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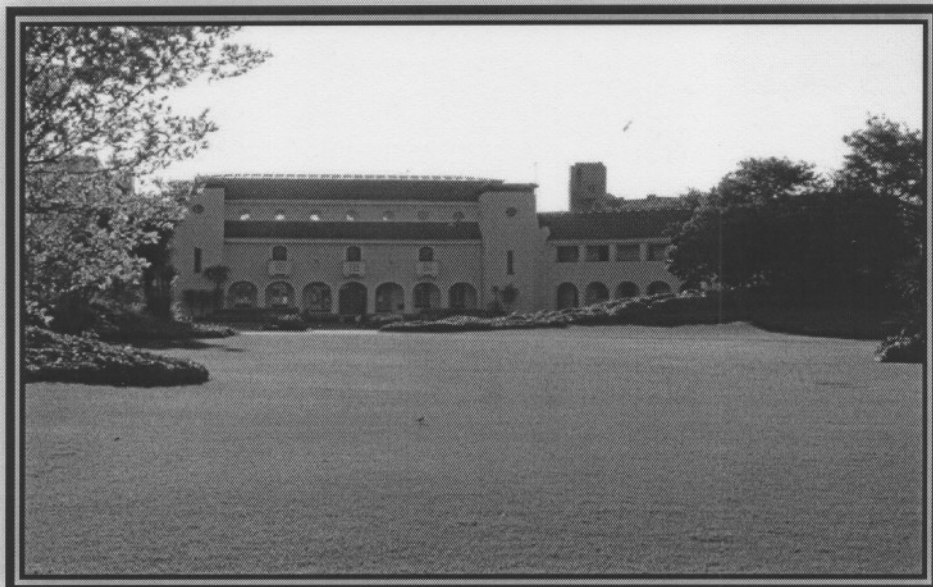NORTH-WEST UNIVERSITY
NOORDWES-UNIVERSITEIT

Meta-analysis and systematic review of the benefits expected when the glycaemic index is used in planning diets

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Handelinge 2:25

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Summary

Motivation: The prevalence of non-communicable diseases such as diabetes mellitus (DM) and cardiovascular disease (CVD) is rapidly increasing in industrialized societies. Experts believe that lifestyle, and in particular its nutritional aspects, plays a decisive role in increasing the burden of these chronic conditions. Dietary habits could, therefore, be modified to exert a positive impact on the prevention and treatment of chronic diseases of lifestyle. It is believed that the state of hyperglycaemia that is observed following food intake under certain dietary regimes contributes to the development of various metabolic conditions. This is not only true for individuals with poor glycaemic control such as some diabetics, but could also be true for healthy individuals. It would, therefore, be helpful to be able to reduce the amplitude and duration of postprandial hyperglycaemia. Selecting the correct type of carbohydrate (CHO) foods may produce less postprandial hyperglycaemia, representing a possible strategy in the prevention and treatment of chronic metabolic diseases. At the same time, a key focus of sport nutrition is the optimal amount of CHO that an athlete should consume and the optimal timing of consumption. The most important nutritional goals of the athlete are to prepare body CHO stores pre-exercise, provide energy during prolonged exercise and restore glycogen stores during the recovery period. The ultimate aim of these strategies is to maintain CHO availability to the muscle and central nervous system during prolonged moderate to high intensity exercise, since these are important factors in exercise capacity and performance. However, the type of CHO has been studied less often and with less attention to practical concerns than the amount of CHO.

The glycaemic index (GI) refers to the blood glucose raising potential of CHO foods and, therefore, influences secretion of insulin. In several metabolic disorders, secretion of insulin is inadequate or impossible, leading to poor glycaemic control. It has been suggested that low GI diets could potentially contribute to a significant improvement of the conditions associated with poor glycaemic control. Insulin secretion is also important to athletes since the rate of glycogen synthesis depends on insulin due to it stimulatory effect on the activity of glycogen synthase.

Objectives: Three main objectives were identified for this study. The first was to conduct a meta-analysis of the effects of the GI on markers for CHO and lipid metabolism with the emphasis on randomised controlled trials (RCT's). Secondly, a systematic review was performed to determine the strength of the body of scientific evidence from epidemiological studies combined with RCT's to encourage dieticians to incorporate the GI concept in meal planning. Finally, a systematic review of the effect of the GI in sport performance was conducted on all available literature up to date to investigate whether the application of the GI in an athlete's diet can enhance physical performance.

Methodology: For the meta-analysis, the search was for randomised controlled trials with a cross-over or parallel design published in English between 1981 and 2003, investigating the effect of low GI *vs* high GI diets on markers of carbohydrate and lipid metabolism. The main outcomes were serum fructosamine, glycosylated haemoglobin (HbA_{1c}), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), total cholesterol (TC) and triacylglycerols (TG). For the systematic review, epidemiological studies as well as RCT's investigating the effect of LGI *vs* HGI diets on markers for carbohydrate and lipid metabolism were used. For the systematic review on the effect of the GI on sport performance, RCT's with either a cross-over or parallel design that were published in English between January 1981 and September 2004 were used. All relevant manuscripts for the systematic reviews as well as meta-analysis were obtained through a literature search on relevant databases such as the Cochrane Central Register of Controlled Trials, MEDLINE (1981 to present), EMBASE, LILACS, SPORTDiscus, ScienceDirect and PubMed. This thesis is presented in the article format.

Results and conclusions of the individual manuscripts:

⇒ For the meta-analysis, literature searches identified 16 studies that met the strict inclusion criteria. Low GI diets significantly reduced fructosamine ($p < 0.05$), HbA_{1c} ($p < 0.03$), TC ($p < 0.0001$) and tended to reduce LDL-c ($p = 0.06$) compared to high GI diets. No changes were observed in HDL-c and TG concentrations. Results from this meta-analysis, therefore, support the use of the GI concept in choosing CHO-containing foods to reduce TC and improve blood glucose control in diabetics.

⇒ The systematic review combined the results of the preceding meta-analysis and results from epidemiological studies. Prospective epidemiological studies showed improvements in HDL-c concentrations over longer time periods with low GI diets *vs*. high GI diets, while the RCT's failed to show an improvement in HDL-c over the short-term. This could be attributed to the short intervention period during which the RCT's were conducted. Furthermore, epidemiological studies failed to show positive relationships between LDL-c and TC and low GI diets, while RCT's reported positive results on both these lipids with low GI diets. However, the epidemiological studies, as well as the RCT's showed positive results with low GI diets on markers of CHO metabolism. Taken together, convincing evidence from RCT's as well as epidemiological studies exists to recommend the use of low GI diets to improve markers of CHO as well as of lipid metabolism.

⇒ From the systematic review regarding the GI and sport performance it does not seem that low GI pre-exercise meals provide any advantages over high GI pre-exercise meals. Although low GI pre-exercise meals may better maintain CHO availability during exercise, low GI pre-exercise meals offer no added advantage over high GI meals regarding performance. Furthermore, the exaggerated metabolic responses from high GI compared

to low GI CHO seems not be detrimental to exercise performance. However, athletes who experience hypoglycaemia when consuming CHO-rich feedings in the hour prior to exercise are advised to rather consume low GI pre-exercise meals. No studies have been reported on the GI during exercise. Current evidence suggests a combination of CHO with differing GI's such as glucose (high GI), sucrose (moderate GI) and fructose (low GI) will deliver the best results in terms of exogenous CHO oxidation due to different transport mechanisms. Although no studies are conducted on the effect of the GI on short-term recovery it is speculated that high GI CHO is most effective when the recovery period is between 0-8 hours, however, evidence suggests that when the recovery period is longer (20-24 hours), the total amount of CHO is more important than the type of CHO.

Conclusion: There is an important body of evidence in support of a therapeutic and preventative potential of low GI diets to improve markers for CHO and lipid metabolism. By substituting high GI CHO-rich with low GI CHO-rich foods improved overall metabolic control. In addition, these diets reduced TC, tended to improve LDL-c and might have a positive effect over the long term on HDL-c. This confirms the place for low GI diets in disease prevention and management, particularly in populations characterised by already high incidences of insulin resistance, glucose intolerance and abnormal lipid levels. For athletes it seems that low GI pre-exercise meals do not provide any advantage regarding performance over high GI pre-exercise meals. However, low GI meals can be recommended to athletes who are prone to develop hypoglycaemia after a CHO-rich meal in the hour prior to exercise. No studies have been reported on the effect of the GI during exercise. However, it has been speculated that a combination of CHO with varying GI's deliver the best results in terms of exogenous CHO oxidation. No studies exist investigating the effect of the GI on short-term recovery, however, it is speculated that high GI CHO-rich foods are suitable when the recovery period is short (0-8 h), while the total amount rather than the type of CHO is important when the recovery period is longer (20-24 h). Therefore, the GI is a scientifically based tool to enable the selection of CHO-containing foods to improve markers for CHO and lipid metabolism as well as to help athletes to prepare optimally for competitions.

Recommendations: Although a step nearer has been taken to confirm a place for the GI in human health, additional randomised, controlled, medium and long-term studies as well as more epidemiological studies are needed to investigate further the effect of low GI diets on LDL-c, HDL-c and TG. These studies are essential to investigate the effect of low GI diets on endpoints such as CVD and DM. This will also show whether low GI diets can reduce the risk of diabetic complications such as neuropathy and nephropathy. Furthermore, the public at large must be educated about the usefulness and application of the GI in meal planning. For sport nutrition, randomised controlled trials should be performed to investigate the role of

the GI during exercise as well as in sports of longer duration such as cricket and tennis. More studies are needed to elucidate the short-term effect of the GI post-exercise as well as to determine the mechanism of lower glycogen storage with LGI meals post-exercise.

Key words: glycaemic index, fructosamine, glycated haemoglobin, high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, total cholesterol, triacylglycerol, carbohydrate metabolism, lipid metabolism, pre-exercise, during exercise, post-exercise and sport performance.

Opsomming

Motivering: Die voorkoms van nie-aansteeklike siektes soos diabetes mellitus (DM) en kardiovaskulêre siektes (KVS) neem vinnig toe in ontwikkelde gemeenskappe. Kenners glo dat leefstyl, meer spesifiek eetgewoontes, 'n deurslaggewende rol speel in die toename van die las van hierdie chroniese siektes. Eetgewoontes kan dus aangepas word om 'n positiewe impak op die voorkoming en behandeling van chroniese leefstylsiektes te hê. Daar word geglo dat die hiperglukemiese toestand wat ontstaan na 'n maaltyd van sekere soorte voedsels kan bydra tot die ontwikkeling van verskeie metaboliese toestande. Hierdie stelling is nie net waar vir individue met verswakte glukemiese kontrole soos sommige diabete nie, maar mag ook waar wees vir gesonde individue. Om hierdie rede sal dit voordelig wees as die omvang en duur van postprandiale hiperglukemie verminder kan word. Deur die regte soort koolhidraatvoedsels te kies mag hiperglukemie minder dikwels voorkom wat dus 'n moontlike strategie is vir die voorkoming en behandeling van chroniese metaboliese siektes. Terselfdertyd is die optimale hoeveelheid koolhidraatinname sowel as die tydsbereking van koolhidraatinname besonder belangrik vir atlete. Die belangrikste voedingsdoelwitte van die atleet is om die liggaam se koolhidraatstore voor oefening aan te vul, om energie te voorsien tydens oefening en om spierglikogeenstore te hervul tydens die herstelfase. Die hoofdoelwit van hierdie strategieë is dus om koolhidraatbeskikbaarheid aan die spiere en sentrale senuweesisteem te handhaaf gedurende langdurige matige tot hoë-intensiteitoefening omdat hierdie faktore belangrik is vir oefenkapasiteit en prestasie. Die tipe koolhidraat wat ingeneem moet word asook praktiese oorwegings is egter minder dikwels en in minder diepte bestudeer as die hoeveelheid koolhidrate.

Die glukemiese indeks (GI) verwys na die potensiaal van koolhidrate om bloedglukosevlakke te laat toeneem en dus insuliensekresie te beïnvloed. By verskeie metaboliese versteurings is insuliensekresie onvoldoende of onmoontlik wat tot swak bloedglukosekontrole aanleiding gee. Daarom is voorgestel dat lae-GI-diëte moontlik kan bydra tot 'n betekenisvolle verbetering in toestande wat met swak bloedglukosekontrole geassosieer word. Insuliensekresie is ook belangrik vir atlete as gevolg van die stimulerende effek daarvan op die aktiwiteit van glikogeensintase.

Doelwitte: Daar is drie hoofdoelwitte geïdentifiseer vir hierdie proefskrif. Die eerste doelwit was om 'n meta-analise van die effek van die GI op merkers vir koolhidraat- en lipiedmetabolisme te ondersoek met die klem op ewekansige gekontroleerde studies (EGS). Tweedens is 'n sistematiese oorsig uitgevoer om die sterkte van bewyse vanaf epidemiologiese studies gekombineer met EGS te beoordeel ten einde dieetkundiges te motiveer om die GI-konsep in dieetbeplanning te inkorporeer. Laastens is 'n sistematiese oorsig van die effek van die GI in sportprestasie uitgevoer op al die beskikbare literatuur tot

op hede om te bepaal hoe die toepassing van die GI in 'n atleet se dieet sportprestasie kan verbeter.

Metodologie: Vir die meta-analise oor die effek van lae-GI-diëte *vs.* hoë-GI-diëte op merkers van koolhidraat- en lipiedmetabolisme het die literatuursoektog hoofsaaklik EGS ingesluit met 'n oorkruis- of parallelle studieontwerp wat in Engels tussen 1981 en 2003 gepubliseer is. Die belangrikste uitkomste was ondermeer serum-fruktosamien, geglikoliseerde hemoglobien (HbA$_{1c}$), hoëdigtheidslipoproteïencholesterol (HDL-c), laedigtheidslipoproteïencholesterol (LDL-c), totale cholesterol (TC) en triasielgliserole (TG). Vir die sistematiese oorsig is epidemiologiese studies sowel as EGS gebruik om die effek van lae-GI teenoor hoë-GI-voedsels op merkers vir koolhidraat- en lipiedmetabolisme te ondersoek. Vir die sistematiese oorsig wat die effek van die GI op sportprestasie ondersoek het, is EGS met 'n oorkruis- of parallele studieontwerp, wat in Engels tussen 1981 en 2004 gepubliseer is, uitgesoek. Al die toepaslike manuskripte wat in die meta-analise en sistematiese oorsigte ingesluit is, is met behulp van databasisse soos die Cochrane Central Register of Controlled Trials, MEDLINE (vanaf 1981 tot op hede), EMBASE, LILACS, SPORTDiscus, ScienceDirect en PubMed, geïdentifiseer. Die proefskrif word in die artikelformaat aangebied.

Resultate en gevolgtrekkings vanuit die individuele manuskripte:
⇒ Vir die meta-analise is 16 studies uit die literatuursoektog geïdentifiseer, wat aan streng insluitingskriteria voldoen het. In vergelyking met hoë-GI-diëte het lae-GI-diëte fruktosamien (p<0.05), HbA$_{1c}$ (p<0.03) en TC (p<0.0001) betekenisvol verlaag en geneig om LDL-c (p=0.06) te verlaag. Geen veranderinge in HDL-c en TG is waargeneem nie. Die resultate van hierdie meta-analise ondersteun dus die gebruik van die GI-konsep om koolhidraatbevattende voedsels te kies sodat TC kan verlaag en bloedglukosekontrole in diabete verbeter kan word.

⇒ Die sistematiese oorsig het die voorafgaande resultate van die meta-analise wat die EGS ingesluit het gekombineer epidemiologiese studies. Prospektiewe epidemiologiese studies het verbeteringe in HDL-c oor langer tydperke aangetoon met lae-GI-diëte terwyl die EGS nie verbetering in HDL-c oor die korttermyn kon aantoon nie. Hierdie resultaat kan moontlik toegeskryf word aan die kort intervensieperiodes waaroor die EGS uitgevoer is. Verder kon geen verband in epidemiologiese studies tussen lae-GI-diëte en LDL-c en TC gevind word nie, terwyl EGS wel 'n verband tussen hierdie lipiede en lae-GI-diëte getoon het. Nietemin het die epidemiologiese studies, net soos die EGS, verbeteringe in merkers vir koolhidraatmetabolisme getoon met lae-GI-diëte in vergelyking met hoë-GI-diëte. Oortuigende bewyse vanaf EGS en epidemiologiese

studies bestaan sodat lae-GI-diëte aanbeveel kan word om merkers vir koolhidraat-asook lipiedmetabolisme te verbeter.

⇒ Vanuit die sistematiese oorsig rakende die GI en sportprestasie, blyk dit nie dat lae-GI-vooroefeningmaaltye enige voordeel bo hoë-GI-vooroefeningmaaltye inhou nie. Alhoewel lae-GI-vooroefeningmaaltye koolhidraatbeskikbaarheid beter handhaaf tydens oefening, bied lae-GI-vooroefeningmaaltye geen verdere voordeel bo hoë-GI-vooroefeningmaaltye in terme van prestasie nie. Verder wil dit voorkom of die vergrote metaboliese respons van hoë-GI-vooroefeningmaaltye in vergelyking met lae-GI-vooroefeningmaaltye nie enige nadelige effekte vir prestasie inhou nie. Uitsonderings is egter atlete wat neig om hipoglukemie te ontwikkel in die uur voor oefening nadat 'n koolhidraatryke maaltyd ingeneem is. Hierdie atlete word dus aangemoedig om eerder 'n lae-GI-vooroefeningmaaltyd te nuttig. Geen studies is nog op die effek van die GI tydens oefening gerapporteer nie. Huidige bewyse toon aan dat 'n kombinasie van koolhidrate met verskillende GI's byvoorbeeld glukose (hoë GI), sukrose (matige GI) en fruktose (lae GI) tydens oefening aanbeveel word omdat dit die beste resultate ten opsigte van koolhidraatoksidasie lewer as gevolg van verskil in transportmeganismes. Alhoewel geen studies nog uitgevoer is om die effek van die GI op korttermyn herstel te bepaal nie, word vermoed dat hoë-GI-koolhidraatryke voedsels ingeneem moet word as die herstelperiode kort is (0-8 uur), terwyl die totale hoeveelheid eerder as die tipe koolhidraat belangrik is wanneer die herstelperiode langer is (20-24 uur).

Gevolgtrekking: Daar bestaan belangrike bewyse ter ondersteuning van die terapeutiese en voorkomende potensiaal van lae-GI-diëte om merkers vir koolhidraat- en lipiedmetabolisme te verbeter. Deur hoë-GI-koolhidraatryke voedsels te vervang met lae-GI-koolhidraatryke voedsels is 'n verbetering in metaboliese kontrole waargeneem. Verder het hierdie diëte TC verlaag, geneig om LDL-c te verlaag en mag dit 'n positiewe effek oor die langtermyn op HDL-c hê. Hierdie bevindings bevestig die belang van lae-GI-diëte in die voorkoming en behandeling van siektes, veral in populasies wat gekenmerk word deur 'n hoë voorkoms van insulienweerstand, glukoseonverdraagsaamheid en abnormale lipiedvlakke. Vir atlete wil dit voorkom of lae-GI-vooroefeningmaaltye nie enige voordeel vir prestasie bo hoë-GI-vooroefeningmaaltye inhou nie. Lae-GI-vooroefeningmaaltye kan egter aanbeveel word vir atlete wat geneig is om hipoglukemie te ontwikkel met die inname van 'n koolhidraatryke maaltyd in die uur voor oefening. Geen studies is nog gerapporteer op die effek van die GI gedurende oefening nie. Daar word egter gespekuleer dat 'n kombinasie van koolhidrate met verskillende GI's die beste resultate lewer in terme van eksogene koolhidraatoksidasie. Verder is ook nog geen studies uitgevoer om die effek van die GI op korttermynherstel te ondersoek nie. Daar word vermoed dat hoë-GI-koolhidraatryke voedsels ingeneem moet word wanneer die herstelperiode kort is (0-8 uur) terwyl die totale

hoeveelheid eerder as die soort koolhidraat belangrik is wanneer die herstelperiode langer is (20-24 uur). Uit bogenoemde resultate blyk dit dat die GI 'n wetenskaplike hulpmiddel is wat 'n mens in staat stel om koolhidraatbevattende voedsel te kies sodat merkers vir koolhidraat- en lipiedmetabolisme kan verbeter en ook atlete in staat te stel om optimaal vir deelname aan kompetisies voor te berei.

Aanbevelings: Alhoewel 'n stap nader geneem is om 'n plek vir die GI in algemene gesondheid te verseker, moet bykomende ewekansig, gekontroleerde, medium- en langtermynstudies sowel as epidemiologiese studies uitgevoer word om die effek van lae-GI-diëte op LDL-c, HDL-c en TG verder te ondersoek. Hierdie studies is ook belangrik om die effek van lae-GI-diëte op eindpunte soos KVS en DM te bestudeer. Hierdie studies sal ook 'n aanduiding gee of lae-GI-diëte die risiko van diabetiese komplikasies soos neuropatie en nefropatie kan verlaag. Verder moet die algemene publiek onderrig word rakende die bruikbaarheid en toepaslikheid van die GI in maaltydbeplanning. Wat sportvoeding betref, moet verdere EGS uitgevoer word om die rol van die GI gedurende oefening sowel as in sportsoorte wat langer duur byvoorbeeld krieket en tennis te ondersoek. Meer studies word ook benodig om die korttermyneffek van die GI op herstel na oefening sowel as die meganisme van laer glikogeenstoring met lae-GI-diëte na oefening, na te vors.

Sleutelwoorde: glukemiese indeks, fruktosamien, geglikoliseerde hemoglobien, hoëdigtheidslipoproteïencholesterol, laedigtheidslipoproteïencholesterol, totale cholesterol, triasielgliserol, koolhidraatmetabolisme, lipiedmetabolisme, vooroefening, gedurende oefening, na-oefening en sportprestasie.

Congress presentations

The following presentations, based on this thesis, have been delivered:

1. OPPERMAN, A.M., VENTER, C.S., OOSTHUIZEN, W., VORSTER, H.H. & THOMPSON, R.L. 2003. Meta-analysis of the health benefits expected when the glycaemic index is used in planning diets. *Association for dietetics in South Africa* (ADSA), Gauteng Branch. 1 October, Pretoria:South Africa.

2. OPPERMAN, A.M., VENTER, C.S., OOSTHUIZEN, W., VORSTER, H.H. & THOMPSON R.L. 2004. Meta-analysis of the health benefits expected when the glycaemic index is used in planning diets. *Journal of the Society for Endocrinology, Metabolism and Diabetes of South Africa,* 9(1):S39. Abstract. SEMDSA Congress, 27-29 March, Durban:South Africa.
   Award: First prize for presentation in nutrition research in the young scientist category at the Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) Congress in Durban, South Africa, 27-29 March 2004.

3. OPPERMAN, A.M., VENTER, C.S., OOSTHUIZEN, W., VORSTER, H.H. & THOMPSON, R.L. 2004. Meta-analysis on the health effects when the glycaemic index is used in meal planning. *Association for dietetics in South Africa* (ADSA), North-West Branch. 18 June, Potchefstroom:South Africa.

4. OPPERMAN, A.M., VENTER, C.S., OOSTHUIZEN, W., VORSTER, H.H. & THOMPSON, R.L. 2004. Meta-analysis on the health effects when the glycaemic index is used in meal planning. *South African journal of clinical nutrition,* 17(2):S1-48. Biennial Nutrition Congress. "Diversity in Nutrition". 23-27 August, Worcester:South Africa.

5. OPPERMAN, A.M. & WRIGHT, H.H. 2004. The glycaemic index in sport nutrition. *South African journal of clinical nutrition,* 17(2):S1-48. Biennial Nutrition Congress. "Diversity in Nutrition". 23-27 August, Worcester: South Africa. Invited Speaker

6. VENTER, C.S., OPPERMAN, A.M., OOSTHUIZEN, W., VORSTER, H.H. & THOMPSON, R.L. 2004. Meta-analysis on the health effects when the glycaemic index is used in meal planning. The Vahouny-ILSI Japan international symposium on non-digestible carbohydrates. 27-29 September, Tokyo:Japan.

List of abbreviations

Abbreviation	Description
κ	Kappa statistic
β-cell	Beta cell
ADA	American Diabetes Association
BG	Blood glucose
BMI	Body mass index
CHD	Coronary heart disease
CHO	Carbohydrate
CI	Confidence interval
CON	Control
CVD	Cardiovascular disease
DM	Diabetes mellitus
DNSG	Diabetes and Nutrition Study Group
EASD	European Association for the Study of Diabetes
EPOC	Effective Practice and Organization of Care
EURODIAB-complications study	European Diabetes Complications Study
FFA	Free fatty acids
GI	Glycaemic index
GLUT-4	Glucose transporter carrier protein-4
GLUT-5	Glucose transporter carrier protein-5
h	hour
HbA_{1c}	Glycated haemoglobin
HDL-c	High-density lipoprotein cholesterol
High GI	High glycaemic index
I^2	Test for heterogeneity
kJ	Kilojoule
LDL-c	Low-density lipoprotein cholesterol
II	Parallel study design
Low GI	Low glycaemic index
MeSH	Medical subject headings
mg/dl	Milligram per desilitre
Min.	Minute
mmol/l	Millimoles per litre
Moderate GI	Moderate glycaemic index
NA	Not applicable
NEFA	Non-esterified fatty acids

Abbreviation	Description
NHANES III	Third National Health and Nutrition Examination Survey
NR	Not reported
RCT's	Randomised controlled trials
RER	Respiratory exchange ratio
RPE	Rate of perceived exertion
RR	Relative risk
SASA	South African Sugar Association
SCFA	Short chain fatty acids
SD	Standard deviation
SEM	Standard error of the mean
SGLT1	Sodium-dependent glucose transporter
TC	Total cholesterol
TG	Triacylglycerols
UKPDS	United Kingdom Prospective Diabetes Study Group
VLDL-c	Very-low density lipoprotein cholesterol
VO_{2max}	Maximal oxygen uptake
X	Cross over study design

Table of content

1

Background and motivation

1. Introduction

One of the most substantial changes in the provision of health care in the last decade has been the shift to managed care using evidence-based clinical practice guidelines. Sackett *et al.* (1996) define evidence-based medicine as the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. This can be applied to the nutrition field where evidence-based nutrition is then defined as the application of the best available systematically assembled evidence in setting nutrition policy in practice (Brunner *et al.*, 2001), meaning that recommendations are based on evidence which has been assessed in an unbiased or impartial manner. Practically evidence-based nutrition provides an objective framework for the development and revision of dietary guidelines and the validation of health claims of foods (Truswell, 2001).

Writing and designing nutrition policy, which incorporates many of the features of an evidence-based approach, has become an evolving science. Confusing and conflicting nutritional advice from the media in combination with a quick reversal of policymakers' nutrition recommendations can lead to public disbelief in both the policy process and published conclusions (Cooper & Zlotkin, 2003). Ambiguous and vague policies can lead to ineffective, irrelevant and inappropriate advice to health professionals, non-governmental organisations, the private sector, regulatory authorities and the public. The consequence of this is that the public and health professionals will ignore these recommendations with potentially adverse outcomes. Therefore, nutrition policy and recommendations that use an evidence-based approach with systematically evaluated evidence are grounded in the needs of both the public and health professionals (Cooper & Zlotkin, 2003). Applying appropriate principles of evidence-based nutrition to public-health nutrition will bring objectivity and the opportunity to have rules of evidence for controversial topics (Truswell, 2001).

The volume of glycaemic index (GI) literature published annually is currently increasing at an exponential rate. GI research is scattered throughout the literature and the traditional way for nutritionists and dieticians to keep in touch with this expansive literature has been original research articles, narrative reviews, editorials or chapters in a book (Hearn *et al.*, 1999). The problems with this approach are now clear. This type of review is subjective and prone to severe bias and error (Horvath & Pewsner, 2004). Selective inclusion of studies that support the view of the author is common where only the most recent trials are used and preference is given to trials with a positive outcome, ignoring studies that came to an opposite conclusion (Horvath & Pewsner, 2004). Similarly, opposite conclusions are often reached with reviews by different authors in different journals without a clear reason, missing potentially important differences. This background discussion will, therefore, evaluate the usefulness and appropriateness of meta-analyses and systematic reviews as tools in

summarising the evidence when the GI is used in planning diets to improve carbohydrate (CHO) and lipid metabolism.

