Effects of low glycaemic index/low glycaemic load vs. high glycaemic index/high glycaemic load diets on overweight/obesity and associated risk factors in children and adolescents: a systematic review and meta-analysis

Lukas Schwingshackl, Lisa Patricia Hobl and Georg Hoffmann*

Abstract

The objective of the present systematic review and meta-analysis was to synthesize the available literature data investigating the effects of low glycaemic index/low glycemic load dietary regimens on anthropometric parameters, blood lipid profiles, and indicators of glucose metabolism in children and adolescents. Literature search was performed using the electronic databases MEDLINE, EMBASE, and the Cochrane Central Register of trials with restrictions to randomized controlled trials, but no limitations concerning language and publication date. Parameters taken into account were: body weight, body mass index, z-score of body mass index, fat mass, fat-free mass, height, waist circumference, hip circumference, waist-to-hip ratio, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, diastolic and systolic blood pressure, fasting serum glucose, fasting serum insulin, HOMA-index, glycosylated haemoglobin, and C-reactive protein. Meta-analyses were performed for each parameter to assess pooled effect in terms of weighted mean differences between the post-intervention (or differences in means) of the low glycaemic index diets and the respective high glycaemic index counterparts. Data analysis was performed using the Review Manager 5.3 software. Nine studies enrolling 1,065 children or adolescents met the inclusion criteria. Compared to diets providing a high glycaemic index, low glycaemic index protocols resulted in significantly more pronounced decreases in serum triglycerides [mean differences −15.14 mg/dl, 95 %-CI (−26.26, −4.00)] and HOMA-index [mean difference −0.70, 95 %-CI (−1.37, −0.04), fixed-effects model only]. Other parameters under investigation were not affected by either low or high glycaemic indices. The present systematic review and meta-analysis provides evidence of a beneficial effect of a low glycaemic index/load diet in children and adolescents being either overweight or obese. Regarding the limitations of this analysis, further studies adopting a homogenous design are necessary to assure the present findings. Since low glycaemic index/load regimens were not associated with a deterioration of the outcome parameters, these diets should not be categorically excluded when looking for alternatives to change lifestyle habits in this age group.
Introduction
According to the World Health Organization (WHO), overweight and obesity remain the leading cause for premature death worldwide [1]. Especially alarming is the increasing number of children who are either overweight or obese. In the United States, the prevalence of childhood obesity nearly tripled between 1980 and 2000 [2]. Because of the fact that overweight children are about 30-50% more likely to suffer from comorbidities such as metabolic syndrome in adulthood than those with normal weight, it is of utmost importance to treat overweight and obesity as soon as possible [3]. Weight management programs designed for the age group of children and adolescents often focus on a reduced fat and/or carbohydrate intake. Diets providing a low glycaemic index (LGI)/low glycaemic load (LGL) seemed to have promising effects on weight reduction, dyslipidaemia and blood glucose values.

The term “glycaemic index” (GI) was introduced by Jenkins and co-workers in 1981 [4] referring to the area under the blood glucose curve measured two hours after consuming 50 g of test carbohydrates in relation to the results obtained by 50 g of glucose or white bread. In 1997 [5, 6] the term glycaemic load (GL) was introduced to quantify the overall glycaemic effect of food with respect to its specific carbohydrate content in typically consumed quantities (i.e. for a specific food, GL equals GI multiplied by the carbohydrate density of the food, usually given as g carbohydrate per 100 g serving). In a meta-analysis published in 2003, LGI diets exerted significant benefits on glycosylated haemoglobin (HbA1c) in type 1 and type 2 diabetics as compared to high GI (HGI) regimens [7]. These results could be confirmed by others demonstrating LGI diets being superior to their HGI counterparts with respect to HbA1c, serum fasting glucose (FG), body weight, fat mass, body mass index (BMI), total cholesterol (TC), LDL-cholesterol (LDL-C), and C-reactive protein (CRP) in overweight and obese study participants being otherwise healthy or diabetic [8–14]. Furthermore, a meta-analyses of cohort studies revealed that the highest category of GI/GL was associated with a significantly increased risk for the development of type 2 diabetes [15]. A correlation between GI/GL and risk of coronary heart disease was postulated as well [16].

