.32 (1.05;1.67) per 10 GI-units
Barclay et al. (2007)[47]	–	1575	<70	M + F	NR	T2D	10 y	FFQ	↑*	HR (95% CI) = 1.75 (1.05;2.92)
Barclay et al. (2007)[47]	–	560	≥70	M + F	NR	T2D	10 y	FFQ	NS (↔)	–
Mosdøl et al. (2007)[38]	Whitehall II	5598	39–63	M + F	329	T2D	65775 py	FFQ	NS (↔)	–
Sahyoun et al. (2008)[46]	Health ABC	1898	70–79	M + F	99	T2D	4 y	FFQ	NS (↔)	–
Glycemic load										
Cross-sectional studies										
Sahyoun et al. (2005)[31]	Health ABC	1079	70–79	M	–	HbA1c	–	FFQ	NS (↔)	–
					–	Fasting ins.	–		NS (↔)	–
Sahyoun et al. (2005)[31]	Health ABC	1169	70–79	F	–	HbA1c	–	FFQ	NS (↔)	–
					–	Fasting ins.	–		NS (↓)	–
Murakami et al. (2006)[32]	JMETS	845	20–78	F	–	HbA1c	–	DHQ	NS (↑)	–
McKeown et al. (2004)[33]	Framingham Offspring	2834	26–82	M + F	–	HOMA-IR	–	FFQ	↑*	HOMA-IR (mean (95% CI)): GL-Q1: 6.7 (6.4;7.0), GL-Q5: 7.0 (6.7;7.3)
Lau et al. (2005)[34]	Inter99	5675	30–60	M + F	–	HOMA-IR	–	FFQ	NS (↓)	–
Liese et al. (2005)[35]	IRAS	979	40–69	M + F	–	S_I	–	FFQ	NS (↓)	–
					–	Fasting ins.	–		NS (↑)	–
					–	AIR	–		NS (↔)	–
					–	Disp. index	–		NS (↔)	–
Mayer-Davis et al. (2006)[36]	IRAS	775	40–69	M + F	–	HbA1c	–	FFQ	NS (↔)	–

Davis et al. (2007)[37]	SOLAR	120	10–17	M + F	–	SI	–	2 × 24-h recall	NS (↔)	–
					–	AIR	–	2 × 24-h recall	NS (↔)	–
					–	Disp. index	–	2 × 24-h recall	NS (↔)	–
Mosdøl et al. (2007)[38]	Whitehall II	5832	39–63	M + F	–	Fasting ins.	–	FFQ	NS (↔)	–
Longitudinal studies										
Salmeron et al. (1997)[39]	HPFS	42759	40–75	M	523	T2D	6 y	FFQ	NS (↑)	–
Salmeron et al. (1997)[26]	NHS	65173	40–65	F	915	T2D	6 y	FFQ	↑**	RR (95% CI) = 1.47 (1.16;1.86) in GL-Q5 vs. Q1
Meyer et al. (2000)[44]	IWHS	35988	55–69	F	1141	T2D	202654 py	FFQ	NS (↓)	–
Hu et al. (2001)[27]	NHS	84941	34–59	F	3300	T2D	1301055 py	FFQ	↑***	RR (95% CI) = 1.4 (1.2;1.55) in GL-Q5 vs. Q1§
Schulze et al. (2004)[40]	NHS II	91249	26–46	F	741	T2D	716300 py	FFQ	NS (↑)	–
Krishnan et al. (2007)[41]	BWHS	40078	21–69	F	1938	T2D	123466 py	FFQ	↑(*)	RR (95% CI) = 1.22 (0.98;1.51) in GL-Q5 vs. Q1
Villegas et al. (2007)[42]	SWHS	64227	40–70	F	1605	T2D	297741 py	FFQ	↑*‡	RR (95% CI) = 1.34 (1.13;1.58) in GL-Q5 vs. Q1
Stevens et al. (2002)[45]	ARIC	9529	45–64	M + F (Wh)		T2D	9 y	FFQ	NS (↔)	–
		2722	45–64	M + F (AA)	1447	T2D	9 y	FFQ	NS (↔)	–
Hodge et al. (2004)[43]	Melbourne Collaborative Cohort Study	31641	40–69	M + F	365	T2D	4 y	FFQ	NS (↓)	–
Mosdøl et al. (2007)[38]	Whitehall II	5598	39–63	M + F	329	T2D	65775 py	FFQ	NS (↔)	–
Sahyoun et al. (2008)[46]	Health ABC	1898	70–79	M + F	99	T2D	4 y	FFQ	NS (↔)	–

† Age at baseline (range).
‡ No *p*-value reported.
§ Data from figure 1D in Hu et al. (2001).[27]
* $P < 0.05$.
(*) $0.05 < P < 0.10$.
** $P < 0.01$.
*** $P < 0.001$.

Abbreviations: AA, African American; AIR, acute insulin response; ARIC, Atherosclerosis Risk in Communities Study; BWHS, Black Women's Health Study; CI, confidence interval; DHI, dietary history interview; DHQ, dietary history questionnaire; Disp. index, insulin disposition index; F, female; FFQ, food frequency questionnaire; GI, glycemic index; GL, glycemic load; HbA1c, hemoglobin A1c; Health ABC, Health, Ageing and Body Composition Study; HPFS, Health Professionals Follow-up Study; HOMA-IR, homeostasis model assessment of insulin resistance; ins., insulin; IRAS, Insulin Resistance Atherosclerosis Study; IWHS, Iowa Women's Health Study; JMETS, Japanese Multi-centered Environmental Toxicants Study; M, male; NHS, Nurses' Health Study; NR, not reported; NS, no significant association; OR, odds ratio; py, person years; Q, quintile; RR, relative risk; SI, serum insulin; S_I, insulin sensitivity; SOLAR, Study of Latino Adolescents at Risk of Diabetes; SWHS, Shanghai Women's Health Study; T2D, type 2 diabetes; Wh, white; y, years; ↑, positive association; ↓, inverse association.

Table 3 **Associations between glycemic index and glycemic load and total cholesterol (TC) in observational studies.**

Reference	Study	Subjects			Outcome	Follow-up time	Diet method	Association	Magnitude
		No.	Age (y)[†]	Sex					
Glycemic index									
Cross-sectional studies									
Van Dam et al. (2000)[16]	Zutphen Elderly Study	394	64–84	M	TC	–	DHI	NS (↔)	–
Milton et al. (2007)[49]	NDNS	582	65 +	M	TC	–	2 × 4-DDR	NS (↔)	–
Amano et al. (2004)[50]	–	32	52.5 ± 7.2	F	TC	–	3-DDR	NS (↔)	–
Murakami et al. (2006)[32]	JMETS	1354	20–78	F	TC	–	DHQ	NS (↔)	–
Milton et al. (2007)[49]	NDNS	570	65 +	F	TC	–	2 × 4-DDR	NS (↔)	–
Levitan et al. (2008)[51]	WHS	18137	45 +	F	TC	–	FFQ	NS (↔)	–
Frost et al. (1999)[52]	Survey of British Adults	1420	18–64	M + F	TC	–	7-DDR	NS (↔)	–
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	TC	–	3 × 24-h recall	NS (↓)	–
Longitudinal studies									
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	172	35–65	M	ΔTC	6 y	DHI	↑*	β (95% CI) = 0.0044 (0.0008;0.008) mmol/L
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	163	35–65	F	ΔTC	6 y	DHI	NS (↔)	–
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	ΔTC	4 y	3 × 24-h recall	NS (↑)	–
Glycemic load									
Cross-sectional studies									
Amano et al. (2004)[50]	–	32	52.5 ± 7.2	F	TC	–	3-DDR	NS (↔)	–
Murakami et al. (2006)[32]	JMETS	1354	20–78	F	TC	–	DHQ	NS (↔)	–
Levitan et al. (2008)[51]	WHS	18137	45 +	F	TC	–	FFQ	NS (↔)	–
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	TC	–	3 × 24-h recall	↓**	β (SE) = −1.85 (0.74) mg/dL
Longitudinal studies									
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	172	35–65	M	ΔTC	6 y	DHI	NS (↑)	–
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	163	35–65	F	ΔTC	6 y	DHI	NS (↓)	–
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	ΔTC	4 y	3 × 24-h recall	↑**	β (SE) = 1.04 (0.36) mg/dL

[†] Age at baseline (mean ± SD or range).