2. Meta-analysis (Quantitative systematic reviews)

2.1 Characteristics and advantages of meta-analyses

A need has been identified to conduct a meta-analysis for the evaluation of GI literature. The primary aim of this meta-analysis is to produce a more accurate estimate of the effect of GI interventions, or groups of interventions, than is possible using only a single study. Since different studies are carried out using different subjects, different study designs and other study-specific factors, it has been suggested that combining the studies will produce an estimate that has broader generalizability than any single study (Sutton *et al.*, 2001). The term meta-analysis has been thoroughly described and several definitions have been linked to meta-analysis. Vorster *et al.* (2003) describe a meta-analysis as the structured result of a literature review in which results from all independent but related or comparable studies are systematically and statistically combined or integrated in order to increase power and precision.

A meta-analysis addresses the potential problems of traditional reviews because of the following characteristics and advantages, which help to minimise bias in results:

- A meta-analysis increases power and precision of statistical results by combining results from different studies, which compensates for low powered research and small studies that find only small effects (Alderson *et al.*, 2004).
- It examines variability between studies (Vorster *et al.*, 2003)
- It answers questions not posed by individual studies. Randomised controlled trials (RCTs) often involve specific types of subjects participating in structured interventions. A selection of studies in which these characteristics differ can allow investigation of the consistency of effect (Alderson *et al.*, 2004).
- It can assist in generating new hypotheses by identifying fields that need more extensive research (Alderson *et al.*, 2004).
- A well-conducted meta-analysis allows for a more objective appraisal of the evidence, which may lead to resolution of uncertainty and disagreement (Egger & Smith, 1997).
- It assures intimacy with the data and field of study. The process of summarizing a research domain in a quantitative fashion forces the reviewer to be complete in finding all the research articles in the literature and to be precise in extracting the necessary data from them and, therefore, to limit bias (Rosenthal & DiMatteo, 2001).

2.2 Basic steps in conducting a meta-analysis

2.2.1 Developing a protocol

The basic steps in conducting a meta-analysis are shown in Figure 1. Preparing a meta-analysis is a complex process that comprises many judgements, as well as decisions about the process and the resources needed. As in any scientific endeavour, the methods to be used should be established beforehand (Alderson *et al.*, 2004). Therefore, a well-planned and feasible protocol should be developed in order to assist the reviewer in conducting a review of good quality.

2.2.2 Formulating a research question/hypothesis

A well-formulated research question will assist the researcher in decisions about what research to include in a review and how to summarise it. As with any research, the first and most important decision in preparing a meta-analysis is to determine its focus. This is best done by asking clearly framed questions. The key components of a research question should include the types of subjects/participants, comparisons/interventions, outcomes and study designs (Alderson *et al.*, 2004).

2.2.3 Literature search and selection of studies

The major goal of a literature search is to implement a search strategy that yields a representative sample of all relevant studies (Durlack & Lipsey, 1991). According to Alderson *et al.* (2004), predetermined standardised subject terms (a more complete description for key words) are useful because they provide a way of retrieving articles that may use different words to describe the same concept and because they provide information beyond what is simply contained in the words of the title and abstract of an article. Using the appropriate standardised subject terms, a simple search strategy can quickly identify articles pertinent to the topic of interest. However, a computer literature search alone is a good start but will not guarantee an unbiased sample of studies because many smaller journals are not indexed on the major databases. The result may be that a significant portion of applicable studies is omitted which may well differ in important ways from those which are found. To prevent publication bias and to obtain a suitable sample of studies, the reviewer should use a combination of search strategies (Alderson *et al.*, 2004).

Multiple search strategies may be necessary to locate relevant studies. An electronic database search on databases such as Medline, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), Lilacs, ScienceDirect, PubMed, SPORTDiscus and SciSearch is usually the first step. Handsearching involves a manual page-by-page examination of the entire contents of a journal issue to identify all eligible reports of trials, whether they appear

Research question

↓

Formulating of a hypothesis

↓

Choose outcomes variables, which are the objectives of investigation

↓

Do a complete literature search (computer based search, handsearch, check reference lists)

↓

QUALITATIVE META-ANALYSIS

↓

Quality assessment of randomised controlled trials

↓

Identify acceptable studies and give scores for quality

Unacceptable studies   Acceptable studies   Good studies
                               ("minor flaws")

QUANTITATIVE META-ANALYSIS

↓

Assess statistical significance of results (*P values*)

Comparing studies   Combining studies
(heterogeneity)   (best estimate across studies)

All studies together   Meta-analysis   All studies together   Meta-analysis

↓

ASSESS

General trend   Disparities and incongruities   New research questions
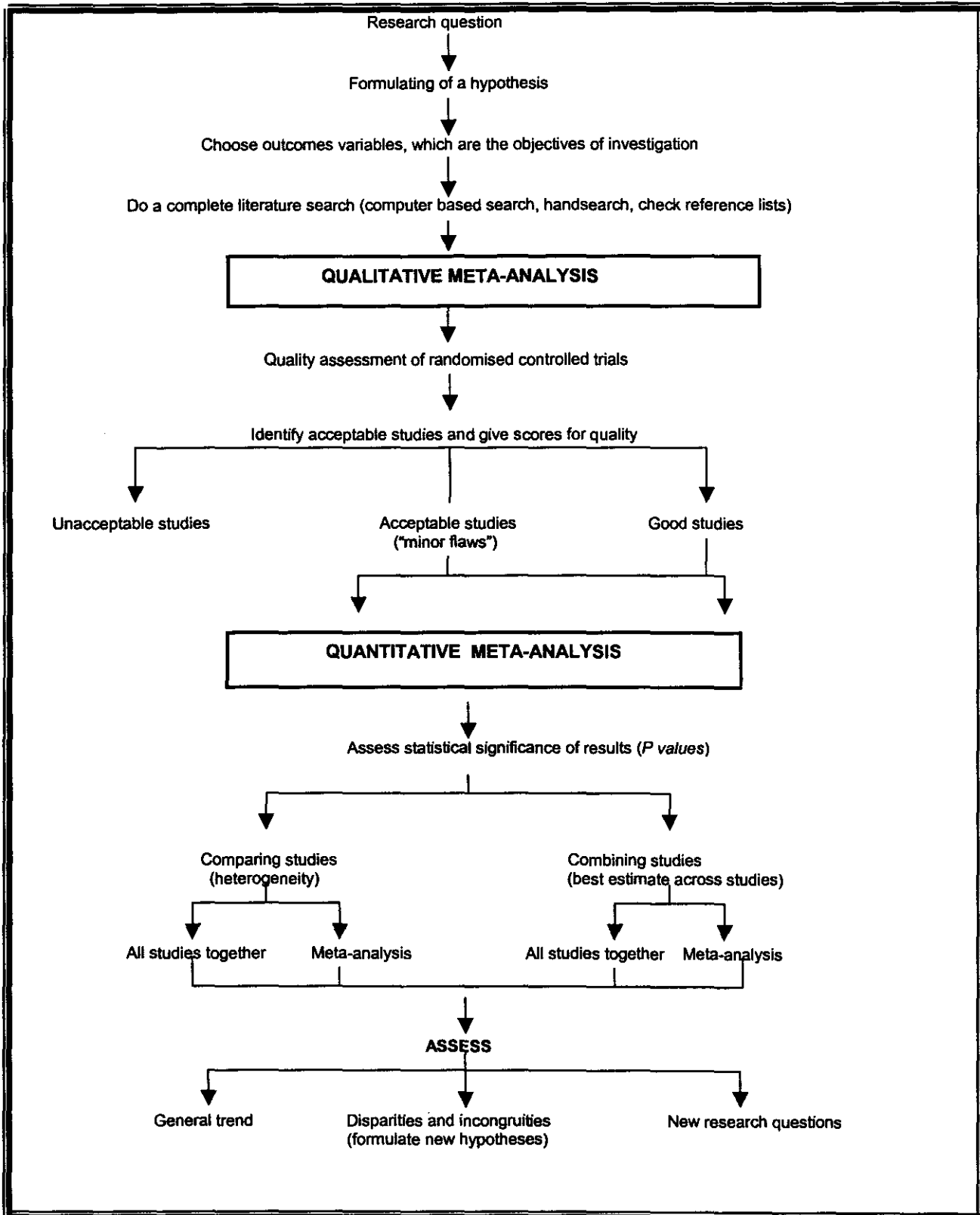   (formulate new hypotheses)

Figure 1: Consecutive steps in conducting a meta-analysis (adapted from Jenicek, 1989)

in articles, abstracts, news columns, editorials, letters or other text (Durlak & Lipsey, 1991). Reviewers should check the reference lists of articles obtained (including those from previously published systematic reviews/meta-analyses) to identify relevant reports. The

reviewer should also check existing reviews for potentially relevant studies. It also sometimes happens that completed studies are never published. Identifying unpublished trials and including them in a meta-analysis, when eligible, may be important to minimise bias. Unfortunately, it is difficult to obtain information about studies that have been completed but were never published (Alderson *et al.,* 2004).

Inclusion and exclusion criteria are generally applied to decide which studies to use in the meta-analysis and is, therefore, a qualitative assessment of the literature. Ideally, this should be carried out in a standardised manner where the reviewers of articles are blinded to the results (Yach, 1990). Reasons for excluding articles may include inappropriate study designs or methodology, types of subjects, exposures, outcomes, confounding factors or other variables in the particular study. Quality assessment of the study is necessary before inclusion in order to reduce bias in the review (Vorster *et al.,* 2003) and might include methods of randomisation, concealment of allocation, blinded assessment to variables as well as treatment and determination whether an intention-to-treat analysis was possible (Alderson *et al.,* 2004). A possible method to decide whether quality criteria are met or not is to award a score, for instance, A, B or C where A represents all criteria met and C represents least criteria met. Good studies are, therefore, studies that meet all the inclusion criteria while unacceptable studies did not meet the inclusion criteria (Figure 1). Quality assessment might also help to gain insight into potential comparisons and to guide interpretation of findings (Alderson *et al.,* 2004).

2.2.4   Data collection

A well-designed data extraction form to collect relevant data is essential. It forms a link between what the primary investigators report (e.g. journal articles, project reports, personal communication) and what a reviewer ultimately reports. Reviewers should consider how many and which variables to collect before adapting or designing a data collection form. Data collection forms should not be over detailed to prevent long and tedious forms to fill in. On the other hand, incomplete forms may lead to omission of key data and reviewers may have to re-abstract studies (Alderson *et al.,* 2004).

It is impossible to specify all variables that should be coded in a meta-analysis. Variables that are usually coded include: general information (published/unpublished), interventions (placebo included), dietary information/diet or test meal provided, comparison interventions, wash out period, participants (sampling random/convenience), exclusion criteria, total number and number in comparison groups, gender, age, weight, assessment of compliance, withdrawals/losses to follow up (reasons/description for drop out), subgroups, statistical

methods and key outcomes (effect sizes) (Adapted from Durlak & Lipsey, 1991; Vorster *et al.*, 2003; Alderson *et al.*, 2004).

Accurate coding is extremely important. Reviewers need instructions and decision rules on the data collection form. To reduce errors, each study must be coded independently by at least two reviewers and controlled by a third reviewer if necessary. All data collection forms should be pilot tested using a representative sample of the studies to be reviewed.

2.2.5 *Statistical analysis*

Statistical analysis includes combining of data in order to arrive at a summary statistic of the best estimate of the effect size, a measure of its variance and confidence intervals (95% or 99%). This step can be described as a quantitative assessment, which also examines heterogeneity between studies (Yach, 1990). Various statistical methods are applied to perform a meta-analysis depending on the type of data being analysed. A conceptual understanding of the principles of meta-analysis is more important for the reviewer than an in depth knowledge of the statistical techniques. The two most common approaches to combine continuous data from RCTs for a meta-analysis are weighted and standardised mean differences. These two summary statistics can be calculated whether the data from each individual are single assessments or changes from baseline measures. It is also possible to measure effects by taking ratios of means, or by comparing statistics other than means (Alderson *et al.*, 2004).

Studies should be combined in a meta-analysis only if they are sufficiently similar to produce a meaningful result (Feuer & Higgins, 1999). The variability across studies is termed heterogeneity and may be troublesome to the reviewer. Variability in the subjects, interventions and outcomes is called clinical heterogeneity and variability in treatment effects being evaluated in the different trials is known as statistical heterogeneity (Alderson *et al.*, 2004). Heterogeneity should be explained and here the inputs of a statistician may be helpful.

2.2.6 *Visual presentation of results*

There are various ways to display the results of a meta-analysis. The Cochrane Review method uses a special programme to generate tables and graphs (RevMan, 4.2). See Figure 2 as an example of a meta-analysis of four studies. This graphical display is called a forest plot. In addition to the graphs, information about the raw data (means and standard deviations), points estimates and confidence intervals, a meta-analysis for each subgroup, the total number of subjects in both control and experimental groups, heterogeneity statistics, a test for the overall effect and percentage weight given to each study, are provided.

In Figure 2 the point estimate is shown as a black square, with the area proportional to the weight given to the trial in the meta-analysis. The horizontal bars represent confidence intervals (usually 95%) for each trial. Large trials with little variation produce larger squares and narrower confidence intervals and, therefore, contribute a larger weight to the meta-analysis. The vertical line in the middle of the forest plot represents the line of no effect. If the confidence intervals cross the line of no effect, then the difference in the effect of treatment versus control is not significant at a 5% level ($P > 0.05$); meaning that there is no evidence of difference between the treatments, either because the sample size is too small or because there is no effect of the experimental treatment (Greenhalgh, 1997).

Comparison: 01 Continuous data
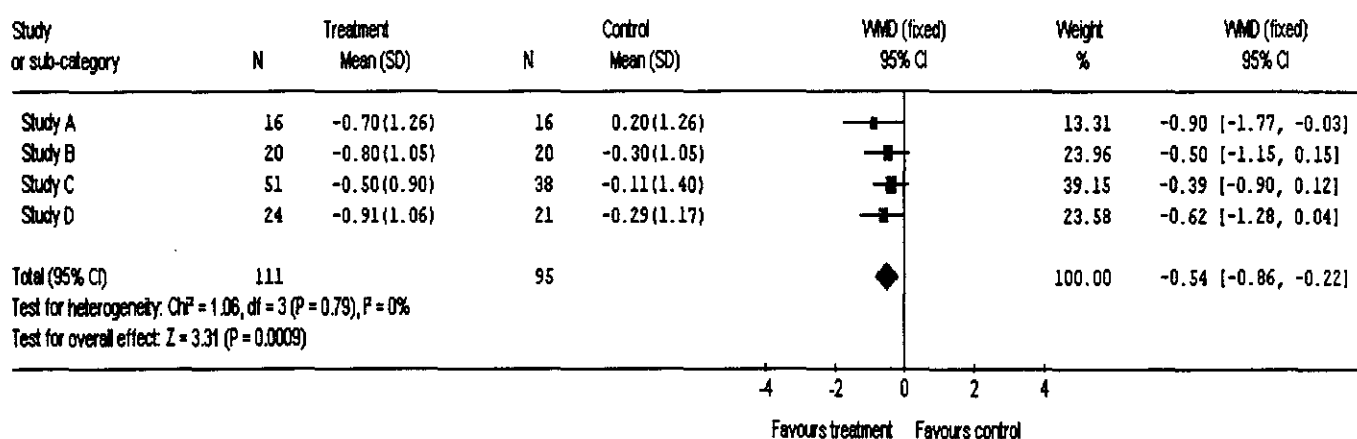Outcome: 01 Example of 4 studies

Study or sub-category	Treatment N	Mean (SD)	Control N	Mean (SD)	WMD (fixed) 95% CI	Weight %	WMD (fixed) 95% CI
Study A	16	-0.70 (1.26)	16	0.20 (1.26)		13.31	-0.90 [-1.77, -0.03]
Study B	20	-0.80 (1.05)	20	-0.30 (1.05)		23.96	-0.50 [-1.15, 0.15]
Study C	51	-0.50 (0.90)	38	-0.11 (1.40)		39.15	-0.39 [-0.90, 0.12]
Study D	24	-0.91 (1.06)	21	-0.29 (1.17)		23.58	-0.62 [-1.28, 0.04]
Total (95% CI)	111		95			100.00	-0.54 [-0.86, -0.22]

Test for heterogeneity: Chi² = 1.06, df = 3 (P = 0.79), I² = 0%
Test for overall effect: Z = 3.31 (P = 0.0009)

```
        -4    -2     0     2     4
     Favours treatment   Favours control
```

Figure 2: Example of a meta-analysis

The diamond at the bottom represents the combined result, calculated using either the fixed or random effects model, with its associated 95% confidence interval. The scale at the bottom of the graph should indicate what side of the line of no effect favours the treatment or control of the intervention. If an entire confidence interval lies to one side of the vertical line, then that particular result is statistically significant. If the confidence interval of the pooled result (black diamond) lies to one side of the vertical line, the overall effect is statistically significant. The scale along the bottom is a scale of the chosen measure of effect size and depends on what type of outcome is measured (Feuer & Higgins, 1999). A simple rule of thumb to determine whether there are any differences between studies (heterogeneity) is to see if it is possible to draw a vertical line that would pass through the confidence intervals of all the studies (Vorster *et al.*, 2003). This forest plot does not show heterogeneity, also indicated by the statistical test for heterogeneity given in Figure 2.

2.3 Limitations of meta-analyses

As with any statistical method, ill conducted and wrongly interpreted meta-analyses may be biased, but on the other hand a well-conducted meta-analysis will allow a more objective appraisal of the available evidence. According to Rosenthal and DiMattio (2001), every meta-analysis has some inherent bias due to inclusion/exclusion criteria and the methods chosen to review the literature. A meta-analysis also includes studies that vary considerably in their sampling units, methods of measuring, data-analytic approaches and statistical findings. A meta-analysis is often criticised for combining apples with oranges because it summarises results from studies that vary notably in methodology and measurement of variables to achieve answers to questions that are similar, though often not identical. It is argued that a meta-analysis is analogous to taking apples and oranges and averaging their measures such as weight, size, colour and flavour. Meta-analyses have also been accused of oversimplifying the results of a specific area of research by focusing on overall effects and downplaying mediating or interaction effects (Wolf, 1986). Furthermore, trials with favourable results are far more likely to be published than those with inconclusive results (Easterbrook *et al.*, 1991). Identification of relevant trials may also be difficult because of publication in less accessible journals (e.g. non-English language) (Flather *et al.*, 1997)

3. Systematic reviews (Unquantitative systematic reviews)

Systematic reviews have rapidly gained an important place in aiding clinical decision-making in nutrition. Systematic reviewing is considered a field of research, although the data are derived from primary studies in the area of interest rather than from direct experimentation. A systematic review can be defined as a review of a clearly formulated question that attempts to minimize bias using systematic and explicit methods to identify, select, critically appraise and summarise relevant research (Needleman, 2002). The steps in conducting a systematic review are more or less the same as in conducting a meta-analysis and involve definition of a research question, development of study inclusion criteria, identification of studies with a search strategy, data collection and critical appraisal of information, pooling of information systematically, summarising of data, drawing conclusions and reporting new findings (Needleman, 2002).

To make sense of the data from the eligible studies, some form of pooling of the information for a systematic review is needed. First of all, data summary tables should be developed. These tables can be constructed for each outcome, grouping together studies with similar study designs, interventions or treatments. This will often be the most sophisticated level of synthesis possible. Sometimes it is possible to perform mathematical analysis on the data, which is then termed a meta-analysis. A meta-analysis is not necessarily part of a systematic review. In some instances it is wise not to combine data formally unless the

studies can be considered similar enough in terms of study characteristics (Needleman, 2002).

A meta-analysis and systematic review differ in the sense that a systematic review is an overview of primary studies that use explicit and reproducible methods while a meta-analysis is a mathematical synthesis of the results of two or more primary studies that address the same hypothesis in the same way (Greenhalgh, 1997). The advantages of systematic reviews are the following:

- Explicit methods limit bias in identifying and rejecting studies.
- Conclusions are more reliable and accurate because of methods used.
- Unmanageable quantities of research on a topic are found, summarised and appraised.
- Time between research discoveries and implementation of effective diagnostic and therapeutic strategies maybe reduced.
- Results of different studies can be compared formally to establish generalisability of findings and consistency of results.
- Reasons for heterogeneity can be identified and new hypotheses generated about particular subgroups.
- Quantitative systematic reviews (meta-analyses) increase the precision of the overall result (Greenhalgh, 1997).

From this discussion it is clear that there is a place and need for well-constructed meta-analyses as well as systematic reviews in evidence-based nutrition. The GI is one of the research areas in which limited amounts of meta-analyses and/or systematic reviews have been conducted so far. Only three meta-analyses on the GI appeared in the literature performed by Brand-Miller (1994), Brand-Miller et al. (2003) and Wolever (2003). The first meta-analysis was conducted more than 10 years ago (Brand-Miller, 1994) investigating the effect of the GI on diabetes management and certain blood lipids, such as total cholesterol and triacylglycerols (TG). Two other meta-analyses on diabetes management investigating fructosamine and HbA_{1c} appeared in 2003 (Brand-Miller et al., 2003; Wolever, 2003), however, no analysis was done on lipids. Because of controversial opinions on the topic (as discussed in the next section), a need has been identified for a complete and updated meta-analysis on the GI and CHO as well as lipid metabolism. This meta-analysis will include the most recent studies, expanding the focus to the whole lipid profile, including high-density lipoprotein cholesterol (HDL-c) and low-density lipoprotein cholesterol (LDL-c) which were shown to be strong independent predictors of cardiovascular disease (Heiss et al., 1980; Gordon et al., 1989; ATP III, 2001). With this meta-analysis the aim is to obtain clearance about the importance of the GI in the planning of diabetic and healthy diets.

Only RCTs were included in the meta-analysis, therefore, a systematic review judging the strength of scientific evidence from epidemiological studies in addition to RCTs was conducted. With this systematic review, strong and weak evidence will be highlighted in order to make well informed and evidence-based recommendations to dieticians when using the GI in meal planning for the public at large and for diabetics.

The GI of a CHO food has been proposed for use in choosing foods to optimise CHO availability during exercise, as well as to influence the rate of glycogen synthesis post-exercise, which could possibly enhance performance (Wright, 2004). Generally, LGI (LGI) CHO foods (GI < 40) have been recommended before an endurance event; moderate (MGI) to high (HGI) (GI ≈ 63-70) CHO foods are recommended during exercise, while HGI (GI > 70) are recommended post-exercise (Walton & Rhodes, 1997). Some of these recommendations are, however, debated and need further investigation. Three reviews concerning the utility of the GI in sport nutrition have been published (Burke *et al.*, 1998, Siu & Wong, 2004) or submitted for publication (Wright, 2004). However, none of the reviews was a systematic review where all relevant studies conducted up to date on the GI and sport nutrition were included. Therefore, it was decided to conduct a comprehensive systematic review to summarise all the literature untill September 2004 on the GI and physical performance.

4. The glycaemic index

4.1   Application of the glycaemic index in health

Over the past 20 years much constructive debate has been at the order of the day about CHO digestion and absorption and this new knowledge has, in many ways, completely changed the way researchers think about CHOs. The effects of CHOs on health may best be described on the basis of their physiological effects (ability to rise blood glucose levels), which depend on the type of constituent sugars (glucose, fructose and galactose), the physical form of the CHO (particle size and degree of hydration), nature of the starch (amylose, amylopectin) and other food components (dietary fibre, fat, organic acids) (Augustin *et al.*, 2002). This classification is referred to as the glycaemic index (GI) and refers to the blood glucose raising potential of the CHO. Jenkins *et al.* (1981) introduced the GI in 1981, proposing the GI as a quantitative assessment of foods based on postprandial blood glucose response, expressed as a percentage of the response to an equivalent CHO portion of a reference food such as white bread or glucose (Jenkins *et al.*, 1981; Jenkins *et al.*, 1984; Wolever *et al.*, 1991).

As a response to high GI CHO, the pancreas secretes insulin in order to restore blood glucose levels and, therefore, results in a greater insulin demand. Hyperinsulinaemia is

characterised by a condition of insulin resistance, which in turn can lead to the onset of type 2 diabetes mellitus (DM) and cardiovascular disease (CVD) (Augustin et al., 2002; Ludwig, 2002). LGI foods, on the other hand are digested and absorbed slowly and may lead to a reduced insulin demand, improved blood glucose control and reduced blood lipid levels (Augustin et al., 2002).

CVD and DM are some of the most common causes of death in Western society and the prevalence is increasing worldwide (King et al., 1998). In South Africa, CVD accounted for 32 919 deaths in the year 2000 which was the second largest cause of death among South Africans, while mortality due to diabetes was estimated to be 13 157, the 10th largest cause of death in South Africa (Bradshaw et al., 2003). The high prevalence of CVD and DM can be attributed to environmental and behavioural factors such as a stressful lifestyle, a low fibre, high saturated fat diet and also inadequate micronutrient intakes (Vorster et al., 1997). The role that the GI may play in preventing the onset of these diseases has been studied during the past few years. Accumulating evidence from randomised control studies has shown that LGI foods may improve overall blood glucose control in people with type 2 diabetes (Brand et al., 1991; Wolever et al., 1992, Frost et al., 1994), reduce serum lipids in people with hypertriglyceridaemia (Jenkins et al., 1987) and improve insulin sensitivity (Frost et al., 1998; Riccardi & Revellese, 2000). Additionally, cross-sectional and cohort studies showed LGI diets are also associated with higher levels of high-density lipoprotein cholesterol (HDL-c) (Frost et al., 1999) and, therefore, reduce the risk for development of type 2 diabetes and CVD (Frost et al., 1999; Salmeron et al., 1997 a, b)

However, the issue of the GI is still a controversial one. The American Diabetes Association (2001) concluded that the total amount of available CHO in food is more important than the source (starch or sugar) or type (low or high GI). Furthermore, they acknowledge that the use of LGI foods may reduce postprandial hyperglycaemia but regard the evidence for long-term benefit as insufficient to recommend LGI diets as a primary strategy in meal planning. Pi-Sunyer (2002) also questions the calculations of the area under the response curve for glucose, the reproducibility of the GI (i.e. the variability in GI values), the effects of a combination of macronutrients on the GI as well as the predictability of the insulin response when consuming low or high GI foods.

In contrast, several other organisations support the use of substituting high GI foods for LGI foods, like the Joint FAO/WHO Expert Consultation on Carbohydrates (Food and Agricultural Organisation/World Health Organisation, 1997), the European Association for the Study of Diabetes (Diabetes and Nutrition Study Group, 2000) and the Dietitians Association of Australia (Dietitians Association of Australia, 1997). They encourage people to apply the GI

when choosing CHO foods. According to Brand-Miller *et al.* (2003), the hypothesis that high GI CHOs increase the risk of chronic disease is supported by experimental evidence such as postprandial hyperglycaemia *per se* is a recognised risk factor for total and cardiovascular mortality. In observational studies it was found that GI and glycaemic load are independent predictors of HDL and triacylglycerol levels and in individuals with type 1 and type 2 diabetes (Ford & Liu, 2001). Furthermore, clinical intervention trials indicate that the GI of the diet affects glycaemic and lipid control (Frost *et al.*, 1994; Bouche *et al*, 2002). Ludwig (2002) is also of the opinion that habitual consumption of high GI foods may increase the risk for type 2 diabetes and heart disease. In order to resolve this controversy, it was decided to conduct a meta-analysis on RCTs, which compared the effects of LGI foods with those of high GI foods. This meta-analysis is the first to investigate the effect of the GI in CHO metabolism as well as lipid metabolism with special reference to total cholesterol, triglycerides, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol. With this meta-analysis and systematic review summarising the epidemiological data also, it is aimed to provide a clear and objective basis for dietary recommendations regarding the use of the GI in meal planning.

4.2 Application of the glycaemic index in sport

Athletes are encouraged to consume CHO prior to, during and after exercise to enhance performance and recovery (Walton & Rhodes, 1997). In spite of all this knowledge, there is a paucity of information available to athletes concerning the types of CHO foods to select.

The main objective for athletes is to optimise blood glucose and muscle glycogen levels. Muscle glycogen is the primary fuel source during prolonged moderate-to-high intensity exercise (Romijn *et al.*, 1993). Depletion of muscle glycogen results in fatigue during prolonged exercise (Jentjens & Jeukendrup, 2003), therefore optimal pre-exercise glycogen levels is a necessity for optimal sport performance (Costill, 1988; Ivy, 1991). The goals of pre-exercise CHO ingestion are to optimize muscle and liver glycogen stores that are needed during exercise, while the intake of CHO during prolonged exercise enhances CHO availability and improves exercise capacity and performance. Post-exercise CHO intake promotes repletion of the body's liver and muscle glycogen stores (Burke *et al.*, 1998).

