



The **overweight/ obesity** **epidemic** revisited

Low fat, low carb, or Mediterranean?

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Abstract

The prevalence of obesity is of monumental concern and has been growing at an exponential rate over the last few decades. Abdominal adiposity is associated with cytokine perturbations leading to prothrombotic and proinflammatory states and these metabolic changes promote cardiometabolic complications. To date, body mass index (BMI) has been strongly and positively linked to an increase risk of type 2 diabetes, cardiovascular disease, sleep apnea, osteoarthritis, dyslipidemia, asthma and certain cancers. Aside from increased co-morbidities obese and overweight populations have a decreased life expectancy compared to their normal weight counterparts. Modest caloric restriction based on energy expenditure is favored long-term over very low calorie diets. Dietary interventions based on macronutrient proportions alone seem over simplistic and fail to demonstrate any clinically relevant difference in weight loss. Weight loss in general improves cardiometabolic parameters; however, no other diet supports the primary and secondary improvement of hard outcomes such as cardiovascular mortality and all-cause mortality as the MedDiet. Both the Mediterranean Diet (MedDiet) and a Low Glycemic Diet (LGD) show effective weight loss results as well as important improvements in common comorbidities. A modified low-glycemic MedDiet includes smaller more frequent meals, moderate consumption of healthy fat (olive oil), high intake of vegetables and fruit, low quantities of red meat using poultry and fish to replace beef and lamb, and the inclusion of high fiber, LG whole grains. Obesity must be viewed as a chronic condition since weight regain is common. A maintenance dietary program, continual support and behavioural strategies are critical for long-term success.

The prevalence of obesity is of monumental concern and has been growing at an exponential rate over the last few decades (WHO 2002). In 2004, according to the Canadian Community Health Survey, 23.1% of adult Canadians were obese (body mass index= 30kg/m²) and an additional 36.1% were overweight (body mass index= 25kg/m²). To give perspective on the magnitude of concern this represents six out of every 10 Canadians are overweight or obese (Tjepkema 2005). Abdominal adiposity is associated with cytokine perturbations leading to prothrombotic and proinflammatory states (Grundy 2004, Grundy 2008) and these metabolic changes promote cardiometabolic complications (Grundy 2004). To date, body mass index (BMI) has been strongly and positively linked to an increase risk of type 2 diabetes, cardiovascular disease, sleep apnea, osteoarthritis, dyslipidemia, asthma and certain cancers (Fabricatore 2006, NHLBI 1998, Schelbert 2009, Tjepkema 2005).

Aside from increased co-morbidities obese and overweight populations have a decreased life expectancy compared to their normal weight counterparts (Peeters 2003). Despite the significance of this prevalence, an initial weight loss of 5-10% can confer positive improvements in cardiometabolic risk factors regardless of initial BMI (Fabricatore 2006, NHLBI 1998). Dietary intervention is an essential component of a comprehensive weight loss strategy and is considered first line therapy in numerous guidelines (NHLBI 1998). Furthermore, the ideal dietary intervention would not only be effective for weight loss but would also prevent, stabilize or reverse the most common

associated comorbidities. A therapeutic lifestyle intervention can be an effective strategy in high risk individuals with coronary heart disease (Gordon 2004). Dietary interventions as they relate to weight loss and the most common comorbidities are the subject of this review.

Regulation of Body Weight and Energy Balance

Daily caloric expenditure depends on three basic elements: basal metabolic rate (BMR), post meal thermogenesis and non-exercise activity thermogenesis. Total caloric expenditure is the sum of an individual's daily caloric expenditure and exercise induced caloric expenditure. It is well accepted that overall caloric deficiency must be induced for weight loss to occur (Schelbert 2009). Regulation of caloric intake is influenced by the central nervous system. Research is burgeoning in this field and the following neuropeptides have been shown to influence eating behavior by modulating hunger and satiety: vagal stimulation, cholecystokinin, Apolipoprotein A-IV, insulin, PYY, Glucagon-like peptide-1, other glucagon-related peptides, leptin, gherlin, tumor necrosis factor- α and obestatin (Jensen 2011).

