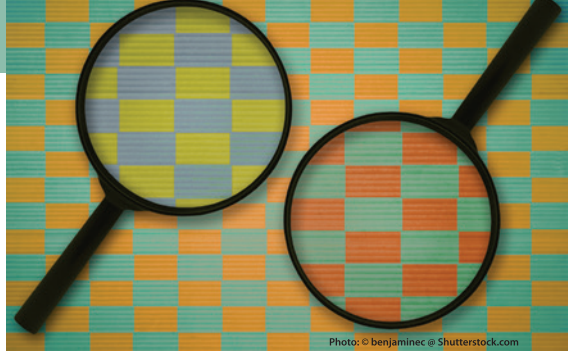
Point: Glycemic Index—An Important but Oft Misunderstood Marker of Carbohydrate Quality



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ABSTRACT

The glycemic index (GI) is a measure of carbohydrate quality that is supported by many international health organizations for the management of chronic diseases and is included on food labels in several different countries to help consumers make healthier food choices. Despite its endorsement by various health and governmental organizations, the GI concept remains controversial. The aim of this article is to address the most recent criticisms of the GI related to its accuracy, precision, and role in cardiometabolic disease prevention and management. Many of the criticisms appear to stem from a misunderstanding of the GI and do not undermine the best evidence from prospective cohort studies and randomized controlled trials, which show important clinical and public health benefits of reducing the GI of the diet.

The glycemic index (GI) was developed more than 30 years ago as a way to classify carbohydrate-containing foods based on their potential to raise blood glucose (1) and is considered a measure of carbohydrate quality (2). Since its introduction, GI values have been reported for more than 2,000 individual foods (3), and many international health organizations have come to support the use of GI in the management of diabetes and cardiovascular disease (CVD), including Diabetes Canada (4), the Canadian Cardiovascular Society (CCS) (5), the American Diabetes Association (ADA) (6), Diabetes Australia (7,8), Diabetes UK (9), the European Association for the Study of Diabetes (EASD) (10), and the European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) (11) (Table I). To help consumers make healthier food choices, the GI has also been successfully included on food labels in different countries, including Australia, New Zealand, the United Kingdom, and South Africa (12,13), and a proposal to introduce a GI symbol program for food labels in Canada has recently been made (14,15).

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Glycemic Index Criticisms and Rebuttals

Despite its endorsement by various health and governmental organizations (4,5,7–10,13), the GI concept has remained controversial since its inception. Over the past few decades several criticisms regarding the methodology and applicability of GI in human health and disease have been debated (Table II). The most recent criticisms have focused on the accuracy and precision of the GI, which has brought into question the value of GI in nutrition labeling and dietary recommendations (16–19). In particular, GI has been criticized for having high intra- and interindividual variation in values, raising concerns about the potential to misclassify foods as being low (≤55 on the glucose scale), medium (56–69), or high (≥70) GI (18,20–22). Most of these concerns, however, are related to glycemic response and not GI, which are not the same thing (19,23). People have a glycemic response to consumption of foods, which is a property of an individual that substantially varies within and between individuals; foods have a GI value, which is a property of a food that is assessed in individuals (i.e., humans are the "assay") and is reliable with the use of standardized methodology—namely the International Organization for Standardization (ISO 26642:2010) methodology (19,24).

These criticisms appear to stem, in part, from conflation of the variation in GI estimates within and between individuals with the GI within and between foods, the measurement of which is based on at least 2 tests of the reference food (glucose or white bread) in at least 10 individuals (19,23,24). A recent example of this common misinterpretation is seen in a study by Matthan et al. (18) in which the authors conclude there is "substantial variability in individual responses to GI value determinations, demonstrating that it is unlikely to be a good approach to guiding food choices." Using the standard deviation (SD) data from this study (SD = 15.3, n = 63) (18) or the SD data from the most recent interlaboratory study (SD = 9, n = 10) (25) for the measurement of GI, the highest margin of error for classification (10.9 based on a t distribution) would be much smaller than the difference between the high-GI and low-GI categories (i.e., 70–55 = 15 on the glucose scale). The result would be a <1% chance of misclassification of a low-GI food as a high-GI food. In fact, the measurement error of GI as expressed by its coefficient of variation (CV) of 17% (25) would meet the allowable variation for macronutrients or fiber (based on a ±20% tolerance limit, in which the amount measured is permitted to vary by up to 20% of the amount declared on the food label) set out in the food labeling requirements of both the U.S. Food and Drug Administration (FDA) (26) and the Canadian Food Inspection Agency (CFIA) (17,19,27).