Most of the epidemiologic data and intervention studies focus on the effects of LGI/LGL diets in adults. In the present systematic review, we investigated the impact of LGI and LGL protocols in randomized controlled trials on anthropometric parameters, blood lipid profiles, and indicators of glucose metabolism in children and adolescents with a mean age below 18 years.

Methods
This systematic review is recorded in the PROSPERO International Prospective Register of Systematic Reviews (crd.york.ac.uk/prospero/index.asp) with the registration number CRD42015016799.

Literature search
Queries of literature were performed using the electronic databases MEDLINE (between 1966 and February 2015), EMBASE (between 1980 and February 2015), and the Cochrane Central Register of trials (until February 2015) with restrictions to randomized controlled trials and age birth to 18 years, but no limitation to language and publication date. Search terms were: “glycaemic index” and “glycaemic load” as well as “glycemic index” and “glycemic load”. Selected articles were screened and sorted out if not all inclusion criteria were met. However, reference lists from retrieved articles were checked to search for further relevant studies, and systematic reviews and meta-analysis were searched as well. This systematic review was planned, conducted, and reported in adherence to standards of quality for reporting meta-analyses [17].

Study selection
To be included in this systematic review, studies had to fulfil all of the following criteria: (1) randomized controlled trials (RCTs); (2) humans; (3) mean age of subjects < 18 years; (4) comparing a LGI or LGL with a HGI or high GL (HGL) dietary pattern; GI and/or GL values must have been reported; (5) report of post mean or mean of two time point values with standard deviation or basic data to calculate these parameters must have been given; (6) assessment of the “outcome of interest” markers: BMI, body weight, height, waist circumference (WC), hip circumference (HC), waist to hip ratio (WHR), fat mass, fat-free mass (FFM), TC, LDL-C, HDL-C, triglycerides (TG), diastolic blood pressure (DBP), systolic blood pressure (SBP), FG, fasting serum insulin (FI), HOMA-Index (HOMA), HbA1c, and CRP.

Risk of bias assessment
Risk of bias was assessed by two authors (LS, GH) using the Risk of bias assessment tool provided by the Cochrane Collaboration. With this tool, the following sources of bias were detected: selection bias, performance/detection bias, attrition bias, reporting bias and other bias (such as contamination via mixing interventions and controls) [18, 19] (Fig. 1).

Data extraction and statistical analysis
The following data were extracted from each study: the first author’s name and the year of publication, duration of the study, number, age and sex of participants, baseline BMI or BMI z-score, dietary descriptions with GI and GL values, amount of energy (kcal) and drop-out rate as well as outcomes and post mean values or differences in mean of two time point values with corresponding standard
deviation. According to the Cochrane Collaboration, it is legit to use both the post-intervention values and differences in means in a meta-analysis [20]. For each outcome parameter a meta-analysis was created to compare the pooled weighted means at the endpoint of the studies or weighted mean differences from the LGI/LGL and HGI/HGL diet groups. All data were analyzed using the software REVIEW MANAGER 5.3, provided by the Cochrane Collaboration (http://tech.cochrane.org/revman). Forest plots were generated to illustrate the study-specific effect sizes along with a 95 %-CI. X²-tests were performed to examine the heterogeneity of the present data results. The I² parameter was used to estimate the inconsistency of the results with I² > 50 % was defined in advance to represent substantial heterogeneity.

Data extraction was conducted independently by all authors, with disagreements resolved by consensus.

Specific data handling
In one of the studies included for meta-analyses [21], two different sets of LGI vs. HGI comparisons were designed distinguished by their protein content. Both designs were included in the study by comparing low protein/LGI with low protein/HGI and high protein/LGI with high protein/HGI separately.