There is still controversy surrounding LGI or high GI food intake before exercise (DeMarco *et al.*, 1999; Thomas *et al.*, 1991; Febbraio & Stewart, 1996; Stannard *et al.*, 2000). LGI foods appear to be less likely than high GI foods to cause hyperglycaemia and hyperinsulinaemia when consumed immediately before exercise (Thomas *et al.*, 1991). This means that LGI foods may reduce the chance of rebound hypoglycaemia at the onset of exercise. Therefore, LGI foods may provide essential substrates to the exercising muscle

late in exercise (Walton & Rhodes, 1997). On the other hand, studies by Sparks *et al.* (1998) and Febbraio and Stewart (1996) demonstrated that there were no significant differences in subsequent exercise performance when comparing consumption of high and LGI CHOs prior to exercise.

During exercise, athletes are advised to consume moderate GI to high GI CHOs (Burke *et al.*, 1998). Blood glucose levels are maintained throughout exercise due to more rapid digestion and absorption of high GI foods. This is in contrast to LGI foods, which have slower digestion and absorption rates and, therefore, do not maintain blood glucose levels and also have the potential to cause gastric distress (El-Sayed *et al.*, 1997). According to Walton and Rhodes (1997), high GI foods should be ingested post-exercise. High GI foods elicit an increased rate of muscle glycogen synthesis compared to LGI foods. A possible explanation for this difference is that high GI foods excite greater substrate availability for glycogen resynthesis.

The manipulation of the GI of CHOs in optimising athletic performance presents an exciting research area in sport nutrition. There is accumulating evidence that supports the use of the GI in planning nutritional strategies of CHO supplementation in sport (Siu & Wong, 2004). The purpose of this review will, therefore, be to evaluate current recommendations on the type of CHO (GI) ingested pre, during and post-exercise, to make informed conclusions regarding the use of the GI in sport nutrition, to motivate and direct future research and to form a firm, evidence-based platform for the use of the GI in sport nutrition.

5. Aims and objectives

5.1 Meta-analysis of the health effects of using the glycaemic index in meal planning.
The main aim was to determine the effects of the GI on risk markers for CHO and lipid metabolism by conducting a meta-analysis of the literature available on the GI since 1981. The objectives were the following:

- To conduct a meta-analysis on published randomised controlled clinical studies that examined the short and long-term effects of LGI diets compared to high GI diets on CHO metabolism by investigating effects on glycated plasma protein (HbA_{1c}) and fructosamine as well as lipid metabolism by investigating effects on triglycerides, total cholesterol, HDL-c and LDL-c.

- To make recommendations and direct future research for the use of the GI in meal planning.

5.2 Some health benefits of low glycaemic index diets: A systematic review

The aim of this systematic review was to determine the total body of strength regarding consistent relevant scientific evidence to encourage dieticians to incorporate the GI concept when planning diets. The objectives were:

- To summarise and judge the strength of scientific evidence from an epidemiological point of view in addition to the strength of RCTs on the effect of LGI diets on markers for CHO and lipid metabolism.

5.3 Systematic review on the effect of the glycaemic index on sport performance

The aim was to investigate if the application of the GI in an athlete's diet can enhance sport performance by conducting a systematic review of all the available literature on the GI and sport since 1981. The objectives were the following:

- To conduct a systematic review on RCTs to determine whether the onset of premature fatigue during exercise can be prevented by eating a LGI meal compared to a high GI meal before the onset of exercise by investigating pre-exercise blood glucose and insulin levels.

- To summarise the literature regarding CHO intake with either an estimated high or medium GI during exercise in order to make recommendations for the use thereof during exercise.

- To determine whether ingesting a high GI meal directly after exercise can increase the rate of glycogen repletion by investigating glycogen levels and rate of glycogen synthesis.

- To make recommendations and direct future research for the use of the GI in sport nutrition.

6. Structure of this thesis

This thesis is presented in article format. The thesis consists of three research articles, one meta-analysis and two systematic reviews, all in the field of clinical nutrition. The introductory chapter gives an overview of the background and motivation for the necessity of a complete and informative meta-analysis on the glycaemic index. This chapter also reviews the literature considered important for conducting a meta-analysis and systematic review. Chapter 2 consists of a manuscript published in the *British Journal of Nutrition* with the title "Meta-analysis of the health effects of using the glycaemic index in meal-planning" (Opperman *et al.*, 2004). Chapter 3 consists of a manuscript accepted by the *South African Journal of Clinical Nutrition* with the title "Some health benefits of low glycaemic index diets: A systematic review". Chapter 4 is a systematic review on the effect of the GI in sport nutrition. A manuscript with the title "Systematic review on the effect of the glycaemic index on sport performance" was submitted for publication in *Sport Medicine*. An example of the data extraction forms for both the meta-analysis and systematic reviews is presented as

Addendum A. In Chapter 5, a general discussion and summary of the findings are provided, conclusions are drawn and recommendations are made. The relevant references of Chapters 2, 3 and 4 are provided at the end of each chapter according to the authors' instructions of the specific journal to which the manuscripts were submitted. The references used in the unpublished Chapters 1 and 5 are provided according to the mandatory style stipulated by the North-West University.

7. Authors' contributions

The principal author of this thesis is Ms. A.M. Opperman. In Table 1.1 the contributions of the co-authors are summarised.

Table 1.1: Co-authors and their contributions

Chapter	Co-author	Contribution
Chapter 2	C.S. Venter	Promoter: Co-reviewer, assistance in writing of article, selection of studies, data extraction, co-drafting of protocol (dietitian)
	W. Oosthuizen	Co-promoter: assistance in writing of article, general recommendations (nutritionist)
	R.L. Thompson	Assistance with statistics (nutritionist)
	H.H. Vorster	General recommendations (nutritionist/physiologist)
Chapter 3	C.S. Venter	Promoter: Co-reviewer, assistance in writing of article, selection of studies, data extraction, co-drafting of protocol (dietitian)
	W. Oosthuizen	Co-promoter: assistance in writing of article, general recommendations (nutritionist)
	R.L. Thompson	Assistance with statistics (nutritionist)
Chapter 4	C.S. Venter	Promoter: Co-reviewer, assistance in writing of article, selection of studies, data extraction, co-drafting of protocol (dietitian)
	H.H. Wright	General recommendations (sport dietitian)
	W. Oosthuizen	Co-promoter: assistance in writing of article, general recommendations (nutritionist)

The following is a statement from the co-authors confirming their individual roles in the reviews and giving their permission that the manuscripts may form part of this thesis.

I declare that I have approved the above mentioned manuscripts, that my role in the review, as indicated above, is representative of my actual contribution and that I hereby give my consent that they may be published as part of the PhD thesis of Maretha Opperman.

_____   _____

Prof. C.S. Venter   Prof. W. Oosthuizen

_____   _____

Dr. R.L. Thompson   Prof. H.H. Vorster

_____

Dr. H.H. Wright

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

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Review article

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

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Diabetes mellitus and CVD are some of the leading causes of mortality and morbidity. Accumulating data indicate that a diet characterised by low-glycaemic index (GI) foods may improve the management of diabetes or lipid profiles. The objective of the present meta-analysis was to critically analyse the scientific evidence that low-GI diets have beneficial effects on carbohydrate and lipid metabolism compared with high-GI diets. We searched for randomised controlled trials with a crossover or parallel design published in English between 1981 and 2003, investigating the effect of low-GI *v.* high-GI diets on markers for carbohydrate and lipid metabolism. Unstandardised differences in mean values were examined using the random effects model. The main outcomes were fructosamine, glycated Hb (HbA$_{1c}$), HDL-cholesterol, LDL-cholesterol, total cholesterol and triacylglycerol. Literature searches identified sixteen studies that met the strict inclusion criteria. Low-GI diets significantly reduced fructosamine by -0.1 (95 % CI -0.20, 0.00) mmol/l ($P=0.05$), HbA$_{1c}$ by 0.27 (95 % CI -0.5, -0.03) % ($P=0.03$), total cholesterol by -0.33 (95 % CI -0.47, -0.18) mmol/l ($P<0.0001$) and tended to reduce LDL-cholesterol in type 2 diabetic subjects by -0.15 (95 % CI -0.31, -0.00) mmol/l ($P=0.06$) compared with high-GI diets. No changes were observed in HDL-cholesterol and triacylglycerol concentrations. No substantial heterogeneity was detected, suggesting that the effects of low-GI diets in these studies were uniform. Results of the present meta-analysis support the use of the GI as a scientifically based tool to enable selection of carbohydrate-containing foods to reduce total cholesterol and to improve overall metabolic control of diabetes.

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

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

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

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

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

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

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

This has led to a constructive debate internationally within the academic field, industry, health practitioners

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

Methods

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

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

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

Data extraction

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

Data analysis

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

Differences between the results of the trials were checked for heterogeneity by visual inspection of the graphs and by statistical test (χ^2).

Results

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

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

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

Explanation of forest plots

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

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

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

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

Table 2. Nutrient composition of high- and low-glycaemic-index diets*

(Mean values and standard deviations)

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

GI, glycaemic index; NR, not reported; TE, total energy.

* For a summary of the studies, see Table 1.

† Low-GI diet contained less fat (25 v. 32 %) and more fibre (21 v. 14 g).

‡ Low-GI diet contained more fibre (26 g/4200 kJ (1000 kcal) v. 21 g/4200 kJ (1000 kcal)).

§ Low-GI diet contained more fibre (50 v. 23 g).

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

Carbohydrate metabolism

Figs 1 and 2 represent the effects of low-GI *v.* high-GI diets on carbohydrate metabolism. For the present study, fructosamine and HbA_{1c} were investigated. No heterogeneity (Higgins *et al.* 2003) was detected for fructosamine (I^2 0 %; Fig. 1). The random effects analysis demonstrated an overall statistically significant reduction in fructosamine in

subjects receiving the low-GI diet compared with the high-GI diet (change −0·1 (95 % CI −0·20, 0·00) mmol/l; $P=0·05$). However, when studies were subgrouped into DM and healthy subjects a non-significant improvement was observed in each group (DM, change −0·11 (95 % CI −0·25, 0·03) mmol/l, $P=0·12$; healthy, change −0·09 (95 % CI −0·24, 0·06) mmol/l, $P=0·25$). The GI reduction for the included studies was 24 (SD 9) units. Frost *et al.* (1994) and Wolever *et al.* (1992a), who had the longest intervention periods, found the biggest change in mean fructosamine concentrations.

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

Lipid metabolism

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

Study or sub-category	Low GI (*n*)	High GI (*n*)	WMD (random) (95 % CI)	Weight (%)	WMD (random) (95 % CI)
1. Diabetic subjects (change in mmol/l)					
Jenkins *et al.* (1988)	8	8		42·61	−0·07 (−0·23, 0·09)
Wolever *et al.* (1992a)	6	6		0·27	−0·63 (−2·59, 1·33)
Frost *et al.* (1994)	25	26		2·53	−0·60 (−1·24, 0·04)
Lafrance *et al.* (1998)	9	9		4·84	−0·20 (−0·67, 0·27)
Jarvi *et al.* (1999)	20	20		3·10	−0·09 (−0·67, 0·49)
Subtotal (95 % CI)	68	69		53·36	−0·11 (−0·25, 0·03)
Test for heterogeneity: χ^2 2·89, df 4 ($P=0·58$), I^2 0 %					
Test for overall effect: Z 1·55 ($P=0·12$)					
2. Healthy subjects (change in mmol/l)					
Jenkins *et al.* (1987a)	6	6		34·15	−0·11 (−0·29, 0·07)
Bouche *et al.* (2002)	11	11		12·50	−0·03 (−0·32, 0·26)
Subtotal (95 % CI)	17	17		46·64	−0·09 (−0·24, 0·06)
Test for heterogeneity: χ^2 0·21, df 1 ($P=0·64$), I^2 0 %					
Test for overall effect: Z 1·16 ($P=0·25$)					
Total (95 % CI)	85	86		100·00	−0·10 (−0·20, 0·00)
Test for heterogeneity: χ^2 3·15, df 6 ($P=0·79$), I^2 0 %					
Test for overall effect: Z 1·92 ($P=0·05$)					

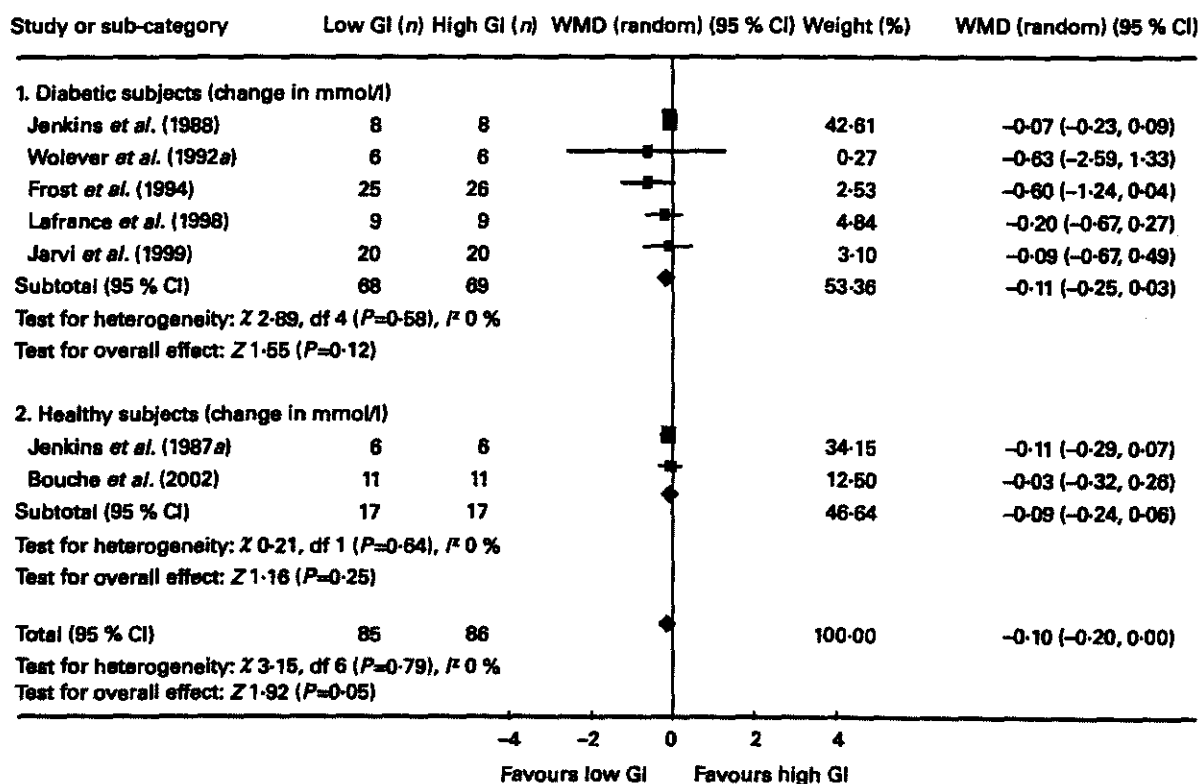−4   −2   0   2   4

Favours low GI   Favours high GI

Fig. 1. Net changes in fructosamine (mmol/l). GI, glycaemic index; WMD, weighted mean difference. For an explanation of the forest plot, see p. 369. For details of selection of studies, see Table 1. GI, glycaemic index.
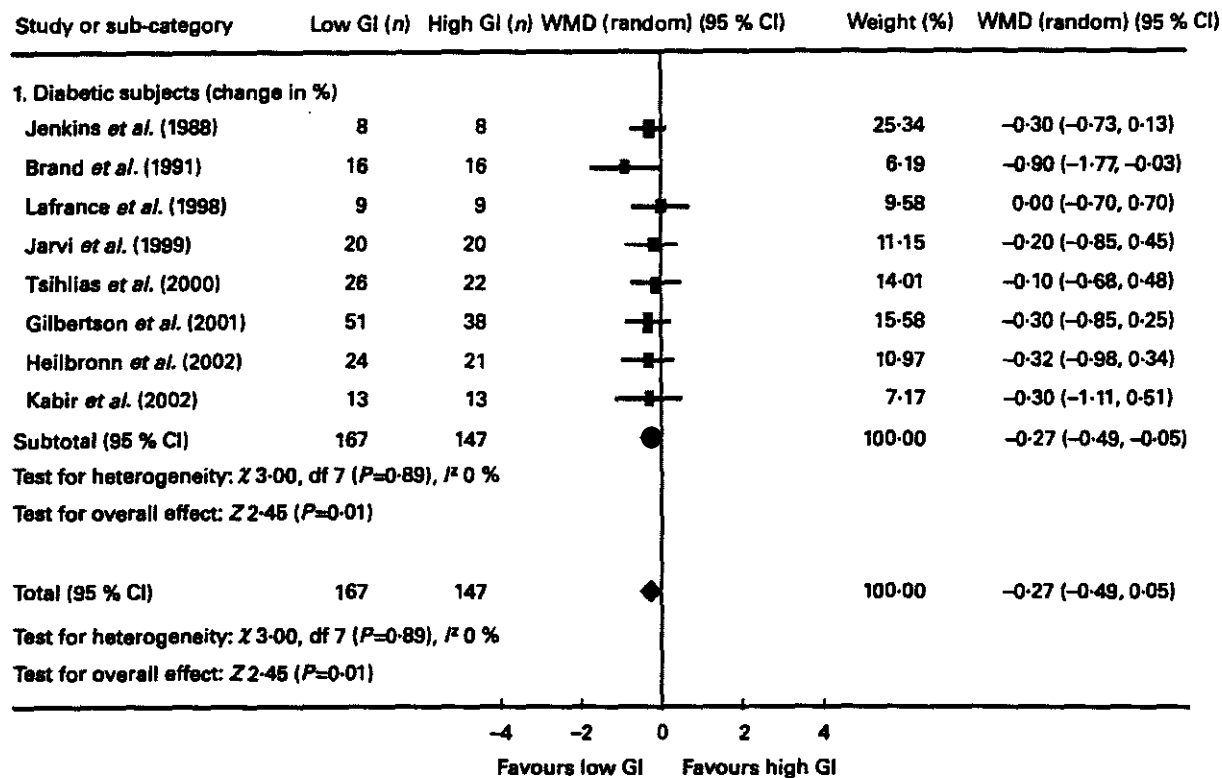
Study or sub-category	Low GI (n)	High GI (n)	WMD (random) (95 % CI)	Weight (%)	WMD (random) (95 % CI)
1. Diabetic subjects (change in %)					
Jenkins et al. (1988)	8	8		25·34	−0·30 (−0·73, 0·13)
Brand et al. (1991)	16	16		6·19	−0·90 (−1·77, −0·03)
Lafrance et al. (1998)	9	9		9·58	0·00 (−0·70, 0·70)
Jarvi et al. (1999)	20	20		11·15	−0·20 (−0·85, 0·45)
Tsihlias et al. (2000)	26	22		14·01	−0·10 (−0·68, 0·48)
Gilbertson et al. (2001)	51	38		15·58	−0·30 (−0·85, 0·25)
Heilbronn et al. (2002)	24	21		10·97	−0·32 (−0·98, 0·34)
Kabir et al. (2002)	13	13		7·17	−0·30 (−1·11, 0·51)
Subtotal (95 % CI)	167	147		100·00	−0·27 (−0·49, −0·05)
Test for heterogeneity: χ 3·00, df 7 (P=0·89), I^2 0 %					
Test for overall effect: Z 2·45 (P=0·01)					
Total (95 % CI)	167	147		100·00	−0·27 (−0·49, 0·05)
Test for heterogeneity: χ 3·00, df 7 (P=0·89), I^2 0 %					
Test for overall effect: Z 2·45 (P=0·01)					

-4   -2   0   2   4

Favours low GI   Favours high GI

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

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

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

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

The random effects analysis demonstrated an overall statistically significant improvement in TC in subjects receiving low-GI diets compared with high-GI diets

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

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

Discussion

Carbohydrate metabolism

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

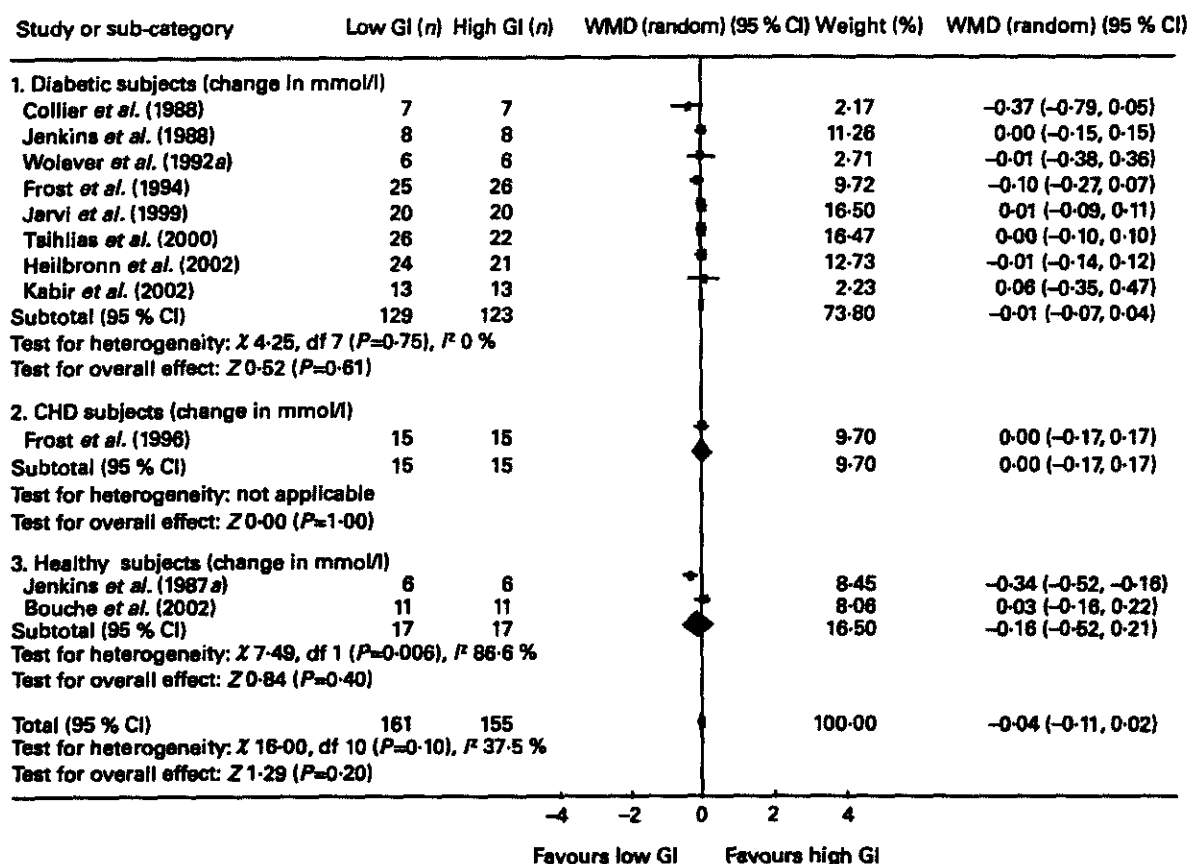| Study or sub-category	Low GI (*n*)	High GI (*n*)	WMD (random) (95 % CI)	Weight (%)	WMD (random) (95 % CI)
1. Diabetic subjects (change in mmol/l)					
Collier *et al.* (1988)	7	7		2·17	−0·37 (−0·79, 0·05)
Jenkins *et al.* (1988)	8	8		11·26	0·00 (−0·15, 0·15)
Wolever *et al.* (1992a)	6	6		2·71	−0·01 (−0·38, 0·36)
Frost *et al.* (1994)	25	26		9·72	−0·10 (−0·27, 0·07)
Jarvi *et al.* (1999)	20	20		16·50	0·01 (−0·09, 0·11)
Tsihlias *et al.* (2000)	26	22		16·47	0·00 (−0·10, 0·10)
Heilbronn *et al.* (2002)	24	21		12·73	−0·01 (−0·14, 0·12)
Kabir *et al.* (2002)	13	13		2·23	0·06 (−0·35, 0·47)
Subtotal (95 % CI)	129	123		73·80	−0·01 (−0·07, 0·04)
Test for heterogeneity: X 4·25, df 7 (*P*=0·75), I^2 0 %					
Test for overall effect: Z 0·52 (*P*=0·61)					
2. CHD subjects (change in mmol/l)					
Frost *et al.* (1996)	15	15		9·70	0·00 (−0·17, 0·17)
Subtotal (95 % CI)	15	15		9·70	0·00 (−0·17, 0·17)
Test for heterogeneity: not applicable					
Test for overall effect: Z 0·00 (*P*=1·00)					
3. Healthy subjects (change in mmol/l)					
Jenkins *et al.* (1987a)	6	6		8·45	−0·34 (−0·52, −0·16)
Bouche *et al.* (2002)	11	11		8·06	0·03 (−0·16, 0·22)
Subtotal (95 % CI)	17	17		16·50	−0·16 (−0·52, 0·21)
Test for heterogeneity: X 7·49, df 1 (*P*=0·006), I^2 86·6 %					
Test for overall effect: Z 0·84 (*P*=0·40)					
Total (95 % CI)	161	155		100·00	−0·04 (−0·11, 0·02)
Test for heterogeneity: X 16·00, df 10 (*P*=0·10), I^2 37·5 %					
Test for overall effect: Z 1·29 (*P*=0·20)					

−4 −2 0 2 4

Favours low GI   Favours high GI

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

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

Fructosamine

Fructosamine is measured as a short-term (2 weeks) index of glycaemic control. Glycated albumin is the main constituent of fructosamine and has a half-life of only 12 d, explaining the usefulness of fructosamine as a short-term marker (Kumar & Clarke, 1998). The studies of Jenkins *et al.* (1987a, 1988) contributed the most weight to the meta-analysis, irrespective of the fact that only six and eight subjects participated in the studies and intervention periods were only 2 weeks long. This could be attributed to the small CI of the studies. Frost *et al.* (1994) and Wolever *et al.* (1992a) found the biggest improvement in mean fructosamine concentrations. These two studies had the longest intervention periods. Although fructosamine is a shorter-term marker for blood glucose control than HbA_{1c}, it seems that the longer low-GI diets are followed, the larger the decreases in fructosamine concentrations that are observed. According to Jones *et al.* (1983), maximum changes in fructosamine take 4–6 weeks to occur. More profound decreases were documented in DM subjects than in healthy subjects. Results would probably be more representative if all available studies conducted on fructosamine and the GI could be included, but due to a lack of complete data (mean values and SD of baseline and end values) this was not possible. However, the combined meta-analysis suggests that low-GI diets will reduce
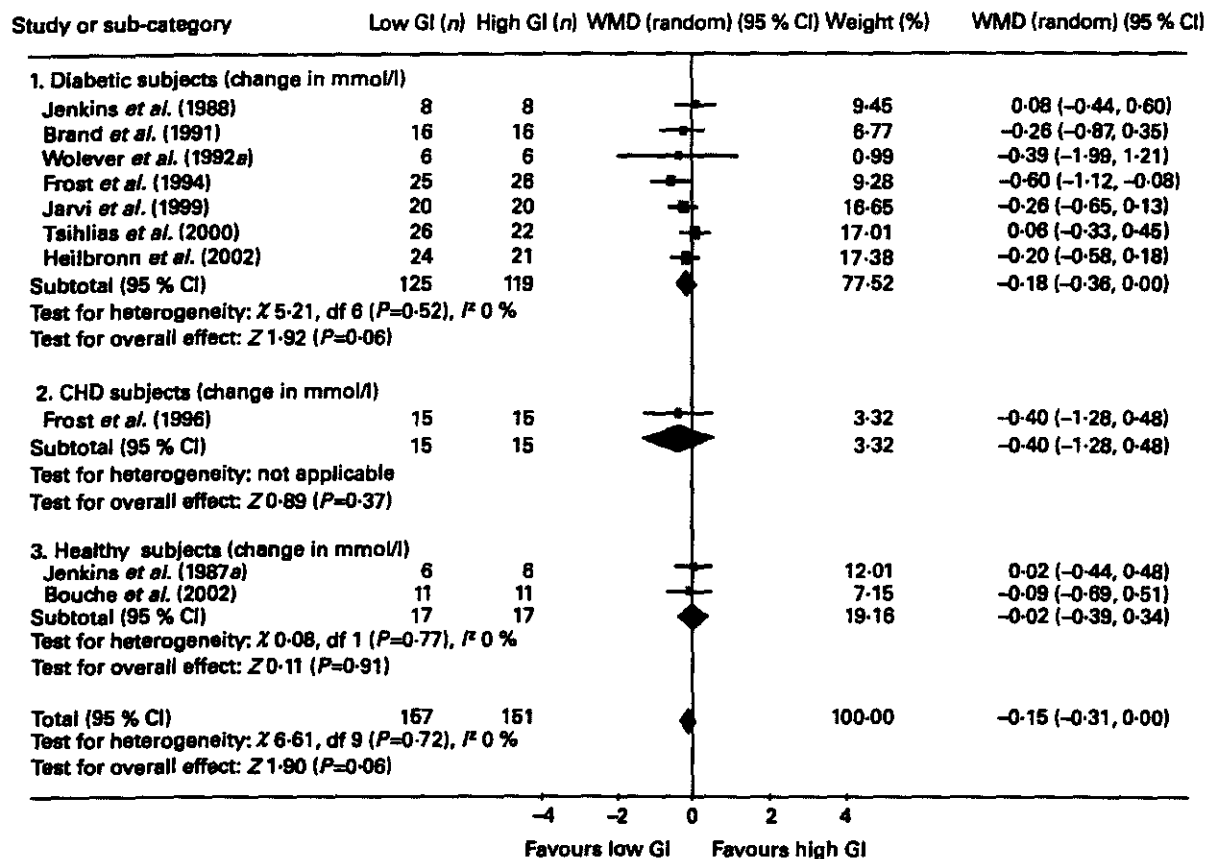
Fig. 4. Net changes in LDL-cholesterol (mmol/l). GI, glycaemic index; WMD, weighted mean difference. For an explanation of the forest plot, see p. 369. For details of selection of studies, see Table 1.