* $P < 0.05$.

** $P < 0.01$.

Abbreviations: β, regression coefficient; CI, confidence interval; DHI, dietary history interview; DHQ, dietary history questionnaire; F, female; FFQ, food frequency questionnaire; JMETS, Japanese Multi-centered Environmental Toxicants Study; MONICA, Monitoring Trends and Determinants in Cardiovascular Disease Study; M, male; NDNS, National Diet and Nutrition Survey (UK); NS, no significant association; SE, standard error; SEASONS, Seasonal Variation of Blood Cholesterol Study; TC, total cholesterol; WHS, Women's Health Study; x-DDR, x-day dietary record; y, years; ↑, positive association; ↓, inverse association.

One study found that GL was inversely associated with TC in the cross-sectional analysis ($\beta = -1.85$, standard error (SE) 0.74, mg/dL) but positively associated with change in TC in the longitudinal analysis ($\beta = 1.04$, SE 0.36, mg/dL).[53] However, two other cross-sectional[32,50] and one longitudinal study[54] did not find significant associations between GL and TC in their overall analyses. In the longitudinal study, the relationship between GL and change in TC among men differed by age category ($P_{interaction} = 0.05$), with a significant positive association for 35-year-old men only (mmol/L: $\beta = 0.16$, 95% CI 0.02–0.30). In women, the association between GL and change in TC differed by BMI ($P_{interaction} = 0.04$) and was inverse for the more obese (mmol/L: BMI ≥ 30, $\beta = -0.14$, 95% CI $^{-}0.27$–$^{-}0.01$)[54] (Table 3).

GI and low-density-lipoprotein cholesterol (LDL-C) were positively associated in one large cross-sectional study including 18,137 women (mg/dL: diff. in LDL-C between first and fifth quintile 2.2, 95% CI 0.5–4.0).[51] No other cross-sectional[32,49,50,52,53] or longitudinal studies[53,54] observed significant associations between GI and LDL-C (Table 4).

Two of four cross-sectional studies did not find associations between GL and LDL-C,[32,50,51] but Ma et al.[53] observed an inverse cross-sectional association between GL and LDL-C ($\beta = -1.73$, SE 0.68, mg/dL) and a positive longitudinal association between GL and change in LDL-C ($\beta = 0.64$, SE 0.33, mg/dL). Oxlund and Heitmann[54] reported a positive longitudinal association among men (mmol/L: $\beta = 0.16$, 95% CI 0.01–0.30), but no overall association among women (Table 4). However, among women, the association between GL and change in LDL-C differed by BMI ($P_{interaction} = 0.03$) and was inverse for the more obese (mmol/L: BMI ≥ 30, $\beta = -0.20$, 95% CI $^{-}0.38$–$^{-}0.10$).[54]

Inverse cross-sectional associations between GI and high-density-lipoprotein cholesterol (HDL-C) were observed in six studies,[38,50–53,55] whereas four other cross-sectional studies did not find significant associations.[16,32,49,56] Neither of the two longitudinal studies identified significant associations between GI and change in HDL-C[53,54] (Table 5).

GL and HDL-C were inversely associated in all nine cross-sectional studies identified,[32,38,50,51,53,55–58] but the results from the two longitudinal studies were contradictory as one observed a borderline significant positive association ($\beta = 0.20$, SE 0.11, $P = 0.07$),[53] while another observed no association between GL and change in HDL-C[54] (Table 5).

Triacylglycerol (TAG) was positively associated with GI in five cross-sectional studies[32,38,50,51,56] but was not associated with GI in another three.[16,49,53] Two longitudinal studies observed non-significant associations, although tendencies towards positive associations were noted[53,54] (Table 6).

Five of six cross-sectional studies found that GL was positively associated with TAG;[32,38,50,51,56] one study did not find an association.[53] Two longitudinal studies showed no associations between GL and change in TAG[53,54] (Table 6).

The associations between GI and GL and different blood lipids are fairly consistent in the cross-sectional studies, with protective effects of both GI and GL on TAG and HDL-C[50,52,55–57,59] and no association with TC and LDL-C.[16,32,49,50,52,53] On the other hand, the two prospective studies that examined associations between GI and GL and these blood lipids[53,54] were unable to replicate the findings from cross-sectional studies; hence, GI and GL do not seem to influence changes in blood lipids. However, the two prospective studies were rather small and the lack of significant associations may be due to type II error.

The positive effects of low GI or GL diets on TC[10,11,13] and LDL-C[11,13] reported in meta-analyses of intervention studies were not generally substantiated by the observational studies we identified (Tables 3 and 4). A possible explanation for the difference is related to the study populations, because the meta-analyses included studies performed on subjects with disturbed metabolism; some even had this as an inclusion criterion.[9,10,13] In observational studies it is most often assumed that participants are healthy at baseline. Therefore, they might not have the same ability as those with disturbed metabolism to improve their metabolic profile enough for an association with GI to be detected, especially if the variation in dietary GI in the study population is small.

OBESITY

Observational studies of associations between GI and BMI, body weight, or body composition measures were primarily cross-sectional and conducted among adults. Furthermore, most of these studies reported unadjusted associations only. The reviewed literature showed that most of the unadjusted associations between GI and obesity measures were non-significant,[5,26,30,35,39,45,49,60] two were inverse,[16,55] and two were positive (data not shown).[35,61]

Independent direct associations between GI and BMI were observed in four studies,[32,60,62,63] whereas three studies did not find significant adjusted associations between GI and obesity measures.[35,37,50] One observed an inverse association between GI and thigh intramuscular fat (IMF) among men but not among women and no association between GI and visceral abdominal fat (VAF) in either men or women.[31] Nielsen et al.[64] studied the associations between GI and BMI and GI and the sum of

Table 4 **Associations between glycemic index and glycemic load and low-density lipoprotein cholesterol (LDL-C) in observational studies.**

Reference	Study	Subjects			Outcome	Follow-up time	Diet method	Association	Magnitude
		No.	Age (y)[†]	Sex					
Glycemic index									
Cross-sectional studies									
Milton et al. (2007)[49]	NDNS	582	65+	M	LDL-C	–	2 × 4-DDR	NS (↔)	–
Amano et al. (2004)[50]	–	32	52.5 ± 7.2	F	LDL-C	–	3-DDR	NS (↔)	–
Murakami et al. (2006)[32]	JMETS	1348	20–78	F	LDL-C	–	DHQ	NS (↔)	–
Milton et al. (2007)[49]	NDNS	570	65+	F	LDL-C	–	2 × 4-DDR	NS (↔)	–
Levitan et al. (2008)[51]	WHS	18137	45+	F	LDL-C	–	FFQ	↑**	Diff. GI-Q5 - GI-Q1 (95% CI): 2.2 (0.5;4.0) mg/dL
Frost et al. (1999)[52]	Survey of British Adults	1420	18–64	M + F	LDL-C	–	7-DDR	NS (↔)	–
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	LDL-C	–	3 × 24-h recall	NS (↔)	–
Longitudinal studies									
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	172	35–65	M	ΔLDL-C	6 y	DHI	NS (↑)	–
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	163	35–65	F	ΔLDL-C	6 y	DHI	NS (↔)	–
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	ΔLDL-C	4 y	3 × 24-h recall	NS (↑)	–
Glycemic load									
Cross-sectional studies									
Amano et al. (2004)[50]	–	32	52.5 ± 7.2	F	LDL-C	–	3-DDR	NS (↔)	–
Murakami et al. (2006)[32]	JMETS	1348	20–78	F	LDL-C	–	DHQ	NS (↔)	–
Levitan et al. (2008)[51]	WHS	18137	45+	F	LDL-C	–	FFQ	NS (↔)	–
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	LDL-C	–	3 × 24-h recall	↓**	β (SE) = −1.73 (0.68) mg/dL
Longitudinal studies									
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	172	35–65	M	ΔLDL-C	6 y	DHI	↑*	β (95% CI) = 0.16 (0.01;0.30) mmol/L
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	163	35–65	F	ΔLDL-C	6 y	DHI	NS (↓)	–
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	ΔLDL-C	4 y	3 × 24-h recall	↑*	β (SE) = 0.64 (0.33) mg/dL

[†] Age at baseline (mean ± SD or range).

