



## Technical Report

# Optimal Dietary Approaches to Reduce Cardiometabolic Risk

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## Optimal Cardiometabolic Diets

*The frequent emergence of new popular diets has presented a great challenge to healthcare practitioners in forming of clear and conclusive recommendations regarding the optimal diet for cardiometabolic health. While newer data has yet to be implemented into formal guidelines, research has already made clear that dietary changes are one of the most potent therapies available for the prevention of type 2 diabetes and cardiovascular disease. Therefore, in light of the rapidly growing cardiometabolic epidemic, it is imperative to understand the influence of and identify the most optimal dietary patterns for reducing cardiometabolic risk, as well as the most successful strategies for implementing dietary changes. This paper will review the data and make an evidence-based recommendation for the optimal dietary patterns for reducing cardiometabolic risk.*

### Introduction

Diabetes and cardiovascular disease (CVD) are two of the biggest health burdens of our time. Heart disease and stroke are responsible for more deaths among Americans of both genders and all racial and ethnic groups than any other disease category; in 2004, the WHO estimated 16.7 million deaths per year attributable to CVD, accounting for 29.2% of total global deaths each year.<sup>1</sup> Furthermore, in 2010, the CDC predicted that 1/3 of the adult U.S. population will have diabetes by the year 2050. These numbers indicate that the “diabetes epidemic” is likely to continue even if obesity numbers remain the same; however, given the increasing prevalence of obesity, it is likely that current figures may actually underestimate future diabetes prevalence.<sup>2</sup>

What has emerged from the past decades of research is the realization that we can no longer assess risk in patients by ignoring the complex relationships between these two chronic disease patterns. Therefore, terms such as “cardiometabolic risk,” which encompasses the risk relationship between the classic definitions of cardiovascular disease and diabetes, are very helpful. Under this new umbrella and its related terms (Metabolic Syndrome, Syndrome X, Insulin Resistant Syndrome), the clinician of today is taught to understand the disease process rather than simply its manifestations. The clustering of components driving cardiometabolic risk are many; but the key factors include central obesity/adiposity, insulin resistance, increased inflammatory burden, and atherogenic dyslipidemia. An abundance of research is now available to show that specific dietary patterns, especially those that drive glycemic/insulin dysregulation and obesity will profoundly increase cardiometabolic risk. Conversely, dietary interventions which specifically aim to reverse these physiological patterns are related to lower cardiometabolic risk and can be the basis of preventative and intervention strategies.

### The epidemiological link between diet and cardiometabolic risk

Dietary patterns have changed dramatically in the U.S. over the last 100 years and increasing numbers of studies have shown that the changes in food distribution and consumption have been harmful for the populations that consume them, leading to a higher risk of chronic disease. Findings from a multitude of population-based, prospective cohort studies have uncovered evidence linking modern dietary patterns with nearly every cardiometabolic risk factor. Hu and Willett have reviewed much of the data on diet and heart disease risk and have consistently found that diets consisting of saturated fat, trans-fatty acids, high glycemic load, and low folate are related to increased risk of coronary heart disease (CHD); while diet consisting of polyunsaturated and monounsaturated fats,

omega-3 fatty acids, low glycemic load and diets high in fruits and vegetables consistently lower cardiometabolic risk in populations that consume them.<sup>3,4</sup> Typical Western diets characterized by high consumption of sugar-sweetened beverages, refined carbohydrates and processed meats, are also repeatedly found to be associated with a significantly increased risk for type 2 diabetes mellitus (DM).<sup>5,6</sup> Furthermore, data from the Nurses' Health Study (NHS) cohort shows that this same dietary pattern is associated with increased inflammatory biomarkers and endothelial dysfunction, two key factors in cardiometabolic risk mediation.<sup>5</sup> Glycemic load, a key dietary parameter, was also positively associated with risk of stroke in the same Nurses' cohort.<sup>7</sup>

The following summarizes some of the common dietary trends and their impact on cardiometabolic (CM) risk:

Dietary trends that increase CM risk

Higher intake of:

- Saturated fat
- Trans fats
- Carbohydrates (glycemic load)
- Red meat
- Sodium

Dietary trends that reduce CM risk

Higher intake of:

- Monounsaturated fat
- Polyunsaturated fat
- Fruits and vegetables/potassium
- Fish
- Nuts
- Folic acid
- Low glycemic load

**National Dietary Guidelines**

One of the main outcomes of the epidemiological evidence linking typical Western dietary trends to CVD and type 2 DM risk factors was the institution of various national dietary guidelines, such as those of the American Diabetes Association and the American Heart Association, which aim to provide authoritative advice about how good dietary habits can promote health and reduce risk for major chronic diseases. The National Cholesterol Education Program (NCEP), launched by the National Heart, Lung, and Blood Institute (NHLBI), issued specific recommendations within its Adult Treatment Panel III (ATP III), evidence-based guidelines on cholesterol management in May 2001. In light of newer findings on cardiometabolic disease, the revised ATP III guidelines include enhanced recommendations including therapeutic lifestyle changes (TLC).<sup>8</sup>

The TLC diet suggests the following guidelines:

- Reduce saturated fat to < 7% of calories
- Reduce cholesterol to < 200 mg/day
- Increase viscous or soluble fiber (10-25 g/day) including oats, barley, psyllium
- Include 2 g/day plant stanols/sterols<sup>9</sup>
- Guidelines also include weight management and increased physical activity

The efficacy of the TLC diet plan has been shown in clinical trials and a number of studies have looked at the TLC in combination with more specific food components which are

promoted by the AHA for cardiometabolic health, such as soy proteins and nuts. This “Dietary Portfolio,” a vegetarian diet which combines four groups of cholesterol-lowering components of plant origin, including viscous fibers, soy protein, plant sterols and almonds,<sup>10</sup> was examined in a landmark study published in JAMA in 2003, in which the Dietary Portfolio was compared to a statin. The randomized, controlled trial of 46 hyperlipidemic adults found that the dietary portfolio group had a mean 28.6% decrease in LDL cholesterol, which was nearly the same as the statin group (30.9%), and well above the placebo (8.0%).<sup>11</sup> Another 2008 study found that the Dietary Portfolio also significantly reduced blood pressure due to almond intake, and suggested that combining cholesterol-lowering plant foods could benefit CVD risk by reducing both serum lipids and blood pressure.<sup>12</sup> The Dietary Portfolio has also been shown to reduce C-reactive protein, a key cardiometabolic inflammatory marker, similarly to a first generation statin.<sup>13</sup>

The Dietary Approaches to Stop Hypertension or DASH diet was another early dietary approach which focused on dietary patterns for controlling hypertension, the leading cause of heart attack, stroke and kidney disease.<sup>14-17</sup> Major trials on the DASH diet, funded by the National Heart, Lung, and Blood Institute, were based upon the results of observational studies which noted the protective effects of vegetarian diets against high blood pressure. DASH investigators hypothesized that a diet rich in fruits, vegetables and low-fat dairy would act in synergy to lower blood pressure,<sup>18</sup> and the goal of the original 1997 trial was to identify an acceptable dietary pattern that lowered blood pressure in the general population. The original DASH diet was:

- Low in saturated fat, cholesterol, and total fat
- High in fruits, vegetables, and fat-free or low-fat milk and milk products
- Inclusive of whole grain products, fish, poultry, and nuts
- Lower in lean red meat, sweets, added sugars, and sugar-containing beverages, compared to the typical Western diet
- Rich in potassium, magnesium, and calcium, as well as protein and fiber<sup>9</sup>

The trials found that the DASH diet lowered systolic and diastolic blood pressure, as well as total, LDL and HDL cholesterol.<sup>14</sup> In a later study, beneficial effects on LDL and other components of metabolic syndrome were also seen.<sup>19,20</sup>