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

Glycated Hb

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

may need to be incorporated into the diet to achieve measurable long-term improvements in glycaemic control. Differences in fructosamine and HbA$_{1c}$ might be confounded by differences in energy intake or weight loss. In most studies body weight, energy intake, fat, protein and carbohydrate and fibre intake were held constant.

Poor blood glucose control has been associated with a greater incidence of long-term macrovascular complications in both type 1 and type 2 DM patients (Balkau *et al.* 1998; UK Prospective Diabetes Study Group, 1998; Couthinho *et al.* 1999; Stratton *et al.* 2000). The UK Prospective Diabetes Study Group found that each 1 % reduction in mean HbA$_{1c}$ concentration was associated with reductions in risk of 21 % for deaths related to diabetes, 14 % for myocardial infarction and 37 % for microvascular complications. It is not clear precisely how low-GI diets improve the markers of carbohydrate metabolism and prevent the onset of type 2 DM. Several mechanisms have been proposed. Briefly, high-GI diets have been associated with high postprandial blood glucose concentrations and increased insulin demands (Ludwig, 2002; Willet *et al.* 2002). Primary hyperinsulinaemia may cause insulin resistance, which reduces insulin sensitivity. In addition, habitual consumption of high-GI meals in the long-term initiates a cycle of hyperinsulinaemia and insulin resistance, leading to a loss of pancreatic β-cell function (Ludwig, 2002); this can result in glucose intolerance and an irreversible state of DM (Willet *et al.* 2002).
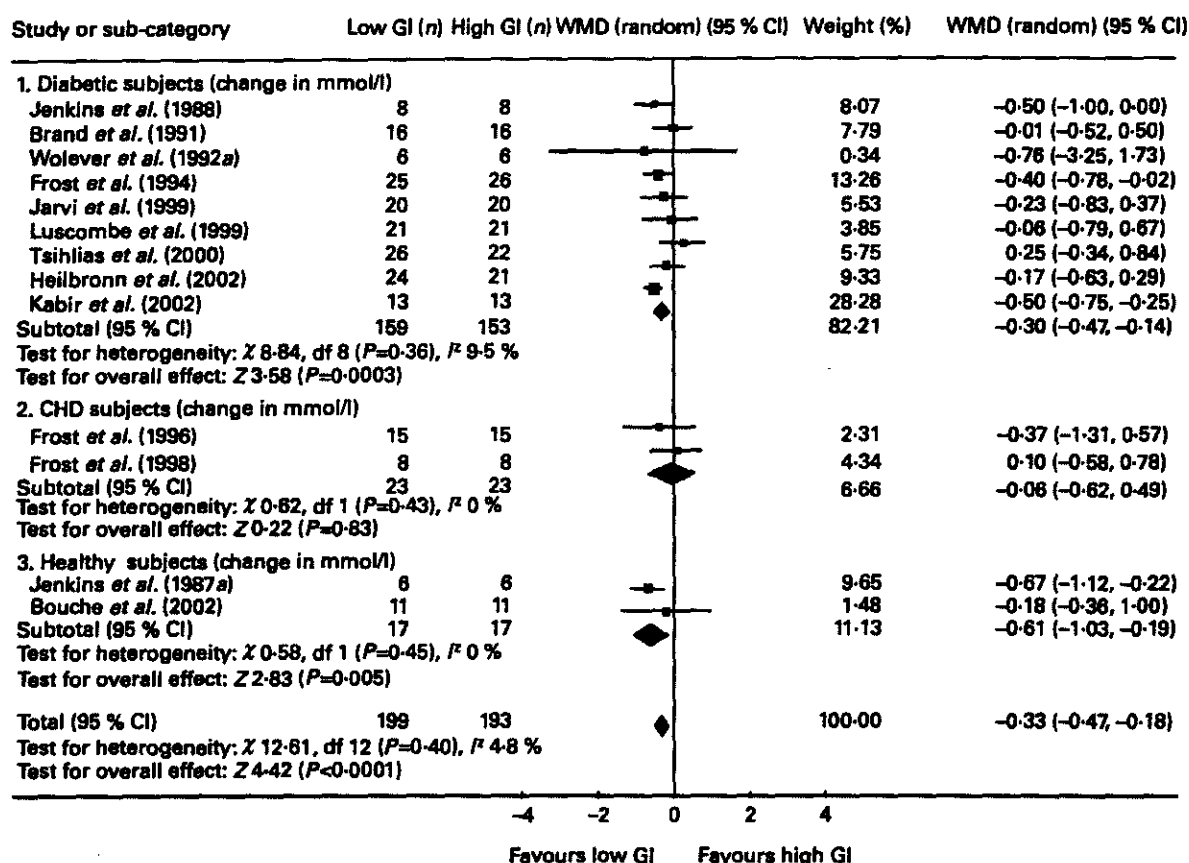
Study or sub-category	Low GI (*n*)	High GI (*n*)	WMD (random) (95 % CI)	Weight (%)	WMD (random) (95 % CI)
1. Diabetic subjects (change in mmol/l)					
Jenkins *et al.* (1988)	8	8		8·07	−0·50 (−1·00, 0·00)
Brand *et al.* (1991)	16	16		7·79	−0·01 (−0·52, 0·50)
Wolever *et al.* (1992a)	6	6		0·34	−0·76 (−3·25, 1·73)
Frost *et al.* (1994)	25	26		13·26	−0·40 (−0·78, −0·02)
Jarvi *et al.* (1999)	20	20		5·53	−0·23 (−0·83, 0·37)
Luscombe *et al.* (1999)	21	21		3·85	−0·06 (−0·79, 0·67)
Tsihlias *et al.* (2000)	26	22		5·75	0·25 (−0·34, 0·84)
Heilbronn *et al.* (2002)	24	21		9·33	−0·17 (−0·63, 0·29)
Kabir *et al.* (2002)	13	13		28·28	−0·50 (−0·75, −0·25)
Subtotal (95 % CI)	159	153		82·21	−0·30 (−0·47, −0·14)
Test for heterogeneity: χ 8·84, df 8 (*P*=0·36), I^2 9·5 %					
Test for overall effect: *Z* 3·58 (*P*=0·0003)					
2. CHD subjects (change in mmol/l)					
Frost *et al.* (1996)	15	15		2·31	−0·37 (−1·31, 0·57)
Frost *et al.* (1998)	8	8		4·34	0·10 (−0·58, 0·78)
Subtotal (95 % CI)	23	23		6·66	−0·06 (−0·62, 0·49)
Test for heterogeneity: χ 0·62, df 1 (*P*=0·43), I^2 0 %					
Test for overall effect: *Z* 0·22 (*P*=0·83)					
3. Healthy subjects (change in mmol/l)					
Jenkins *et al.* (1987a)	6	6		9·65	−0·67 (−1·12, −0·22)
Bouche *et al.* (2002)	11	11		1·48	−0·18 (−0·36, 1·00)
Subtotal (95 % CI)	17	17		11·13	−0·61 (−1·03, −0·19)
Test for heterogeneity: χ 0·58, df 1 (*P*=0·45), I^2 0 %					
Test for overall effect: *Z* 2·83 (*P*=0·005)					
Total (95 % CI)	199	193		100·00	−0·33 (−0·47, −0·18)
Test for heterogeneity: χ 12·61, df 12 (*P*=0·40), I^2 4·8 %					
Test for overall effect: *Z* 4·42 (*P*<0·0001)					

−4 −2 0 2 4

Favours low GI   Favours high GI

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

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

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

Lipid metabolism

The present meta-analysis pooled the results of fourteen randomised controlled trials studying low-GI *v.* high-GI diets and their effects on markers for lipid metabolism.

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

HDL-cholesterol

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

A low HDL-cholesterol concentration is a strong independent predictor of CHD and has several causes, many
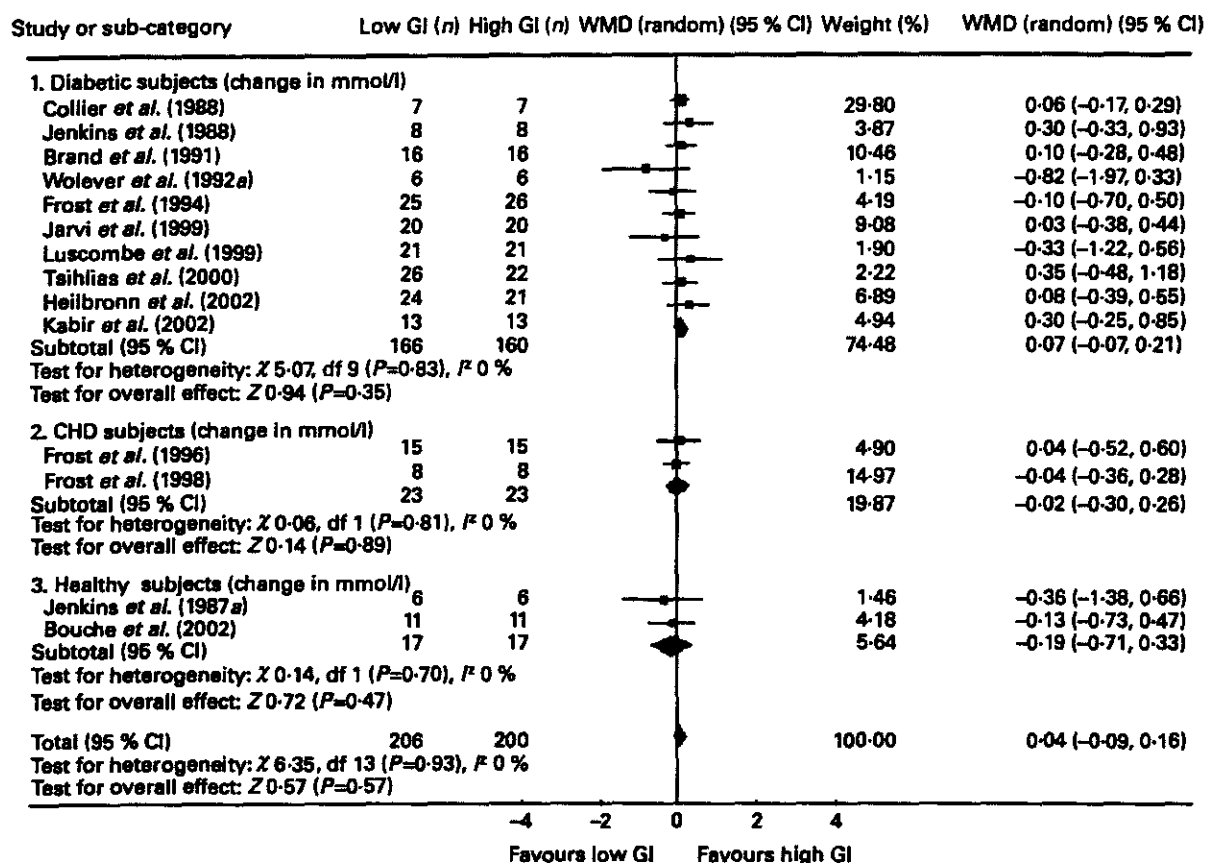
Study or sub-category	Low GI (n)	High GI (n)	WMD (random) (95 % CI)	Weight (%)	WMD (random) (95 % CI)
1. Diabetic subjects (change in mmol/l)					
Collier et al. (1988)	7	7		29·80	0·06 (−0·17, 0·29)
Jenkins et al. (1988)	8	8		3·87	0·30 (−0·33, 0·93)
Brand et al. (1991)	16	16		10·46	0·10 (−0·28, 0·48)
Wolever et al. (1992a)	6	6		1·15	−0·82 (−1·97, 0·33)
Frost et al. (1994)	25	26		4·19	−0·10 (−0·70, 0·50)
Jarvi et al. (1999)	20	20		9·08	0·03 (−0·38, 0·44)
Luscombe et al. (1999)	21	21		1·90	−0·33 (−1·22, 0·56)
Tsihlias et al. (2000)	26	22		2·22	0·35 (−0·48, 1·18)
Heilbronn et al. (2002)	24	21		6·89	0·08 (−0·39, 0·55)
Kabir et al. (2002)	13	13		4·94	0·30 (−0·25, 0·85)
Subtotal (95 % CI)	166	160		74·48	0·07 (−0·07, 0·21)

Test for heterogeneity: χ 5·07, df 9 (P=0·83), I^2 0 %
Test for overall effect: Z 0·94 (P=0·35)

2. CHD subjects (change in mmol/l)					
Frost et al. (1996)	15	15		4·90	0·04 (−0·52, 0·60)
Frost et al. (1998)	8	8		14·97	−0·04 (−0·36, 0·28)
Subtotal (95 % CI)	23	23		19·87	−0·02 (−0·30, 0·26)

Test for heterogeneity: χ 0·06, df 1 (P=0·81), I^2 0 %
Test for overall effect: Z 0·14 (P=0·89)

3. Healthy subjects (change in mmol/l)					
Jenkins et al. (1987a)	6	6		1·46	−0·36 (−1·38, 0·66)
Bouche et al. (2002)	11	11		4·18	−0·13 (−0·73, 0·47)
Subtotal (95 % CI)	17	17		5·64	−0·19 (−0·71, 0·33)

Test for heterogeneity: χ 0·14, df 1 (P=0·70), I^2 0 %
Test for overall effect: Z 0·72 (P=0·47)

Total (95 % CI)	206	200		100·00	0·04 (−0·09, 0·16)

Test for heterogeneity: χ 6·35, df 13 (P=0·93), I^2 0 %
Test for overall effect: Z 0·57 (P=0·57)

−4　−2　0　2　4

Favours low GI　　Favours high GI

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

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

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

a 0·09 mmol/l difference in HDL-cholesterol concentration between the lowest and the highest quintiles of the GI.

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

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

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

LDL-cholesterol

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

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

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

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

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

Total cholesterol

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

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

Triacylglycerol

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

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

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

Conclusion

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

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

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

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3

Some health benefits of low glycaemic index diets: A systematic review

A.M. Opperman, C.S Venter, W. Oosthuizen & R.L. Thompson

Abstract

Background: There is controversy on the practical use of the glycaemic index (GI), often with reference to the responsibility of health professionals to only advise consumers when scientific evidence supports their recommendations. There are indications that low GI diets may improve health, but the strength of the evidence is not known.

Objectives: The objective of this systematic review is to determine the strength of scientific evidence to encourage dieticians to incorporate the GI concept when planning diets.

Design: A meta-analysis that is part of the systematic review was performed. We searched for randomised controlled trials with a crossover or parallel design published in English between 1981 and 2003, investigating the effect of low GI vs. high GI diets on markers for carbohydrate and lipid metabolism. The main outcomes were fructosamine, HbA_{1c}, HDL-cholesterol, LDL-cholesterol, total cholesterol and triacylglycerols.

Results: Literature searches identified 13 studies that met strict inclusion criteria. Low GI diets significantly reduced fructosamine by -0.1 mmol/L (CI -0.20,0.00; P=0.05), HbA_{1c} by -0.27% (CI -0.5,-0.03; P=0.03), LDL-cholesterol in type 2 diabetics by -0.24 mmol/L (CI -0.45, -0.04; P=0.02) and total cholesterol by -0.33 mmol/L (CI -0.47,-0.18; P<0.0001) compared to high GI diets. No effects were observed in HDL-c and triacylglycerols.

Conclusion: This systematic review presents convincing evidence to recommend the use of the GI as a scientifically based tool to choose carbohydrate-containing foods to reduce total cholesterol and LDL-c concentrations and to improve overall metabolic control of diabetes.

1. Introduction

There is controversy in the literature on the practical use of the glycaemic index (GI) concept,[1] often with reference to the responsibility of health professionals to advise consumers only when the scientific evidence supports their recommendations. The evidence-based approach has recently been implemented as an objective framework in which to gather and review all available evidence in setting nutrition policy and practice.[2] This paper is a systematic review of the results of studies which compared the effects of low GI *vs* high GI diets on markers of carbohydrate and lipid metabolism.

A systematic review is regarded by Egger and Smith[3] as "most appropriate for denoting any review of a body of data that uses clearly defined methods and criteria", whilst a meta-analysis is defined as a statistical technique used to combine the results of studies addressing the same question into a one number summary.[4] According to the definition of Egger and Smith,[3] a meta-analysis can, if appropriate, be part of a systematic review. Therefore, the results of a meta-analysis performed on the data gathered is included in this paper.

In order to assess the scientific evidence on the health benefits of lowering the GI of the diet as a basis for dietary recommendations designed to improve the serum lipid profile and overall metabolic control of diabetes, the terminology suggested by the Journal of the American Medical Association will be used.[5] This hierarchy of evidence includes: systematic reviews and meta-analyses, randomised controlled trials (RCT's), cohort studies, case-control studies, cross-sectional surveys and case reports.[5]

2. Scientific evidence

The ultimate purpose of applied health research is to improve health care. Summarising the literature to adduce recommendations for clinical practice is an important part of the process. It is, therefore, important to differentiate between strong *vs* weak evidence because recommendations based on inadequate evidence often require reversal when sufficient data become available. Furthermore, it is time consuming and expensive to replace old recommendations and implement new recommendations. In this systematic review the most recent evidence, including epidemiological evidence as well as a meta-analysis conducted on RCT's regarding the health benefits of low GI diets, are presented.

3. Epidemiological studies

3.1 Diabetes Mellitus

Table 1 summarises cross-sectional and cohort studies of the relation of the GI to the risk of diabetes and coronary heart disease (CHD) (Adapted from Jenkins *et al.*[6]). Considering

epidemiological evidence, the cross-sectional EURODIAB Complications Study reported that the lower GI diet of European outpatients with type 1 diabetes was associated with significantly lower (P = 0.0001) HbA_{1c} concentrations. Compared with the highest GI quartile (GI = 89), HbA_{1c} concentrations in the lowest quartile (GI = 75) was 11% lower in patients from Southern European centres and 6% lower in patients from the rest of the European centres.[10] Furthermore, the Framingham cohort showed a strong positive association between prevalence of CHD and increased HbA_{1c} concentrations, suggesting the importance of hyperglycaemia in the development of CHD.[15]

The Nurses' Health Study[7], the Health Professionals Study[8] and the Iowa Women's Health Study[9] investigated the long-term effects of the GI on the development of type 2 diabetes. Salmeron *et al.*[7] found a positive association with the GI and the development for type 2 diabetes in women after adjustment for age, body mass index (BMI), smoking, physical activity, family history of diabetes, alcohol and cereal fibre intake and total energy intake. Comparing the highest with the lowest quintile of the GI of the diet, the relative risk (RR) of diabetes was 1.37 (95% CI, 1.09,1.71, P trend = 0.05). A similar association was observed in men after adjusting for the same factors.[8] Comparing the highest and lowest quintiles, the RR of diabetes was 1.37 (95% CI, 1.02,1.83, P trend = 0.03). However, in the Iowa Women's Health Study no association was reported between the GI and the risk for the development for diabetes[9] (Table 1). The pattern of risk across quintiles of GI was inconsistent since the RR first rose to 1.22 in the 3rd quintile and then dropped to 0.84 in the 5th quintile.

3.2 Coronary heart disease

A low HDL-c concentration is a strong independent predictor of CHD and has several causes, many of which are associated with insulin resistance, elevated triacylglycerols, overweight and obesity, physical inactivity and type 2 diabetes.[16] In the Third National Health and Nutrition Examination Survey (NHANES III) (1988-1994), an inverse relationship was found between the GI and HDL-c concentrations (13 907 participants).[13] Ford and Liu[13] reported a statistically significant change in HDL-c concentration of –0.6 mmo/L per 15 unit increase in the GI, after adjusting for covariates such as gender, BMI, smoking status, alcohol intake, physical activity and energy intake derived from fat and carbohydrate. HDL-c concentrations for the lowest and the highest GI quintiles were 1.36 mmol/L and 1.27 mmol/L, respectively. Data from the Nurses' Health Study reported by Liu *et al.*[55] indicated an inverse relationship between the GI, HDL-c and TG in postmenopausal women. For the lowest and highest quintiles of overall dietary GI, multivariate-adjusted geometric mean HDL-c concentrations were 1.45 and 1.29 mmol/L and the geometric mean TG concentrations were 1.16 and 1.37 mmol/l.

Table 1: Cross-sectional and cohort studies of the relation of the glycaemic index (GI) to the risk of diabetes and cardiovascular disease and its association with HDL and glycated haemoglobin (HbA_{1c}) (Adapted from Jenkins *et al.*[6])

Author	Subjects	Main outcome	Type of study	Duration	Difference in GI	Main effect
Salmeron *et al.*[7]	Nurses' Health Study aged 45-65y (n=65 173)	Diabetes	Cohort	6 years	Quintiles, GI:64-79	Positive association between GI and development of type 2 diabetes in women
Salmeron *et al.*[8]	Health Professionals study	Diabetes	Cohort	6 years	Quintiles, GI:65-79	Positive association between GI and development of type 2 diabetes in men
Meyer *et al.*[9]	Iowa Women's Health Study aged 55-69 years, n=35 988	Diabetes	Cohort	6 years	Quintiles, GI: <58 to >80	No association between GI and development of diabetes in older women
Buyken *et al.*[10]	EURODIAB Complications study; Type 1 diabetics aged 33y, BMI=26.7kg/m^2, n=2810	HbA_{1c}	Cross-sectional	NR	Quartiles, GI: 74.9-88.55	Low GI diets associated with significantly lower (P=0.0001) HbA_{1c} concentrations
Liu *et al.*[11]	Nurses' Health Study, aged 38-63y, BMI=25.7kg/m^2, n=75 521	CHD risk	Cohort	10 years	Quintiles, 72-80 (by Glycaemic load)	CHO with high GI associated with increased risk for CHD
Liu *et al.*[55]	Nurses' Health Study, aged 38-63y, BMI=25.7kg/m^2, n=75 521	HDL-c & TG	Cohort	10 years	Quintiles, GI:75	Positive inverse association between GI and HDL-c and TG in postmenospausal women
Van Dam *et al.*[12]	Zutphen Elderly Study aged 65-84 in 1955, BMI=25.57kg/m^2 (555 of 1088 men still alive from original survey plus 711 new men of same age)	CHD risk	Cohort and cross-sectional	10 years 1985-1995	Quintiles, GI:74-85	No association between GI and HDL-c concentrations as well as risk of developing CHD
Ford , Liu[13]	NHANES III 20-y survey n=6825 M, 7052 =F, BMI=26.57kg/m^2	HDL-c	Cross-sectional survey	NR	Quintiles, GI: ≤75 to ≥88	Inverse relationship between GI and HDL-c concentrations
Frost *et al.*[14]	British Adults (1986-1987) aged 16-64y, n=699 M, 721 F	HDL-c	Cross-sectional survey	NR	Quintiles, mean GI: 86	Inverse relationship between GI and HDL-c concentrations
Buyken *et al.*[10]	EURODIAB Complications study; Type 1 diabetics aged 33y, BMI=26.77kg/m^2, n=2810	HDL-c	Cross-sectional	NR	Quartiles, GI: 74.9-88.55	Inverse relationship between GI and HDL-c concentrations

CHD = Coronary heart disease; HDL-c = high-density lipoprotein cholesterol; NR = not reported; RR = Relative Risk; NHANES III = Third National Health and Nutrition Examination Survey; CHO = carbohydrate; M = male; F = female

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Frost *et al.*[14] who reported data from the Survey of British Adults (1986-1987), found a significant negative relationship between serum HDL-c concentration and the GI of the diet for both men (P=0.02) and women (P<0.0001). For women, the improvement in HDL-c concentrations between the lowest and the highest quintile of the GI was 0.25 mmol/L, representing a possible 29% reduction in CHD morbidity. In men, the potential decrease in CHD morbidity was found to be 7% reflecting a 0.09 mmol/L difference in HDL-c concentration between the lowest and the highest quintiles of the GI.

In the EURODIAB Complications Study, higher HDL-c concentrations were observed in patients from the Northern, Eastern and Western European centres who consumed low GI diets. The observed relations of the dietary GI with HDL-c concentrations were independent of dietary fibre intake[10]. However, in the Zutphen Elderly Study conducted on elderly male subjects, no associations were found between the GI and HDL-c concentrations. These differences in findings between the epidemiological studies could possibly be attributed to the age and gender differences between study populations.[12] In contrast to these findings, epidemiological evidence failed to prove a significant relationship between LDL-c, TC, TG and low GI diets.[10,12,14] Furthermore, Liu *et al.*[11] found a positive association between high GI diets and the development of CHD, while Van Dam *et al.*[12] could not find any relationship (Table 1).

4. Clinical intervention studies

In a recent meta-analysis by Opperman *et al.*[17] conducted on RCT's, the effect of low GI diets on markers for carbohydrate and lipid metabolism in healthy as well as CHD and type 1 and type 2 diabetic subjects was analysed. For the meta-analysis glucose was used as reference food to standardise GI's of the different studies. Significant improvements were observed in HbA$_{1c}$, fructosamine, LDL-c and TC suggesting that low GI diets improve blood glucose control as well as lipid metabolism. No effects were found on HDL-c and TG. Some of the results will be reported here, supported by plausible biological mechanisms to explain the outcomes of the meta-analysis.
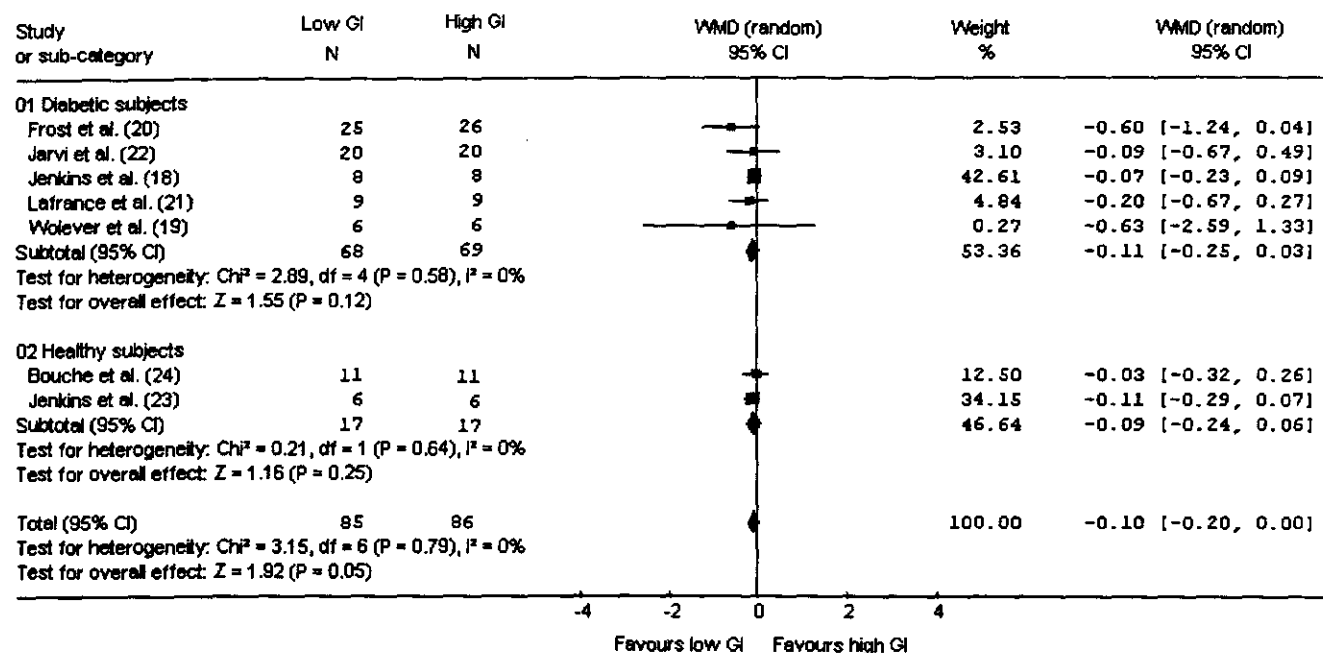
4.1   Carbohydrate metabolism
Fig. 1 and 2 represent the effects of low *vs* high GI diets on carbohydrate metabolism. For this meta-analysis, fructosamine and glycosylated haemoglobin (HbA$_{1c}$) were investigated.