Ethical approval
Not required for this systematic review.

Results
Literature search and study characteristics
A total of nine studies enrolling 1,065 subjects extracted from 1,359 articles met the inclusion criteria and were enclosed for meta-analyses [21–29]. The detailed steps
of the systematic article search and selection process are given as a flow chart in Fig. 2.

All nine studies were randomized controlled trials (RCTs) with a duration between 10 and 96 weeks and a publication date between the years 2003 and 2014. General study characteristics are summarized in Table 1. The data by Damsgaard et al. [30] were not suitable for meta-analyses, since not enough information was given by the authors to calculate standard deviations. For the other trials, the pooled estimates of effect size for the results of LGI/LGL compared to HGI/HGL for all outcome parameters are summarized in Table 2.

**Anthropometric parameters**

None of the anthropometric data was affected significantly by an LGI/LGL dietary protocol (Table 2). Since most of the data came from the DIOGenes Study [21] enrolling many children with normal weight, sensitivity analyses were performed including only trials investigating the effects of LGI/LGL vs. HGI/HGL on children and adolescents being either overweight and/or obese. However, still no significant differences were found between the two dietary regimens (Table 2).

**Blood lipids**

TG levels were significantly more decreased in the LGI/LGL groups as compared to their HGI/HGL counterparts [MD $-15.14$ mg/dl, 95 % CI $(−26.26, −4.00)$, $p = 0.008$] (Fig. 3). GI did not influence any of the other blood lipid values extracted for this systematic review (Table 2).

**Parameters of glucose control**

Decreases in HOMA-index [MD $-0.70$, 95 % CI $(−1.37, −0.04)$, $p = 0.04$] were significantly more pronounced following an LGI/LGL diet as compared to the HGI/HGL protocols (Fig. 4) when fixed-effects models were applied. Following random-effects data synthesis, results were not statistically significant [MD $-0.87$, 95 % CI $(−1.75, 0.02)$, $p = 0.06$].

**Discussion**

By synthesizing data of nine randomized controlled trials, the present meta-analysis provides evidence that a low GI/GL diet may exert beneficial effects on TG and HOMA-index in children and adolescents as compared to a high GI/GL dietary approach.
### Table 1 General characteristics of randomized controlled intervention trials included in the meta-analysis

| Reference          | Participants | Age (yrs) | Duration (weeks) | Dietary intervention (as indicated by the investigators) | Energy amount (end of the study), or energy restriction | Drop Out |
|--------------------|--------------|-----------|------------------|----------------------------------------------------------|--------------------------------------------------------|----------|
| Casazza et al. 2012 [22] | 26 | 12.4 | 16 | Specialized diet | 346, 129 | 2019 kcal | 0 % |
| Ebbeling et al. 2003 [23] | 16 | 16.9 | 24 | Reduced glycemic load diet vs Standard diet | 53, 68 (g/1000 kcal) | 1621 | 12.5 % |
| Ianuzzi et al. 2008 [24] | 26 | Range: 7-13 | 24 | diet high glycemic index vs Low-fat diet | 60 | 1981.6 kcal | 48.1 % |
| Kirk et al. 2012 [25] | 66 | 9.8 | 48 | Low carbohydrate diet vs Portion controlled diet | <55, 73.2 (g/1000 kcal) | 1950 kcal | 25.7 % |
| Kong et al. 2014 [26] | 104 | 16.8 | 24 | Low glycemic index diet vs Control diet | 74.4, 117.7 | 1565 kcal | 34.6 % |
| Mirza et al. 2013 [27] | 113 | 11.65 | 96 | Low glycemic load diet vs Low fat diet | 55.5, 77.2 | 1148 kcal | 52.6 % |
| Papadaki et al. 2010 [21] | 647 | 12.15 | 26 | Low protein/LGI vs Low protein/HGI | 60.8, 153.4 | 1692.4 kcal | 37 % |
| Ramon-Krauel et al. 2013 [28] | 17 | 12.8 | 24 | LGI diet vs Low fat | 54.6, 56.4 | 1271 kcal | 12.5 % |
| Rouhani et al. 2013 [29] | 50 | 13.89 | 10 | LGI vs Healthy nutrition recommendations | 43.22 | 1503 kcal | 24 % |