Physiologic Impact of Caloric Deficiency

Dietary caloric restriction antagonizes weight loss efforts by reducing BMR through reductions in thyroid hormones, triiodothyronine (T₃) from thyroxine (T₄) as well as preferential use of lean muscle mass over adipose tissue for energy. This phenomenon can be mitigated by the inclusion of exercise which favors the maintenance of lean muscle tissue and increases BMR (Jensen 2011).

Dietary Interventions for Weight Loss

Caloric Restriction

Caloric restriction is a critical component of successful weight loss (Schelbert 2009). A very low calorie diet (VLCD) is defined as less than 800 kcal/day while a low calorie diet (LCD) is defined as 800-1350kcal/day. A meta-analysis of randomized trials evaluated the efficacy of caloric restriction on short and long term efficacy of weight loss. At the end of six months the average lost was 16.1% and 9.7% of body weight in the VLCD and LCD respectively (Tsai 2006). Despite this initial short statistical difference between the two diets, a greater regain of weight in the VLCD was seen which subsequently equalized the benefits of the diets by one year so that there was no difference in weight loss between the groups (Tsai 2005).

The literature is devoid of studies assessing the long-term metabolic impact of caloric restriction (Kim 2008). A study by Wadden (1990) assessed the influence of caloric restriction influence on thyroid hormones: T3, T4 and reverse T3. Reverse T3 (rT3) is the enzyme responsible for converting T3 (the more active thyroid hormone) to the less active T4. In the VLCD group serum T3 was reduced by 66% while rT3 increased by 27%. When the VLCD group returned to a LCD thyroid function increased but remained 22% lower than baseline at the end of study (Wadden 1990). Further research is needed to better understand if T3 depression and rT3 augmentation effect are temporary or longer term.

Moderate caloric restriction based on estimated total energy expenditure is preferred over VLCD long term. Mild caloric deficiency will result in less antagonizing reflective mechanisms, less thyroid suppression and less BMR suppression. Even with successful weight loss obesity should be viewed as a chronic condition as long-term weight gain is common and should be monitored regularly (Wadden 1993).

Macronutrient Quantity

Many commercial and popular diets tout that their clinical weight loss success is based on a particular combination of carbohydrate, protein and fat. This topic has indeed earned the interest of several investigators.

Low Carbohydrate, High Protein Diet vs. Low Fat, High Carbohydrate Diet

A systematic review analyzed 13 randomized controlled trials that compared low carbohydrate, high protein (LC/HP) 'ketogenic'

diet to low fat, high carbohydrate (LF/HC) diets. By 12 months a statistically significant difference of 1.05 kg ($P < 0.05$) favored the LC/HP diet (Hession 2009). Despite a statistical significance at 12 months it is questionable whether a modest 1.05 kg difference is of clinical significance at 12 months.

LC/HP Diet vs. LF/HC Diet vs. MedDiet

A two-year prospective trial evaluated three diets head to head. An LC/HP diet according to Atkin's guidelines, LF/HC diet according to the American Heart Association guidelines and a Mediterranean Diet (MedDiet). The caloric restriction for LF/HC and MedDiet was 1500 kcal per day for women and 1800 kcal a day for men. The LC/HP diet was restricted based on 20g of carbohydrates per day (Shai 2008).

The greatest amount of weight loss occurred in the first six months for all diet types. At six months, LC/HP showed the most significant weight loss. At the two-year mark, the MedDiet and the Atkin's diet demonstrated a close to equal average weight loss of 4.4kg and 4.7kg respectively. The LF/HC diet demonstrated inferior weight loss throughout the two-year period with an average 2.9kg of weight loss (Shai 2008). Systematic reviews and prospective studies have consistently reproduced these findings. The statistical differences between the diets are inconsistent at the end of one year. After two years weight regain to some degree is common across all diet types. At two years the LF/HC appears to be inferior to the Mediterranean and LC/HP diet to questionable degree of clinical relevance.