Many of the criticisms, therefore, appear to stem from a misunderstanding of GI. It is important to continue to address these misunderstandings in order for progress to be made in

Table I. Glycemic index and glycemic load recommendations in diabetes and cardiovascular disease guidelines

Guideline	Recommendation	Grade Assessment
Diabetes Canada (4)	"Dietary advice may emphasize choosing carbohydrate food sources with a low glycemic index to help optimize glycemic control [type 1 diabetes [AND] type 2 diabetes]."	Grade B, level 2
American Diabetes Association (ADA) (6)	"Carbohydrate intake from vegetables, fruits, legumes, whole grains, and dairy products, with an emphasis on foods higher in fiber and lower in glycemic load, is preferred over other sources, especially those containing added sugars."	Grade B
Diabetes UK (9)	"Offer individualized education to support people to identify and quantify their dietary carbohydrate intake, encourage low glycaemic index foods and consider reducing the total amount of carbohydrates."	Not graded
Diabetes Australia (7,8)	"Commonly used diets for blood glucose control include low fat, high unrefined carbohydrate (approximately 25–30% of energy from fat and 50% of total energy from unrefined carbohydrate), or low glycaemic index diets usually both in combination with weight reducing advice."	Not graded
European Association for the Study of Diabetes (EASD) (10)	"When carbohydrate intake is at the upper end of the recommended range it is particularly important to emphasise foods rich in dietary fibre and with a low glycaemic index. (See recommendations on fibre, glycaemic index and micronutrients)."	Grade A
	"Carbohydrate-rich, low glycaemic index foods are suitable as carbohydrate-rich choices provided other attributes of the foods are appropriate."	Grade A
European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) (11)	"Lifestyle interventions to increase HDL-C levels…. Among carbohydrate-rich foods prefer those with low glycaemic index and high fibre content."	Grade C
Canadian Cardiovascular Society (CCS) (5)	"We suggest that all individuals be encouraged to…adopt a healthy dietary pattern to lower their CVD risk: [including]…ix. Low-glycemic load (GL)… or low-glycemic index (GI)…dietary patterns."	Conditional recommendation (low-quality evidence)
	"We suggest the following dietary patterns for LDL-C lowering: [including]… ii. Low GI dietary patterns."	Conditional recommendation (moderate-quality evidence)

this area and to help consumers make better dietary choices for their health.

Glycemic Index and Health Outcomes

Another main source of debate has been over whether the GI concept has meaningful advantages in the prevention and management of cardiometabolic diseases. Individual "negative" studies have often been invoked as evidence that the GI concept does not improve outcomes. A recent example is the OmniCarb randomized clinical trial (28), in which a low-GI dietary pattern failed to show improvements in insulin sensitivity, lipid levels, or systolic blood pressure. The accompanying editorial took the study as providing sufficient evidence to conclude that the GI concept may not be relevant for heart health (29). It has been correctly pointed out that this randomized controlled trial may have failed to show the expected improvements due to its short duration (<5 weeks), focus on relatively healthy insulin-sensitive individuals, and higher drop-out rate in the high-GI comparator arm (30). It is also only one among many studies of GI and cardiometabolic outcomes—the majority of which have longer follow-up durations and include individuals with a range of cardiometabolic phenotypes.

Systematic reviews and meta-analyses of the highest quality evidence from prospective cohort studies and randomized controlled trials have reached the opposite conclusion. Evidence from the most recent pooled analyses of >20 prospective cohort studies, involving >600,000 participants with 4–25 years of follow-up, show high-GI dietary patterns are associated with significant increases in incident type 2 diabetes (31), CVD (32), and coronary heart disease (CHD), especially in women (33,34), and a nonsignificant increase in incident stroke (35) (Fig. 1).