**BMI** = body mass index; **HGI** = high glycaemic index; **HGL** = high glycaemic load; **LGI** = low glycaemic index; **LGL** = low glycaemic load; **LP** = low protein
### Table 2  Pooled estimates of effect size for the results of low glycaemic index/low glycaemic load compared to high glycaemic index/high glycaemic load

| Outcome parameter (I²) | Mean difference | 95% confidence interval | p-Value | No. of studies | Sample size | I² (%) |
|------------------------|-----------------|------------------------|---------|----------------|-------------|--------|
| Body mass index, kg/m² | −0.54 (−1.19, 0.12) | 0.11 | 7 | 836 | 13 |
| Body mass index, kg/m²¹ | −1.00 (−2.31, 0.31) | 0.13 | 5 | 119 | 24 |
| Body mass index z-score | −0.09 (−0.19, 0.01) | 0.08 | 4 | 777 | 0 |
| Body mass index z-score ¹ | −0.11 (−0.23, 0.02) | 0.10 | 2 | 40 | 0 |
| Weight, kg | −0.10 (−1.86, 1.67) | 0.92 | 5 | 794 | 9 |
| Weight, kg ¹ | −0.37 (−2.82, 2.08) | 0.77 | 3 | 103 | 0 |
| Waist circumference, cm | −1.23 (−3.22, 0.77) | 0.23 | 5 | 794 | 0 |
| Waist circumference, cm ¹ | −1.40 (−5.46, 2.66) | 0.50 | 3 | 103 | 0 |
| Hip circumference, cm | −1.07 (−3.25, 1.12) | 0.34 | 3 | 664 | 0 |
| Hip circumference, cm ¹ | −8.00 (−23.5, 7.50) | 0.31 | 1 | 16 | NA |
| Waist-to-hip ratio | 0.00 (−0.02, 0.01) | 0.53 | 3 | 664 | 13 |
| Waist-to-hip ratio ¹ | 0.00 (−0.05, 0.05) | 1.00 | 1 | 16 | NA |
| Body fat, kg | −0.43 (−2.01, 1.14) | 0.59 | 4 | 777 | 40 |
| Body fat, kg ¹ | 0.44 (−1.52, 2.40) | 0.66 | 2 | 87 | 28 |
| Fat mass, kg | −1.04 (−2.50, 0.43) | 0.17 | 4 | 689 | 26 |
| Fat mass, kg ¹ | −1.87 (−3.96, 0.22) | 0.08 | 2 | 42 | 64 |
| Fat-free mass, kg | 0.81 (−1.10, 2.72) | 0.40 | 2 | 647 | 71 |
| Diastolic blood pressure, mm Hg | 0.65 (−2.11, 3.41) | 0.64 | 4 | 213 | 39 |
| Systolic blood pressure, mm Hg | 1.63 (−1.52, 4.78) | 0.31 | 4 | 213 | 39 |
| LDL-cholesterol, mg/dl | −1.61 (−8.09, 4.87) | 0.63 | 4 | 237 | 0 |
| HDL-cholesterol, mg/dl | 0.27 (−2.13, 2.66) | 0.83 | 5 | 263 | 0 |
| Triglycerides, mg/dl | −15.14 (−26.26, −4.00) | 0.008 | 5 | 263 | 0 |
| Total cholesterol, mg/dl | −3.72 (−11.71, 4.27) | 0.36 | 4 | 246 | 0 |
| C-reactive protein, mg/l | 0.58 (−0.25, 1.41) | 0.17 | 1 | 26 | NA |
| HOMA index | −0.70 (−1.37, −0.04) | 0.04 | 4 | 172 | 30 |
| Fasting serum insulin, μU/ml | 2.67 (−6.32, 0.9) | 0.15 | 3 | 109 | 0 |
| Fasting serum glucose, mg/dl | −0.13 (−2.25, 1.98) | 0.90 | 4 | 213 | 0 |