Protein vs. Carbohydrate vs. Fat

A study by Sacks and colleagues (2009) investigated four diet groups based on intakes of carbohydrates, protein and fat. All four groups received the same guidelines for healthy choices of each macronutrient. At six months, 12 months and 24 months there were no significant differences between the four groups regarding weight loss, satiety, hunger and satisfaction with the diet. The greatest weight loss was seen at six months and regain began after 12 months. All diets improved fasting insulin levels and cholesterol panels equally, possibly reflecting a decrease in adiposity and cytokine perturbation rather than the diets (Sacks 2009).

Therefore, from a simple weight loss perspective the optimal diet may be patient dependent since compliance and adherence are the greatest predictors for weight loss (Fabricatore 2006).

“Reduced-calorie diets result in clinically meaningful weight loss regardless of which macronutrients they emphasize (Sacks 2009).”

Impact of Glycemic Index and Glycemic Load on Weight Loss

Glycemic index ranks foods based on the rate that they impact blood sugar levels. Glycemic load is a reflection of the glycemic index plus the total absolute amount of carbohydrates (Wolever 1991). Factors that decrease the glycemic index are the co-ingestion of carbohydrates with fat, protein and/or fiber.

The glycemic index (GI) and glycemic load (GL) of the average North American diet has increased as food-processing advancements and refined carbohydrate intake have risen (Ludwig 2002). High glycemic index/load diets among individuals without diabetes are associated with physiological 24-hour hyperglycemia, hyperinsulinemia, higher C-peptide excretion and higher glycosylated hemoglobin (Hb A1C) concentrations. Homeostasis of glucose are tightly regulated by the endocrine pancreas via insulin and glucagon. A high glycemic-index meal results in rapid postprandial hyperglycemia leading to reactive hyperinsulinemia. Two to four hours postprandial following a high glycemic meal, mild hypoglycemia occurs inducing hunger and hyperphagia in order re-establish homeostasis. This cycle has metabolic consequences promoting weight gain. Furthermore, this chronic glucotoxicity can lead to β -cell failure and increase the risk of type II diabetes. A low glycemic index meal induces a milder, more prolonged and controlled release of insulin and return to euglycemic state resulting in better glycemic control and satiety (Ludwig 2002).

A randomized controlled trial assessed four diets: high carbohydrate or high protein with low or high GI respectively. Lowering the GI in the high carbohydrate diets resulted in the doubling of fat loss from 2.8kg to 4.5kg in 12 weeks. In the high-protein diets GI did not impact fat loss. In addition, women were more responsive to changes in glycemic index (McMillan-Price 2006). Two Cochrane reviews support low glycemic index/load meals for both the treatment of obesity (Thomas 2007) and glycemic control of type II diabetes (Thomas 2009).

Critical review of the Cochrane database concluded that there was statistically and significantly greater weight loss in the low glycemic diet (LGD) group as compared to the LF diets. Parameters such as weight loss from fat mass improved as well as satiety. In addition, the resting energy expenditure was not antagonized to the same degree as in the low fat group (Pereira 2004). High GI and GL diets are associated with higher weight gain, fat mass and waist circumference (Hare-Bruun

2006). The limitations of the current research are inconsistent cut-offs between LGD and HGD. This may contribute to some inconsistencies in the literature (Esfahani 2011).

Weight loss can be realized by a degree of caloric deficiency, regardless of macronutrient proportions. Nonetheless, one of the greatest hurdles of weight loss is the very common subsequent weight regain. Typical Western diets induce high glycemic responses that promote postprandial carbohydrate oxidation rather than fat oxidation. This may be a plausible mechanism for the long-term promotion of weight gain. Low glycemic diets support weight control by promoting satiety, maintaining insulin sensitivity and blunting insulin secretion (Brand-Miller 2002).

Dietary Intervention Impact on Mortality and Common Comorbidities

From a simplistic weight loss perspective the review of the literature indicates a slight superiority of the MedDiet and LC/HP diet over that of the LF/HC. The clinical relevance of these findings is disputable given the negligible magnitude of difference on weight loss. Individuals who are overweight and obese are at increased risk of various comorbidities. Choosing a dietary intervention for weight loss should place a special emphasis on the impact the dietary intervention could have not only on weight loss but also on mortality and common comorbidities.