4.1.1 Fructosamine
There was an overall statistically significant reduction in fructosamine in subjects receiving the low GI diet compared to the high GI diet (change -0.1 mmol/L, 95% CI -0.20, 0.00; P=0.05) (Fig. 1). However, when studies were sub grouped into diabetic and healthy

subjects, a non-significant improvement was observed in each group [DM (change -0.11 mmol/L, 95% CI -0.25, 0.03; P=0.12); healthy (change -0.09 mmol/L, 95% CI -0.24, 0.06; P=0.25)]. The GI reduction for the included studies was 24±9 units (mean±SD).

Study or sub-category	Low GI N	High GI N	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
01 Diabetic subjects					
Frost et al. (20)	25	26		2.53	-0.60 [-1.24, 0.04]
Jarvi et al. (22)	20	20		3.10	-0.09 [-0.67, 0.49]
Jenkins et al. (18)	8	8		42.61	-0.07 [-0.23, 0.09]
Lafrance et al. (21)	9	9		4.84	-0.20 [-0.67, 0.27]
Wolever et al. (19)	6	6		0.27	-0.63 [-2.59, 1.33]
Subtotal (95% CI)	68	69		53.36	-0.11 [-0.25, 0.03]
Test for heterogeneity: Chi² = 2.89, df = 4 (P = 0.58), I² = 0%					
Test for overall effect: Z = 1.55 (P = 0.12)					
02 Healthy subjects					
Bouche et al. (24)	11	11		12.50	-0.03 [-0.32, 0.26]
Jenkins et al. (23)	6	6		34.15	-0.11 [-0.29, 0.07]
Subtotal (95% CI)	17	17		46.64	-0.09 [-0.24, 0.06]
Test for heterogeneity: Chi² = 0.21, df = 1 (P = 0.64), I² = 0%					
Test for overall effect: Z = 1.16 (P = 0.25)					
Total (95% CI)	85	86		100.00	-0.10 [-0.20, 0.00]
Test for heterogeneity: Chi² = 3.15, df = 6 (P = 0.79), I² = 0%					
Test for overall effect: Z = 1.92 (P = 0.05)					

-4 -2 0 2 4

Favours low GI   Favours high GI

WMD = Weighted mean difference   df = degrees of freedom (number of studies minus 1)

95% CI = 95% Confidence interval   N = Number of subjects

Fig. 1: Net changes in fructosamine

Fructosamine is measured as a short-term (two weeks) index of glycaemic control. Glycosylated albumin is the main constituent of fructosamine and has a half-life of only 12 days, explaining the usefulness of fructosamine as a short-term marker.[32] Although fructosamine is a shorter term marker for blood glucose control than HbA_{1c}, it seems that the longer low GI diets are followed the larger decreases in fructosamine concentrations are observed. According to Jones et al.,[33] maximum changes in fructosamine take 4-6 weeks to occur. More profound decreases were documented in diabetic subjects than in healthy subjects. Results would probably be more representative if all available studies conducted on fructosamine and the GI could be included, but due to a lack of complete data (means and SDs of baseline and end values) this was not possible. However, the combined meta-analysis suggests that low GI diets will reduce mean fructosamine concentrations by 0.1 mmol/L over and above that seen with high GI diets during a period of 4.6±3 weeks. GI reductions of 24±9 units were achieved.

4.1.2 Glycosylated haemoglobin

There was a statistically significant decrease in mean HbA_{1c} concentrations in subjects receiving low GI diets (change −0.27%, 95% CI -0.5, -0.03; P=0.03) (Fig. 2). The difference in GI between the low and high GI diets was 21±7 units. All the included studies that measured HbA_{1c} in this meta-analysis were performed on diabetic subjects.

Study or sub-category	Low GI N	High GI N	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
01 Diabetic subjects					
Brand et al. (25)	16	16		7.34	-0.90 [-1.77, -0.03]
Heilbronn et al (27)	24	21		13.00	-0.32 [-0.98, 0.34]
Jarvi et al. (22)	20	20		13.21	-0.20 [-0.85, 0.45]
Jenkins et al. (18)	8	8		30.01	-0.30 [-0.73, 0.13]
Kabir et al. (28)	13	13		8.50	-0.30 [-1.11, 0.51]
Lafrance et al. (21)	9	9		11.34	0.00 [-0.70, 0.70]
Tsihlias et al. (26)	26	22		16.60	-0.10 [-0.68, 0.48]
Subtotal (95% CI)	116	109		100.00	-0.27 [-0.50, -0.03]
Test for heterogeneity: Chi² = 2.99, df = 6 (P = 0.81), I² = 0%					
Test for overall effect: Z = 2.21 (P = 0.03)					
Total (95% CI)	116	109		100.00	-0.27 [-0.50, -0.03]
Test for heterogeneity: Chi² = 2.99, df = 6 (P = 0.81), I² = 0%					
Test for overall effect: Z = 2.21 (P = 0.03)					

-4 -2 0 2 4

Favours low GI   Favours high GI

WMD = Weighted mean difference   df = degrees of freedom (number of studies minus 1)
95% CI = 95% Confidence interval   N = Number of subjects

Fig. 2: Net changes in HbA_{1c}

HbA_{1c} is a longer term marker for carbohydrate metabolism than fructosamine. This test provides an index of the average blood glucose concentration over the half-life of the haemoglobin molecule (approximately six weeks).[32] From these results one may conclude that low GI diets beneficially influenced long-term glycaemic control. A significant reduction of 0.27% in HbA_{1c} concentrations may be expected over a period of 8.5±7 weeks with a GI reduction of 21±7 units. Additionally, more than one type of low GI food may need to be incorporated into the diet to achieve measurable long-term improvements in glycaemic control.

Poor blood glucose control has been associated with a greater incidence of long-term macrovascular complications in both type 1 and type 2 diabetic patients.[34-37] The UK Prospective Diabetes Study Group (UKPDS) group found that each 1% reduction in mean HbA_{1c} concentration was associated with reduction in risk of 21% for deaths related to diabetes, 14% for myocardial infarction and 37% for microvascular complications. It is not clear precisely how low GI diets improve the markers of carbohydrate metabolism and prevent the onset of type 2 diabetes. Several mechanisms have been proposed. Briefly,

high GI diets have been associated with high postprandial blood glucose concentrations and increased insulin demands.[38,39]   Primary hyperinsulinaemia may cause insulin resistance, which reduces insulin sensitivity. Additionally, habitual consumption of high GI meals over the long-term initiates a cycle of hyperinsulinaemia and insulin resistance leading to a loss of pancreatic β-cell function[38] that can result in glucose intolerance and an irreversible state of diabetes.[39] Hyperglycaemia also showed deleterious effects on counterregulatory hormone secretion, increased late postprandial serum free fatty acid concentrations[38] and led to the occurrence of oxidative stress.[40] Low GI diets, on the other hand, tend to delay glucose absorption, therefore, resulting in reduced peak insulin concentrations and overall insulin demand.[40]

4.2   Lipid metabolism

This meta-analysis pooled the results of 13 randomised controlled trials studying low *vs* high GI diets and their effects on markers for lipid metabolism. In the studies reviewed, low GI diets showed a statistically significant improvement in TC concentrations, while non-significant improvements were observed in LDL-c. No significant change was found in TG and HDL-c with low GI diets, although an inverse relationship was found in epidemiological studies between the GI and HDL-c with lower GI diets. [10, 13, 14] Contrary to the general belief, an inverse relationship between low GI diets and TG was found[19]. According to Wolever *et al.,*[19] insulin regulates both cholesterol and TG synthesis. One would, therefore, expect an improvement in TG concentrations because markers for carbohydrate metabolism (HbA$_{1c}$) in this meta-analysis improved significantly. Furthermore, it appears obvious that improved blood glucose control would reduce insulin resistance accompanied by an improvement in TG concentrations. Nevertheless, intra-individual biological variation in TG concentrations has been well documented. [52, 53] According to Nazir *et al.*[52] and Castro Cabezas *et al.,*[53] several factors contribute to the variation of TG such as intervention diet (amount of fat and carbohydrate), exercise, alcohol consumption, diurnal and seasonal variation and smoking and could possibly explain the lack of effects on TG concentrations. A possible explanation for the unchanged HDL-c concentrations can be attributed to the length of studies. Intervention periods differed from only two weeks to six months.[17]

4.2.1   LDL-cholesterol

Overall, low GI diets tended to lower mean LDL-cholesterol concentrations although not statistically significantly (change -0.15 mmol/L, 95% CI -0.31, 0.00; P=0.06). The GI of the diets was decreased by 21±10 units. In type 2 diabetics, it seems that mean LDL-c concentrations were decreased to a larger extent than in CHD and healthy subjects. Larger decreases in LDL-c were reported for longer studies in well-controlled type 2 DM

subjects,[20,25] except for an unexpected non-significant increase in mean LDL-c concentrations after six months, as reported by Tsihlias et al.[26] (Fig. 3).

The study of Tsihlias et al.[26] showed a non-significant increase in LDL-c concentration over a period of 6 months. However, when this study is excluded from the meta-analysis, the effect of low GI diets on LDL-c is significant in type 2 diabetics (change -0.24 mmol/L, 95% CI -0.45, -0.04; P=0.02) as well as for the overall effect. The negative results from this study may be attributed to a relatively small GI reduction of 11 units, the GI of only one meal (breakfast) was lowered and the possibility of poorer compliance with longer studies. Furthermore, not all available studies conducted on the GI and LDL-c could be included. RCT's that showed promising results on low GI diets and LDL-c, but did not report means and SDs for the change, were those of Jenkins et al.[41,42] Both these studies found significant improvements in LDL-c concentrations with low GI diets.

When comparing corresponding studies that measured markers for carbohydrate metabolism and LDL-c,[22,25,27] improvements in LDL-c concentrations were observed where decreases in fructosamine and HbA$_{1c}$ were perceived. But how can low GI diets contribute to lower LDL-c concentrations? A possible mechanism may be that insulin resistance may occur with consumption of a high GI diet because of the direct effects of hyperglycaemia.[38] Insulin resistance impairs normal suppression of free fatty acid (FFA) release from adipose tissue in the postprandial state.[43] According to Timar et al.,[44] increased FFA released from abdominal adipose tissue, delivered to the liver, offers an efficient substrate for enhanced synthesis of TG and very-low density lipoprotein cholesterol (VLDL-c), resulting in elevated cholesterol concentrations. Furthermore, with the prevalence of insulin resistance as seen in type 2 diabetics, LDL-receptor activity is reduced resulting in less LDL-c removal from the blood and, therefore, contributing to higher LDL-c concentrations.[45] Barakat et al.[46] explain that reduced receptor activity may be attributed to glycosylation of the LDL-particle in the presence of hyperglycaemia. Glycosylated LDL-c cannot bind as efficiently as non-glycosylated LDL-c because of impairments in the binding of the LDL-particles to LDL-receptors and, therefore, glycosylated LDL-particles will remain longer in circulation.

From these results, excluding the study of Tsihlias et al.,[26] it seems that low GI diets have favourable effects on LDL-c concentrations of type 2 diabetic subjects. A reduction of 0.20 mmol/L in LDL-c concentrations with low GI diets can be expected over a period of 10±7 weeks together with a GI reduction of 28±8 units of the diet.

Study or sub-category	Low GI N	High GI N	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
01 Diabetic subjects					
Brand et al. (25)	16	16		6.77	-0.26 [-0.87, 0.35]
Frost et al. (20)	25	26		9.28	-0.60 [-1.12, -0.08]
Heilbronn et al (27)	24	21		17.38	-0.20 [-0.58, 0.18]
Jarvi et al. (22)	20	20		16.65	-0.26 [-0.65, 0.13]
Jenkins et al. (18)	8	8		9.45	0.08 [-0.44, 0.60]
Tsihlias et al. (26)	26	22		17.01	0.06 [-0.33, 0.45]
Wolever et al. (19)	6	6		0.99	-0.39 [-1.99, 1.21]
Subtotal (95% CI)	125	119		77.52	-0.18 [-0.36, 0.00]
Test for heterogeneity: Chi² = 5.21, df = 6 (P = 0.52), I² = 0%					
Test for overall effect: Z = 1.92 (P = 0.06)					
02 CHD subjects					
Frost et al. (29)	15	15		3.32	-0.40 [-1.28, 0.48]
Subtotal (95% CI)	15	15		3.32	-0.40 [-1.28, 0.48]
Test for heterogeneity: not applicable					
Test for overall effect: Z = 0.89 (P = 0.37)					
03 Healthy subjects					
Bouche et al. (24)	11	11		7.15	-0.09 [-0.69, 0.51]
Jenkins et al. (23)	6	6		12.01	0.02 [-0.44, 0.48]
Subtotal (95% CI)	17	17		19.16	-0.02 [-0.39, 0.34]
Test for heterogeneity: Chi² = 0.08, df = 1 (P = 0.77), I² = 0%					
Test for overall effect: Z = 0.11 (P = 0.91)					
Total (95% CI)	157	151		100.00	-0.15 [-0.31, 0.00]
Test for heterogeneity: Chi² = 6.16, df = 9 (P = 0.72), I² = 0%					
Test for overall effect: Z = 1.90 (P = 0.06)					

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        -4      -2       0       2       4
        Favours low GI    Favours high GI
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WMD = Weighted mean difference   df = degrees of freedom (number of studies minus 1)
95% CI = 95% Confidence interval   N = Number of subjects

Fig. 3: Net changes in LDL-cholesterol

4.2.2   Total cholesterol

There was an overall statistically significant improvement in TC in subjects receiving low GI diets compared to high GI diets (change -0.33 mmol/L, 95% CI -0.47, -0.18; P<0.001). This improvement was achieved by lowering the GI of the intervention diet by 22±8 units. Larger decreases in TC concentrations were observed in patients with elevated TC baseline concentrations (>5.2 mmol/L).[18-20,22,24,25,27-30]   Two studies showed that mean TC concentrations of healthy subjects significantly improved on low GI diets[18,24] while the studies of Frost _et al._ [29,31] found no change in patients with CHD (Fig. 4). The results of Frost _et al._[29,31] could be attributed to the short intervention period of only three weeks. In all the studies, low GI intervention diets improved TC to a larger or lesser extent. No significant improvements were observed in the two studies conducted on CHD patients while a significant reduction was observed in the two studies performed on healthy subjects. From these findings it can be concluded that by lowering the GI by 19±8 units over a time period of 8±6 weeks, a significant decrease of 0.3 mmol/L can be expected in TC concentrations of type 2 diabetic subjects.

Study or sub-category	Low GI N	High GI N	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
01 Diabetic subjects					
Brand et al. (25)	16	16		7.79	-0.01 [-0.52, 0.50]
Frost et al. (20)	25	26		13.26	-0.40 [-0.78, -0.02]
Heilbronn et al (27)	24	21		9.33	-0.17 [-0.63, 0.29]
Jarvi et al. (22)	20	20		5.53	-0.23 [-0.83, 0.37]
Jenkins et al. (18)	8	8		8.07	-0.50 [-1.00, 0.00]
Kabir et al. (28)	13	13		28.28	-0.50 [-0.75, -0.25]
Luscombe et al. (30)	21	21		3.85	-0.06 [-0.79, 0.67]
Tsihlias et al. (26)	26	22		5.75	0.25 [-0.34, 0.84]
Wolever et al. (19)	6	6		0.34	-0.76 [-3.25, 1.73]
Subtotal (95% CI)	159	153		82.21	-0.30 [-0.47, -0.14]

Test for heterogeneity: Chi² = 8.84, df = 8 (P = 0.36), I² = 9.5%
Test for overall effect: Z = 3.58 (P = 0.0003)

02 CHD subjects					
Frost et al. (29)	15	15		2.31	-0.37 [-1.31, 0.57]
Frost et al. (31)	8	8		4.34	0.10 [-0.58, 0.78]
Subtotal (95% CI)	23	23		6.66	-0.06 [-0.62, 0.49]

Test for heterogeneity: Chi² = 0.62, df = 1 (P = 0.43), I² = 0%
Test for overall effect: Z = 0.22 (P = 0.83)

03 Healthy subjects					
Bouche et al. (24)	11	11		1.48	-0.18 [-1.36, 1.00]
Jenkins et al. (23)	6	6		9.65	-0.67 [-1.12, -0.22]
Subtotal (95% CI)	17	17		11.13	-0.61 [-1.03, -0.19]

Test for heterogeneity: Chi² = 0.58, df = 1 (P = 0.45), I² = 0%
Test for overall effect: Z = 2.83 (P = 0.005)

Total (95% CI)	199	193		100.00	-0.33 [-0.47, -0.18]

Test for heterogeneity: Chi² = 12.61, df = 12 (P = 0.40), I² = 4.8
Test for overall effect: Z = 4.42 (P < 0.0001)

```
-4    -2     0     2     4
Favours Low GI    Favours High GI
```

WMD = Weighted mean difference   df = degrees of freedom (number of studies minus 1)
95% CI = 95% Confidence interval   N = Number of subjects

Fig. 4: Net changes in total cholesterol

The mechanisms by which low GI diets may reduce TC concentrations remain unclear. Speculatively, these mechanisms involve lower insulin-stimulated HMG-CoA reductase activity as a result of a reduced rate of carbohydrate absorption; impaired bile acid and cholesterol reabsorption from the ileum due to the high fibre content of low GI foods and inhibition of hepatic cholesterol synthesis by short chain fatty acids such as propionate.[40]

5. Judging the evidence

According to Guyatt *et al.*,[5] standard notation for the relative weight carried by the different types of primary study when making decisions about clinical interventions places them into the following hierarchy:

1. Systematic reviews and meta-analysis

2. Well-designed randomised controlled trials with definite results (i.e. confidence intervals which do not overlap the threshold clinically significant effect)

3. Randomised controlled trials with non-definitive results (i.e. a point estimate which suggests a clinically significant effect but with confidence intervals overlapping the threshold for this effect)

4. Cohort studies

5. Case-control studies

6. Cross-sectional surveys

7. Case reports

Considering the evidence obtained from this systematic review it seems that this review conform to the first two criteria presented. This proves that there is convincing evidence to recommend the use of low GI diets to improve markers for carbohydrate and lipid metabolism profiles. One could, therefore, expect significant improvements in fructosamine of -0.1 mmol/L with a reduction in the GI of 24±9 units and HbA_{1c} will improve by -0.27% with a reduction of 21±7 GI units. For lipid metabolism, low GI diets will significantly decrease LDL-c concentrations by -0.24 mmol/L with a reduction of 21±10 units and TC by -0.33 mmol/L with a GI reduction of 20±9 units. Therefore, it is strongly recommended that the concept of the GI should be implemented in a healthy diet and dieticians should be encouraged to use the GI in practice, especially with regard to diets of patients with diabetes and other lifestyle diseases where hyperlipidaemia and poor glycaemic control are present.

6. Recommendations

Considering the information obtained from this review, the following recommendations are proposed. Firstly, epidemiological evidence showed positive associations between HDL-c concentrations and low GI diets when low GI diets were consumed over long-term periods, while the meta-analysis of RCT's showed no effect over periods from two weeks to six months. It is, therefore, recommended that more long-term (>6 months) intervention studies should be performed to assess the effects of low GI diets on HDL-c concentrations. It is also important to recruit highly motivated participants to ensure optimal compliance over such a long period.

Secondly, the possible relationship between low GI diets and other non-communicable diseases should be investigated more thoroughly, focusing on low GI (< 55) *vs.* high GI (> 70) foods. There are indications that low GI diets may benefit the prevention of obesity,[24,47,48, 54] colon cancer and breast cancer[49-51] and a meta-analysis analysing the effect of low GI diets on these diseases is suggested. Additionally, a meta-analysis on epidemiological data regarding the glycaemic load and its effect on TG should be performed. Finally, the use of the GI concept in sport performance should be exploited fully. A systematic review on the GI and sport performance is a priority.

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4

Systematic review on the effect of the glycaemic index on sport performance

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Carbohydrate (CHO) ingestion prior to, during and after exercise is essential. Ingestion of CHO at these times will optimise performance by either delaying glycogen depletion or enhancing restoration of glycogen stores. Fatigue is often associated with hypoglycaemia and muscle glycogen depletion. To improve performance and avoid early fatigue athletes are encouraged to consume CHO to optimise muscle glycogen stores prior to exercise and maintain blood glucose (BG) levels during exercise. This can only be achieved by ingestion of the correct type and amount of CHO. The glycaemic index (GI) has been proposed as a tool in choosing CHO for optimal sport nutrition. However, there is inconsistency in the literature regarding recommendations for the use of the GI and, therefore, needs extensive investigation. The aim of this systematic review will be to evaluate current recommendations on the use of the GI pre, during and post-exercise, to make informed conclusions regarding the use of the GI as well as to direct future research. Eighteen randomised controlled trials (RCT's) that met the quality criteria were included in the systematic review. Studies had either a cross-over or parallel design and were published in English between January 1981 and September 2004. All manuscripts were obtained through a literature search on relevant databases such as the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, LILACS, SPORTDiscus, ScienceDirect and PubMed. Although it is generally recommended to consume low GI CHO pre-exercise it appears that low GI pre-exercise meals do not provide any advantages over high GI pre-exercise meals. Furthermore, low GI pre-exercise meals seem to better maintain CHO availability during exercise, however, in terms of performance low GI pre-exercise meals offer no added advantage over high GI meals. Additionally, the exaggerated metabolic responses from high GI compared to low GI CHO seems not be detrimental to exercise performance. However, athletes who experience hypoglycaemia when consuming CHO-rich feedings in the hour prior to exercise are advised

to rather consume low GI pre-exercise meals. Recommendations suggest that moderate to high GI CHO should be consumed during exercise, however, no studies have been reported on the GI during exercise. Current evidence suggests that a combination of CHO with differing GI's such as glucose (high GI), sucrose (moderate GI) and fructose (low GI) will deliver the best results in terms of exogenous CHO oxidation due to different transport mechanisms. Although no studies are conducted on the effect of the GI on short-term recovery it is speculated that high GI CHO is most effective when the recovery period is between 0-8 hours, however, evidence suggests that when the recovery period is longer (20-24 hours), the total amount of CHO is more important than the type of CHO.

KEY WORDS: Glycaemic index, pre-exercise, during exercise, post-exercise, sport performance

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1. Introduction

It is widely documented that athletes should consume carbohydrate (CHO) prior to, during and after exercise[1]. Ingestion of CHO at these times will optimise performance by either delaying glycogen depletion or enhancing restoration of glycogen stores on multiple training days[2]. Muscle glycogen is the primary fuel source during prolonged moderate-to-high intensity exercise[3]. Despite its importance, muscle glycogen stores are present in only limited amounts, with depletion of these stores occurring rapidly during prolonged high-intensity exercise[4]. Fatigue during exercise is often associated with hypoglycaemia[5] and muscle glycogen depletion[3,6]. In an attempt to avoid early fatigue and improve performance, athletes are encouraged to consume CHO to optimise muscle glycogen stores prior to exercise and maintain blood glucose (BG) levels during exercise[1].

The goals of pre-exercise CHO ingestion are to optimise muscle and liver glycogen stores that are needed during exercise, while the intake of CHO during prolonged exercise enhances CHO availability and improves exercise capacity and performance. Post-exercise CHO intake promotes repletion of the body's liver and muscle glycogen stores[7]. The optimal amount and timing of CHO consumption has been investigated extensively. However, the type of CHO that an athlete should consume before, during and after exercise needs further investigation[8]. CHO and CHO foods can be functionally classified according to the extent to which they increase BG levels. This has led to the concept of the glycaemic index (GI), which is a measure expressed as a percentage value based on the area under the BG response curve of a food containing 50 g of available CHO, divided by the area of the BG response of 50 g of CHO in a reference food, multiplied by 100[9]. Therefore, the GI reflects the rate of digestion and absorption of a CHO-rich food.

There has been much constructive debate about the usefulness of the GI in sport nutrition. In general it is recommended that low GI foods must be consumed before prolonged exercise to promote CHO availability[10]. Moderate GI to high GI foods and drinks are considered appropriate during prolonged exercise as well as immediately after exercise[1]. Since glycogen storage is influenced both by insulin and a rapid supply of glucose substrate, it seems logical that CHO sources with a moderate GI to high GI would enhance post-exercise recovery[11]. There is, however, inconsistency in the literature regarding recommendations for the use of the GI pre, during and post-exercise and needs extensive investigation. Hence, it seems imperative that a systematic review of the use of the GI as a tool in sport nutrition for increased exercise performance should be conducted. The purpose of this review will, therefore, be to evaluate current published evidence on the type of CHO (GI) ingested pre, during and post-exercise, to make informed conclusions regarding the use

of the GI in sport nutrition, to motivate and direct future research and to form a firm, evidence based platform for the use of the GI in sport nutrition.

2. Methods

2.1 Identification of clinical trials

Randomised controlled trials (RCT's) with a cross-over or parallel design that were published between January 1981 and September 2004 were selected through a computer-assisted literature search. A title scan was conducted of each database such as the Cochrane Central Register of Controlled Trials, MEDLINE (1981 to present), EMBASE, LILACS, SPORTDiscus, ScienceDirect and PubMed. Medical subjects' headings (MeSH) such as "glycemic index" or "glycaemic index" combined with key words such as BG, insulin, muscle glycogen concentration, muscle glycogen usage, lactate, free fatty acids, glycerol, epinephrine, norepinephrine, rate of glycogen synthesis, time trials, performance, rate of perceived exertion, CHO oxidation and respiratory exchange ratio were used to search for manuscripts. Titles were rejected if they indicated that the study did not include a dietary component, did not clearly involve any form of exercise or the subjects suffered from an abnormal health condition. The titles of the indexed references were then selected or rejected in accordance with the title scan mentioned above. The abstracts of the preliminary citations were then examined for the following criteria: 1) a low GI, moderate GI or high GI food/meal had to be supplied to athletes either pre, during or post-exercise and 2) an exercise intervention had to form part of the study. If any of these criteria were unclear on analysis of the title or abstract, the full text article was examined. Reference lists of all available published trials and relevant reviews were cross-checked manually to ensure that all applicable manuscripts were included. Citations were rejected if they were found to be a thesis, an abstract, a roundtable discussion, a letter or a comment.

Studies from all languages were included while only studies conducted on humans were considered. Accepted interventions included high GI, moderate GI, and low GI intervention meals, which investigated the effect of the GI pre and post-exercise. However, no studies were found where the effect of the GI during exercise was investigated. This review was not concerned with comparing single nutrients but rather CHO rich meals with different GIs as pre, during or post-exercise meals. Comparison of fructose and glucose as only CHO sources during exercise lies beyond the scope of this review and, therefore, the discussion of the effect of different types of CHO consumed during exercise will be a general one.

The participants were either athletes (elite or endurance athletes) or well-trained subjects or people that were accustomed to exercise or physical activity. No specific sporting events were favoured. Only studies of good quality regarding methodology were considered.

Quality criteria were adapted from the Effective Practice and Organization of Care (EPOC) Cochrane Group and included methods of randomisation and blinded assessment of variables with regard to blood samples.

Additionally, food intake had to be controlled (either advice given, key foods provided or all foods provided) and described (low GI, moderate GI and high GI meals); the subject population had to be homogenous, at least with regard to the type of athletes who participated in the exercise intervention, and a standardised diet or meal prior to intervention had to be followed to ensure equal muscle substrate concentrations among participants.

2.2 Data extraction and evaluation

Each potentially relevant study was assessed for inclusion independently by at least two reviewers. Two investigators (AMO and CSV), by means of an agreed standardized data collection form, independently extracted the relevant data. Co-investigators adjudicated areas of disagreement or uncertainty and resolved them by discussion or referred the query to a third reviewer. Information about the outcome variables that were extracted from the RCT's included: general information (study number, journal of publication, title of manuscript, authors, country, language of publication, publication date, primary purpose of study, setting); trial characteristics (study design, duration of study, randomisation, blinding); interventions (standardised diet prior to intervention, placebo/control included, dietary information/ diet or test meal provided, GI of test meal, reference food for GI, method of manipulating GI, control of dietary intake, nutrient content of test meals, exercise bout, wash out period); participants [sampling (random/convenience), inclusion criteria, exclusion criteria, total number and number in comparison groups, gender, age, weight, VO_{2max}, assessment of compliance, withdrawals/ losses to follow up; outcomes and results (for outcomes) and times of assessment]. Variables that were considered for this review included: muscle glycogen concentration, BG, insulin, lactate, free fatty acids (FFA), CHO oxidation, rate of perceived exertion (RPE), respiratory exchange ratio (RER), time trials and performance. No formal statistical analysis was performed due to results that were reported as graphs making it impossible to obtain means and standard deviations to conduct a meta-analysis as well as the different exercise protocols used. Furthermore, blood samples were taken at different time intervals during exercise to test the effect of the GI meal/drink. If only baseline and end values were used (as in a meta-analysis) this would not supply comprehensive information to what the effect of the meal is pre, during or post-exercise.