## **Cardiometabolic diets**

Though the TLC and DASH diets effectively address high cholesterol and hypertension, research continued to seek out more specific dietary interventions which may reverse the physiological patterns associated with higher cardiometabolic risk, especially insulin sensitivity. Some of the accumulating research has spawned a debate over the past decades about the benefits of reducing calories from fat and cholesterol, versus reducing caloric intake from carbohydrates. The result is a deeper understanding of the complex nature of both fat and carbohydrates as macronutrients and an emphasis on the fact that not all fats and carbohydrates are equal in their benefits or detriments. One example would be the notion that hydrogenated

polyunsaturated fats, which are rich in trans-fats, should be consumed in place of saturated fats to prevent heart disease. We now know that these fats actually increase LDL and total cholesterol and promote an atherogenic profile.<sup>21-23</sup> It is now also known that the nutritional value of refined carbohydrates such as white bread differs greatly from that of high fiber whole grains and that they have very different effects on insulin and glycemic control. Research has found that among similar diets which differ in glycemic index, diets with a lower glycemic impact exert a more beneficial effect on CVD risk factors, and nearly all measures of insulin resistance and atherogenic lipoprotein measures.<sup>24-31</sup>

In the past decade, two dietary patterns have become popular, leading to numerous well-designed clinical trials with regards to cardiometabolic risk. These are the Mediterranean diet and the low carbohydrate diet; both of which emphasize the replacement of high glycemic carbohydrates with monounsaturated and polyunsaturated fats or protein, respectively, and include some of the key elements of the TLC and DASH diets.

### Low carbohydrate diet

The low carbohydrate/high protein diet is a popular method for weight loss around the world, whether by the more extreme version popularized by Dr. Atkins, or other commonly used low carbohydrate diets such as the *South Beach Diet*<sup>32</sup> and *The Zone*.<sup>33</sup> A low carbohydrate diet can be defined by a fixed amount or percentage of total carbohydrates in the diet or by lowering a diet's glycemic load; the latter of which can be achieved when dietary carbohydrate content is rich in dietary fiber, instead of sugars and starch. While early studies questioned the safety and long term impact of low carbohydrate diets on health, recent research shows consistent positive evidence for their efficacy not only in weight loss but also in controlling various biomarkers of cardio-metabolic risk due to the glycemic impact of reducing carbohydrates.

One systematic review of 13 randomized, controlled trials on low carbohydrate diets (include less than 60 g of carbohydrates per day) vs. low-fat/high carbohydrate diets (30% or less daily energy from fat) revealed that low carbohydrate and high protein diets are as or more effective at 6 months than low-fat/high carbohydrate diets in reducing both weight and the overall risk of CVD, for up to 12 months.<sup>34</sup> Low carbohydrate diets significantly improve HDL levels at 6 and 12 months and reduce systolic blood pressure after 12 months. While this review found total cholesterol to be elevated in low carbohydrate diets, it was suggested that this finding is likely explained by the increase in beneficial HDL levels.<sup>34</sup> Another key study looked at the differences in cardiometabolic risk factors of high protein or high carbohydrate diets in overweight and obese adults, focusing on dyslipidemia and post-prandial insulin response, which was measured with a mixed meal challenge (similar to a glucose tolerance test). Post-prandial response at 1 and 2 hours was found to be significantly lower in the high protein group, as were lower fasting insulin levels,<sup>35</sup> suggesting benefits of a low carbohydrate diet for insulin sensitivity.