* $P < 0.05$.

** $P < 0.01$.

Abbreviations: β, regression coefficient; CI, confidence interval; DHI, dietary history interview; DHQ, dietary history questionnaire; F, female; FFQ, food frequency questionnaire; GI, glycemic index; JMETS, Japanese Multi-centered Environmental Toxicants Study; LDL-C, LDL cholesterol; M, male; MONICA, Monitoring Trends and Determinants in Cardiovascular Disease Study; NDNS, National Diet and Nutrition Survey (UK); NS, no significant association; SE, standard error; SEASONS, Seasonal Variation of Blood Cholesterol Study; WHS, Women's Health Study; x-DDR, x-day dietary record; y, years; ↑, positive association; ↓, inverse association.

Table 5 **Associations between glycemic index and glycemic load and high-density lipoprotein cholesterol (HDL-C) in observational studies.**

Reference	Study	Subjects			Outcome	Follow-up time	Diet method	Association	Magnitude
		No.	Age (y)†	Sex					
Glycemic index									
Cross-sectional studies									
Van Dam et al. (2000)[16]	Zutphen Elderly Study	394	64–84	M	HDL-C	–	DHI	NS (↔)	–
Milton et al. (2007)[49]	NDNS	582	65+	M	HDL-C	–	2 × 4-DDR	NS (↔)	–
Liu et al. (2001)[56]	NHS	280	45–70	F	HDL-C	–	FFQ	NS (↓)	–
Amano et al. (2004)[50]	–	32	52.5 ± 7.2	F	HDL-C	–	3-DDR	↓***	HDL-C (mean (95% CI)): GI-T1: 1.87 (1.69;2.05), GI-T3: 1.47 (1.37;1.58) mmol/L
Murakami et al. (2006)[32]	JMETS	1354	20–78	F	HDL-C	–	DHQ	NS (↔)	–
Milton et al. (2007)[49]	NDNS	570	65+	F	HDL-C	–	2 × 4-DDR	NS (↔)	–
Levitan et al. (2008)[51]	WHS	18137	45+	F	HDL-C	–	FFQ	↓***	Diff. GI-Q5 – GI-Q1 (95% CI): –2.6 (–3.3;–2.0) mg/dL
Frost et al. (1999)[52]	Survey of British Adults	1420	18–64	M + F	HDL-C	–	7-DDR	↓***	β (95%CI) = –0.14 (–0.016;–0.012) mmol/L
Ford & Liu (2001)[55]	NHANES III	13907	20+	M + F	HDL-C	–	FFQ	↓***	HDL-C (mean (SE)): GI-Q1: 1.36 (0.01), GI-Q5; 1.28 (0.01) mmol/L
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	HDL-C	–	3 × 24-h recall	↓**	β (SE) = –0.89 (0.38) mg/dL
Mosdøl et al. (2007)[38]	Whitehall II	6581	39–63	M + F	HDL-C	–	FFQ	↓***	β (SE) = –0.035 (0.008) mmol/L
Longitudinal studies									
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	172	35–65	M	ΔHDL-C	6 y	DHI	NS (↑)	–
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	163	35–65	F	ΔHDL-C	6 y	DHI	NS (↔)	–
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	ΔHDL-C	4 y	3 × 24-h recall	NS (↔)	–
Glycemic load									
Cross-sectional studies									
Liu et al. (2001)[56]	NHS	280	43–69	F	HDL-C	–	FFQ	↓*	HDL-C (mean (95% CI)): GL–Q1: 1.50 (1.40;1.60), GL–Q5: 1.34 (1.24;1.45) mmol/L

Table 5 **Continued**

Reference	Study	Subjects			Outcome	Follow-up time	Diet method	Association	Magnitude
		No.	Age (y)[†]	Sex					
Amano et al. (2004)[50]	–	32	52.5 ± 7.2	F	HDL-C	–	3-DDR	↓*	HDL-C (mean (95% CI)): GL–T1: 1.82 (1.64;2.00), GL–T3: 1.42 (1.26;1.60) mmol/L
Murakami et al. (2006)[32]	JMETS	1354	20–78	F	HDL-C	–	DHQ	↓**	HDL-C (mean (SE): GL–Q1: 67.2 (1.3), GL–Q5: 60.8 (1.4) mg/dL
Levitan et al. (2008)[51]	WHS	18137	45+	F	HDL-C	–	FFQ	↓***	Diff. GI–Q5 – GI–Q1 (95% CI): –4.9 (–6.0;–3.8) mg/dL
Ford & Liu (2001)[55]	NHANES III	13907	20+	M + F	HDL-C	–	FFQ	↓***	HDL-C (mean (SE)): GL–Q1: 1.35 (0.01), GL–Q5: 1.26 (0.01) mmol/L
Slyper et al. (2005)[57]	–	32	11–25	M + F	HDL-C	–	3-DDR	↓*	GL predicted 21.1% of the variation in HDL-C
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	HDL-C	–	3 × 24-h recall	↓**	β (SE) = –0.77 (0.20) mg/dL
Mosdøl et al. (2007)[38]	Whitehall II	6581	39–63	M + F	HDL-C	–	FFQ	↓**	β (SE) = –0.009 (0.003) mmol/L
Radhika et al. (2007)[58]	CURES	2043	20–84	M + F	HDL-C	–	FFQ	↓***	HDL-C (mean (SE): GL–Q1: 44.1 (11.5), GL–Q5: 41.2 (9.6) mg/dL
Longitudinal studies									
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	172	35–65	M	ΔHDL-C	6 y	DHI	NS (↑)	–
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	163	35–65	F	ΔHDL-C	6 y	DHI	NS (↓)	–
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	ΔHDL-C	4 y	3 × 24-h recall	↑(*)	β (SE) = 0.20 (0.11) mg/dL

[†] Age at baseline (mean ± SD or range).
(*) $0.05 < P < 0.10$.
* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.
Abbreviations: β, regression coefficient; CI, confidence interval; CURES, Chennai Urban Rural Epidemiology Study; DHI, dietary history interview; DHQ, dietary history questionnaire; F, female; FFQ, food frequency questionnaire; GI, glycemic index; GL, glycemic load; HDL-C, HDL cholesterol; JMETS, Japanese Multi-centered Environmental Toxicants Study; M, male; MONICA, Monitoring Trends and Determinants in Cardiovascular Disease Study; NDNS, National Diet and Nutrition Survey (UK); NHANES, National Health and Nutrition Examination Survey; NHS, Nurses' Health Study; NS, no significant association; Q, quintile; SE, standard error; SEASONS, Seasonal Variation of Blood Cholesterol Study; T, tertile; WHS, Women's Health Study; x-DDR, x-day dietary record; ↑, positive association; ↓, inverse association.