3. Results

The literature search yielded 65 references (titles and abstracts, original research and review papers). Out of these, 25 original research papers were identified as possible studies to

include in the systematic review. Two investigators examined the full text publications from which 18 studies met the inclusion criteria. Fourteen studies were included to investigate the effect of the GI pre-exercise. No studies investigated the effect of the GI during exercise while only four studies examined the application of the GI during the recovery period. All the studies included were RCT's.

3.1 Pre-exercise meals

Table 1 summarises the effect on exercise performance by applying the GI pre-exercise. Eleven of the 14 studies compared the effect of a low GI *vs.* a high GI meal or drink pre-exercise while only three studies compared moderate GI *vs.* high GI meals and moderate GI vs. control meals (e.g. water, sweetened placebo) respectively. Time of ingestion of meals varied from 45 minutes to 3 hours pre-exercise. Glycaemic indices of low GI meals varied from 21 to 50, moderate GI meals 60 to 70 and high GI meals 70 to 100 when glucose was used as reference food. Only one of the studies did not report the GI of the test meals (Wee *et al.,* 1999). The number of participants in the included studies varied between six and ten. Six studies recruited participants that were endurance trained[12-17], three studies used trained cyclists[10,18,19], three studies used active males or females[20-22], and two studies used recreational runners[24,25].

Of the 11 studies that compared low GI vs. high GI pre-exercise meals, six served the pre-exercise meals ≤ 60 min. prior to exercise[10,13-16,19] while five studies served the meals ≥60 min. prior to exercise[12,17,18,24,25]. Of the remaining three studies, one study investigated moderate GI pre-exercise meals vs. a control given 45 min. prior to exercise[20], one investigated only a moderate GI meal 45 min. prior to exercise[21] and one investigated the difference between moderate GI and high GI pre-exercise meals 45 min. prior to exercise[22].

When summarising the studies that provided pre-exercise meals, the study of Thomas *et al.*[10] was the first to investigate the effect of high GI vs. low GI meals fed prior to exercise and its subsequent effects during exercise. Eight trained cyclists pedalled to exhaustion at 65-70% VO_{2max} 1 h after ingesting one of four test foods, which consisted either of lentils (low GI), potato (high GI), glucose (high GI) and water (CON). BG and insulin concentrations were significantly higher after the high GI than the low GI foods from 30-60 min. after ingestion. Higher FFA concentrations were observed with low GI *vs.* high GI foods. Lactate and CHO oxidation remained higher in the high GI trials throughout exercise. Time to exhaustion was prolonged by 20 min. in the group fed low GI pre-exercise foods. Thomas *et al.*[10] suggested that low GI pre-exercise meals may prolong endurance due to reduced postprandial hyperglycaemia and hyperinsulinaemia, lower lactate levels during exercise as well as maintenance of higher BG and FFA concentrations during exercise.

Table 1: Effect on exercise performance by applying the glycaemic index pre-exercise

Author(s) and year	Study participants	GI of meal/drink	Time of meal	Outcomes (Major results)	Authors' conclusion(s)
Thomas *et al.*[10]	Trained cyclists (n=8)	29[a]/98[b]&100[c]	60 min. pre-exercise	↑ BG [b vs a] (15, 30, 45 and 60 min. postprandial), insulin [c vs a] (30 and 45 min. postprandial), lactate [b vs a] (45 and 60 min. postprandial; at 15 and 45 min. of exercise), RER [c,b vs a] (during exercise), CHO oxidation [b vs a] (during exercise) ↓ BG [c vs a] (at 75 and 90 min. of exercise), FFA [b,c vs a] (during the whole trial), time to exhaustion [b,c vs a]	Low GI pre-exercise meals may prolong endurance during strenuous exercise by inducing less postprandial hyperglycaemia and hyperinsulinaemia, lower levels of lactate before and during exercise and maintaining BG and FFA at higher levels during critical periods of exercise. No hypoglycaemia (2.5-2.8mmol/l) was reported.
Thomas *et al.*[19]	Trained cyclists (n=6)	36[d] & 30[e]/ 73[f] & 100[g]§	60 min. pre-exercise	↑ BG [g vs d,e] (30 min. postprandial), insulin [f,g vs d,e] (30 min. postprandial), RER [g vs d,e,f] (during exercise) ↔ Lactate ↓ BG [f,g vs d,e] (at 120 min. of exercise), FFA [g vs e] (during exercise).	Low GI foods are associated with higher blood-borne muscle fuel substrate levels after more than 90 min. of exercise. No hypoglycaemia was reported.
Febbraio and Stewart[15]	Endurance (n=6)	29/80	45 min. pre-exercise	↑ BG (30 min. postprandial), insulin (15, 30 and 45 min. postprandial) ↔ [Muscle glycogen], lactate, CHO oxidation, total work performed, RER (postprandial and during exercise) ↓ FFA (after 20, 40 and 60 min. of exercise)	Pre-exercise CHO ingestion has no effect on muscle glycogen utilisation or exercise performance, irrespective of the glycaemic or insulinaemic responses to ingested meals.
Burke *et al.*[12]	Endurance trained cyclists (n=6)	37/87	120 min. pre-exercise	↑ Insulin (30, 60 and 90 min. postprandial) ↔ BG, FFA, CHO oxidation, total CHO oxidation, RER (postprandial and during exercise)	When CHO is ingested during exercise in amounts presently recommended (1998), pre-exercise CHO intake has little effect on metabolism or on subsequent performance during prolonged cycling (≈ 2.5 h).
Sparks *et al.*[18]	Endurance (n=8)	29/83	60 min. pre-exercise	↑ BG (30 and 45 min. postprandial), insulin (30, 45 and 60 min. postprandial; at 10 and 20 min. of exercise), CHO oxidation (during exercise), RER (during exercise) ↔ Lactate (postprandial and during exercise), BG (onset of exercise; at 20 min. of exercise); insulin (at 30 min. to end of exercise), performance (during exercise), RPE (during exercise), ↓ BG (at 10 and 15 min. of exercise), FFA (at 20 and 50 min. of exercise)	Pre-exercise CHO feedings with varying GIs do not affect exercise performance following short-term submaximal exercise despite alterations in metabolism. No hypoglycaemia was reported.
Kirwan *et al.*[20]	Active females (n=6)	60-70	45 min. pre-exercise	↑ †BG (15 and 30 min. postprandial), insulin (15, 30 and 45 min. postprandial), FFA (at 0 (onset of exercise), 30, 60 and 90 min. of exercise), RER (at 90 and 120 min. of exercise), time to exhaustion ↔ † [Muscle glycogen], muscle glycogen utilisation, epinephrine, norepinephrine, total CHO oxidation ↓ †Glycerol (at onset of exercise)	Significant improvement in exercise time when a moderate GI meal is ingested 45 min. prior to exercise compared to water.
DeMarco *et al.*[13]	Endurance (n=6)	36/69	30 min. pre-exercise	↑ Insulin (15 and 30 min. postprandial; after 20 min. of exercise), time to exhaustion (20 min. shorter than low GI), RPE, RER (at 20, 40, 60, 80 and 120 min. of exercise) ↔ BG (after 40 to 100 min. of exercise) ↓ BG (after 120 min. of exercise)	Pre-exercise low GI meals may positively affect maximal performance following sustained exercise by maintaining higher plasma glucose levels at the end of 2 h of strenuous exercise. No hypoglycaemia was reported.
Wee *et al.*[24]	Recreational runners (n=6)	NR/NR	3 h pre-exercise	↑ Lactate (1st postprandial hour), BG (15, 30 and 60 min. postprandial), insulin (postprandial), RPE (at 60 min. of exercise), CHO oxidation (30-180 min. postprandial; at 60 and 80 min. of exercise), RER (30-180 min. postprandial; at 60 and 80 min. of exercise) ↔ Lactate (during exercise), insulin (during exercise), time to exhaustion ↓ BG (at 20 min. of exercise), FFA (postprandial and during exercise)	The GI of a CHO meal ingested 3 hours prior to exercise does not influence subsequent endurance running capacity. No hypoglycaemia was reported.

Table 1: Effect on exercise performance by applying the glycaemic index pre-exercise (continued)

Author(s) and year	Study participants	GI of meal/drink	Time of meal		Outcomes (Major results)	Authors' conclusion(s)
Febbraio et al.[14]	Endurance (n=8)	52/80	30 min. pre-exercise	↑	BG, insulin (10, 20, 30 min. postprandial), CHO oxidation (during exercise)	Pre-exercise high GI feedings but not low GI feedings augment CHO utilisation during exercise but do not affect exercise performance.
				↔	[Muscle glycogen], lactate, total work performed (postprandial and during exercise)	
				↓	FFA (20 and 30 min. postprandial and during exercise)	
Stannard et al.[18]	Highly trained cyclists (n=10)	41/100	65 min. pre-exercise	↑	Lactate (postprandial at 45 and 60 min. of exercise), BG (15, 30 and 45 min. postprandial)	High GI meals 65 min. prior to exercise non-significantly decrease plasma glucose and increase plasma lactate levels compared to a low GI meal, but not enough to be detrimental to incremental exercise performance. No hypoglycaemia was reported.
				↔	BG (onset of exercise), time to exhaustion (during exercise), RER (during exercise)	
Kirwan et al.[22]	Active men (n=6)	61/82	45 min. pre-exercise	↑	#BG (30 min. postprandial)	Eating a moderate GI breakfast 45 min. before onset of exercise may improve performance time by maintaining euglycaemia for a longer period during exercise. Hyperglycaemia reported for both meals.
				↔	#[Muscle glycogen], insulin, FFA, glycerol, epinephrine, norepinephrine, performance, CHO oxidation, RER (postprandial and during exercise)	
				↓	#BG (after 60 and 90 min. of exercise)	
Kirwan et al.[21]	Active females (n=6)	61	45 min. pre-exercise	↑	†BG (15, 30 and 45 min. postprandial), insulin (15, 30 and 45 min. postprandial; after 30 min. of exercise), FFA (after 0, 30, 60, 90 and 120 min. of exercise), glycerol (after 60 min. of exercise), RER (after 30, 60, 90 and 120 min. of exercise)	Ingestion of a moderate GI meal 45 min. prior to endurance exercise does not alter exercise duration compared to a control (water).
				↔	†[Muscle glycogen], muscle glycogen utilisation, epinephrine and norepinephrine (postprandial and during exercise)	
Garcin et al.[17]	Endurance (n=10)	50/100	Throughout 3 h pre-exercise	↔	Lactate, BG, RPE, hunger feelings	RPE does not depend on the GI of pre-exercise foods during 1h exercise at 80% VO₂max.
Wu et al.[25]	Recreational runners (n=9)	37/77	3 h pre-exercise	↑	BG (30 and 60 min. postprandial), insulin (90 and 120 min. postprandial)	Low GI meals result in a higher rate of fat oxidation during exercise compared to a high GI meal. The greater rate of fat oxidation with low GI meals may be beneficial in improving endurance performance by delaying depletion of muscle glycogen. No hypoglycaemia was reported.
				↔	Lactate (during exercise), insulin (during exercise), RPE (during exercise), CHO oxidation (postprandial), RER (postprandial and during exercise), satiety (during exercise)	
				↓	Lactate (15-120 min. postprandial), BG (at 15 min. of exercise), FFA (at 30, 45 and 60 min. of exercise), glycerol (at 60 min. of exercise), satiety (15 and 30 min. postprandial)	

↑ = High GI significantly higher than low GI   # = High GI significantly higher than moderate GI   † = Moderate GI significantly higher than control   ᵃ = Lentils   ᵈ = Lentils

↔ = No difference between low GI & high GI   # = No difference between moderate GI & high GI   † = No difference between moderate GI & control   ᵇ = Potato   ᵉ =Bran cereal

↓ = High GI significantly lower than low GI   # = High GI significantly lower than moderate GI   † = Moderate GI significantly lower than control   ᶜ = Glucose   ᶠ = Rice cereal

     ᵍ = Potato flakes

[ ]   = Concentration   NR   = Not reported   § = Potato used as reference food (GI = 100)

BG   = Blood glucose   RPE   = Rate of perceived exertion

CHO   = Carbohydrate   RER   = Respiratory exchange ratio

FFA   = Free fatty acids

In a follow-up study by Thomas *et al.*[19], with the same exercise protocol they compared lentils and bran cereal (low GI) with potato flakes and rice cereal (high GI), providing 1 g CHO/kg body mass. FFA and BG concentrations were found to correlate inversely with the GI of the foods during the last 60-90 min. of exercise. Both these studies' results implicate that slow digestion of CHO in a pre-exercise meal favours higher plasma/serum substrate concentrations towards the end of exercise, which seem to improve exercise performance.

These results are in accordance with a more recent study conducted by DeMarco *et al.*[13] where they compared postprandial metabolic and physiologic responses of a low GI *vs.* a high GI pre-exercise meal. Ten men accustomed to cycling consumed a meal providing 1.5 g CHO/kg body mass, consisting either of cornflakes, banana and milk (high GI) or bran flakes, apple and low fat yoghurt (low GI), with water as the control. The meals were consumed 30 min. prior to a cycle test (2 h at 70% VO_{2max} followed by cycling to exhaustion at 100% VO_{2max}). Significantly lower insulin levels were observed at 20 min. of exercise, as well as higher BG and RPE ($p<0.05$) at 2 h of exercise after ingesting the low GI compared to the high GI pre-exercise meal. Additionally, RER was significantly higher with the high GI test meal throughout exercise. Furthermore, time to exhaustion was 59% longer with the low GI than with the high GI pre-exercise meal implicating that a low GI pre-exercise meal may positively influence performance following prolonged exercise by maintaining BG concentrations towards the end of exercise.

Febbraio and associates conducted two studies to explore the effect of the GI on exercise performance. In the first study they examined the effect of pre-exercise CHO intake on muscle CHO metabolism and performance during endurance exercise[15]. Six endurance-trained men ingested lentils (low GI), mashed potato (high GI) or diet jelly (CON) 45 min. pre-exercise (cycled at 70% VO_{2max} for 120 min. followed by a 15 min. performance cycle). BG and insulin concentrations were significantly higher 15-45 min. postprandially and FFA levels were suppressed throughout the exercise period following the high GI meal. Regardless of these results, no differences were found in either the rate of muscle glycogen utilisation during exercise or work output during the performance cycle between athletes ingesting high GI or low GI foods. These results suggested that irrespective of the glycaemic or insulinaemic response of the pre-exercise meals, pre-exercise CHO intake has no influence on muscle glycogen utilisation or exercise performance. In the second study, Febbraio *et al.*[14] further examined the influence of pre-exercise ingestion of CHOs with differing GIs on substrate metabolism. Eight trained men cycled at 70%VO_{2max} for 120 min. followed by a 30 min. performance cycle 30 min. after ingesting either muesli (low GI), mashed potato (high GI) or diet jelly (CON). Once again BG and insulin concentrations were higher postprandially and FFA levels were lower in the high GI compared to the low GI meal ($p<0.05$) throughout

exercise. At the onset of exercise, BG concentrations dropped significantly so that it were lower after the high GI meal compared to the low GI meal at 15 and 30 min. during exercise. Furthermore, CHO oxidation was higher throughout exercise, whereas glycogen usage tended to be higher after the high GI meal compared to the low GI meal. However, no differences were observed in work output also between athletes ingesting high GI or low GI meals. The authors concluded that pre-exercise feedings with a high GI (but not a low GI) meal increase CHO utilisation during exercise but do not seem to affect exercise performance.

The effects of pre-exercise meals with varying GIs on metabolism during exercise and an "all out" performance cycle was the subject of investigation in a study conducted by Sparks *et al.*[16]. Eight endurance trained triathletes consumed three meals consisting either of lentils (low GI), instant mashed potato (high GI) or a diet soft drink (CON) 45 min. prior to cycling for 50 min. at 67% VO_{2max} followed by a performance ride to exhaustion. BG concentrations were significantly higher 30 min. postprandially in the high GI group and declined towards the onset of exercise to be significantly lower than the low GI group at 10 min. of exercise and up to 30 min. of exercise. Insulin concentrations were significantly higher with the high GI meal postprandial and during exercise compared to low GI. FFA concentrations were lower at the onset and termination of exercise in the high GI compared to the low GI trial. Additionally, RER and CHO oxidation were higher in the high GI *vs.* the low GI trial. Again no differences in work output between the groups during the performance cycle were observed. These findings indicate that pre-exercise CHO meals with varying GIs do not have a detrimental effect on exercise performance despite the changes in metabolism.

Kirwan and colleagues conducted three studies on the effect of moderate GI pre-exercise meals and exercise. In the first study, Kirwan *et al.*[20] determined the effects of two moderate GI breakfast cereals (sweetened whole grain oats or sweetened whole-oats flour) with different amounts of dietary fibre, on the metabolic response to prolonged moderate-intensity exercise. Six active women consumed in a randomised order either water (CON) or 75 g available CHO from the breakfast cereals, 45 min. prior to cycling at 60% VO_{2max} up to exhaustion. FFA concentrations were significantly lower for the first 60-90min. of exercise while RER was significantly higher at 90 and 120 min. of exercise in the moderate GI cereal groups compared to the CON. At the end of the workout there were no differences in glucose, insulin, FFA, glycerol, epinephrine, norepinephrine, RER and muscle glycogen concentrations between the groups. Time to exhaustion was, however, 16% longer during the sweetened whole-oat flour trial compared to CON. The authors concluded that ingesting a moderate GI meal with a high dietary fibre content before prolonged exercise significantly enhances exercise capacity. In the second study Kirwan *et al.*[21], with the same exercise

protocol they further studied the effects of a moderate GI meal on exercise duration and substrate utilisation. Six active women again consumed 75 g available CHO in the form of whole grain rolled oats (moderate GI), water was used as a control. FFA and glycerol concentrations were significantly lower during the first 120 min. of exercise while RER was higher (p<0.05) during the same period of time in the moderate GI group. However, at the end of the workout there was once again no difference in glucose, insulin, FFA, glycerol, epinephrine, norepinephrine, RER and muscle glycogen concentrations between the moderate GI and CON groups. This time exercise duration tended to be longer with the moderate GI meal compared to CON but differences were not significant. It was concluded that ingesting a moderate GI meal prior to endurance exercise does not prolong time to exhaustion. A third study by Kirwan *et al.*[22], with the same exercise protocol as the above mentioned studies, examined the effects of moderate GI and high GI meals on metabolism and exercise performance. Six male volunteers ingested 75 g available CHO in the form of rolled oats (moderate GI) or puffed rice (high GI), which was compared to water (CON). Before the onset of exercise both the moderate GI and high GI meals induced significant hyperglycaemia and hyperinsulinaemia. During exercise BG levels were significantly higher at 60 and 90 min. after the moderate GI meal compared to both the high GI meal and CON. Total CHO oxidation was significantly higher during exercise in the moderate GI group than in CON and correlated with exercise performance time. There was no difference in FFA concentrations between moderate GI and high GI trials during exercise. However, FFA was significantly suppressed 30 and 45 min. after ingestion of the high GI meal, 45 min. after ingestion of the moderate GI meal, as well as 30, 60 and 120 min. after the onset of exercise for both high GI and moderate GI meals compared to the CON. Again no differences were found between the groups for glucose, insulin, FFA, glycerol, epinephrine, norepinephrine and muscle glycogen usage at the end of the workout. Exercise time was significantly prolonged in the moderate GI group, regardless of FFA suppression during exercise, compared to the CON. No difference was, however, observed in exercise time between the high GI and CON groups. To conclude, ingesting a moderate GI meal 45 min. pre-exercise, offered a greater advantage by enhancing time to exhaustion, maintaining of euglycaemia for a longer period during exercise even though total CHO oxidation was increased during exercise.

The topic of investigation in a study by Stannard and collaborators was whether the GI of a pre-exercise meal has an effect on BG and lactate levels during incremental exercise[18]. Ten trained cyclists started to cycle 65 min. postprandial with an initial workload of 50 watts. Workload was increased every 3 min. by 50 watts until exhaustion (350 watts). Pre-exercise meals supplied 1 g CHO/kg body mass and consisted of either pasta (low GI), glucose (high GI) or an artificially sweetened placebo (CON). BG concentrations were significantly higher

at 15-45 min. postprandial and significantly lower during exercise (up to 200 watts) with the high GI meal compared to the low GI meal. Plasma lactate concentration was significantly higher from 45 min. postprandial through to the end of the 100-watt workload in the high GI group. At higher intensities, no difference in blood values was observed between the groups. No difference in time to exhaustion was found between the three groups. Additionally, these outcomes suggest that although high GI CHO consumed 65 min. pre-exercise decreases BG and increases lactate concentrations pre and during exercise, it does not seem to be detrimental to incremental exercise performance.

Regarding the studies that fed pre-exercise meals between two to three hours prior to exercise, the study of Garcin *et al.*[17] assessed the effect of CHO foods with various GIs on the relationships between RPE and BG concentrations or hunger during a 1 h exercise bout. Ten triathletes cycled for 1 h at 80% VO_{2max} after consuming either glucose (high GI), whole-wheat biscuits (low GI) or water (CON) 3 h pre-exercise. The test meals provided 0.3 g CHO/kg body mass. RPE values increased as a logarithmic function of time. No significant difference regarding BG, lactate, RPE or hunger feelings were noted between the three meals at any time. Additionally, no correlations were found between RPE and BG concentrations during exercise. These results indicate that RPE during exercise does not seem to depend on the GI of the pre-exercise meal.

The purpose of the study by Burke *et al.*[12] was to investigate whether the GI of a pre-exercise meal has an influence on exercise performance when large amounts of CHO are also consumed during exercise. Six trained cyclists pedalled for 2 h at 70% VO_{2max} followed by a performance ride. Meals supplied 2 g CHO/kg body mass and consisted either of potato (high GI), pasta (low GI) or low energy jelly (CON) consumed 120 min. pre-exercise. Additionally, subjects consumed a glucose solution every 20 min. throughout exercise to yield 2.4 g CHO/kg body mass. The high GI group produced significantly higher glucose and insulin responses and lower FFA responses postprandially. Regardless of these results, both total CHO oxidation and oxidation of the ingested CHO for high GI, low GI and CON were comparable during the 2 h exercise bout. Furthermore, no difference in time to completion of the performance ride was observed between the three groups. These results suggest that the type (GI) of pre-exercise CHO consumed has a small effect on metabolism and subsequent performance during prolonged cycling when CHO is ingested during exercise in amounts currently recommended (1998).

In a study by Wee and associates, the outcome of high GI compared to low GI pre-exercise meals on endurance running capacity was assessed[24]. Eight active subjects ran on a treadmill at 70% VO_{2max} to exhaustion after consuming an isoenergetic meal containing either

high GI or low GI foods providing 2 g CHO/kg body mass 3 h pre-exercise. The high GI meal resulted in a significantly higher insulin and BG response curve postprandial compared to the low GI meal. Fat oxidation was significantly lower and CHO oxidation significantly higher during the first 80 min. of exercise in the high GI compared to the low GI trial. Even though insulin concentrations were not different between groups, BG concentrations were significantly lower at 20 min. into exercise in the high GI than in the low GI trial, however, BG concentrations did not reach hypoglycaemic levels (2.5-2.8 mmol/l)[26]. For the duration of exercise, glycerol and FFA concentrations were lower in the high GI trial than in the low GI trial. No difference was observed in performance times between the two groups. These results show that regardless of the shift in substrate utilisation from CHO to fat with a low GI compared to a high GI pre-exercise meal, no difference in endurance running capacity was detected[24].

Finally, Wu *et al.*[25] investigated the effects of mixed high-CHO meals with different GIs on substrate utilisation during subsequent exercise. Nine runners exercised for 1 h at 65% VO_{2max} 3 h after ingesting an isoenergetic high GI, low GI or water (CON) pre-exercise meal. The meals provided 2 g CHO/kg body mass. Hyperglycaemia and hyperinsulinaemia were detected after ingestion of the high GI meal. FFA concentrations were significantly lower at 30-60 min. of exercise following the high GI than the low GI meal. Fat oxidation during exercise was significantly higher for the low GI than the high GI trial. It was proposed that the greater rate of fat oxidation with the low GI meal might be favourable in improving endurance performance by delaying depletion of muscle glycogen.

3.2 Post-exercise meals

Table 2 summarises the effect on recovery by applying the glycaemic index post-exercise One of the four studies investigating the GI and recovery compared high GI *vs.* low GI meals[27], two studies provided high GI recovery meals either as snacks (nibbling) or meals (gorging)[28,29] while one study compared high GI meals given either as immediate or delayed feedings[30]. Subjects that participated in the recovery studies included trained cyclists, triathletes, endurance trained athletes and trained runners. The study of Burke *et al.*[27] that compared low GI *vs.* high GI recovery meals defined the low GI meal as 51 and the high GI meal as 77. The studies of Burke *et al.*[28] and Parkin *et al.*[30] did not indicate the GI of the recovery meal and just stated that it was high GI. Siu *et al.*[29] reported a GI of 77 for their recovery meal.

Concerning feeding patterns post-exercise, three trials [27,28,29] assessed the effects of high GI or low GI meals given at different time intervals during the recovery period. Burke and associates[27] examined the effect of the GI of post-exercise CHO intake on muscle glycogen

Table 2: Effect on recovery by applying the glycaemic index post-exercise

Author(s) and year	Study participants	GI of meal	Time of meal		Outcomes (Major results)	Authors' conclusion(s)
Burke et al.[27]	Elite junior cyclists (n=5)	50/77†	0, 4h, 8h and 21h post-exercise	↑	**[Muscle glycogen]** (high GI vs. low GI 24 h post-exercise), **BG and insulin incremental areas** (high GI vs. low GI at 24 h post-exercise without meal immediately post-exercise)	High GI CHO foods after prolonged exercise produce significantly greater glycogen storage than low GI foods.
Burke et al.[28]	Triathletes (n=8)	NR	Gorging = 0 h, 4h, 8h and 20 h post-exercise	↑	BG, insulin (in gorging trial 60-90 min. after both meals, then returned to baseline)	Large high GI meals are as effective as small snacks in achieving glycogen storage during 24 h of recovery from prolonged exercise given that the total CHO intake was adequate.
			Nibbling = 0-11 h (hourly) & 20-23 h (hourly) post-exercise	↔ ↓	**[Muscle glycogen]** TG (in gorging trial over 24 h trial)	
Parkin et al.[30]	Endurance (n=6)	NR	Immediate feeding = 0, 2h, 4h, 8h and 24 h post-exercise Delayed feeding = 2h, 4h, 6h, 8h and 22h post-exercise	↔	**[Muscle glycogen]**, **BG, insulin** (at any time point between immediate and delayed feeding)	Delaying ingestion of high GI foods by 2 h has no effect on muscle glycogen storage provided that a sufficient amount of CHO is ingested during the recovery period.
Siu et al.[29]	Trained male runners (n=8)	77†	Gorging = Single bolus 20 min. after 90 min. run Nibbling = 3 equal meals 20 min., 1h and 2 h after 90 min. run	↑	BG (gorging vs. nibbling at 60 min. of recovery; nibbling vs. gorging at 2h and 3h of recovery), **insulin** (gorging vs. nibbling at 60 min. of recovery; nibbling higher than gorging at 3h of recovery), **FFA** (gorging higher than nibbling at 3h of recovery and after second bout of exercise), **rate of CHO oxidation** (gorging higher than nibbling at 30 min. into second exercise bout and at exhaustion)	Three small feedings of a high GI meal in a 4h recovery period increased the reliance on CHO oxidation for energy provision in a subsequent endurance capacity run, compared with the responses after ingestion of the same meal in one feeding.
				↔	**Lactate** (at any time point)	

† Reference food is glucose

BG	= Blood glucose	Low GI	= Low glycaemic index
CHO	= Carbohydrate	FFA	= Free fatty acids
High GI	= High glycaemic index	[ ]	= Concentration
↑	= Significantly higher	NR	= Not reported
↔	= No difference between groups		
↓	= Significantly lower		

storage. Five trained cyclists followed a muscle glycogen depletion exercise protocol by cycling for 2 h at 75% VO_{2max} followed by four 30 second all out sprints. Subjects ingested isocaloric high CHO meals that supplied 10 g CHO/ kg body mass, consisting mainly either of rolled oats, pasta, parboiled rice and lentils (low GI) or cornflakes, whole-meal bread and instant mashed potato (high GI), evenly distributed between four meals eaten at 0, 4, 8 and 21 h post-exercise. A higher muscle glycogen content was observed after 24 h of recovery with groups ingesting the high GI compared to the low GI meals. When the effects of the immediate post-exercise meal were excluded, the total incremental areas for BG and insulin after each meal were greater for the high GI than the low GI meals, suggesting that high GI recovery meals during the first 24 h of recovery lead to greater muscle glycogen stores compared to low GI recovery meals[27].