### Mediterranean Diet

The Mediterranean diet is one of the most well-known diets for promoting cardiovascular health. Modeled upon the traditional diets of Greece, Spain, southern Italy, Portugal, and Turkey, the diet was popularized by the book *Eat, Drink and be Healthy*, though even as early as the

fifties and sixties, researchers noted that those who lived in the Mediterranean region had a much lower risk of heart disease than populations consuming a Western diet, despite a high intake of monounsaturated fatty acids.<sup>36,37</sup> An early, large study on 13,000 subjects that spanned 30 years confirmed the exceptionally low death rates of the Cretan population from heart disease.<sup>36,37</sup>

The traditional Mediterranean diet is characterized by a high intake of:

- fresh and cooked vegetables and fresh fruits
- legumes/plant proteins and whole grains
- fresh fish
- nuts and olive oil

and includes

- moderate intake of wine
- moderate intake of dairy, mainly yogurt & cheeses
- low consumption of red meat, refined grains and sugary foods<sup>38</sup>

The Mediterranean diet has grown in popularity over the years and is recommended for its benefits in lowering rates of CVD, cancer and cognitive decline, as well as its ability to increase longevity.<sup>39</sup> Its high phytonutrient content and substitution of refined and high glycemic foods with monounsaturated fats are largely responsible for the positive data on lower cardiometabolic risk factors in those following a Mediterranean diet. The diet has also been shown to reduce immune cell activation and decrease concentrations of inflammatory biomarkers such as C-reactive protein related to atherogenesis,<sup>40</sup> both important factors in the development of cardiometabolic risk. A meta-analysis of 7 prospective studies published in the last 2 years found that a 2-point increase in adherence to the Mediterranean diet was associated with a significant reduction of overall mortality (RR = 0.92; 95% CI: 0.90, 0.94), and cardiovascular incidence or mortality (RR = 0.90; 95%; CI: 0.87, 0.93), confirming the significant and consistent protection provided through adherence to the Mediterranean diet.<sup>41</sup>

While both diets have clear benefits for lowering cardiometabolic risk, there are subtle but important differences in the mechanisms of each diet which modulate the reduction of risk factors in each diet. In one key, long-term study, each of these popular diets was compared to a low-fat diet with the aim of assessing their efficacy in facilitating weight loss. Over 300 moderately obese subjects were divided into 3 diet groups. The low-fat, restricted calorie diet was based on AHA guidelines, and aimed for 1500 kcal per day for women and 1800 for men, with 30% of calories from fat, 10% from saturated fat, and an intake of 300 mg cholesterol per day. The Mediterranean diet was a moderate fat, restricted calorie diet rich in vegetables and low in red meat and emphasizing poultry and fish. The low carbohydrate diet was non-restricted in caloric intake and aimed to provide 20 g carbohydrates per day with a gradual increase to 120 g to maintain weight loss. Participants on the low fat diet lost a mean of 2.9 kg, while higher averages of 4.4 kg were lost in the Mediterranean group and 4.7 kg in the low carbohydrate group. All three groups experienced significant decreases in waist circumference and blood pressure, though the reduction in this marker was not statistically significant. The low carbohydrate group experienced the greatest increase in HDL cholesterol levels and reduction in triglyceride levels, and both the Mediterranean and low carbohydrate groups experienced significant decreases in the inflammatory marker, C-reactive protein during both weight loss and

maintenance phases. In addition, diabetic patients on the Mediterranean diet experienced a decrease in fasting glucose levels, while those on the higher carbohydrate diet had increased levels of this marker.<sup>42</sup>

Table 1<sup>42</sup>

| Change in value       | Low-fat (24 mo)  | Med. (24 mo)     | Low Carb (24 mo) |
|-----------------------|------------------|------------------|------------------|
| Fast. Glucose (mg/dL) | not depicted     | D: -32.8 ND: 3.1 | D: 1.2 ND: 1.3   |
| Fast. Insulin (mU/ml) | D: -1.5 ND: -1.4 | D: -4.0 ND: -1.8 | D: -2.2 ND: -3.7 |