LF/HC Diet and Cardiometabolic Risk Factors

As reviewed a LF/HC diet has the tendency to be a higher in carbohydrates notably higher simple carbohydrates resulting in an overall higher glycemic index diet. It positively impacts triglyceride to a much lesser degree than both the LC/HP and MedDiet. Furthermore, the LF/HC promotes less glucose control than the Mediterranean Diet (Shai 2008).

HP/LC Diet and Cardiometabolic Risk Factors

A HP/LC diet has been associated with higher mortality from all causes (Trichopoulos 2007), increased risk of renal stone formation, high renal acid load, negative calcium balance and theoretically increased risk for bone loss (Reddy 2002, Fung 2010). While offering benefit relative to a LF/HC diet for the endpoint of weight loss as reviewed above, such a list of complications is concerning. Recommendation of such a strategy for long-term weight maintenance should be done with caution.

MedDiet and Cardiometabolic Risk Factors

The MedDiet has shown positive impact on various health parameters including mood, cognition, erectile function and endothelial function (Féart 2009, Giugliano 2010, Rallidis 2009,



Sánchez-Villegas 2009). The MedDiet impacts risk factors such as cholesterol panel improvements as well as reducing the risk of subsequent coronary events (de Lorgeril 2008, Shai 2008).

The MediDiet resulted in a 52% four-year relative risk reduction in the incidence of type II diabetes in high-risk individuals (Salas-Salvadó 2011). With regards to secondary prevention among individuals newly diagnosed with type II diabetes there were 26% fewer individuals started on antihyperglycemics at the end of four years in MedDiet group as compared to the American Diabetic Association diet. We could expect to see much greater impact if the MedDiet was compared to a typical western diet.

Weight loss in general improves cardiometabolic parameters; however, no other diet supports the primary and secondary improvement of hard outcomes such as cardiovascular mortality and all-cause mortality as the MedDiet.

A Low-Glycemic Modified MedDiet, The Future?

A Cochrane review confirmed that glycemic control is improved in a low-glycemic index diet without any increased risk of hypoglycemic events (Thomas 2009). A low glycemic index diet improves glycemic control among individuals with normal glucose control as well as individuals with type II diabetes (Thomas 2009), and improves body composition (Thomas 2007). Combining both the low glycemic diet with MedDiet food composition seems a promising future to synergize their independent benefits.

Adjunctive Consideration on Weight Loss

Several adjunctive treatments have appeared to enhance the results of diets. Adding structure to the diet with menus, recipes and

grocery lists improved weight loss (Fabricatore 2009, Heymsfield 2003, Wing 1996). The added structure of incorporating partial meal replacement has also been shown to produce greater weight loss than a conventional weight loss diet alone (Heymsfield 2003). Non-dietary interventions also play a major role in a comprehensive therapeutic lifestyle intervention. It is beyond the scope of this review to discuss these in any detail but their importance should be noted. Behavioural strategies including cognitive behavioural therapy, motivational interviewing, social support network and exercise regimen synergistically improve adherence, compliance, effectiveness and body composition.

Summary

Modest caloric restriction based on energy expenditure is favored long-term over very low calorie diets. Dietary interventions based on macronutrient proportions alone seem over simplistic and fail to demonstrate any clinically relevant difference in weight loss. Both the MedDiet and a LGD show effective weight loss results as well as important improvements in common comorbidities. A modified low-glycemic MedDiet including smaller more frequent meals, moderate consumption of healthy fat (olive oil), high intake of vegetables and fruit, low quantities of red meat, using poultry and fish to replace beef and lamb, the inclusion of high fiber, and LG whole grains appears to be a desirable intervention strategy given the current state of the literature. The plan must be individualized to the needs of each patient, however, and certain cultural/ religious/ personal preferences may force modification in order to maximize long term compliance. Obesity must be viewed as a chronic condition since weight gain is common. A maintenance dietary program, continual support and behavioural strategies are critical for long-term success. •

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