I² = inconsistency (heterogeneity); NA = not applicable

¹ For anthropometrical parameters, sensitivity analyses were performed including only trials investigating the effects of glycaemic index/load on children and adolescents being either overweight and/or obese (no such data were available for fat-free mass)
Overweight and obesity in children and adolescents represent a worldwide problem with grave consequences for those affected. Increased body fat mass is considered to be a major risk factor for the development of cardiovascular and metabolic diseases such as type 2 diabetes. Lifestyle modifications aiming at a normalisation of body weight with subsequent weight management are a core principle in primary and secondary prevention for those being either overweight or obese. The influence of variations in macronutrient compositions on body weight indices is discussed controversially both in adults as well as in children and adolescents. A number of dietary regimens differing in macronutrient content were compared in a systematic review by Gow and co-workers [31] with respect to their effects on children and adolescents with overweight and obesity. Results suggest that expressive indicators such as BMI z-score will show positive developments regardless of the dietary macronutrient composition as long as a hypocaloric diet is given. According to Gow et al., short-term advantages of a low carbohydrate regime as compared to high carbohydrate counterparts were no longer detectable in long-term follow-up investigations. In interventions by Demol et al. [32] and by Krebs et al. [33], BMI z-score was found to be decreased by an average of 0.25 following a low carbohydrate regimen. In our own study, we could observe a tendency towards a more prominent reduction in BMI z-score of −0.09 following a low GI/GL diet as compared to a high GI/GL protocol. Although these changes are smaller in scope and non-significant, the trials enrolled in the present meta-analysis are characterized by a longer running time of 24–96 weeks as compared to the studies by Demol et al. (12 weeks) and Krebs et al. (13 weeks), respectively. This finding can be interpreted as an indication that a special focus on GI/GL might exert long-term benefits regarding body weight management. However, none of the other anthropometric parameters observed in this meta-analysis was affected in a different manner by either GI/GL dietary regimens.

An increased level of TG is regarded to be a predictor of atherosclerosis and subsequent cardiovascular diseases. When compared to their normal weight peers, children with overweight (+0.21 mmol/L) or obesity (+0.26 mmol/L) were reported to have significantly increased serum TG concentrations [34]. In the present meta-analysis, reduction in TG levels was significantly stronger following low GI/GL diets with improved values averaging 17 mg/dL (~0.17 mmol/L) which indicates a favourable change regarding the predictive power of increased TG concentrations.
Another target of low GI/GL diets is insulin resistance, which is commonly associated with overweight and obesity and is regarded to be a precursor of the corresponding cardiovascular and metabolic consequences [35, 36]. Insulin resistance can be assessed via euglycaemic hyperinsulinaemic patch clamp, however, this procedure is not applicable for every trial due to its costs and invasiveness. Thus, it is more appropriate to use a surrogate marker when recording insulin resistance. Both surrogate markers used in our meta-analyses (HOMA index and fasting insulin) were classified to be inadequate in the assessment of insulin resistance in children and adolescents during a consensus conference on the topic in 2010 [37]. HOMA index is known to correlate well with FI [38], however, FI itself is regarded to be no suitable alternative for the gold standard [39–41]. Still, the fact remains that both parameters are measured in numerous intervention studies to assess the impact of lifestyle on insulin resistance. We could observe a reduction in HOMA-index that was significantly stronger (mean difference −0.70 units) in individuals subjected to a low GI/GL protocol as compared to its high GI/GL counterparts. Although there is no unanimously accepted cut-off value for HOMA-index to indicate insulin resistance in children and adolescents, some studies have suggested that values near to 3.0 might be adequate in the pediatric population [42]. Thus, changes like the ones found in the present study may be of clinical relevance. Decrease in FI was more pronounced, albeit not statistically significant, following a low GI/GL dietary protocol (−2.67 μU/mL) in the present analysis based upon three trials. Significantly improved FI values in a pediatric population following lifestyle interventions based upon changes in dietary habits and/or physical activity were described by Ho et al. [43, 44].