D-Diabetic

ND-Non-diabetic

Table 2<sup>42</sup>

| Change in value         | Low-fat (6 mo) | Low-fat (24 mo) | Change in value         | Low Carb (6 mo) | Low Carb (24 mo) |
|-------------------------|----------------|-----------------|-------------------------|-----------------|------------------|
| HDL Cholesterol (mg/dL) | 1.7            | 6.4             | HDL Cholesterol (mg/dL) | 4.8             | 8.4              |
| LDL Cholesterol (mg/dL) | -0.2           | -0.05           | LDL Cholesterol (mg/dL) | 1               | -3               |
| Triglycerides (mg/dL)   | -11.7          | -2.8            | Triglycerides (mg/dL)   | -40             | -23.7            |
| CRP (mg/L)              | -0.2           | -0.5            | CRP (mg/L)              | -0.7            | -1.3             |
| Change in value         | Med. (6 mo)    | Med. (24 mo)    |                         |                 |                  |
| HDL Cholesterol (mg/dL) | 2              | 6.3             |                         |                 |                  |
| LDL Cholesterol (mg/dL) | -4.3           | -5.6            |                         |                 |                  |
| Triglycerides (mg/dL)   | -23            | -21.8           |                         |                 |                  |
| CRP (mg/L)              | -0.5           | -0.9            |                         |                 |                  |

While the diabetic participants experienced greater benefits in markers of insulin sensitivity on the Mediterranean diet, non-diabetic subjects were influenced more profoundly by the reduction in carbohydrates. The greater benefits experienced by diabetics on the Mediterranean diet was likely due to the higher content of insulin-sensitizing phytonutrients in that diet, which, in light of these participants' reduced pancreatic beta cell function, would have a greater impact on insulin sensitivity in peripheral tissues such as muscle and fat. Non-diabetic study participants experienced a greater benefit from the reduction of carbohydrates, as a result of the heightened sensitization of their cells to insulin. These findings highlight the benefits of each diet in improving biomarkers of cardiometabolic risk, including components of insulin resistance and inflammation, in various populations.

### A low glycemic Mediterranean diet

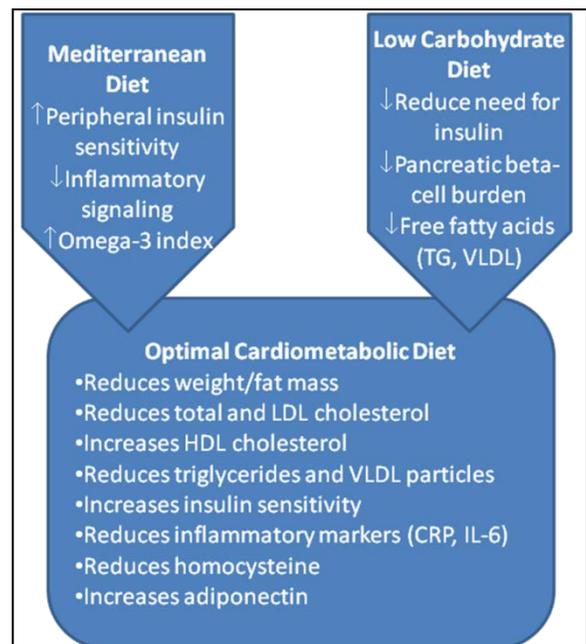
Recently, newer studies have shown evidence that specific elements of each of these diets may work in synergy to yield an even more significant impact on cardiometabolic health. While the benefits of the low carbohydrate diet stem from reduced carbohydrate content, the Mediterranean diet's focus on plant-based foods, including herbs and spices, as well as key features like the inclusion of large quantities of monounsaturated fatty acids, in the form of olive oil and nuts are key components which contribute to its cardiometabolic benefits.

In a recent study on overweight patients with type 2 DM that compared a traditional Mediterranean diet with a low carbohydrate -Mediterranean diet and to the current ADA diet

over 12-months, the combination low carbohydrate -Mediterranean diet was found to be superior in improving glycemic control and caused a significantly greater reduction in HbA1C and increased HDL levels<sup>43</sup>. Another key intervention on the combined diets compared the traditional Mediterranean diet with a Mediterranean diet enriched with soy protein and phytosterols, and a low glycemic load diet. A more than twofold improvement was found in total cholesterol, non-HDL cholesterol, triglycerides (TG), cholesterol/HDL, and TG/HDL, when phytosterols, soy protein, hops and acacia were added to the diet.<sup>44</sup> Additionally, at 12 weeks, almost double the number of subjects on the phytonutrient-enriched diet experienced a resolution of their metabolic syndrome, compared with the traditional Mediterranean group.<sup>45</sup>