In a follow-up study with the same exercise protocol Burke *et al.*[28] examined the significance of greater incremental BG and insulin concentrations on glycogen repletion by comparing the intake of large CHO meals, referred to as gorging, to a pattern of frequent small CHO snacks, referred to as nibbling. The reason for this was that nibbling simulates the flattened glucose and insulin responses that would occur after ingesting of a low GI CHO meal. Eight triathletes ingested in random order meals providing 10 g CHO/kg body mass in total, consisting of high GI foods such as corn flakes, glucose, whole-meal bread and instant mashed potatoes. The meals of the gorging trial were divided into four meals of equivalent CHO content consumed at 0, 4, 8 and 20 h of recovery, while the nibbling trial was divided into 16 snacks of equivalent CHO content that were consumed hourly throughout the 24 h recovery period. Although there were significant differences between the two trials in incremental BG, insulin and triacylglycerol, concentrations no significant differences were found in muscle glycogen concentrations between the nibbling and gorging trial. These results suggest that there is no difference in glycogen storage during a 24 h recovery period when a high GI diet is consumed either as small frequent snacks or as less frequent large meals.

A more recent study by Siu *et al.*[29], the effect of the feeding pattern of high GI meals during short-term recovery on subsequent endurance capacity was examined. Eight trained runners ran on a treadmill at 70% VO_{2max} for 90 min. followed by a 4 h recovery period and a further exhaustive run at the same speed on two separate occasions. During the recovery period, a high GI meal supplying 1.5 g CHO/kg body mass, was ingested in either a nibbling or gorging pattern. During the gorging trial the test meal was consumed as a single meal 20 min. after the first run, while the nibbling trial supplied the same amount of food, divided into three equal snacks. The first snack was consumed 20 min. after the first run and the other two snacks at hourly intervals thereafter. Time to exhaustion during the second run was not

different between the nibbling or gorging trial. On the other hand, CHO oxidation was significantly lower and fat oxidation significantly higher during the second run in the gorging trial compared with the nibbling trial. Even though there was no difference in time to exhaustion between the nibbling and gorging trials, these results indicate that high GI CHO provided as small frequent meals during a 4 h recovery period, increases the dependence on CHO oxidation for energy provision during a subsequent exhaustive run when compared to a single meal.

Up to date there was only one study that assessed the effect of altering the timing of ingestion of high GI CHO during recovery. Parkin and colleagues investigated whether there was a difference in muscle glycogen storage following prolonged exercise when a high GI recovery meal was ingested immediately or delayed by two hours after exercise[30]. Six endurance trained subjects cycled for 2 h at 70% VO_{2max} followed by four all-out 30 second sprints on two separate occasions. Five high GI meals were fed either immediately after exercise or delayed by 2 h. Meals were fed at 2 h intervals over a period of 24 h. Muscle biopsies were taken immediately, 8 h and 24 h after exercise. No differences were detected in the incremental glucose and insulin areas or muscle glycogen concentrations when comparing the immediate or delayed feeding trials. From these findings it is proposed that delaying a post-exercise high GI meal for 2 h has no effect on the rate of muscle glycogen resynthesis at 8 h and 24 h post-exercise, however, adequate amounts of CHO should be ingested during the recovery period.

4. Discussion

4.1 The glycaemic index and pre-exercise meals

The ability to sustain prolonged aerobic exercise is determined to a large extent by substrate availability. The maintenance of euglycaemia and CHO oxidation late in exercise can delay fatigue, suggesting that CHO intake before and/or during exercise may be crucial to prolong the duration of exercise[20]. It has been proposed that pre-exercise CHO feedings enhance muscle glycogen availability and improve performance[32] by optimising liver and muscle glycogen concentrations[33]. It also has an effect on metabolic responses and substrate utilisation during subsequent exercise[24,34].

However, earlier studies have shown potential disadvantages with pre-exercise CHO intake. It was suggested that CHO feedings in the hour prior to exercise might impair exercise performance by causing a rapid decrease in blood glucose concentrations and an accompanying acceleration of muscle glycogenolysis[35] via a reduced glucose supply to the active muscle[16]. This can be attributed to associated hyperinsulinaemia that increases glucose uptake by the exercising muscles and furthermore, reduces hepatic glucose output,

resulting in hypoglycaemia. Another potential disadvantage is that these elevated insulin concentrations also suppresses lipolysis and fat utilisation, thereby accelerating CHO oxidation causing premature glycogen depletion[35].

High GI CHO is known to cause above mentioned hypoglycaemic (2.5-2.8 mmol/l)[26] and hyperinsulinaemic symptoms 30-60 min. after ingestion, while low GI CHO does not have such an exacerbated response[7]. Figure 1 illustrates these differences in blood glucose and insulin responses between low GI and high GI CHO ingestion. The dotted line represents the difference in insulin concentrations between low GI and high GI CHO intake, while the solid line represents the difference in BG concentrations. It was, therefore, suggested that CHO sources that produce a minimal glycaemic and insulinaemic response would attenuate these metabolic disturbances. For this reason low GI CHO was proposed to formulate pre-exercise feedings. The motivation for this was that by consuming low GI foods in the immediate pre-exercise period, CHO would be digested and absorbed into the blood at a relatively slow rate. Consequently, any surge of insulin would be eliminated and at the same time provide a steady supply of "slow-release" CHO that would be available from the gastrointestinal tract during the exercise period[36]. Therefore, one of the aims of this systematic review was to investigate whether this holds any truth or not.

Regarding studies providing meals 30-60 min. pre-exercise, Thomas *et al.*[10,19] and DeMaro *et al.*[13] indeed found an improvement in endurance time with low GI pre-exercise meals. The study of Thomas *et al.*[10] has led to widespread advice that endurance athletes should choose pre-exercise meals based on low GI foods and drinks. Criticism, however, against the studies of Thomas *et al.*[10,19] was that their low GI test foods provided two to three times as much protein and almost twice the energy to yield the same amount of CHO that was used for the high GI pre-exercise test meal. Consequently the pre-exercise meals were neither isoenergetic nor had the same macronutrient composition and for this reasons, their results should be interpreted with care. In addition, Thomas *et al.*[10] failed to address the fact that there was no difference in exercise performance when the low GI pre-exercise meal was compared to the high GI pre-exercise meal[16]. Another important observation was raised by Burke *et al.*[7] regarding the measurement of performance. Thomas *et al.*[10,19] defined performance as the "time to exhaustion at a fixed sub-maximal work rate". Protocols applying time to exhaustion have been shown to have a high coefficient of variation. Additionally these protocols cannot be applied to competitive sport since work rates vary during a match or competitive run and do not occur at a fixed rate.
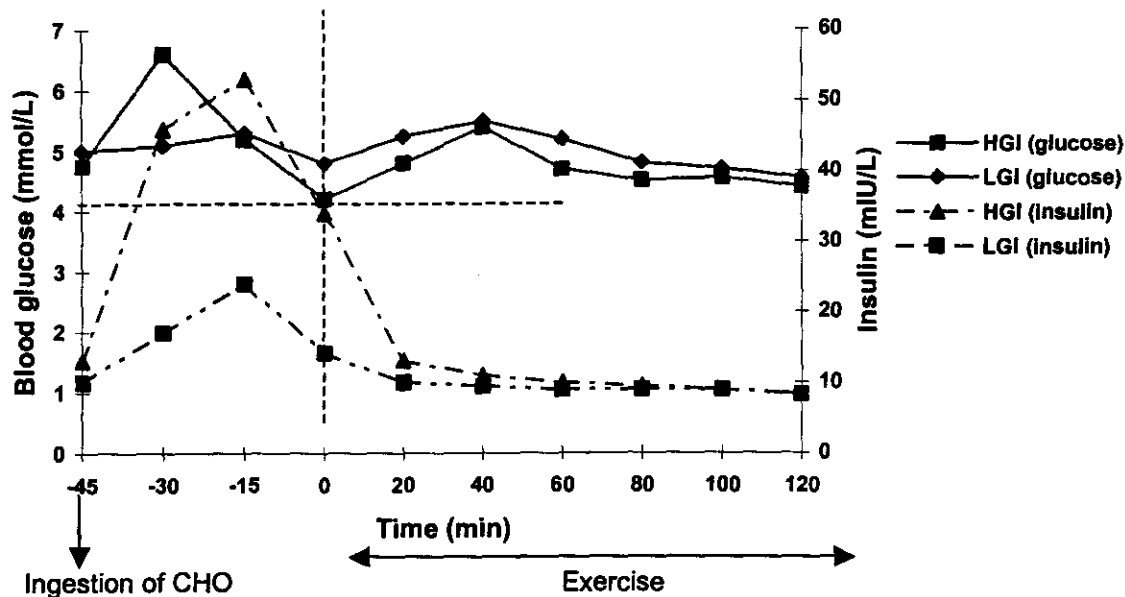
Figure 1: Glycaemic and insulinaemic responses after carbohydrate ingestion

Moreover, a dependant variable with a low degree of reliability is less likely to show or detect a real change[37]. Hence, it is difficult to apply these changes in time to exhaustion to real sport situations, making it complicated to translate the results of these studies into practical advice for competitive athletes. A possible solution for this problem is to have subjects perform a time trial after a period of fixed sub-maximal exercise. By combining a more reliable and sport-specific measurement of performance with a period of steady-state exercise, one can compare the metabolic responses to different treatments[7].

None of the other studies investigating the effect of pre-exercise meals 30-65 min. prior to exercise found that low GI pre-exercise meals will improve exercise performance more than high GI pre-exercise meals[14-16,18]. Similarities between the studies were the observation of significantly higher blood glucose and insulin concentrations during the postprandial period with the high GI compared to the low GI pre-exercise either directly before or at the onset of exercise. This was accompanied by a decrease in FFA and an increase in CHO oxidation and, therefore, RER which could contribute to premature depletion of glycogen stores and early onset of fatigue[23,35]. Despite these observations no difference in work output and performance was reported whether a high GI or low GI pre-exercise meal was ingested[14-16,18,23]. Moreover, taking in consideration other metabolites such as lactate, no detrimental effects were observed with high GI compared to low GI pre-exercise meals[14-18,23]. There were also no differences found in muscle glycogen concentration whether low GI or high GI pre-exercise meals were fed[14,15]. When viewing the studies that investigated low GI compared

to high GI pre-exercise meals fed 2-3 h prior to exercise, they also failed to show any detrimental effects with high GI pre-exercise meals regarding exercise performance[12,17,24,25].

Considering the studies that investigated the effect of moderate GI vs. CON and moderate GI vs. high GI CHO fed 45 min. prior to exercise, no difference was found between the trials in variables such as BG, insulin, FFA, glycerol and muscle glycogen concentration at the onset of fatigue[20-22]. Nevertheless, duration of exercise was prolonged when moderate GI pre-exercise meals were ingested compared to a CON and a high GI pre-exercise meal[21]. Up to date no other studies were conducted to investigate the effect of moderate GI pre-exercise meals on exercise performance and, therefore, may warrant some further investigation.

To conclude, although low GI compared to high GI pre-exercise meals seem to provide more stable metabolic responses postprandial as well as at the early stages of exercise, most studies failed to show an improvement in exercise performance when low GI pre-exercise meals are compared to high GI pre-exercise meals. Therefore, low GI pre-exercise meals do not have any additional advantages over high GI pre-exercise meals. However, there are exceptional circumstances where athletes may benefit from low GI pre-exercise meals. Athletes who respond negatively to CHO feedings in the hour prior to exercise, experience exaggerated CHO oxidation and decreases in BG concentrations at the onset of exercise, causing a rapid onset of fatigue and symptoms of hypoglycaemia. The reason for this severe reaction is not known. To combat this extreme reaction it is recommended that adequate amounts (>70 g) of low GI CHO should be consumed as well as a high-intensity warm-up session pre-exercise to sustain BG and insulin concentrations[38].

Finally, every athlete must consider the benefits of pre-exercise meals, whether the pre-exercise meal is to prevent hunger feelings during competition or for sustained energy supply during an exercise bout. Athletes must trust their own preferences and previous experience in choosing pre-exercise meals. Another challenge is to ensure that pre-exercise feedings do not cause excessive fullness or result in gastrointestinal discomfort like vomiting or diarrhoea during exercise[7].

4.2 The glycaemic index during exercise

CHO ingestion during exercise leads to performance benefits such as increased exercise time to fatigue[39], enhanced work output during exercise[58] and improved sprint performance after prolonged exercise[40]. However, the mechanism underlying these ergogenic effects is less clear. Proposed mechanisms are maintenance of euglycaemia and oxidation of blood glucose at high rates late in exercise when the body's endogenous glycogen stores are depleted and a decreased rate of muscle glycogen utilisation occurs, therefore, sparing

muscle glycogen. Other possible factors are type and intensity of exercise, amount, type and timing of CHO intake and pre-exercise nutritional and training status of subjects[41]. The mechanisms for above mentioned ergogenic effects of CHO may be different for relatively short-duration (~1 h) high-intensity exercise (80-85 % VO_{2max}) than for long-duration (>2 h) low- to moderate-intensity exercise (60-75% of VO_{2max})[42].

Although it sounds reasonable that the type of CHO ingested during exercise should be easily digested and absorbed to ensure a rapid supply of glucose to the exercising muscle, the effect of the GI of CHO-rich foods and drinks during exercise has not been studied. The recommendation, however, is that moderate GI to high GI CHO should be consumed during endurance type exercise[1]. Of the monosaccharides, glucose (high GI)[43] is found to be oxidised at relatively high rates (up to 1 g/min) while fructose and galactose are oxidised at much lower rates during exercise[44,45]. Reasons for adding fructose (low GI) to sport drinks are firstly to improve the palatability of a sport drink. Furthermore, it causes a 20-30% smaller increase in insulin levels compared to glucose consequently reducing lypolysis to a smaller extent[46]. Fructose also seems to prevent exercise-induced rebound hypoglycaemia[47,48]. However, several studies showed that fructose has a 25% lower oxidation rate than glucose[47,49,50]. The reason for this is that fructose is absorbed more slowly from the gut than glucose. Fructose must first be metabolised in the liver, where it undergoes phosphorylation by fructokinase and is then converted to glucose and only after this process fructose will be available as energy to the exercising muscle[23]. The oxidation rate of galactose is even lower[44], due to the limited absorption and conversion to glucose into the liver[46].

Regarding disaccharides, maltose (high GI)[43] has been found to have similar oxidation rates to glucose[51], while sucrose (moderate GI) has either lower[52] or similar oxidation rates compared to glucose[51]. For polysaccharides, glucose polymers such as maltodextrin (high GI)[43] have been widely used in sport drinks because of their neutral taste and relatively low osmolality[46]. Oxidation rates as well as rates of gastric emptying and consequently the rate of delivery of CHO into the digestive system were found to be similar between glucose and maltodextrins[53]. Amylopectin (high GI) and amylose (low GI)[43] are two major types of starches which make up to 50% of total daily CHO intake. Most naturally occurring starches are a mixture of amylose and amylopectin[46]. In a study conducted by Saris *et al.*[54], the rate of gastric emptying and oxidation rate of insoluble starch (23% amylose and 77% amylopectin) and soluble starch (100% amylopectin) were compared. Gastric emptying rate was higher with the soluble starch, however, not significantly so. Oxidation rate on the other hand was significantly higher with the soluble starch. Furthermore, insoluble starch may cause gastrointestinal discomfort due to the slower absorption rate[54].

In conclusion, CHO with a high oxidation rate such as the monosaccharide glucose, is preferable to use in beverages for athletes during exercise. On the contrary, low GI CHO such as fructose and galactose, are slowly digested and absorbed and are, therefore, not suitable to include as single CHO in sport drinks. Fructose is also known to cause gastrointestinal discomfort as a result of its slower oxidation rate[55]. The high GI disaccharides maltose and sucrose as well as the high GI polysaccharides maltodextrin and amylopectin have oxidation rates similar to glucose and are for this reason appropriate CHO sources to include in sport drinks[56,57].

RCT's have shown that with the exception of fructose, all the other types of CHO (glucose, sucrose and polymers) on their own or in mixtures that could include fructose, have the ability to reduce muscle glycogen utilisation and improve exercise performance[58-60]. A study by Shi et al.[61] investigated the addition of two or three CHOs (glucose, fructose and sucrose) to a sport drink during exercise. They found an increase in CHO and water absorption despite an increase in osmolality. This could partially be explained by the different transport mechanisms across the intestinal wall for glucose, fructose and sucrose[46,61].

Further investigation by the laboratory of Jentjens and Jeukendrup also reported higher oxidation rates with the combination of CHO's during exercise. The first study compared exogenous CHO oxidation rates when a low glucose (1.2 g/min), high glucose (1.8 g/min) or a mixed solution of fructose (0.6 g/min) and glucose (1.2 g/min) was ingested during exercise. They found that when fructose and glucose were consumed simultaneously during exercise, exogenous CHO oxidation rates reached peak values of approximately 1.3 g/min[62]. In the second study, a glucose solution (2.4 g/min) or a mixed glucose (1.2 g/min), fructose (0.6 g/min) and sucrose (0.6 g/min) solution was ingested during exercise[63]. The authors found that when glucose, fructose and sucrose were ingested simultaneously at high rates (2.4 g/min), exogenous CHO oxidation rates reached peak values of 1.7 g/min and estimated endogenous CHO oxidation is reduced compared with the ingestion of an isocaloric amount of glucose. A possible explanation for this is the fact that sucrose and fructose are absorbed by intestinal transport mechanisms that are, in part, different from glucose transport[63]. This conclusion supports the findings and explanation of Shi et al.[61]. Jentjens et al.[63] explain that glucose absorption occurs via a sodium-dependent glucose transporter (SGLT1), whereas fructose is absorbed from the intestine by a glucose transporter carrier protein-5 (GLUT-5). It has been suggested that sucrose is hydrolysed into the monosaccharides glucose and fructose at the brush-border membrane. Fructose and glucose is then subsequently absorbed by conventional monosaccharide transport mechanisms. Another suggestion is that disaccharides like sucrose are absorbed by a specific disaccharidase-related transport system[63].

The combination of different CHO sources in sport drinks sounds promising. From this discussion it seems that the combination of single CHO sources with differing GIs such as glucose (high GI), sucrose (moderate GI) and fructose (low GI) deliver the best results in terms of exogenous CHO oxidation. This could to a certain extent be explained by different transport mechanisms. However, because of limited research on the effect of the GI during endurance type exercise, this review may support the conduction of additional research in this area. Furthermore, no studies were found investigating the effect of the GI during team sport e.g. cricket and tennis, which are played over long time periods with variations in activity level.

4.3 The glycaemic index and recovery meals

According to Romijn et al.[3], muscle glycogen is the major source of energy during prolonged moderate to high intensity exercise. The onset of fatigue is generally associated with the depletion of muscle glycogen stores[64], which are in a large part dependant on the preceding recovery period. The time needed to recover following exhaustive exercise is determined by the restoration of muscle glycogen stores[8]. Complete restoration of muscle glycogen stores depends on the extent of glycogen depletion during exercise and also the type and amount of CHO consumed during the recovery period, which can take up to 24 h[64,65]. Therefore, the first 24 h of recovery is crucial and CHO intake must be optimal. However, the training and competition schedules of athletes often allows considerably less time than this, especially athletes who train or participate more than once daily[66].

Two laboratories described the refilling of glycogen stores during the recovery period when CHO is ingested[8,67]. In a study conducted by Adamo et al.[67], they observed the existence of two structural forms of skeletal muscle glycogen that function as different metabolic pools under physiological conditions. Macroglycogen shows the greatest relative depletion at exhaustion while proglycogen is more sensitive to dietary CHO and is synthesised more rapidly following glycogen depletion. After 24 h of a high CHO diet ($\geq$75% total energy), the proglycogen concentration reaches a plateau while the macroglycogen pool continues to expand and is responsible for the supercompensation seen in the days following exhaustive exercise[67]. Therefore, it appears that immediate CHO ingestion directly after exercise reloads the proglycogen pool, while continued CHO resynthesis over time refills the macroglycogen pool[68].

Jentjens and Jeukendrup[8] suggest that the pattern of muscle glycogen synthesis following glycogen-depleting exercise occurs in two phases. The rapid phase of muscle glycogen synthesis is independent of insulin, which lasts about 30-60 min. and is characterised by increased permeability of the muscle cell membrane to glucose. This can be attributed to an

exercise-induced translocation of glucose transporter carrier protein-4 (GLUT-4) to the cell surface. The slow phase of glycogen synthesis follows the rapid phase and is characterised by a marked increase in the sensitivity of muscle glucose uptake and glycogen synthesis to insulin[69] and could last for up to 48 hours. Insulin and muscle contraction have been shown to augment the activity of glycogen synthase, the rate-limiting enzyme in glycogen synthesis[8].

The study of Burke et al.[27] formed the basis for the use of high GI CHO during the recovery phase. Unfortunately data from earlier studies cannot be applied to the GI since they referred to simple (glucose, fructose, sucrose) and complex CHO[70,71]. It should be noted that simple and complex CHO are not synonymous with high GI and low GI. Many foods with a "complex" structure such as bread and potatoes have a high GI while "simple" CHO such as fructose have a low GI[68]. Additionally, glucose and insulin concentrations as well as responses were not always measured and food intake and intervention meals not well described. Importantly, the activation of glycogen synthase by insulin is well documented[64].

Since glycogen storage is influenced by both insulin and a rapid supply of glucose substrate, it has been proposed that high GI CHO sources might enhance the recovery process since it is also more easily digested and absorbed[68]. In an earlier study conducted by Kiens et al.[78], they found higher muscle glycogen concentrations with a high GI recovery meal during the first 6 h of recovery than with a low GI recovery meal. However, at 20, 32 and 44 h after exercise, muscle glycogen concentrations were similar on the low GI and the high GI diets. Results should, however, be interpreted with caution since the foods supplied were not described and the diets were described interchangeably as complex CHO/low GI and simple CHO/high GI. In the study of Burke et al.[27], they found greater glycogen storage with a high GI compared to a low GI recovery meal at 24 h post-exercise. Complicating the interpretation of their results is the observation that the magnitude of increase in glycogen storage with the high GI diet group was greater than the 24 h blood glucose and insulin response. However, in the follow-up study by Burke et al.[28], no difference in glycogen storage over 24 h after the nibbling trial (simulating low GI) and the gorging trial (simulating high GI) could be found despite the differences in BG and insulin responses postprandially.

Nevertheless, it is possible that the diets may have caused differences in glycogen storage during the earlier hours (0-8 h) of recovery. From the aforementioned results it seems that manipulating glucose and insulin levels during a longer recovery period (i.e. 24 h) is not critical for optimal glycogen storage. Therefore, the emphasis should be on the amount rather than the type of CHO ingested during the recovery period[28]. According to Jentjens

and Jeukendrup[8], maximal glycogen synthesis rates occur at a CHO intake of approximately 1.2 g/kg body mass/h.

No studies were conducted up to date on the effect of the GI on short-term recovery, however, it seems that low GI foods are not recommended for recovery periods between 0-8 h. Criticism against the ingestion of low GI foods for short-term recovery may include the fact that low GI foods delay digestion and absorption[72]. Furthermore, a considerable amount of the CHO in low GI foods is not absorbed[73,74]. Therefore, low GI CHO might cause a slower supply of glucose to skeletal muscle, impairing glycogen storage. In a study conducted by Jozsi et al.[75] they investigated the effect of starch structure on muscle glycogen resynthesis and cycling performance. Subjects ingested one of four CHO solutions consisting of glucose, maltodextrin and waxy starch (100% amylopectin), both high GI[43] and resistant starch (100% amylose), which is low GI[43]. Higher glycogen synthesis rates were observed with the high GI CHO, while the low GI CHO impaired glycogen storage[75]. The authors concluded that the resistant starch mixture resulted in lower glycogen storage due to the poor digestibility thereof. Such indigestible CHO forms a poor substrate for muscle glycogen-resynthesis[75].

Regarding the frequency of recovery meals, an earlier study[70] reported that large meals were as effective as small frequent snacks in achieving glycogen storage during a 24 h recovery period. With reference to the results section, Burke et al.[28] reported similar findings. However the study of Siu et al.[29] found that when the recovery period is very short (< 4 h) the frequency of the high GI CHO feeding might be more important than when the recovery period is longer (> 8 h). This could be attributed to the fact that small frequent feedings compared to a single meal increase the reliance on CHO oxidation for energy when the recovery period is followed by subsequent exercise[29]. Unfortunately muscle glycogen concentration was not measured during this study, making it difficult to explain whether the increased CHO utilisation with more frequent high GI snacks during subsequent exercise was due to oxidation of muscle glycogen or blood glucose, or both. However, this was the first study investigating the frequency of CHO feedings during short-term (< 4 h) recovery and warrants further investigation.

Finally, concerning timing of recovery meals, preliminary research by Ivy et al.[76] showed that muscle glycogen storage has been higher at 4 h post exercise following the immediate ingestion of a glucose polymer compared with ingestion after a 2 h delay, probably as a result of the combined effects of insulin and the insulin-like effects of muscle contractions. Although it appears that earlier feedings are most important when the recovery period is short (4-8 h), it may have less impact over a longer recovery period as illustrated by Parkin et

al.[30]. Major findings from the study were that no difference in muscle glycogen concentrations was observed at 8 and 24 h of recovery whether carbohydrate intake was immediately after exercise or delayed by 2 h[30]. Burke *et al.*[11] emphasised that when recovery intervals are short, athletes should maximise the effective recovery time by ingesting CHO as soon as possible. On the other hand, when recovery periods are longer, athletes can consume their preferred recovery meal, given that the total CHO intake goals are achieved (7-10 g/kg body mass/day)[8,77].

No studies have been conducted on the effect of the GI on short-term recovery. However, it can be speculated that high GI CHO recovery meals are most effective when the recovery period is short (<8 h) to restore glycogen levels as a result of greater insulinaemic responses that stimulate activation of glycogen synthase and also provide a more rapid supply of glucose substrate. Low GI CHO recovery meals seem to be less efficient with short recovery periods since they might cause a lower supply of glucose to skeletal muscle and, therefore, are a poor substrate for glycogen synthesis. However, evidence suggests that when the recovery period is longer (20-24 h), the total amount of CHO is more important than the frequency, timing and GI of the recovery meal.

5. Conclusion

Pre-exercise it does not seem that low GI meals provide any advantages over high GI meals. Although low GI pre-exercise meals may better maintain CHO availability during exercise low GI pre-exercise meals offer no added advantage over high GI pre-exercise meals regarding performance. Furthermore, the exaggerated metabolic responses from high GI compared to low GI CHO seems not be detrimental to exercise performance. However, athletes who experience hypoglycaemia when consuming CHO-rich feedings in the hour prior to exercise are advised to rather consume low GI pre-exercise meals. Regarding during exercise CHO intake, no studies have been conducted on the effect of the GI during exercise. Current evidence suggests a combination of CHO with differing GI's such as glucose (high GI), sucrose (moderate GI) and fructose (low GI) will deliver the best results in terms of exogenous CHO oxidation due to different transport mechanisms. Finally, although no studies have been conducted on the effect of the GI so far on short-term recovery it is speculated that high GI CHO is most effective when the recovery period is between 0-8 h, however, evidence suggests that when the recovery period is longer (20-24 h) the total amount of CHO is more important than the type of CHO.

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Combined discussion, conclusions and recommendations

1. Introduction

The overall purpose of this thesis was to evaluate and summarise the body of evidence regarding the fundamental role of the GI in health and sport. To achieve this the first comprehensive and complete meta-analysis investigating markers for carbohydrate and lipid metabolism was conducted in order to examine the health effects of using the GI in meal planning. This meta-analysis was also the first to study the effect of the GI on the whole lipid profile. Additionally, this manuscript has already been published in the British Journal of Nutrition (Opperman *et al.*, 2004). Following the meta-analysis, a systematic review judging the strength of evidence from both randomised controlled trials as well epidemiological studies for application of the GI in a healthy eating plan was performed. This manuscript has been accepted for publication in the South African Journal of Clinical Nutrition. The final manuscript was a complete systematic review, also the first of its kind, on all the literature published up to date about the usefulness of the GI in planning pre, during and post-exercise meals for athletes (submitted for publication in Sport Medicine).