Table 6 **Associations between glycemic index and glycemic load and triacylglycerol (TAG) in observational studies.**

Reference	Study	Subjects			Outcome	Follow-up	Diet method	Association	Magnitude
		No.	Age (y)†	Sex					
Glycemic index									
Cross-sectional studies									
Van Dam et al. (2000)[16]	Zutphen Elderly Study	360	64–84	M	TAG	–	DHI	NS (↔)	–
Milton et al. (2007)[49]	NDNS	582	65+	M	TAG	–	2 × 4-DDR	NS (↑)	
Liu et al. (2001)[56]	NHS	185	43–69	F	TAG	–	FFQ	↑*	TAG (mean (95% CI)): GI–Q1: 1.16 (0.99;1.36), GI–Q5: 1.37 (1.13;1.64) mmol/L
Amano et al. (2004)[50]	–	32	52.5 ± 7.2	F	TAG	–	3-DDR	↑***	TAG (mean (95% CI)): GI–T1: 0.70 (0.48;0.91), GI–T3: 1.44 (1.02;1.86) mmol/L
Murakami et al. (2006)[32]	JMETS	1349	20–78	F	TAG	–	DHQ	↑***	TAG (mean (SE)): GI–Q1: 87.1 (3.0), GI–Q5: 103.1 (3.0) mg/dL
Milton et al. (2007)[49]	NDNS	570	65+	F	TAG	–	2 × 4-DDR	NS (↔)	–
Levitan et al. (2008)[51]	WHS	18137	45+	F	TAG	–	FFQ	↑***	Ratio GI–Q5/GI–Q1 (95% CI): 1.11 (1.08;1.14) mg/dL
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	TAG	–	3 × 24-h recall	NS (↔)	–
Mosdøl et al. (2007)[38]	Whitehall II	6600	39–63	M + F	TAG	–	FFQ	↑***	β (SE) = 0.074 (0.017) mmol/L
Longitudinal studies									
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	172	35–65	M	ΔTAG	6 y	DHI	NS (↑)	–
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	163	35–65	F	ΔTAG	6 y	DHI	NS (↑)	–
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	ΔTAG	4 y	3 × 24-h recall	NS (↔)	–

Table 6 **Continued**

Reference	Study	Subjects			Outcome	Follow-up	Diet method	Association	Magnitude
		No.	Age (y)[†]	Sex					
Glycemic load									
Cross-sectional studies									
Liu et al. (2001)[56]	NHS	185	43–69	F	TAG	–	FFQ	↑***	TAG (mean (95% CI)): GL–Q1: 0.99 (0.84;1.14), GL–Q5: 1.74 (1.46;2.07) mmol/L
Amano et al. (2004)[50]	–	32	52.5 ± 7.2	F	TAG	–	3-DDR	↑**	TAG (mean (95% CI)): GL–T1: 0.74 (0.52;0.95), GL–T3: 1.48 (1.08;1.88) mmol/L
Murakami et al. (2006)[32]	JMETS	1349	20–78	F	TAG	–	DHQ	↑*	TAG (mean (SE)): GL–Q1: 91.0 (4.1), GL–Q5: 105.4 (4.4) mg/dL
Levitan et al. (2008)[51]	WHS	18137	45+	F	TAG	–	FFQ	↑***	Ratio GL–Q5/GL–Q1 (95% CI): 1.13 (1.08;1.17) mg/dL
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	TAG	–	3 × 24-h recall	NS (↔)	–
Mosdøl et al. (2007)[38]	Whitehall II	6600	39–63	M + F	TAG	–	FFQ	↑***	β (SE) = 0.026 (0.007) mmol/L
Longitudinal studies									
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	172	35–65	M	ΔTAG	6 y	DHI	NS (↓)	–
Oxlund & Heitmann (2006)[54]	MONICA (Danish part)	163	35–65	F	ΔTAG	6 y	DHI	NS (↓)	–
Ma et al. (2006)[53]	SEASONS	574	20–70	M + F	ΔTAG	4 y	3 × 24-h recall	NS (↔)	–

[†] Age at baseline (mean ± SD or range).
* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.
Abbreviations: β, regression coefficient; CI, confidence interval; DHI, dietary history interview; DHQ, dietary history questionnaire; F, female; FFQ, food frequency questionnaire; GI, glycemic index; GL, glycemic load; M, male; NS, no significant association; Q, quintile; SE, standard error; T, tertile; TAG, triacylglycerol; x-DDR, x-day dietary record; ↑, positive association; ↓, inverse association.

four skin folds (ΣSF) in 10- and 16-year-old children from the Danish European Youth Heart Study (EYHS) cohort. Among 16-year-old boys there was a positive association between GI and ΣSF but no association was observed between GI and BMI (Table 7).

Longitudinal studies are less frequent and, in total, only three studies have examined associations between GI and changes in obesity measures. Ma et al.[62] found a positive association between the 1-year change in dietary GI and the 1-year change in BMI with a five unit increase in dietary GI associated with a 0.04 unit increase (95% CI 0.01–0.07) in BMI. Only two prospective studies were identified. Kolagotla et al.[65] reported, in a conference abstract, no association between baseline GI and the 7-year change in BMI among children with a baseline age of 3–5 years. However, when dividing the population into tertiles according to fat intake, they found a significant inverse association between baseline GI and BMI change in the highest tertile of fat intake.[65] We conducted a prospective 6-year follow-up study in adults. This study demonstrated weak positive associations between baseline dietary GI and changes in body weight (percent change: $\beta = 0.2$, 95% CI 0.01–0.40), body fat percentage (percent body fat: $\beta = 0.09$, 95% CI 0.004–0.17), and waist circumference (cm: $\beta = 0.16$, 95% CI $^{-}0.01$–$^{+}0.32$) among women but not among men, whereas changes in hip circumference were not associated with baseline dietary GI among either men or women[66] (Table 7). Physical activity was found to modify the association among women, with associations being present and strong for sedentary women but not for more active women or for men. Among the sedentary women, there was a 6% (95% CI 2–9%, $p = 0.001$) increase in body weight (equal to 3.8 kg for a woman with a median body weight of 62.8 kg at baseline), a three percentage-point increase in body fat percentage (95% CI 1–4 percentage points, $p = 0.002$) and a 4 cm increase in waist circumference (95% CI 1–7 cm, $p = 0.008$) after 6 years per 10-unit increase in baseline GI.

Unadjusted cross-sectional associations between GL and obesity measures have been reported in ten papers. GL and BMI were positively associated in one study[35] and inversely associated in six studies.[17,55,60,61,67,68] Three studies observed no association (data not shown).[5,18,30]

Of the nine studies reporting adjusted cross-sectional analyses, three did not find significant associations between GL and various obesity measures,[32,37,62] whereas four observed positive associations in adults.[35,50,60,63] The study by Sahyoun et al.[31] found an inverse association between GL and VAF in men but no association in women, and GL and thigh IMF were not associated in either men or women.[31] Finally, the more recent study among children, performed by Nielsen et al.,[64] found that GL was associated with ΣSF among 16-year-old boys, with a 10% difference in dietary GL associated with a 1% (SE = 0.6%) higher ΣSF.[64] However, no other significant associations between GL and BMI or ΣSF were found in either 10-year-old boys or 10- or 16-year-old girls.

Ma et al.[62] were unable to show an association between the 1-year change in GL and the 1-year change in BMI. Finally, in our study, we observed no association between baseline GL and the 6-year change in body weight, body fat percentage or hip circumference, in either men or women, and only a borderline significant inverse association between baseline GL and change in waist circumference among women but not among men[66] (Table 7).