Other important components of the Mediterranean diet include an emphasis on ample fish, moderate amounts of cultured dairy products and beneficial polyphenols from red wine, as well as the importance of enjoying meals with family and friends. The enhancement of glycemic control through the selection of unprocessed, high fiber foods and the higher phytonutrient content of the Mediterranean diet are both examples of the diet's glycemic impact. The glycemic impact of a food or meal takes into account the impact of the all the other macronutrients (proteins, fats, non-digestible carbohydrates, fermentable fibers) and micronutrients (vitamins, minerals, phytonutrients) that impact glucose disposal and insulin secretion. While many are familiar with glycemic index (GI), a number that reflects the glycemic effect of *available carbohydrates* in food relative to the effects of an equal amount of glucose, and glycemic load (GL), the amount of carbohydrate exposure over a certain length of time (calculated by taking the GI/100 and multiplying this by the weight of the food and the percent of available carbohydrates in the food), both GI and GL are based on relative units and do not correlate easily to grams of total carbohydrates or calories consumed.

Soluble and fermentable fibers (carbohydrates that can be fermented into short chain fatty acids by gut micro-flora), appear to have an especially profound effect on glycemic impact, not only on the glycemic response of the initial meal consumed, but on subsequent meals, as well. Research from the Lund University in Sweden has shown that a single breakfast meal containing high amounts of soluble and fermentable fibers will decrease the glycemic impact of the subsequent lunch and dinner meals.<sup>46</sup> This effect was also noted for fibers consumed in the evening; impacting the glycemic response of the breakfast meal.<sup>47,48</sup> Consequently, combining a phytonutrient-rich, Mediterranean diet with a focus on fiber-rich, low glycemic carbohydrates allows one to reap the benefits of both diets.



### **Key Dietary Recommendations**

When implementing a low Glycemic impact, Mediterranean diet, low glycemic carbohydrates should comprise about 40% of the diet, protein should comprise another 30% and fats 30%. Some of the main foods to emphasize in such a diet are as follows:

- fresh and cooked vegetables and fruits
- legumes/plant proteins and whole grains
- fish and chicken
- moderate intake of wine
- moderate dairy: yogurt & cheeses
- nuts, olive oil
- low consumption of red meat, refined grains and sweet foods

### Other Dietary Recommendations:

- Increase both soluble and fermentable fiber content and supplement the diet, if necessary, with soluble and fermentable fibers (FOS, inulin etc.)
- Reduce the frequency of refined carbohydrate consumption (i.e. white bread, white pasta, muffins, cakes and cookies) and focus instead on whole grains-based foods
- Increase phytonutrients by using brightly colored vegetables, spices and herbs to improve insulin sensitivity
- Do not skip breakfast as this meal sets the tone of blood sugar stability for the day
- Consider small, high protein snacks between meals to keep blood sugar stable
- Remember that even small decreases in weight or increases in physical activity can have tremendous benefits and emphasis should be placed upon improving insulin sensitivity and decreasing inflammation

### **Conclusion**

The cardiometabolic epidemic will have a major impact on global public health in the next fifty years, and addressing it effectively requires a shift from the current medical paradigm towards lifestyle therapies. Implementing and educating patients about diet plans such as a low glycemic Mediterranean diet that addresses overall cardiometabolic risk is an integral aspect of prevention and treatment and offers physicians and patients an alternative to pharmacological agents for attaining optimal glycemic control and reducing cardiometabolic risk.<sup>43</sup> Helping each patient find a dietary pattern that will allow them to attain optimal health, while enjoying the foods they choose, is part of the lost art of healing.

*“Let food be thy medicine and medicine be thy food” - Hippocrates*

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