

Use of The Mediterranean Diet to Manage Progression of Type 2 Diabetes

By

Christopher B. Orange

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Dr. Paul Chelminski, MD, MPH, FACP
Director and Clinical Professor of Medicine
UNC-Chapel Hill PA Program

Date

John Vrnak, PA-C
Chapel Hill Internal Medicine

Date

Introduction

The various aspects that comprise metabolic syndrome such as pre-diabetes, dyslipidemia and pre-hypertension epitomize prodromal phases of severe cardiometabolic disorders.¹ Lifestyle modifications have demonstrated the ability to mitigate or arrest the subsequent advancement of various components of metabolic syndrome. The cardio protective benefits of the adoption of the Mediterranean diet have been well established in the medical literature. But can this supposed panacea be more effective in preventing the progression from pre-diabetes to type 2 diabetes than traditional pharmacological interventions such as the use of Metformin? That is what this paper will endeavor to ascertain.

Adherence to the Mediterranean diet has been touted as the most ideal way to maintain overall good health and prevent the onset of certain disease processes.² However the traditional Mediterranean diet usually referenced in academic literature is not a distinct or unique diet, it is in fact an amalgamation of dietary patterns adhered to by the various populations of the numerous countries that lay on the verge of the Mediterranean Sea. The diet points to a nutritional pattern readily accessible in the Mediterranean in the 1960's that includes complex carbohydrates, vegetables, fruits, legumes, with olive oil as the primary source of fats and low to moderate amounts red wine and lean animal protein such as chicken & fish.² Adherence to this dietary practice has been shown to lower the probability of onset of chronic diseases and lower the risk of mortality in various extensive epidemiological studies.²

Pathophysiology

A diagnosis pre-diabetes indicates impaired glucose tolerance (IGT) along with impaired fasting glucose (IFG). Together they represent a transitional stage with diabetes on one end of the spectrum and normal glucose tolerance on the other.¹ IGT is characterized with a plasma glucose reading of 140-199 mg/dl 2 hours after consumption of 75 gm oral glucose solution, IFG is characterized with a fasting plasma glucose of 100-125 mg/dl.¹ IGT & IFG give patients an increased probability of advancement to type 2 diabetes.

The development and full manifestation of type 2 diabetes is in and of itself a seminal event but it also increases the probability and severity of certain other disease processes; namely being in a pre-diabetic state raises one's risk for cardiovascular disease. If one then advances to an established diagnosis of type 2 diabetes there is an associated increased probability of stroke, CVD and peripheral vascular disease in comparison with patients w/o the same disease burden in the general population.¹ There appears to be a corollary relationship between macrovascular disease and the state of pre-diabetes, many patients that display hypertriglyceridemia, hypertension, insulin resistance, lowered HDL cholesterol and upper body obesity are pre-diabetic even if they do not carry that official diagnosis.¹ The constellation of signs and symptoms of metabolic syndrome can be seen concurrently or retroactively before an official diagnosis of Type 2 DM is made.¹ (All issue of metabolic syndrome can be mitigated with Med Diet)

Metabolic Syndrome

	Men	Women
Central obesity	Waist > 40 inches	Waist > 35 inches
Fasting triglycerides	> 150 mg/dL	> 150 mg/dL
Low HDL-C	< 40 mg/dL	< 50 mg/dL
Blood pressure	> 130/85	> 130/85
Fasting glucose	> 110 mg/dL	> 110 mg/dL

Persistent over abundance of the body's primary fuel source glucose is the main pathogenic circumstance that leads to the development of type 2 diabetes mellitus in persons who are genetically or more importantly epigenetically predisposed to presentation of this disease state.³ However not all people who are overweight and whose caloric intake exceeds daily requirements develop type 2 diabetes. In some the glucose intolerance remains minimal or non existent, and some people store the extra energy consumed in the form of subcutaneous adipose tissue as opposed to having it deposited to the pancreas, liver, heart, skeletal muscles. This is due to a compensatory mechanisms of the islet B-cells that keep blood nutrient levels within normal range i.e. blood glucose levels, nominal accrual of liver fat, lower amounts of visceral adipose tissue as opposed to subcutaneous adipose tissue and the limited presence of insulin resistance.³ Through these compensatory factors vital organ systems do not undergo longer term damage.

In individuals who go on to develop type 2 diabetes the aforementioned compensatory are hindered, minimally present or absent all together. When combined with other metabolic factors-the evolution of tangential resistance to insulin, systemic inflammation of adipose tissue, elevated glucagon secretion and lowered incretin reaction, elevated internal glucose production the failure of the islet B-cells to indemnify for surplus glycogen inexorably leads to the development of diabetes mellitus may occur.