Most of the significant associations from adjusted cross-sectional analyses of GI or GL and obesity measures were positive.[32,35,50,60,62–64] However, in some of these studies the associations were significant only among subgroups,[31,64] and frequently there were inconsistencies between the GI and GL analyses in the studies reporting both.[31,32,35,50,62] Two of the three longitudinal studies on GI and obesity measures are consistent with the observations from the cross-sectional studies and found significant positive associations in either the whole population[62] or in subgroups.[66] However, one study observed an inverse association between GI and change in BMI among children with a high fat intake.[65] The two longitudinal studies of GL and obesity measures observed no or very weak inverse associations.[62,66]

A meta-analysis by the Cochrane collaboration[13] reviewed the effects of GI and GL on overweight and obesity in intervention studies and observed a larger loss of body weight and total fat mass, as well as a larger reduction in BMI, on low-GI compared to high-GI diets; this led them to conclude that a lowering of the GI or GL appears to be an effective method of losing weight. These results are in line with those of Livesey et al.,[14] who observed reductions in body weight on both low-GI and low-GL diets. The results contrast with our mixed findings on the associations between GI and GL and obesity measures. However, a major difference is the focus on treatment studies and consequently on weight loss among overweight and obese people in the meta-analyses; the observational studies cited in this review focused on prevention of weight gain and reported on the associations between the GI and GL of the habitual diet and weight change over longer time periods.

CONCLUSION

Generally, the associations between GI or GL and heart disease, measures of insulin sensitivity, diabetes, blood lipids, or measures of obesity were mixed. Studies reporting unadjusted associations (both cross-sectional and

Table 7 **Associations between glycemic index and glycemic load and obesity measures in observational studies.**

Reference	Study	Subjects			Outcome	Follow-up	Diet method	Association	Magnitude
		No.	Age (y)†	Sex					
Glycemic index									
Cross-sectional studies									
Nielsen et al. (2005)[64]	EYHS (Danish part)	223	10	M	ΣSF	–	24-h recall	NS (↓)	–
					BMI	–		NS (–)	–
Nielsen et al. (2005)[64]	EYHS (Danish part)	181	16	M	ΣSF	–	24-h recall	↑**	β (SE) = 0.60 (0.21) mm
					BMI	–		NS (–)	–
Sahyoun et al. (2005)[31]	Health ABC	1079	70–79	M	VAF	–	FFQ	NS (↓)	–
					Thigh IMF	–		↓*	Thigh IMF (mean (SE)): GI–Q1: 9.9 (0.3), GI–Q5: 8.9 (0.3) cm^2
Amano et al. (2004)[50]	–	32	52.5 ± 7.2	F	BW	–	3-DDR	NS (↑)	–
					BMI	–		NS (↑)	–
					BF%	–		NS (↑)	–
Nielsen et al. (2005)[64]	EYHS (Danish part)	262	10	F	ΣSF	–	24-h recall	NS (↑)	–
					BMI	–		NS (–)	–
Nielsen et al. (2005)[64]	EYHS (Danish part)	183	16	F	ΣSF	–	24-h recall	NS (↓)	–
					BMI	–		NS (–)	–
Sahyoun et al. (2005)[31]	Health ABC	1169	70–79	F	VAF	–	FFQ	NS (↑)	–
					Thigh IMF	–		NS (↔)	–
Murakami et al. (2006)[32]	JMETS	1354	20–78	F	BMI	–	DHQ	↑*	BMI (mean (SE)): GI–Q1: 23.7 (0.2), GI–Q5: 24.4 (0.2) kg/m^2
Murakami et al. (2007)[63]	–	3931	18–20	F	BMI	–	DHQ	↑*	BMI (mean (SE)): GI–Q1: 20.8 (0.1), GI–Q5: 21.2 (0.1) kg/m^2
Liese et al. (2005)[35]	IRAS	979	40–69	M + F	BMI	–	FFQ	NS (↔)	–
					WC	–		NS (↔)	–
Ma et al. (2005)[62]	SEASONS	572	20–70	M + F	BMI	–	FFQ	↑**	β (95% CI) = 0.75 (0.21;1.30)‡ kg/m^2
Lau et al. (2006)[60]	INTER99	6334	30–60	M + F	BMI	–	FFQ	↑*	β (95% CI) = 0.261 (0.05;0.48) kg/m^2
Davis et al. (2007)[37]	SOLAR	120	10–17	M + F	BMI	–	2 × 24-h recall	NS (↔)	–
					BMI z-score	–	2 × 24-h recall	NS (↔)	–
					BF (kg)	–	2 × 24-h recall	NS (↔)	–
					LBM (kg)	–	2 × 24-h recall	NS (↔)	–
Longitudinal studies									
Hare-Bruun et al. (2006)[66]	MONICA (Danish part)	185	35–65	M	ΔBW	6 y	DHI	NS (↔)	–
					ΔBF%	6 y		NS (↑)	–
					ΔWC	6 y		NS (↑)	–
					ΔHC	6 y		NS (↔)	–

Hare-Bruun et al. (2006)[66]	MONICA (Danish part)	191	35–65	F	ΔBW	6 y	DHI	↑*	β (95% CI) = 0.2 (0.01;0.4)[§,‖]
					ΔBF%	6 y		↑*	β (95% CI) = 0.09 (0.004;0.17)[‖] %-points
					ΔWC	6 y		↑(*)	β (95% CI) = 0.16 (−0.01;0.32)[‖] cm
					ΔHC	6 y		NS (↑)	–
Kolagotla et al. (2003)[65] (abstr.)		103	3–5	M + F	ΔBMI	7 y	FFQ	NS (↓)	–
Ma et al. (2005)[62]	SEASONS	572	20–70	M + F	ΔBMI	1 y	FFQ	↑*	β (95% CI) = 0.04 (0.01;0.07)[¶] kg/m^2
Glycemic load									
Cross-sectional studies									
Nielsen et al. (2005)[64]	EYHS (Danish part)	223	10	M	ΣSF	–	24-h recall	NS (↓)	–
					BMI	–		NS (–)	–
Nielsen et al. (2005)[64]	EYHS (Danish part)	181	16	M	ΣSF	–	24-h recall	↑**	β (SE) = 0.15 (0.06) mm
					BMI	–		NS (–)	–
Sahyoun et al. (2005)[31]	Health ABC	1079	70–79	M	VAF	–	FFQ	↓*	VAF (mean (SE)): GL–Q1: 157.2 (3.8), GL–Q5: 144.5 (3.6) cm^2
					Thigh IMF	–		NS (↓)	–
Amano et al. (2004)[50]	–	32	52.5 ± 7.2	F	BW	–	3-DDR	↑(*)	BW (mean (95% CI)): GL–T1: 60.0 (56.0;64.0), GL–T3: 67.6 (62.3;72.9) kg
					BMI	–		↑(*)	BMI (mean (95% CI)): GL–T1: 25.2 (23.7;26.7), GL–T3: 27.6 (26.0;29.3) kg/m^2
					BF%	–		↑(*)	BF% (mean (95% CI)): GL–T1: 34.1 (30.0;38.3), GL–T3: 41.7 (37.9;45.5) %-points
Nielsen et al. (2005)[64]	EYHS (Danish part)	262	10	F	ΣSF	–	24-h recall	NS (↑)	–
					BMI	–		NS (–)	–
Nielsen et al. (2005)[64]	EYHS (Danish part)	183	16	F	ΣSF	–	24-h recall	NS (↑)	–
					BMI	–		NS (–)	–
Sahyoun et al. (2005)[31]	Health ABC	1169	70–79	F	VAF	–	FFQ	NS (↔)	–
					Thigh IMF	–		NS (↔)	–
Murakami et al. (2006)[32]	JMETS	1354	20–78	F	BMI	–	DHQ	NS (↔)	–