This observational evidence aligns with the evidence from randomized controlled trials (Fig. 2). The most recent systematic pooled analyses of >50 randomized controlled trials, involving >4,000 participants with 4–68 weeks of follow-up, show that low-GI diets reduce glycated blood proteins (HbA1c and fructosamine) in people with diabetes (36) by the equivalent of ~0.5% in HbA1c, an absolute reduction that is at the lower limit of efficacy of most antihyperglycemic agents and exceeds the FDA threshold of 0.3% for the development of new antihyperglycemic agents. These reductions are in addition to protective effects on blood lipids (total cholesterol and the primary lipid target for cardiovascular disease prevention, LDL-C) (37) and weight maintenance (38) in people with and without diabetes and on blood pressure in people without diabetes (39), all without any adverse effects on other cardiometabolic risk factors. Thus, the totality of the highest level of evidence used to support clinical practice guidelines and public health policy shows that reducing GI may have meaningful benefits for the prevention and management of diabetes and CVD—a conclusion shared by international diabetes and heart association guidelines (4–6,9,27,28).

Other Lines of Evidence

The large body of evidence supporting a causal role of low-GI interventions in cardiometabolic disease prevention is strengthened further by an important biological analogy. The α-glucosidase inhibitor acarbose, an oral prandial agent that effectively converts the diet to a low-GI dietary pattern, provides compelling evidence of the ability of an intervention that lowers GI to improve hard clinical outcomes (2). Individual randomized controlled trials (40,41) and systematic reviews and meta-analyses of randomized controlled trials (42,43) have shown that acarbose

Table II. Summary of major criticisms and rebuttals concerning major criticisms of the glycemic index (GI)

Criticism (against GI)	Rebuttal (for GI)
Accuracy and precision of GI	
1. GI methodology is not well standardized—The GI has been criticized for its methodological variations, with the complaint that "GI methodology is not well standardized and has several flaws" (23,47).	1. GI methodology is standardized—Determination of the GI and recommendation for food classification has been established and standardized via the International Organization for Standardization (ISO 26642:2010) (24); however, standardization of the methodology does not mean that it is used correctly (23,24,49).
2. High variation of GI values is seen within food categories in international GI tables—The GI value of wholemeal wheat flour bread, for example, varies from 52 to 87, encompassing both "low" and "high" GI classifications. High variation in GI is even seen in foods that require no preparation (e.g., the GI of raw apple varies from 28 to 44), diminishing usability (3,48).	2. Variations in GI values in international GI tables are due to real differences—Some of the variation may be due to methodological errors, but much of the variation is due to real differences among foods within the same category (see also counterpoint 3) (3,23).
3. GI values are influenced by many factors—Geographic location, maturity of food during harvest and consumption, processing, packaging, preparation, etc. of food items can potentially alter GI (7,8,16,48).	3. Various factors affecting GI values of foods can be beneficial—It is acknowledged that differences in variety, growing conditions, processing, etc. can affect GI; however, this provides an opportunity to reduce GI without making major changes to the nature of one's diet (23). Furthermore, several studies show no significant effect of age, gender, BMI (body mass index), ethnicity, or glucose tolerance on mean GI values (23,49–51).
4. High variation in GI between individuals makes it unreliable for guiding food choices—Healthy individuals exhibit different glycemic responses than those with glucose intolerance, prediabetes, or diabetes. Even between healthy individuals glycemic responses are variable (7–9,18).	4. Concerns about high between-individual variation are related to glycemic response, not GI values, which do not differ significantly among individuals (50,52). Although within-individual variation does influence the accuracy and precision of GI values, GI methodology has been designed to minimize these effects (23,24).
5. High variation in GI within individuals makes it unreliable for guiding food choices (18,49).	5. Variation in GI values has been misinterpreted—Although there can be high within-individual variation in GI values, there is not high variation in the GI values of foods, which are based on the means of estimates for at least 10 subjects (19,23,49). Accordingly, GI values are not intended to indicate what an individual's glycemic response will be on any one eating occasion, but rather to indicate which carbohydrate-containing foods, on average, will produce relatively lower or higher glycemic responses, where low-GI foods will produce lower responses and high-GI foods will produce higher responses.
6. GI methodology is not precise enough for clinical utility (47,48).	6. GI is clinically useful—GI methodology can distinguish between low-GI (≤55 on the glucose scale) and high-GI (≥70) foods with ≥95% certainty (17,23) and, thus, can be used clinically to classify foods as being low, medium, or high GI, with the advice of consuming low-GI foods more often.
7. The GI does not apply to mixed meals (8).	7. Comparing mixed meals with the same macronutrient composition, meal GI is closely correlated with glycemic response (53)—Numerous factors independently influence the glycemic response associated with mixed meals, including GI and the amounts of fat, protein, and carbohydrate they contain (23).
8. Addition of fat and protein to carbohydrate-containing foods changes the GI—Consumption of white bread (a high-GI food) with cheese, for example, will result in a reduced GI value (8).	8. Similar to the counterpoint for mixed meals (counterpoint 7), adding fat and protein sources to a food does not change the GI of that food, it changes the glycemic response to the combination of food components (53). In the example of adding cheese to white bread, the GI value of the white bread remains the same, because the GI is a property of the food, while the glycemic response observed following consumption of white bread and cheese together is influenced both by the GI of the white bread and the separate effect of the cheese. It follows that if one were to consume the same combination as a low-GI bread (e.g., coarse rye kernel bread [3,54]) with cheese, then the glycemic response would be even lower. The more relevant question is what kind of bread will you choose to eat with the cheese?