Epidemiology

The approximated prevalence of diabetes in adults worldwide was 285 million in 2010. Striking are the projections that this figure is forecasted to increase by an estimated 154 million by 2030.³ Type 2 diabetes is by far the most common form encompassing almost 90% of cases. The increase is estimated to be much more drastic in 2nd and 3rd world nations. This sharp rise in the prevalence of type 2 diabetes is no doubt connected to the these developing countries increased rates of obesity linked to the gradual adoption of what some would term a traditional western diet.³

Twenty to thirty years ago the incidence of type 2 diabetes mellitus was unusual in developing countries, and in the most populated country in the world China the proportion was estimated to be less than 1%.⁴ However a large percentage of the burden of future cases will not be incurred by developed western countries, but by developing countries in Asia and the Middle East, with only 20% of cases of type 2 diabetes occurring in the developed world. The causes of this are multifactorial. In Asia the primary causal agents are increased urbanization

driven by robust economic development which in turn has led to a change in traditional dietary trends i.e. shift toward a more western diet with higher proportions of meat, processed foods and saturated fat.⁴

Type 2 Diabetes is becoming the preeminent chronic disease of our time, diabetes is the primary cause for non-traumatic limb amputation, end stage renal failure and blindness along with being the main driver of increased incidence of CVD, heart disease and PVD as previously noted.¹ Polycystic ovarian syndrome and non-alcoholic fatty liver disease have also been linked to type 2 diabetes.³

Financial & Pub Health Implications

With the current status of Type 2 Diabetes Mellitus as “Primus Inter Pares” with respect to other chronic medical conditions and the preeminence it is projected attain with respect to future healthcare expenditures and resources-it is worthwhile to explore the true cost of this pervasive disease process.

The straightforward costs of the disease burden of DM in the form of increased medical expenditures is well known and somewhat easier to quantify; however, the hidden costs in the form of diminished quality of life, diminished work productivity and career analogous absences

are less well known but often not taken into consideration when mitigation measures are considered and undertaken at a macroeconomic level.⁵ A study from 2007 by the American Diabetes Association estimated an increase of 174 billion dollars in expenditures on care related to diabetes along with diminished productivity.⁵ With the number of individuals in the US living with type 2 DM expected to increase to an estimate of one third of the population by 2050 and healthcare spending accounting for almost 18 percent of Gross Domestic Product (GDP) or 3.2 trillion dollars it is easy to see how the projected increased incidence of DM and its ancillary problems could put a considerable burden not only on the US healthcare system but on the entire economy as a whole.⁵⁶

It is believed that those living with Diabetes Mellitus tend to utilize healthcare resources at a higher rate than persons without diabetes. This is primarily due to the fact that diabetes raises your probability of ophthalmic, renal, cardiovascular, neurological and peripheral vascular complications. The price of treating routine medical conditions not related to diabetes is also increased.⁵

The ancillary cost of diabetes in the form of work absenteeism, inability to participate in the workforce due to early mortality and diabetes related disability, diminished productivity at work and overall reduction in quality of life due to disease burden are the hidden but far more pervasive and costly consequences of this chronic illness.⁵ Persons with diabetes tend to lose more work days than those who do not have diabetes. This is due primarily to treatment of other conditions often present with diabetics such as hypertension, hyperlipidemia and

increase BMI. The loss of personal autonomy along with the inability to work due to disability associated with diabetic complications is also very substantial cost borne by society as whole, nearly 70,000 lower limb amputations are done each year due to complications from diabetes as estimated by the Centers for Disease Control.⁵ Premature death due to diabetes is not only disagreeable but severely limits prospective productivity and hidden behind the supposed cause of many of these deaths is diabetes as the driving force, nearly 20% of cardiovascular disease deaths can be accredited to diabetes,⁷ nearly 60% of deaths caused by renal failure and almost 30% of deaths due to cerebrovascular disease can be accredited to diabetes.⁵

The approximated cost of treatment of diabetes for 2012 was nearly 246 billion dollars with nearly 176 billion dollars accounting for direct spending on care associated with diabetes and the other 70 billion dollars attributed to premature deaths, reduced productivity and those not participating in the workforce due to sustained disability from diabetic disease process complications.⁵ In 2012 43.1 million inpatient hospital days out of an estimated 168 million were spent caring for patients with a diagnosis of diabetes type 1 or 2, with 61% of those days directly correlated with diabetes care.⁵ Nearly 50% of total emergency department visits, provider office visits, and prescriptions written for those with diabetes are in some manner or another ascribed to their chronic illness. With what has been termed the “Greying of America” i.e. the percentage of person greater than 65 years of age rapidly rising with the ensuing retirement of the Baby Boomer generation this trend in healthcare expenditure will not only continue to climb but rise exponentially over the coming decades. Those greater than the age of 65 utilize a considerable quantity of health care resources and with an increasing number of

Americans being diagnosed with type 2 diabetes the problem really begins to come into focus.⁵ This burden will be shared or endured depending on your outlook by all citizens in the United State since the brunt of these cost will be satisfied through Medicare, on average those with diabetes tend to be less healthy and older due to the aforementioned cultural pressure the that is to be put on our healthcare infrastructure in the coming decades.⁵

Most concerning is that estimates from a diabetes study 10 years prior point out that healthcare expenditures connected to medical states associated with diabetes and its complications along with generic medical issues treated inpatient that are not associated with diabetes end up requiring a more protracted hospital stays irrespective of the circumstances of admission.⁵ In addition to more than a third of outpatient and physician office visits that list diabetes as the primary diagnosis being addressed, this ends up consuming 23% of an estimated \$1.5 trillion in total healthcare spending according to most recent estimates.