Table 7 **Continued**

Reference	Study	Subjects			Outcome	Follow-up	Diet method	Association	Magnitude
		No.	Age (y)[†]	Sex					
Murakami et al. (2007)[63]	–	3931	18–20	F	BMI	–	DHQ	↑***	BMI (mean (SE)): GI–Q1: 20.5 (0.2), GI–Q5: 21.5 (0.2) kg/m^2
Liese et al. (2005)[35]	IRAS	979	40–69	M + F	BMI	–	FFQ	↑***	β (SE) = 0.09 (0.03) kg/m^2
					WC	–		↑***	β (SE) = 0.24 (0.06) cm
Ma et al. (2005)[62]	SEASONS	572	20–70	M + F	BMI	–	FFQ	NS (–)	–
Lau et al. (2006)[60]	INTER99	6334	30–60	M + F	BMI	–	FFQ	↑***	β (95% CI) = 0.173 (0.095;0.252) kg/m^2
Davis et al. (2007)[37]	SOLAR	120	10–17	M + F	BMI	–	2 × 24-h recall	NS (↔)	–
					BMI z-score	–	2 × 24-h recall	NS (↔)	–
					BF (kg)	–	2 × 24-h recall	NS (↔)	–
					LBM (kg)	–	2 × 24-h recall	NS (↔)	–
Longitudinal studies									
Hare-Bruun et al. (2006)[66]	MONICA (Danish part)	185	35–65	M	ΔBW	6 y	DHI	NS (↑)	–
					ΔBF%	6 y		NS (↓)	–
					ΔWC	6 y		NS (↓)	–
					ΔHC	6 y		NS (↓)	–
Hare-Bruun et al. (2006)[66]	MONICA (Danish part)	191	35–65	F	ΔBW	6 y	DHI	NS (↓)	–
					ΔBF%	6 y		NS (↓)	–
					ΔWC	6 y		↓ (*)	β (95% CI) = –0.5 (–1.0;0.01)[#]
					ΔHC	6 y		NS (↓)	–
Ma et al. (2005)[62]	SEASONS	572	20–70	M + F	ΔBMI	1 y	FFQ	NS (–)	–

[†] Age at baseline (mean ± SD or range).
[‡] Increase in BMI per 5 unit increase in GI.
[§] Percentage change in body weight (due to log transformation of BW in the statistical analysis).
[||] Change in outcome variable per unit increase in baseline GI.
[¶] Change in BMI per 5-unit increase in intra-individual GI.
[#] Change in waist circumference (cm) per 10% increase in baseline GL.
(*) $0.05 < P < 0.10$.
* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.

Abbreviations: AA, African American; β, regression coefficient; BF%, body fat percentage; BMI, body mass index; BW, body weight; CI, confidence interval; DHI, dietary history interview; DHQ, dietary history questionnaire; EYHS, European Youth Heart Study; F, female; FFQ, food frequency questionnaire; GI, glycemic index; GL, glycemic load; HC, hip circumference; Health ABC; Health, Ageing and Body Composition Study; IMF, intramuscular fat; IRAS, Insulin Resistance Atherosclerosis Study; JMETS, Japanese Multi-centered Environmental Toxicants Study; M, male; MONICA, Monitoring Trends and Determinants in Cardiovascular Disease Study; NS, no significant association; Q, quintile; ΣSF, sum of four skin folds; SE, standard error; SEASONS, Seasonal Variation of Blood Cholesterol Study; SOLAR, Study of Latino Adolescents at Risk of Diabetes; T, tertile; VAF, visceral abdominal fat; WC, waist circumference; Wh, white; WHR, waist-hip-ratio; x-DDR, x-day dietary record; y, years; ↑, positive association; ↓, inverse association.

longitudinal) generally showed inconsistent results that were weak or non-significant. However, unadjusted analyses may be modified by both dietary and non-dietary factors, which can be different for different populations.

When looking at adjusted analyses only, the picture is still inconclusive. The majority of analyses show non-significant associations, and the significant associations reported show a mixed picture with both positive and inverse associations observed for several outcomes.

Results from cross-sectional and longitudinal studies were not generally in agreement. For several outcomes, the longitudinal studies were unable to replicate the findings from cross-sectional studies (GI and GL vs. TC, GI, and GL vs. LDL-C, GI, and GL vs. HDL-C, GI, and GL vs. TAG and GL vs. obesity). However, as cross-sectional studies allow no interpretation of the temporal sequence, it is not possible to deduce whether the association is due to a causal relationship between the two variables in question, or if some underlying relationship is responsible for the apparent association. In longitudinal studies, the prospective feature secures the temporal relation to ensure that the exposure preceded the outcome, which is an indicator for a cause and effect relationship.[69] Other factors, such as residual confounding, may also have influenced the results of some of the studies in unpredictable ways and may contribute to the mixed results seen for some of the outcomes. Only the positive association between GI and the development of type 2 diabetes was fairly consistent in both cross-sectional and longitudinal studies and between both sexes.

There seems to be a difference in the effects of GI and GL between healthy subjects and those with metabolic disturbances. Possibly, a protective effect of GI or GL may be detectable only among persons with greater potential for improvement in metabolic risk factors, i.e., persons with type 2 diabetes or disturbed lipid metabolism, rather than among healthy persons. Furthermore, with regard to heart disease, TAG, and possibly obesity, it seems that women may benefit more from reducing their dietary GI and GL than men. Whether this is related to the known gender differences in the overall diet or to potentially better compliance of women with dietary recommendations would be interesting to explore.

The choice of dietary measurement method may influence the calculated GI of the diet in observational studies because the methods have different levels of detail and different strengths and weaknesses. Of the 35 observational studies identified for this paper, 24 studies[17,19,26,30,31,33–36,39,40,43–45,55,56,60–62,65,67,68] used a food frequency questionnaire (FFQ) for dietary assessment. Those studies may have missed some of the variation in dietary GI because of the limited number of possible food items included in a FFQ and the limitations in quantifying individual amounts and combinations of foods eaten. The dietary measurement methods used in the remaining studies were dietary history methods ($n = 5$[5,16,32,54,66]) diet records ($n = 4$[49,50,52,57]) and 24-h recalls ($n = 2$[53,64]). These methods may be more detailed and better suited for calculating GI and GL. One drawback to a single 24-h recall, in particular, is that the period covered may be too short to reflect habitual intake. The comparison of studies using different methods of dietary measurement may exaggerate the differences and reduce comparability between studies and, thus, partly explain the mixed results. However, if the effect of GI on health outcomes is robust, the method of dietary measurement should not be of great importance, as long as it is carried out carefully and thoroughly.

The present review found little evidence for a relationship between dietary GI and several of the health-related outcomes considered, which might also depend on type II error in the individual studies. Differences in dietary GI are often small in observational studies, making it difficult to detect associations because sample sizes need to be large in order to obtain significant results. Indeed, a number of the studies identified for the present review were rather small, with 1000 individuals or less in the population studied. However, other studies included more than 10,000 participants and still did not observe significant associations in all[17,44] or in subgroups of participants,[21,39,40,43,51] indicating that the null-results are not due to type II error.

Another important issue is publication bias. It has been shown that not all studies in a specific research field reach publication, in part because null-results are published less frequently than positive results.[70–72] Whether publication bias is a problem in studies of GI and/or GL and health has not been assessed, but it is likely that this research field suffers from the same problems with publication bias as documented in other research fields. GI and GL may therefore be even more weakly associated with cardiovascular health and its risk factors than suggested by the present results, with diabetes potentially being an exception.

Whether a lowering of dietary GI and GL should be part of the dietary recommendations for healthy populations is, in our opinion, still debatable. The evidence from this review is not strong, aside from a small protective effect of GI on a few outcomes. Furthermore, if the present Danish dietary recommendations[73] (as an example) are followed, dietary GI will most likely be moderate (low GI ≤ 55, medium GI 56–69, high GI ≥ 70).[75] The Danish recommendations are as follows: high intakes of fruit (GI ca. 30–60; extracted from Foster-Powell et al.[74]) and vegetables (GI ca. 45–55); daily intakes of potatoes (GI ca. 50–85), rice (GI ca. 35–70), pasta (GI ca. 38–45), or wholegrain bread (GI ca. 30–70); weekly intake of fish (200–300 g; GI not relevant); and low intakes of

sugar-sweetened beverages, sweets, cakes, and dietary fat. Therefore, the feasibility of reducing dietary GI in the general population, beyond the level achieved by the dietary recommendations, is questionable. In addition, the barriers to adopting new health messages and incorporating them into the habitual diet may be great, since the public receives large numbers of more-or-less substantiated health messages through the media every day. Furthermore, it may be difficult for individuals to apply the GI concept to the usual diet, as this requires some nutritional knowledge, or at least a dedicated effort to learn how to use the concept in practice.