CRP is generally accepted as a biomarker for chronic low-grade inflammation usually observed in association with obesity, diabetes, or cardiovascular diseases [45, 46]. Observational as well as interventional studies reported a beneficial effect of a diet focusing on low GI/GL on serum CRP concentrations [12, 47]. This is in contrast to the results of Iannuzzi et al. [24] in the present analysis who could not observe a superior effect of low GI/GL on CRP when compared to high GI/GL diets. This seems to be more in line with data by Griffith et al. [48], who could not find a correlation between GI/GL and CRP in normal weight individuals with even lower levels of serum CRP in overweight and obese individuals following a high GI/GL diet.

One major limitation of the present systematic review is the fact that there is only a low a number of studies assessing the specific outcome parameter chosen for data synthesis. This might explain that statistically significant differences between LGI/LGL and HGI/HGL could only be observed for TG and HOMA index, while other parameters were characterized by tendencies towards an improvement following diets adopting a low glycaemic index. In addition, there was a broad range of dietary measures with different setups for low or high GI/GL (e.g. via an additional variation in protein content) or the respective thresholds to distinguish between both protocols. Assessment of adhesion to dietary protocols, drop outs, and randomization of study participants were presented and grouped in different ways as well. This might be of special importance concerning a potential study immanent low adherence of volunteers to the prescribed dietary intervention. Although most of the studies enrolled in the present meta-analysis were characterized by a clear difference between initial LGI and HGI protocols, there was a tendency towards an approximation of dietary GI between groups at the end of the studies (e.g. Damsgaard et al. [30], who reported a dietary GI that was only four points lower in their LGI groups as compared to the HGI counterparts by the end of their trial). This can be explained by numerous reasons such as lack of taste stimuli affecting flavour of the diet. Although these limitations are characteristic for nutritional intervention studies [49], they nevertheless affect the validity of the data.

Conclusion
The present systematic review and meta-analyses provide evidence of a beneficial effect of a low GI/GL diet in children and adolescents being either overweight or obese. Although no improvements could be found with respect to anthropometrical parameters such as body weight, BMI, BMI z-score, or waist circumference, a statistically significant positive impact was found for TG and HOMA index. Regarding the limitations of this analysis, the results are not solid enough to justify a clear recommendation. Further - esp. long-term - studies are necessary to assure the present findings. Since low GI/GL regimens were not associated with a deterioration of the outcome parameters, these diets should not be categorically excluded when looking for alternatives to change lifestyle habits in this age group.

Abbreviations
BMI: Body mass index; CRP: C-reactive protein; DBP: Diastolic blood pressure; FFMI: Fat-free mass; FG: Fasting glucose; FI: Fasting insulin; HbA1c: Glycosylated haemoglobin; HC: Hip circumference; HDLC: High density lipoprotein-cholesterol; HOMA: (high) glycaemic index; HOMA-GL: (high) glycaemic load; I²: Inconsistency; LDL-C: Low density lipoprotein-cholesterol; LGI: (low) glycaemic index; LGL: (low) glycaemic load; TC: Total cholesterol; SBP: Systolic blood pressure; TG: Triglycerides; WC: Waist circumference; WHR: Waist-to-hip ratio; WMD: (weighted) mean difference.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
GH and LS developed the idea for this systematic review, GH prepared the protocol. Literature search was performed by LS and LPH, while data
References

1. World Health Organization (WHO). Obesity and overweight. 2014. http://www.who.int/mediacentre/factsheets/fs311/en/. Accessed December 12th, 2014.