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reduces incident type 2 diabetes, hypertension, CVD, myocardial infarction, and stroke in people at risk for type 2 diabetes (40,41,43) and myocardial infarction and CVD in people with type 2 diabetes (42); these reductions correspond with improvements in glycemic control and blood pressure that are similar to those seen in low-GI interventions (36–43) and have estimates that overlap with those observed for the association of low-GI dietary patterns with the same clinical outcomes (i.e., the 95% CIs contain the reciprocal of the estimates for the associations of high-GI dietary patterns with type 2 diabetes, CHD, and stroke) (31–35).

Research Priorities

There remains a need for more research to address the existing uncertainties regarding GI. The available studies have identified several limitations, including the incorrect use of methodology to measure GI and a failure to achieve large enough differences in GI (>15 on the glucose scale) between intervention and control arms in randomized trials. To help address these limitations, it is suggested that policy makers, grant committees, and journal editors enforce the use of standardized GI methodology in the design, conduct, and reporting of future intervention studies (5). Future trials should also consider the use of metabolically controlled (full or partial) designs, with the provision of key low-GI study foods to ensure sufficient differences in GI are achieved. Several longer term randomized trials conducted in individuals with diabetes have already taken this approach and have achieved large differences in GI that corresponded to significant improvements in cardiometabolic risk factors (44–46).

Conclusions

Overall, many of the criticisms of GI appear to stem from misunderstanding of its meaning and utility. GI is a property