In conclusion, we suggest it seems premature to include GI in the dietary recommendations for healthy populations. However, large-scale observational and intervention studies, such as the Diogenes study (http://www.diogenes-eu.org/), are ongoing; when the results are available, it will be necessary to reevaluate the evidence. For now, we believe attention should be called to the current dietary recommendations and efforts to encourage the populace to follow them should be intensified.

Acknowledgment

Supported by The Danish Medical Research Council. *Declaration of interest.* None of the authors have any relevant interests to declare.

REFERENCES

1. Robertson A, Tirado C, Lobstein T, et al. Food and health in Europe: a new basis for action. WHO Regional Publications. European Series. 2004;96:1–385.
2. Jenkins DJ, Wolever TM, Taylor RH, et al. Glycemic index of foods: a physiological basis for carbohydrate exchange. Am J Clin Nutr. 1981;34:362–366.
3. Ludwig DDS. The glycemic index – Physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. Jama 2002;287:2414–2423.
4. Chiu CJ, Hubbard LD, Armstrong J, et al. Dietary glycemic index and carbohydrate in relation to early age-related macular degeneration. Am J Clin Nutr. 2006;83:880–886.
5. Liu SM. 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 2002;21:298–306.
6. Brand-Miller JC, Holt SHA, Pawlak DB, McMillan J. Glycemic index and obesity. Am J Clin Nutr. 2002;76(Suppl):S281–S285.
7. Liu S, Willett WC, Manson JE, Hu FB, Rosner B, Colditz G. Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle-aged women. Am J Clin Nutr. 2003;78:920–927.
8. Ludwig DS. Dietary glycemic index and obesity. J Nutr. 2000;130(Suppl):S280–S283.
9. Brand-Miller J, Hayne S, Petocz P, Colagiuri S. Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. Diabetes Care. 2003;26:2261–2267.
10. Kelly S, Frost G, Whittaker V, Summerbell C. Low glycaemic index diets for coronary heart disease. Cochrane Database Syst Rev. 2004;CD004467.
11. Opperman AM, Venter CS, Oosthuizen W, Thompson RL, Vorster HH. Meta-analysis of the health effects of using the glycaemic index in meal-planning. Br J Nutr. 2004;92:367–381.
12. Anderson JW, Randles KM, Kendall CW, Jenkins DJ. Carbohydrate and fiber recommendations for individuals with diabetes: a quantitative assessment and meta-analysis of the evidence. J Am Coll Nutr. 2004;23:5–17.
13. Thomas D, Elliott E, Baur L. Low glycaemic index or low glycaemic load diets for overweight and obesity. Cochrane Database Syst Rev. 2007;3:CD005105.
14. Livesey G, Taylor R, Hulshof T, Howlett J. Glycemic response and health – a systematic review and meta-analysis: relations between dietary glycemic properties and health outcomes. Am J Clin Nutr. 2008;87(Suppl):S258–S268.
15. Barclay AW, Petocz P, Millan-Price J, et al. Glycemic index, glycemic load, and chronic disease risk – a meta-analysis of observational studies. Am J Clin Nutr. 2008;87:627–637.
16. van Dam RM, Visscher AWJ, Feskens EJM, Verhoef P, Kromhout D. Dietary glycemic index in relation to metabolic risk factors and incidence of coronary heart disease: the Zutphen Elderly Study. Eur J Clin Nutr. 2000;54:726–731.
17. Levitan EB, Mittleman MA, Hakansson N, Wolk A. Dietary glycemic index, dietary glycemic load, and cardiovascular disease in middle-aged and older Swedish men. Am J Clin Nutr. 2007;85:1521–1526.
18. Liu SM, Willett WC, Stampfer MJ, et al. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. Am J Clin Nutr. 2000;71:1455–1461.
19. Beulens JW, de Bruijne LM, Stolk RP, et al. High dietary glycemic load and glycemic index increase risk of cardiovascular disease among middle-aged women: a population-based follow-up study. J Am Coll Cardiol. 2007;50:14–21.
20. Tavani A, Bosetti C, Negri E, Augustin LS, Jenkins DJ, La VC. Carbohydrates, dietary glycaemic load and glycaemic index, and risk of acute myocardial infarction. Heart. 2003;89:722–726.
21. Halton TL, Willett WC, Liu S, et al. Low-carbohydrate-diet score and the risk of coronary heart disease in women. N Engl J Med 2006;355:1991–2002.
22. Brand-Miller JC. Glycemic load and chronic disease. Nutr Rev. 2003;61(Suppl):S49–S55.
23. Leeds AR. Glycemic index and heart disease. Am J Clin Nutr 2002;76(Suppl):S286–S289.
24. Jenkins DJA, Kendall CWC, Augustin LSA, et al. Glycemic index: overview of implications in health and disease. Am J Clin Nutr. 2002;76(Suppl):S266–S273.
25. Liu S, Willett WC. Dietary glycemic load and atherothrombotic risk. Curr Atheroscler Rep. 2002;4:454–461.
26. Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. Jama. 1997;277:472–477.
27. Hu FB, Manson JE, Stampfer MJ, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med. 2001;345:790–797.
28. Barclay AW, Petocz P, Millan-Price J, et al. Glycemic index, glycemic load, and chronic disease risk – a meta-analysis of observational studies. Am J Clin Nutr. 2008;87:627–637.