2. Ogden CL, Kuczmarski RJ, Flegal KM, Mei Z, Guo S, Wei R, et al. Centers for Disease Control and Prevention 2000 growth charts for the United States: improvements to the 1977 National Center for Health Statistics version. Pediatrics. 2002;109(1):45–60.

3. Swingshackl L, Ascherio A, Rimm EB, Colditz GA, Spiegelman D, Jenkins DJ, et al. Dietary fiber, glycemic load, and risk of NIDDM in men. Diabetes Care. 1997;20(4):545–50. doi:10.2327/diacare.20.4.545.

4. Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of noninsulin-dependent diabetes mellitus in women. JAMA. 1997;277(6):472–76. doi:10.1001/jama.1997.035409010331.

5. 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(8):2261–7.

6. Goff LM, Cowland DE, Hooper L, Frost GS. Low glycemic index diets and blood lipids: a systematic review and meta-analysis of randomized controlled trials. Nutr Metab Cardiovasc Dis. 2012;22(1):101–10. doi:10.1016/j.numecd.2012.06.002.

7. Kelly S, Frost G, Whittaker V, Summerbell C. Low glycemic index diets for coronary heart disease. Cochrane Database Syst Rev. 2004;4:CD004647. doi:10.1002/14651858.CD004647.pub2.

8. Livsey 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(1):595–605.

9. Opperman AM, Venter CS, Oosthuizen W, Thompson RL, Vorster HH. Meta-analysis of the health effects of using the glycemic index in meal-planning. Br J Nutr. 2004;92(3):367–81.

10. Schwingshackl L, Hoffmann G. Long-term effects of low glycemic index/low glycemic load vs. high glycemic index/load diets on parameters of obesity and obesity-associated risks: A systematic review and meta-analysis. Nutr Metab Cardiovasc Dis. 2012;22(8):699–706. doi:10.1016/j.numecd.2012.03.008.

11. Thomas DE, Elliott EJ, Baur L. Low glycemic index or low glycemic load diets for overweight and obesity. Cochrane Database Syst Rev. 2007;3:CD005105. doi:10.1002/14651858.CD005105.pub2.

12. Thomas D, Elliott EJ. Low glycemic index, low glycemic load, diets for diabetes mellitus. Cochrane Database Syst Rev. 2009;1:CD002696. doi:10.1002/14651858.CD002696.pub2.

13. Dong JY, Zhang L, Zhang YH, Qin LQ. Dietary glycemic index and glycemic load in relation to the risk of type 2 diabetes: a meta-analysis of prospective cohort studies. Br J Nutr. 2011;106(1):1649–54. doi:10.1017/S0007114511005480.

14. Mente A, De Koning L, Shannon HS, Anand SS. A systematic review of the evidence supporting a causal link between dietary factors and coronary heart disease. Arch Intern Med. 2009;169(7):669–69. doi:10.1001/archinternmed.2009.38.

15. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7), e1000097. doi:10.1371/journal.pmed.1000097.

16. Higgins JP, Altman DG, Gøtzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.

17. Hooper L, Summerbell CD, Thompson R, Sills D, Roberts FG, Moore HJ, et al. Reduced or modified dietary fat for preventing cardiovascular disease. Cochrane Database Syst Rev. 2012;2:CD005237. doi:10.1002/14651858.CD005237.pub6.

18. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Collaboration; updated March 2011.

19. Papadaki A, Linardakis M, Larsen TM, van Baak MA, Lindroos AK, Pfeiffer AF, et al. The effect of protein and glycemic index on children's body composition: the DiOGenes randomized study. Pediatrics. 2012;126(5):e1435–52. doi:10.1542/peds.2009-3533.

20. Casaza K, Cardel M, Dullin-Keita A, Hanks LJ, Gower BA, Newton AL, et al. Reduced carbohydrate diet to improve metabolic outcomes and decrease adiposity in obese peripubertal African American girls. J Pediatr. 2011;158(3):336–42. doi:10.1016/j.jpeds.2010.04.018.