Table II. *(continued from previous page)*

Criticism (against GI)	Rebuttal (for GI)
Applicability of GI	
1. The GI is too complex, making it difficult to learn and follow (55).	1. GI education is feasible and successful—Studies show clinicians and clients can understand and apply GI knowledge and skills, resulting in reductions in dietary GI (61–63).
2. There is a lack of reliable GI education tools (56).	2. Educational tools have been created and continue to be developed by clinicians and researchers—These resources are available through associations such as Diabetes Canada and Dietitians of Canada (64,65). In some countries inclusion of GI information on food labels is permitted, including Australia, New Zealand, the United Kingdom, and South Africa (12,13,66), and has been proposed in other countries such as Canada (14,15).
3. The GI does not reflect the overall healthfulness of a food—It has been argued that the GI is limited as an indicator of carbohydrate quality because many high-GI foods, such as whole grains and starchy vegetables, are linked to positive health outcomes, whereas some low-GI foods, such as foods high in fructose and other nutrients of concern, are linked to negative health outcomes (16,23,57–59). Furthermore, through the encouragement of consumption of low-GI foods that are high in fructose and other nutrients of concern, the GI could be used to promote the intake of "unhealthy" foods that do not align with dietary guidelines promoted by government agencies (16).	3. All else being equal, the GI does reflect the healthfulness of a food—The GI is intended to be included as part of standard dietary guidelines, not as an alternative, stand-alone dietary recommendation (67). Additionally, it is incorrect to assert that all whole grains and starchy vegetables have a high GI, because the GI of both of these types of foods and their metabolic effects vary widely depending on type, variety, composition, and processing (23). In addition, the effects of fructose are not uniform. Whereas overfeeding of fructose has been shown to have adverse metabolic effects, small to moderate doses in the context of weight-maintaining diets have shown improvements in glycemic control and blood pressure without any adverse metabolic effects, suggesting that overconsumption is the issue (68–70). Although some low-GI foods can be high in fructose or other nutrients of concern, this issue is not unique to the GI and applies equally to whole grain and fiber, both of which can be used in cakes, cookies, and sugary breakfast cereals. To address this concern, nutrient-profiling criteria can be used to prevent "unhealthy" foods from carrying low-GI claims, a system that is already well established to regulate health claims for fiber from oats, barley, and psyllium in the United States and Canada, as well as low-GI claims in Australia and New Zealand (17).
4. The GI is not as good an indicator of carbohydrate quality as is dietary fiber or whole grains (59), and it is difficult to discern the independent effect of fiber compared with that of GI on glycemic control and other outcomes (60).	4. The GI is a good indicator of carbohydrate quality—Low-GI diets have at least as many, if not more, statistically significant effects on health outcomes as do diets high in whole grains or dietary fiber. The three markers of carbohydrate quality also tend to be complementary, with a combination of shared and separate effects on cardiometabolic risk factors. Although it is true that low-GI diets may have some of their shared effects mediated by the effects of the dietary fiber (especially viscous fiber) they contain, it is the GI more than the fiber that predicts cardiometabolic effects (23). Therefore, there is no need to disentangle the relative contributions of the different factors. The focus should be on whether, as a marker of carbohydrate quality, the GI helps to improve health outcomes.
5. The GI does not respond to serving size, whereas glycemic response does, thus it is more appropriate to focus on glycemic response to help guide food choices (16).	5. Reducing glycemic response does not necessarily improve health outcomes—The effect of reduced glycemic response on health depends on how the glucose response is reduced. Because GI does not vary in response to the amount of food consumed, it allows for more direct comparisons between food products with standardized serving sizes (17).
6. The GI is only applicable to those with diabetes, not to the general (nondiabetic) population (16).	6. The GI is applicable to the general population for prevention of various chronic diseases, such as diabetes and cardiovascular disease, as evidenced by findings from systematic reviews and meta-analyses (31–34).

of food, the purpose of which is not to indicate what an individual's glycemic response will be on any one eating occasion, but rather to indicate which carbohydrate-containing foods will produce, on average, relatively lower or higher responses (19). As such, many of the criticisms do not call into question the validity of GI or undermine the evidence from prospective cohort studies and randomized controlled trials that when taken together show important clinical and public health benefits of reducing the GI of the diet. The GI remains an important marker of carbohydrate quality that can be considered complementary to other markers of carbohydrate quality, such as dietary fiber, and food-based approaches, such as whole grains, dietary pulses, and fruit.