29. Austin MA, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. Am J Cardiol. 1998;81:7B–12B.
30. Scaglioni S, Stival G, Giovannini M. Dietary glycemic load, overall glycemic index, and serum insulin concentrations in healthy schoolchildren. Am J Clin Nutr. 2004;79:339–340.
31. Sahyoun NR, Anderson AL, Kanaya AM, et al. Dietary glycemic index and load, measures of glucose metabolism, and body fat distribution in older adults. Am J Clin Nutr. 2005;82:547–552.
32. Murakami K, Sasaki S, Takahashi Y, et al. Dietary glycemic index and load in relation to metabolic risk factors in Japanese female farmers with traditional dietary habits. Am J Clin Nutr. 2006;83:1161–1169.
33. McKeown NM, Meigs JB, Liu S, Saltzman E, Wilson PW, Jacques PF. Carbohydrate nutrition, insulin resistance, and the prevalence of the metabolic syndrome in the Framingham Offspring Cohort. Diabetes Care. 2004;27:538–546.
34. Lau C, Faerch K, Glumer C, et al. Dietary glycemic index, glycemic load, fiber, simple sugars, and insulin resistance: the Inter99 study. Diabetes Care. 2005;28:1397–1403.
35. Liese AD, Schulz M, Fang F, et al. Dietary glycemic index and glycemic load, carbohydrate and fiber intake, and measures of insulin sensitivity, secretion, and adiposity in the insulin resistance atherosclerosis study. Diabetes Care. 2005;28:2832–2838.
36. Mayer-Davis EJ, Dhawan A, Liese AD, Teff K, Schulz M. Towards understanding of glycaemic index and glycaemic load in habitual diet: associations with measures of glycaemia in the Insulin Resistance Atherosclerosis Study. Br J Nutr. 2006;95:397–405.
37. Davis JN, Alexander KE, Ventura EE, et al. Associations of dietary sugar and glycemic index with adiposity and insulin dynamics in overweight Latino youth. Am J Clin Nutr. 2007;86:1331–1338.
38. Mosdol A, Witte DR, Frost G, Marmot MG, Brunner EJ. Dietary glycemic index and glycemic load are associated with high-density-lipoprotein cholesterol at baseline but not with increased risk of diabetes in the Whitehall II study. Am J Clin Nutr. 2007;86:988–994.
39. Salmeron J, Ascherio A, Rimm EB, et al. Dietary fiber, glycemic load, and risk of NIDDM in men. Diabetes Care. 1997;20:545–550.
40. Schulze MB, Liu S, Rimm EB, Manson JE, Willett WC, Hu FB. Glycemic index, glycemic load, and dietary fiber intake and incidence of type 2 diabetes in younger and middle-aged women. Am J Clin Nutr. 2004;80:348–356.
41. Krishnan S, Rosenberg L, Singer M, et al. Glycemic index, glycemic load, and cereal fiber intake and risk of type 2 diabetes in US black women. Arch Intern Med. 2007;167:2304–2309.
42. Villegas R, Liu S, Gao YT, et al. Prospective study of dietary carbohydrates, glycemic index, glycemic load, and incidence of type 2 diabetes mellitus in middle-aged Chinese women. Arch Intern Med. 2007;167:2310–2316.
43. Hodge AM, English DR, O'Dea K, Giles GG. Glycemic index and dietary fiber and the risk of type 2 diabetes. Diabetes Care. 2004;27:2701–2706.
44. Meyer KA, Kushi LH, Jacobs Jr DR, Slavin J, Sellers TA, Folsom AR. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. Am J Clin Nutr. 2000;71:921–930.
45. Stevens J, Ahn K, Juhaeri, Houston D, Steffan L, Couper D. Dietary fiber intake and glycemic index and incidence of diabetes in African-American and white adults: the ARIC study. Diabetes Care. 2002;25:1715–1721.
46. Sahyoun NR, Anderson AL, Tylavsky FA, Lee JS, Sellmeyer DE, Harris TB. Dietary glycemic index and glycemic load and the risk of type 2 diabetes in older adults. Am J Clin Nutr. 2008;87:126–131.
47. Barclay AW, Flood VM, Rochtchina E, Mitchell P, Brand-Miller JC. Glycemic index, dietary fiber, and risk of type 2 diabetes in a cohort of older Australians. Diabetes Care. 2007;30:2811–2813.
48. Barclay AW, Petocz P, Millan-Price J, et al. Glycemic index, glycemic load, and chronic disease risk – a meta-analysis of observational studies. Am J Clin Nutr. 2008;87:627–637.
49. Milton JE, Briche B, Brown IJ, Hickson M, Robertson CE, Frost GS. Relationship of glycaemic index with cardiovascular risk factors: analysis of the National Diet and Nutrition Survey for people aged 65 and older. Public Health Nutr. 2007;10:1321–1325.
50. Amano Y, Kawakubo K, Lee JS, Tang AC, Sugiyama M, Mori K. Correlation between dietary glycemic index and cardiovascular disease risk factors among Japanese women. Eur J Clin Nutr. 2004;58:1472–1478.
51. Levitan EB, Cook NR, Stampfer MJ, et al. Dietary glycemic index, dietary glycemic load, blood lipids, and C-reactive protein. Metabolism 2008;57:437–443.
52. Frost G, Leeds AA, Dore CJ, Madeiros S, Brading S, Dornhorst A. Glycaemic index as a determinant of serum HDL-cholesterol concentration. Lancet 1999;353:1045–1048.
53. Ma Y, Li Y, Chiriboga DE, et al. Association between carbohydrate intake and serum lipids. J Am Coll Nutr. 2006;25:155–163.
54. Oxlund AL, Heitmann BL. Glycaemic index and glycaemic load in relation to blood lipids – 6 years of follow-up in adult Danish men and women. Public Health Nutr. 2006;9:737–745.
55. Ford ES, Liu SM. Glycemic index and serum high-density lipoprotein cholesterol concentration among US adults. Arch Intern Med 2001;161:572–576.
56. Liu SM, Manson JE, Stampfer MJ, et al. Dietary glycemic load assessed by food-frequency questionnaire in relation to plasma high-density-lipoprotein cholesterol and fasting plasma triacylglycerols in postmenopausal women. Am J Clin Nutr. 2001;73:560–566.
57. Slyper A, Jurva J, Pleuss J, Hoffmann R, Gutterman D. Influence of glycemic load on HDL cholesterol in youth. Am J Clin Nutr. 2005;81:376–379.
58. Radhika G, Ganesan A, Sathya RM, Sudha V, Mohan V. Dietary carbohydrates, glycemic load and serum high-density lipoprotein cholesterol concentrations among South Indian adults. Eur J Clin Nutr. 2007;(Epub ahead of print).
59. Buyken AE, Toeller M, Heitkamp G, et al. Glycemic index in the diet of European outpatients with type 1 diabetes: relations to glycated hemoglobin and serum lipids. Am J Clin Nutr 2001;73:574–581.
60. Lau C, Toft U, Tetens I, et al. Association between dietary glycemic index, glycemic load, and body mass index in the Inter99 study: is underreporting a problem? Am J Clin Nutr. 2006;84:641–645.
61. Jonas CR, McCullough ML, Teras LR, Walker-Thurmond KA, Thun MJ, Calle EE. Dietary glycemic index, glycemic load, and risk of incident breast cancer in postmenopausal women. Cancer Epidemiol Biomarkers Prev. 2003;12:573–577.
62. Ma Y, Olendzki B, Chiriboga D, et al. Association between dietary carbohydrates and body weight. Am J Epidemiol. 2005;161:359–367.
63. Murakami K, Sasaki S, Okubo H, Takahashi Y, Hosoi Y, Itabashi M. Dietary fiber intake, dietary glycemic index and

load, and body mass index: a cross-sectional study of 3931 Japanese women aged 18–20 years. Eur J Clin Nutr. 2007;61: 986–995.
64. Nielsen BM, Bjornsbo KS, Tetens I, Heitmann BL. Dietary glycaemic index and glycaemic load in Danish children in relation to body fatness. Br J Nutr. 2005;94:992–997.
65. Kolagotla L, Singer MR, Cook J, Moore LL. Dietary glycemic index and change in body fat throughout childhood. Pediatr Res. 2003;53:168A.
66. Hare-Bruun H, Flint A, Heitmann BL. Glycemic index and glycemic load in relation to changes in body weight, body fat distribution, and body composition in adult Danes. Am J Clin Nutr. 2006;84:871–879.
67. Higginbotham S, Zhang ZF, Lee IM, Cook NR, Buring JE, Liu S. Dietary glycemic load and breast cancer risk in the Women's Health Study. Cancer Epidemiol Biomarkers Prev 2004;13:65–70.
68. Silvera SA, Jain M, Howe GR, Miller AB, Rohan TE. Glycaemic index, glycaemic load and ovarian cancer risk: a prospective cohort study. Public Health Nutr. 2007;10: 1076–1081.
69. Hill AB. The environment and disease: sasociation or causation? Proc R Soc Med 1965;58:295–300.
70. Stern JM, Simes RJ. Publication bias: evidence of delayed publication in a cohort study of clinical research projects. BMJ 1997;315:640–645.
71. Bardy AH. Bias in reporting clinical trials. Br J Clin Pharmacol. 1998;46:147–150.
72. Misakian AL, Bero LA. Publication bias and research on passive smoking: comparison of published and unpublished studies. JAMA 1998;280:250–253.
73. Astrup AV, Andersen NL, Stender S, Trolle E. [Dietary Recommendations 2005]. Ugeskr Laeger 2005;167:2296–2299.
74. Foster-Powell K, Holt SHA, Brand-Miller JC. International table of glycemic index and glycemic load values: 2002. Am J Clin Nutr. 2002;76:5–56.
75. Aston LM. Glycaemic index and metabolic disease risk. Proc Nutr Soc. 2006;65:125–134.