21. Papadaki A, Linardakis M, Larsen TM, van Baak MA, Lindroos AK, Pfeiffer AF, et al. The effect of protein and glycemic index on children's body composition: the DiOGenes randomized study. Pediatrics. 2012;126(5):e1435–52. doi:10.1542/peds.2009-3533.

22. Casaza K, Cardel M, Dullin-Keita A, Hanks LJ, Gower BA, Newton AL, et al. Reduced carbohydrate diet to improve metabolic outcomes and decrease adiposity in obese peripubertal African American girls. J Pediatr. 2011;158(3):336–42. doi:10.1016/j.jpeds.2010.04.018.
38. Schwartz B, Jacobs DR, Moran A, Steinberger J, Hong CP, Sinaiko AR. Measurement of insulin sensitivity in children: comparison between the euglycemic-hyperinsulinemic clamp and surrogate measures. Diabetes Care. 2006;31(14):785–8. doi:10.2337/dci06-1376.

39. Brandou F, Brun JF, Mercier J. Limited accuracy of surrogates of insulin resistance during puberty in obese and lean children at risk for altered gluoregulation. J Clin Endocrinol Metab. 2005;90(2):761–7. doi:10.1210/jc.2004-0329.

40. Gungor N, Saad R, Janosky J, Arslanian S. Validation of surrogate estimates of insulin sensitivity and insulin secretion in children and adolescents. J Pediatr. 2004;144(1):47–55. doi:10.1016/j.jpeds.2003.09.045.

41. Huang TT, Johnson MS, Goran MI. Development of a prediction equation for insulin sensitivity from anthropometry and fasting insulin in prepubertal and early pubertal children. Diabetes Care. 2002;25(7):1203–10.

42. Tresaco B, Bueno G, Pineda I, Moreno LA, Garagori JM, Bueno M. Homeostatic model assessment (HOMA) index cut-off values to identify the metabolic syndrome in children. J Physiol Biochem. 2005;61(2):381–8.

43. Ho M, Garnett SP, Baur L, Burnows T, Stewart L, Neve M, et al. Effectiveness of lifestyle interventions in child obesity: systematic review with meta-analysis. Pediatrics. 2012;130(3):e1647–71. doi:10.1542/peds.2012-1176.

44. Ho M, Garnett SP, Baur L, Burnows T, Stewart L, Neve M, et al. Impact of dietary and exercise interventions on weight change and metabolic outcomes in obese children and adolescents: a systematic review and meta-analysis of randomized trials. JAMA Pediatr. 2013;167(8):759–68. doi:10.1001/jamapediatrics.2013.1453.

45. Shoelson SE, Herrero L, Naaz A. Obesity, inflammation, and insulin resistance. Gastroenterology. 2007;132(6):2169–80. doi:10.1053/j.gastro.2007.03.059.

46. Xu H, Barnes GT, Yang Q, Tan G, Yang D, Chou CJ, et al. Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. J Clin Invest. 2003;112(12):1821–30. doi:10.1172/JCI19451.

47. Buyken AE, Goletzke J, Joslowski G, Feltick A, Cheng G, Herder C, et al. Association between carbohydrate quality and inflammatory markers: systematic review of observational and interventional studies. Am J Clin Nutr. 2014;99(4):813–33. doi:10.3945/ajcn.113.074252.

48. Griffith JA, Ma Y, Chasan-Taber L, Olendzki BC, Chiriboga DE, Stanek EJ, 3rd et al. Association between dietary glycemic index, glycemic load, and high-sensitivity C-reactive protein. Nutrition (Burbank, Los Angeles County, Calif). 2008;24(5):401–6. doi:10.1016/j.nut.2007.12.017.

49. Sacks FM, Bray GA, Carey VJ, Smith SR, Ryan DH, Anton SD, et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. N Engl J Med. 2009;360(9):859–73. doi:10.1056/NEJMoa0804748.