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Competing Interests

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Cardiometabolic Disease Outcome	SRMA	No. Cohort Comparisons	N	No. Events	Follow-up Duration, *yrs*	Pooled Effect Estimates RR (95% CI)	RR (95% CI)	I^2
CVD	Ma et al. 2012	17	356 031	7708	6-18	1.13 (1.04, 1.22)		15.2%
CHD	Fan et al. 2012	12	297 053	7137	5-25	1.13 (1.04, 1.22)		32%
	Mirrahimi et al. 2012	12	233 655	6940	6-25	1.11 (0.99, 1.24)		45%
Stroke	Cai et al. 2015	10	225 205	3046	5-18	1.10 (0.99, 1.21)		23%
T2DM	Bhupathiraju et al. 2014	20	437 047	35 715	4-24	1.19 (1.14, 1.24)		68.5%

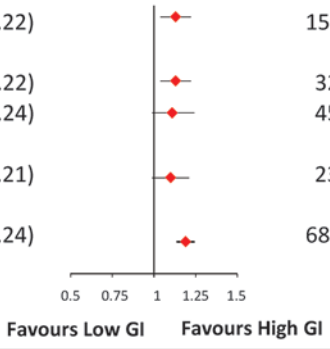

Fig. 1. Summary of findings from most recent systematic review and meta-analyses (SRMAs) of prospective cohort studies assessing the relationship between glycemic index (GI) and cardiometabolic disease outcomes. CHD = chronic heart disease; CVD = cardiovascular disease; N = number of participants; RR = relative risk; T2DM = type 2 diabetes mellitus.

Cardiometabolic Risk Factor	SRMA	No. Trial Comparisons	N	Participant Characteristics	Achieved GI in Control	Achieved GI in Intervention	Follow-up Duration, *wks*	Pooled Effect Estimates MD (95% CI)	SMD (95% CI)	SMD (95% CI)	I^2
Glycemic Control											
HbA1c, *%*	Schwingshackl et al. 2013	4	486	Mixed	~64.8	~72.9	24–52	-0.09 (-0.52, 0.33)	-0.21 (-1.20, 0.76)		72%
	Wang et al. 2015	15	738	Diabetes	-	-	2–144	-	-0.42 (-0.69, -0.16)		64%
FG, *mmol/L*	Schwingshackl et al. 2013	13	2059	Mixed	~54.2	~63.4	26–68	0.03 (-0.07, 0.12)	0.17 (-0.40, 0.69)		52%
FI, *pmol/L*	Schwingshackl et al. 2013	11	1741	Mixed	~53.4	~62.7	24–68	-5.16 (-8.45, -1.88)	-0.93 (-1.52, -0.34)		48%
Fructosamine	Wang et al. 2015	9	148	Diabetes	-	-	2–12	-	-0.44 (-0.82, -0.06)		50%
Blood Lipids											
TC, *mmol/L*	Goff et al. 2013	27	1441	Mixed	~63.5	~47.0	4–52	-0.13 (-0.22, -0.04)	-0.54 (-0.92, -0.17)		0%
LDL-C, *mmol/L*	Goff et al. 2013	23	1281	Mixed	~63.4	~47.3	4–52	-0.16 (-0.24, -0.08)	-0.82 (-1.23, -0.41)		0%
HDL-C, *mmol/L*	Goff et al. 2013	24	1331	Mixed	~63.4	~47.1	4–52	-0.03 (-0.06, 0.00)	-0.40 (-0.80, 0.00)		0%
TG, *mmol/L*	Goff et al. 2013	27	1412	Mixed	~63.5	~46.5	4–52	0.01 (-0.06, 0.08)	0.05 (-0.32, 0.43)		0%
Body Weight & Adiposity											
BW, *kg*	Schwingshackl et al. 2013	16	2325	Mixed	~64.2	~52.4	24-68	-0.62 (-1.28, 0.03)	-0.46 (-0.96, 0.02)		0%
WC, *cm*	Schwingshackl et al. 2013	10	1726	Mixed	~61.8	~55.9	24-68	0.06 (−0.83, 0.96)	0.06 (-0.83, 0.96)		0%
Fat mass, *kg*	Schwingshackl et al. 2013	6	868	Mixed	~62.0	~52.2	24-68	-0.56 (-1.24, 0.12)	-0.66 (-1.46, 0.14)		0%
Blood Pressure											
SBP, *mmHg*	Schwingshackl et al. 2013	13	2034	Mixed	~62.5	~51.7	24-68	0.08 (−1.12, 1.28)	0.04 (-0.51, 0.58)		0%
	Evans et al. 2017	16	1097	Healthy	~61.9	~50.3	8-52	-1.13 (-2.51, 0.25)	-0.40 (-0.89, 0.09)		8.5%
DBP, *mmHg*	Schwingshackl et al. 2013	13	2034	Mixed	~62.5	~51.7	24-68	-0.75 (-1.71, 0.21)	-0.42 (-0.97, 0.12)		13%
	Evans et al. 2017	16	1097	Healthy	~61.9	~50.3	8-52	-1.26 (-2.30, -0.22)	-0.59 (-1.08, -0.10)		19.7%