2. Main results

From the meta-analysis, the main results were that low GI diets (mainly consisting of CHO known to have a low GI such as peas, lentils, beans, pasta, barley, parboiled rice and oats) significantly reduced fructosamine by -0.1 mmol/L (CI -0.20,0.00; P=0.05), glycosylated haemoglobin (HbA$_{1c}$) by -0.27% (CI -0.5,-0.03; P=0.03), total cholesterol (TC) by -0.33 mmol/L (CI -0.47,-0.18; P<0.0001) and tended to reduce low-density lipoprotein cholesterol (LDL- c) in type 2 diabetics by -0.15 mmol/L (CI -0.31, - 0.00; P=0.06) compared to high GI diets. High GI diets were those that contained potato, wheatmeal, white bread and breakfast cereals known to have a high GI. No changes were observed in high-density lipoprotein cholesterol (HDL-c) and triacylglycerol (TG) concentrations. Results of this meta-analysis support the use of the GI as a scientifically based tool to choose CHO-containing foods to reduce TC and to improve overall metabolic control of diabetes.

From the systematic review, prospective epidemiological studies showed positive associations between low GI diets and HDL-c concentrations over longer time periods, while this was not the case with the short-term randomised controlled trials (RCTs), probably because of the short intervention period during which the RCTs were conducted. Furthermore, epidemiological evidence failed to prove a significant relationship between LDL-c, TC, TG and low GI diets. Nevertheless, the epidemiological studies, as with the RCTs showed positive results with low GI diets on markers for carbohydrate metabolism. Additionally, RCTs illustrated improvements in TC and a tendency to improve LDL-c with low GI diets and epidemiological studies illustrated that low GI diets might prevent the onset of CVD. The evidence obtained from this systematic review seems to be convincing enough to

recommend the use of low GI diets in improving markers for carbohydrate and lipid metabolism.

Regarding the systematic review about the effect of the GI on physical performance, evidence suggests that low GI compared to high GI pre-exercise meals provide a more stable metabolic response postprandially as well as in the early stages of exercise. However, most studies failed to show an improvement in exercise performance when comparing low GI and high GI pre-exercise meals, demonstrating that low GI meals have no additional benefits over high GI pre-exercise meals. However, athletes who are sensitive to carbohydrate feedings in the hour prior to exercise might benefit from low GI pre-exercise meals. During exercise it is recommended that CHO with high oxidation rates such as glucose, sucrose, maltose, maltodextrin and amylopectin (moderate GI to high GI) should be added to sport drinks. Low GI CHO such as fructose and galactose during exercise is not recommended due to its low oxidation rates as well as the fact that it slowly digested and absorbed which may result in gastrointestinal distress. High GI CHO recovery meals are recommended when the recovery period is short (0-8 hours), while low GI recovery meals are not recommended during short recovery periods since it is a poor substrate for glycogen synthesis. However, with a longer recovery period (20-24 h) the total amount of CHO ingested is more important than the frequency, timing and GI of the recovery meal.

3. Limitations of the study and suggested solutions

This section includes the limitations of the current study. A brief discussion on suggested solutions will be added:

- Regarding the meta-analysis, certain studies were not included because of incomplete baseline and end values as well as standard deviations (SD's) of variables. This could have influenced the results of the meta-analysis. The SD's of the differences between baseline and end values could not be calculated according to the Follman method used in the meta-analysis (Follman *et al.,* 1992). The authors of the studies that supplied incomplete data were contacted to supply comprehensive information. Unfortunately feedback was received from only one author. One option would be to summarise main outcomes and conclusions of those studies that were excluded and incorporate it into the discussion section. The other option would be to use a different statistical method such as the method of Petitti (Petitti, 2000) if no SD's of individual low GI and high GI differences for the specified studies were supplied. The variance of each study can then be calculated under two assumptions: firstly, the baseline and end values for each person were independent and secondly, the two values for each person were dependent and then calculated with the help of a correlation factor. Studies are then weighted by the

reciprocal of the variance. The overall effect is then estimated and 95% confidence intervals are then computed using these weights (Brand-Miller *et al.*, 2003).

- Studies with different study designs such as crossover and parallel studies were not separated, attributing the same weight to all the studies included. However, when study designs were separated, similar results were observed.

- Earlier studies might have been underpowered since as few as five or six subjects were included. Previous work from the author's laboratory indicated that if a 10% range for the GI of a food is sought with 80% confidence, between 24 and 90 subjects should be included in a study using venous plasma samples (Nell, 2001).

- The relatively short duration (2 weeks – 6 months) of the RCTs used in this meta-analysis.

- There has been doubt surrounding dietary compliance that compromises any free-living study with humans (Brand-Miller *et al.*, 2003). Tightly controlled nutrition studies are notoriously difficult to conduct. Variation in any study weakens its power and *ad-libitum* studies (where individuals can vary their energy intake) need greater numbers. Controlled metabolic studies have their own problems of regulating energy intake. Also, it is difficult to measure compliance. Furthermore, work with diets with a low GI or high GI is complicated by food choices and other factors such as fibre content and palatability. It is here that tightly controlled animal work can supplement human studies to overcome the problem of compliance (Daly, 2004). Pawlak and colleagues (2004) showed that diets with a higher GI could have adverse effects on body composition, postprandial glycaemia and insulinaemia and TG concentrations. They recently studied the effects of low GI *vs.* high GI diets on adiposity, glucose homeostasis and plasma lipids in partially pancreatectomised rats. Despite having similar mean bodyweight, rats fed high GI diets had more body fat, less lean body mass, greater increases over time in the areas under the curve for blood glucose and plasma insulin after oral glucose, lower plasma adiponectin and higher plasma TG concentrations as well as severe disruption of islet-cell architecture. Rats on the high GI diet had almost twice the body fat of those on the low GI diet after 9 weeks. Furthermore, rats with higher postprandial insulin concentrations at baseline were more susceptible to weight gain with the high GI diets. Pawlak *et al.* (2004) suggested that this increased susceptibility to weight gain might be related to improved insulin action in the periphery, because insulin sensitivity (in the insulin tolerance test) was unchanged and insulin concentrations were increased. However, a more simple explanation might be that adequate insulin-secretory capacity was necessary to achieve weight gain on diets with a high GI. However, the possibility remains that higher initial concentrations of insulin reflect reduced insulin sensitivity and, therefore, the insulin resistant rats gained the most weight on diets with a high GI. Perhaps a suitable parallel for partially pancreatectomised (insulin-resistant) rats in

human beings would be insulin-resistant individuals with impaired fasting glucose or impaired glucose tolerance that are a group very susceptible to adverse changes in lipids, insulin and bodyweight. Finally, these findings may provide a mechanistic basis for interpretation of studies of GI in human subjects

- From the results of the meta-analysis and systematic review, it is not known what the level of disease reduction that will come from intervention with low GI diets. There is a scarcity of published primary intervention studies with low GI foods that examine prevention of clinical disease in subjects at risk, such as those who are glucose intolerant. There appears to be improved pancreatic β-cell function with low GI diets among subjects who are glucose intolerant (Wolever and Mehling, 2002). Furthermore, in the STOP-NIDDM randomised, trial the glycaemic response to diet was reduced by slowing digestion with an α-glucosidase inhibitor (acarbose), consequently significantly fewer conversions of glucose-intolerant to type 2 diabetes patients and more reversions to normal were observed (Chiasson _et al._, 2002). It might be reasoned that low GI foods may have similar effects via the same mechanism. However, so far no studies have been conducted in humans on this mechanism. Nevertheless, the future burden of disease from diabetes (obesity, stroke and heart disease) is expected to overburden health budgets. Waiting for conclusive proof of the magnitude of efficacy of low GI CHO foods on clinical end points may, therefore, be unwise, given the suggested absence of risk from reduced postprandial glycaemia and the prospective evidence from epidemiological studies that low GI diets appear to lower the advent of type 2 diabetes, coronary heart disease and possibly stroke (all disease outcomes rather than biochemical markers of disease (Salmeron _et al._, 1997a, b; Liu _et al._, 2000; Liu, 2002; Hodge _et al._, 2004).

- The effect of low GI _vs._ high GI diets on insulin secretion/sensitivity has not been incorporated in the meta-analysis due to incompatible units and results that were reported with the help of response curves. Therefore, actual data were not available to calculate means and SD's, which the method of Follman _et al._ (1992) required. However, there is an increasing number of studies in a variety of groups of human subjects which are consistent with the hypothesis that diets with a lower GI may reduce insulin resistance (Wolever, 2000). Two studies by Frost _et al._ (1996; 1998) illustrated that there might be a positive association between the GI and insulin resistance. In their first study it was shown that 4 weeks of a low GI compared to a high GI diet tended to reduce the area under the glycaemic response curve in response to oral glucose and significantly reduced the insulin response area in patients who were at risk for developing coronary heart disease (CHD) (Frost _et al._, 1996). In the following study they found that a low GI compared to a high GI diet improves _in vitro_ insulin responsiveness of adipocytes from women at risk for cardiovascular disease (CVD) and improves _in vivo_ insulin sensitivity as

measured by the rate of fall of plasma glucose after an intravenous insulin injection (Frost *et al.,* 1998). Criticism towards these two studies is that they did not use validated tests such as the euglycaemic, hyperinsulinaemic clamp technique or the sampled intravenous glucose tolerance test (Wolever, 2000). Jarvi and associates (1999) studied the effect of low GI *vs.* high GI diets on insulin resistance in type 2 diabetic subjects. Significant lower daylong plasma insulin excursions and improvements in insulin sensitivity with low GI diets were observed when compared to high GI diets. Chiasson *et al.* (1996) studied the pharmacological inhibition of CHO absorption on insulin sensitivity in subjects with impaired glucose tolarance (IGT). IGT subjects received either acarbose or a placebo for 4 months. Insulin sensitivity was assessed by the insulin suppression test. Steady-state plasma, the measure for insulin sensitivity, did not change in the placebo group, but on acarbose, improved to within 1 SD of the mean of a group of age-matched controls. According to the authors, this improvement in insulin sensitivity could be attributed to the significant reduction in 12 h mean plasma glucose and insulin concentrations. However, an increase in colonic fermentation, as judged by significant increases in serum acetate and butyrate, was also observed. The short-chain fatty acids generated by colonic fermentation have effects on glucose metabolism which might influence insulin sensitivity (Wolever, 1995). Low GI foods may have the same effect by increasing the amount of CHO entering the colon (Food and Agriculture Organisation/ World Health Organisation, 1997). Most recent data from the cross-sectional Framingham Offspring Cohort, which examined the relationship between CHO related dietary factors, insulin resistance and the prevalence of the metabolic syndrome, illustrated a positive relationship between the GI and insulin resistance. Conversely, the prevalence of the metabolic syndrome, of which insulin resistance is part, was significantly higher among individuals in the highest relative to the lowest quintile category of the GI (Relative risk 1.41; 95% CI 1.04-1.91) (McKeown *et al.,* 2004). Finally, in a study by Harbis *et al.* (2004), they tested the hypothesis that subjects with central obesity and some degree of insulin resistance have postprandial alterations in both hepatic and intestinal lipoproteins that are influenced by the glycaemic and insulinaemic responses to a meal. Mixed meals with either rapidly available glucose (RAG) or slowly available glucose (SAG) were consumed. They found that in comparison with ingestion of a mixed meal rich in RAG, ingestion of a meal rich in SAG significantly lowered both the postprandial increase in insulinaemia and the accumulation of circulating TG and other TG-rich lipoproteins.

- Limitations for the systematic review about the GI and sport nutrition were that studies might have been underpowered due to the small number (5-9) of subjects that participated in the studies.

- Exercise protocols of the different studies were not comparable.

- Most data were not reported as means and SD's so that a meta-analysis could not be performed.

- Some of the studies did not provide standardised diets or meals prior to intervention to ensure equal muscle substrate concentrations amongst participants.

- The different GI's of the meals have not always been reported.

- In some studies meals given pre or post-exercise were not well described.

4. Integrated discussion

Evidence for and against the application of the GI has been accumulated during the past 20 years. Several organisations such as the American Dietetic Association (1999), the American Heart Association (Krauss *et al.*, 2000), the American Diabetes Association (2004) and individual scientists such as Coulston and Reaven (1997), Pi-Sunyer (2002) and Franz *et al.* (2003) question the usefulness of the GI in human health. Associations that endorse the application of the GI are the Joint Food and Agriculture Organisation/World Health Organisation Expert Consultation on Carbohydrates (Food and Agriculture Organisation/ World Health Organisation, 1997), the Dietitians' Association of Australia (1997), the European Association for the Study of Diabetes (Diabetes and Nutrition Study Group (DSNG) of the European Association for the Study of Diabetes (EASD), 2000), the New Zealand Dietetic Association (2000), the Canadian Diabetes Association (2000) and Diabetes UK (2003). Scientists who support the use of the GI in human health are Salmeron *et al.* (1997 a, b), Frost *et al.* (1998), Liu *et al.* (2000), Wolever (2003) and Brand-Miller *et al.* (2003), amongst others. Countries that have decided to use the GI in labelling of CHO containing foods are Egypt, Japan, Sweden and Australia. Although legislation regarding food labelling in South Africa has not yet been approved, the GI already appears on the labels of some South African beverages (Venter *et al.*, 2003).

4.1 Some objections against the use of the glycaemic index.

Reasons supplied by the American Diabetes Association (ADA) (2004) for not supporting the use of the GI is that although low GI diets may reduce postprandial hyperglycaemia, there is not sufficient evidence of long-term benefits to recommend the use of low GI diets as primary strategy in meal planning (B-level evidence). Additionally, the ability of individuals to maintain these diets long-term (and therefore achieve glycaemic benefit) has not been established. Furthermore, the application of the GI may severely limit the food choices of diabetics. Recommendations from the ADA, supported by A-level evidence, are that the total amount of CHO rather than the source or type of CHO is important and that foods containing CHO from whole grains, fruit, vegetables and low-fat milk should be included in a healthy diet (ADA, 2004).

Other points of criticism against the GI stem from the requirement that 50 grams of CHO must be consumed and then compared to 50 grams of a standard food like white bread or glucose to establish the GI of a food (Jenkins *et al.,* 1981). According to Pi-Sunyer (2002) these amounts of CHO do not reflect actual amounts of CHO contributed by individual foods in the usual diet. Franz *et al.* (2003) pointed out the example of carrots consumed in usual portion sizes would supply minimal amounts of CHO and despite having a high GI, would not elicit much of a glycaemic response. Pizza may have a lower GI, but the usual portion size consumed would contribute a considerably greater amount of total CHO, resulting in a higher glycaemic response. Pi-Sunyer (2002) also questioned the calculation of the area under the blood glucose response curve; factors that affect the reproducibility of the GI such as ripeness of fruit, physical form of foods and the variability within food classes; the effects of a combination of macronutrients (mixed meals) on the GI and also the predictability of the insulin response. Regarding mixed meals the argument of Coulston *et al.* (1987) was that the GI of each separate component of a meal cannot predict the glycaemic response to a meal. Furthermore, Coulston and Reaven (1997) are of the opinion that the emphasis must rather be on lower saturated fat intake, weight loss and substitution of refined CHO for whole grains than on the type of CHO.

Regarding the fibre content of food, Pi-Sunyer (2002) questioned the extent to which the fibre in a particular food is responsible for its GI. According to Pi-Sunyer (2002), the presence of naturally occurring fibre in foods has little effect on the glycaemic response of food. Comparison between brown and white rice, brown and white spaghetti and whole-wheat and white bread showed small differences in the GI, although the fibre content was quite different. Furthermore, Jenkins *et al.* (1981) could not find correlations between the GI and fibre content of a food, while Holt *et al.* (1997) found no relation between the postprandial insulin response and the fibre content of a food. This concern of Pi-Sunyer (2000) is justified. According to Björk *et al.* (2000), a high dietary fibre content is not a prerequisite for low GI properties in food and the naturally occurring levels of viscous fibre in common cereals have only marginal impact on glycaemia. Wholemeal cereal products, therefore, produce GI's as high as those of white bread. However, dietary fibre as part of an intact botanical structure as in barley and pumpernickel bread, may be effective in reducing glycaemia.

Other concerns that are frequently expressed are that the GI concept is too complex. It introduces another burden on patients who may be led to ignore other important nutritional recommendations and information about the GI of many familiar foods which may be difficult to find, especially when novel foods are introduced (Coulston & Reaven, 1997).

When the emphasis of the utility of the GI moves to physical performance, the argument is offered that it is not only the exhaustion of glycogen stores that leads to fatigue, but an alternative hypothesis attributes fatigue to a central (brain) governor. The function of this central governor is to prevent bodily damage. The central governor regulates the mass of skeletal muscle that is activated and then determines the appropriate exercise intensity that is safe under the prevailing conditions: less muscle mass is activated during hypoglycaemia and more when muscle glycogen stores are intact (Valeriani, 1991). According to this hypothesis, the GI of CHO ingested pre-exercise does not influence subsequent exercise performance provided CHO is ingested during exercise so that hypoglycaemia is prevented (Brand-Miller *et al.*, 2001).

4.2 *Support for the use of the glycaemic index*

Results on markers for carbohydrate metabolism from the published meta-analysis (Opperman *et al.*, 2004) are in accordance with the findings of earlier meta-analyses conducted by Brand-Miller (1994), Wolever (2003) and Brand-Miller *et al.* (2003). Some new findings on the effect of the GI on markers for lipid metabolism were also observed in this meta-analysis. The 1994 publication of Brand-Miller found a significant improvement of 9% in glycaemic control with glycosylated hemoglobin (HbA_{1c}) when low GI diets were compared to high GI diets. Fructosamine, TC and TG improved by 8%, 6% and 9% respectively, however, the changes were not significant. Wolever (2003) observed a highly significant reduction of 6.4% in glycated plasma proteins (HbA_{1c} and fructosamine), while Brand-Miller *et al.* (2003) found an improvement of 0.43% in HbA_{1c} and 0.2 mmol/l for fructosamine. When combining the results of the glycated plasma proteins, a 7.4% reduction was observed.

This meta-analysis also showed highly significant improvements in HbA_{1c} of 0.27% (P=0.03) and fructosamine of 0.1 mmol/l (P=0.05), however, the changes were not as explicit as with the other three meta-analyses due to exclusion of studies with incomplete data for the method that we used. Other reasons for differences between the results of the meta-analyses were different selection criteria used and the different time frames in which the studies were conducted. Some of the more recent published studies (Bouche *et al.*, 2002; Kabir *et al.*, 2002) were not submitted for publication when the meta-analysis of Brand-Miller *et al.* (2003) was compiled. Moreover, different subsets of data may have been used. For example Brand-Miller *et al.* (2003), reported the results of 104 subjects in their meta-analysis when the study of Gilbertson *et al.* (2001) were analysed, while this meta-analysis reported the results of 89 subjects, not taking the results of the drop-outs into account (Petocz, 2004). Other studies excluded were those of Jenkins *et al.* (1985; 1987), Wolever *et al.* (1992), Calle-Pascual *et al.* (1988), Fontvielle *et al.* (1988; 1992), Brynes *et al.* (2003), Gilbertson *et*

al. (2003) and Wolever and Mehling (2003). The main reason for exclusion of such high profile studies was that baseline and end values of variables were not included, therefore, standard deviations could not be calculated, according to the Follman method (Follman *et al.,* 1992). The HbA_{1c} data of Collier *et al.* (1988), who found a 27% decrease in HbA_{1c}, were excluded for the same reason, however, HDL-c and TG data were complete and have been included.

With the above-mentioned results in mind, an increasing realisation of the relationship between blood glucose control and non-communicable diseases is truly remarkable given that just over a decade ago starch in particular seemed as though it was just a source of energy and only because it seemed to help to cut the fat content of the diet. Postprandial hyperglycaemia is now emerging as one of the major risks that the public encounters and in the meantime, consumers in most countries are neither empowered via food labelling or local authoritative food tables nor advised to protect themselves in this regard. In addressing this problem, one ought not now lose sight of other possible dietary approaches and also consider a role for lower postprandial glycaemia as contributing to the benefits of both increased physical activity and energy restriction (Livesey, 2002).

For markers for lipid metabolism, the only other meta-analysis to report about the changes in the lipid profile when applying the GI was performed by Brand-Miller in 1994. Brand-Miller (1994) found only minor improvements in TC and TG, while in this study significant differences were found in TC and a tendency for LDL-c to improve with low GI diets. The reasons for these improvements are comprehensively discussed in the meta-analysis (Chapter 2). Additionally, since Brand-Miller's study in 1994, more studies have been conducted and subject populations were also larger. Results from the systematic review where findings from epidemiological studies were reported also supported the findings of the RCTs for markers for CHO as well as lipid metabolism. However, the RCTs were unable to show an improvement in HDL-c with shorter-term (2 weeks - 6 months) studies, while epidemiological data showed increases in HDL-c over long-term (>1 year) periods with low GI diets (see Chapter 3). Additional data from a follow-up cohort from the prospective cohort Nurses' Health Study II, only published in 2004 (Schulze *et al.,* 2004), similarly found a significant association between the GI and increased risk of diabetes comparable with the studies included in the systematic review (Schulze *et al.,* 2004). In addition, the glycaemic load (GL; the product of the GI value of a food and its CHO content) has been used to represent both the quality and quantity of the CHO consumed. However, dietary GL is more strongly associated with higher fasting TG and lower HDL-c levels compared with the GI. In a cohort of the Nurses' Health Study a strong positive association between GL and risk of CHD was observed among 75 521 women during 10 years of follow-up (Liu *et al.,* 2000).

The above-mentioned improvements on markers for lipid metabolism were found in studies where mixed meals based on high GI and low GI foods were consumed. These studies controlled for the effects of fat and protein. Criticism against mixed meals is that when individual CHO foods are taken as part of a mixed meal, differences in glycaemic responses between foods are abolished (Jenkins *et al.*, 1988). Discrepancies in results between studies where mixed meals with different GI's were consumed may be explained partially by methodological differences, principally the method of calculation of the glycaemic response area, method of blood sampling (venous *vs.* arterial blood) and the length of the study (the time between the meal and the last glycaemic measurement) (Augustin *et al.*, 2002). When using standardized methodology, the GI of mixed meals can be predicted consistently by calculating the mean GI value of their components weighted by the CHO content of each component and by the fact that the correlation between the GI of mixed meals and the mean GI value for their components ranges from 0.84 to 0.99 (Wolever & Jenkins, 1986; Wolever *et al.*, 1991).

It seems as if low GI diets are not only effective in improving markers for CHO and lipid metabolism but also for other variables. Research on thrombolytic factors such as plasminogen activator inhibitor-1, a marker of increased coagulation (Jarvi *et al.*, 1999); endothelial cell dysfunction (Couthino *et al.*, 1999); insulin resistance (Frost *et al.*, 1996); obesity (Ludwig *et al.*, 1999) and various types of cancer (Brunning *et al.*, 1992) have shown that low GI compared to high GI diets can play a preventative role in the prevalence of these conditions. Taken together, a low GI diet appears to have not only a therapeutic role, but also preventative potential (Bjork *et al.*, 2000). Therefore, existing evidence supports the clinical utility of the GI concept in human health.

Regarding the concerns that the GI concept is too complex, implementation of the GI is simpler than the vast tables of numerical values would suggest. Practical recommendations for the lowering of the GI of a diet include: use breakfast cereals based on oats, barley and bran; use grainy bread made with whole seeds; reduce the amount of potatoes (rather use cooled potato); enjoy all types of fruit and vegetables (except potatoes); eat plenty of salad vegetables with vinaigrette dressing (Brand-Miller, 2004); use peas, beans and lentils (as thickening agent); pasta, semolina and high amylose rice like Basmati (Slabber, 2004); make dried beans part of every meal; rather use greenish bananas than ripe bananas; mix lentils with rice and use barley in mixed dishes and soup. Furthermore, these suggestions do not limit food choices but actually expand the amount of CHO that can be used in meal planning.

The GI provides a new form of nutrition information which some athletes have already incorporated into their meal plans. However, the GI is not intended to provide a universal

system to rank the virtues of CHO rich foods. The nutritional content of the food, palatability, portability, cost, gastric comfort and ease of preparation may also be important attributes in preparation for events. These are often specific to the individual and the exercise situation, and the athlete should choose food according to his or her nutritional goals (Burke *et al.*, 1998). Furthermore, this systematic review shows that there is insufficient evidence to support universal benefits of low GI CHO-rich meals pre-exercise. There are, however, exceptions where low GI pre-exercise meals may be beneficial, for example, athletes who show an exaggerated and detrimental response to CHO-rich foods pre-exercise, or events in which the athlete cannot consume significant amounts of CHO during the session. In these cases, the pre-exercise meal may have a positive impact on metabolism and CHO availability during the event and a low GI CHO-rich meal may enhance performance by better maintaining CHO availability throughout the event.

Athletes are advised to consume CHO during prolonged exercise to enhance performance. According to Jeukendrup (2004), exogenous CHO oxidation is optimal at ingestion rates of 1.0-1.2 g/min. Athletes use a variety of CHO-rich drinks and foods to achieve this CHO intake during an event. Decisions on which CHO sources to use are based on previous experience, practical requirements of the event, gastrointestinal comfort and fluid needs (Burke *et al.*, 1998). Although no studies have been performed on the usefulness of the GI during exercise, it appears sensible that moderate GI to high GI CHO should be taken during exercise. Low GI CHO like fructose has a low oxidation rate and is slowly digested and absorbed, leading to gastrointestinal discomfort and a slow delivery of CHO to muscle during exercise. Moderate GI to high CHO-rich foods seem to enhance glycogen storage ingested post-exercise compared to low GI foods. Reasons for this are still speculative. While low GI CHO-rich foods can contribute to total CHO intake, it is reasonable to focus on CHO-rich foods and drinks with a moderate GI to high GI.

5. Conclusion

Low GI diets have clinical implications in the prevention and management of chronic diseases such as diabetes and cardiovascular disease. The literature proves that the low-fat/high-carbohydrate diets advocated by health organisations in Western countries could be further improved by including two low GI foods daily (Brand-Miller *et al.*, 1997), or including one low GI food at each meal or replacing 50% of CHO in the diet with low GI sources (Katanas, 1999). When introduced *ad-libitum* in the diet, low GI foods would often confer an array of advantages with their low energy density and discrete content of dietary fibre. Most evidence from biochemical markers suggests that low GI foods have a beneficial effect on markers for blood glucose control, however, more long-term research is needed to confirm low GI diet's effects on markers for lipid metabolism. Furthermore, it is still not clear what the

effect of low GI diets will be on endpoints such as cardiovascular disease. With the knowledge up to date, it seems that there is a place for low GI diets in disease prevention and management, particularly in populations characterised by already high incidences of insulin resistance, glucose intolerance and abnormal lipid levels. For the sporting community, there is insufficient evidence to support the use of low GI CHO pre-exercise, except when athletes are prone to develop hypoglycaemia when a CHO-rich meal is consumed pre-exercise. During exercise it is accepted that moderate GI to high GI CHO is beneficial, while post-exercise it seems that moderate GI to high GI CHO's are most efficient to restore glycogen levels.

6. Recommendations

Although one meta-analysis/systematic review cannot provide all the answers about the usefulness of the GI in human health as well as in sport nutrition, it can at least provide some directions for future research. Although one is a step closer confirming a place for the use of the GI in human health, additional basic and epidemiological research and large, multi-centre, prospective, randomised, controlled clinical trials with good compliance are required to investigate the effect of low GI diets further on LDL-c, HDL-c as well as TG. Such long-term studies are also essential to investigate the effect of low GI diets on endpoints such as CVD and DM. This research will also indicate whether low GI diets decrease the risk of complications of DM such as nephropathy and neuropathy. This requires GI testing of local products according to standardised *in vivo* methodology to expand the list of low GI foods so that dietary variety and palatability are not compromised. Furthermore, nutrition education is especially important to educate the public at large about the usefulness and application of the GI in meal planning. Regarding the GI and physical performance, more clinical trials should be conducted on the use of the GI during exercise as well as post-exercise. Although it is accepted that moderate GI to high GI CHO's are beneficial during exercise, the effect of the GI of CHO-rich foods and drinks during exercise has not been studied. So far only four studies have been performed on the application of the GI post-exercise. Therefore, more research is required to elucidate the mechanism of lower glycogen storage with low GI foods post-exercise. Furthermore, no studies exist investigating the effect of the GI in events which are of longer duration such as cricket or tennis matches. This is a weakness in sport nutrition and needs to be addressed.

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Appendices

Appendices

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