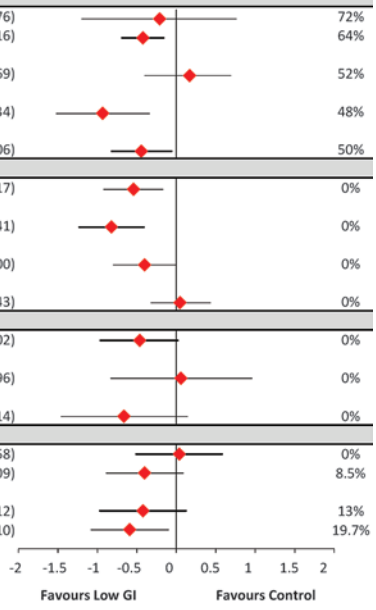

Fig. 2. Summary of findings from most recent systematic review and meta-analyses (SRMAs) of randomized controlled trials assessing the effect of low-glycemic index (GI) diets on cardiometabolic risk factors. To allow summary estimates for each end point to be displayed on the same axis, mean differences (MDs) were transformed to standardized mean differences (SMDs) and pseudo-95% CIs, which were derived directly from the original MD and 95% CI. Achieved GI = average GI of intervention or control arm across all trials included in the meta-analysis; BW = body weight; DBP = diastolic blood pressure; FG = fasting glucose; FI = fasting insulin; MD = mean difference; Mixed = participants with different metabolic phenotypes; N = number of participants; SBP = systolic blood pressure; SMD = standardized mean difference; TC = total cholesterol; TG = triglycerides; WC = waist circumference. (Figure adapted from several figures in Ha et al. [71])

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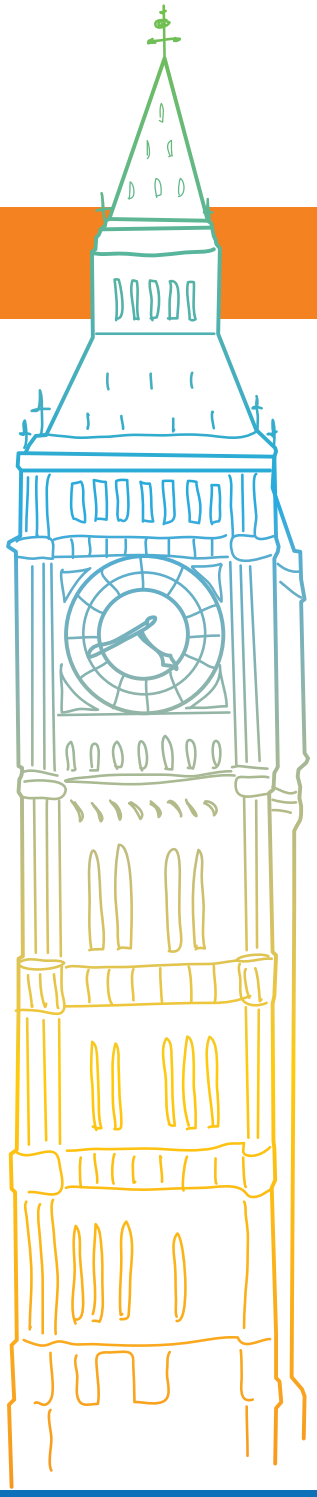

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