Methods

A Google Scholar search was done utilizing the terms diabetes prevention with diet, Mediterranean diet for prevention of diabetes, diabetes prevention study, prevention of diabetes with diet vs medication. Supplementary terms used were economic cost of diabetes, worldwide/national cost of diabetes, GDP percentage used to treat diabetes, teaching kitchens for diabetes care, chronic complications of diabetes. The same terms were used to search PubMed.

Results

Cochran Risk-of-Bias Tool

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants & Personnel	Blinding of outcome data	Incomplete Outcome Data	Selective Reporting	Other Bias
Estruch 2013	Low	Low	Low	Low	Low	Low	Low
Esposito 2014	Low	Low	Low	Low	Low	Unclear	Low
Chrysohoou 2004	Low	Low	High	Low	Low	High	Low
DPPRG 2009	Low	Unclear	High	Low	Unclear	Low	Low
DPPRG 2002	Low	Low	Low	Low	Low	Low	Low

Estruch et al. 2013; Esposito et al. 2014; Diabetes Prevention Program Research Group et al.

2009; Chrysohoou et al. 2004)

Author/year	Sample Size	Objective	Follow-Up	Sex	Components	Key Findings
Estruch et al, 2013 Primary prevention of Cardiovascular disease with Mediterranean Diet	7447	Confirm adherence to Mediterranean Diet is inversely related to Cardiovascular Risk	4.8 years	M/F	Adherence to diet consisting of: -Olive oil -Tree Nuts -Legumes -Wine with meals -Fresh fruits -Vegetables -Fish -White meat -Sofrito	Persons at elevated cardiovascular risk put Med diet with olive oil or nuts lowered incidence of cardiovascular events
Esposito et al, 2014 Effects of Mediterranean diet on the need for Diabetes Drugs and Remission of Newly diagnosed Type 2 Diabetes	215	Assess long term effects of diet interventions on glycemic control, need for diabetic medication and remission of type 2 diabetes	10 years	M/F	2 tier design in which overweight participants with newly diagnosed type 2 diabetes were randomly assigned to a Low carbohydrate Mediterranean diet or a Low Fat diet	Newly diagnosed type 2 diabetics on Med Diet had greater reduction in HbA1c levels, Higher rates of remission, and delay in

						need for diabetes medication
Chrysohoou et al, 2004 Adherence to Med Diet Attenuates Inflammation and Coagulation process in Healthy Adults	3042	Effect of Mediterranean diet on plasma levels of C-reactive protein, white blood cell counts, and other inflammation markers		M/F	Participants living in Attica, Greece adherence to Mediterranean diet was assessed using questionnaire by healthcare professionals and assigned diet score	Med diet led to reduction in systemic inflammation
Diabetes Prevention Program Research Group 2009, 10 Yr follow up outcome study	3150	Follow up with those assigned to all cohorts to determine in continued lifestyle interventions prevented onset of type 2 diabetes	10 years	M/F		Cumulative incidence of diabetes lowest in lifestyle intervention group
Diabetes Prevention Program Research Group 2002	3234	Determine what's more effective in reducing incidence of type diabetes: Lifestyle VS Metformin	2.8 years	M/F	Intensive lifestyle interventions such as: -Weight reduction -Increased activity level -Low fat diet	Lifestyle intervention more effective than metformin

Literature Review

Several dietary patterns have been studied by nutritional epidemiologists with regard to development or prevention of type 2 diabetes mellitus,⁸ the analysis was based on food frequency questionnaires of those studied in sizeable cohorts.⁸ It distinguished two considerable dietary patterns that correlate to ideal and non-ideal health outcomes, the first

was the “Prudent diet”. The prudent diet consists of poultry, low-fat dairy products, and high volumes of fruit, vegetables, whole grains, legumes and fish.⁸ The second was the “Western Diet” consisting of high fat dairy products, and high volumes of sweets, refined grains, eggs, processed & red meat. Their analysis showed that almost all dietary behavioral patterns correlated to diabetes risk are encompassed in the “western diet”.⁸ While almost all the dietary behavioral patterns associated with safeguards against the development of diabetes are encompassed in the “prudent diet”.⁸ The prudent diet has many of the hallmarks of the Mediterranean diet elucidated earlier in this text. The analysis identified a third dietary pattern, the Mediterranean diet which as mentioned earlier is strikingly similar to the “prudent diet” but has a larger monounsaturated fatty acid content due to incorporation of olive oil and modest amounts of red wine.⁸ I surmise that the incorporation of olive and red wine makes this option the most viable and appetizing in addition to gaining some modest cardio protective effects due to the red wine consumption.

It has been shown from prior trials that newly diagnosed type 2 diabetes patients that are put on a Mediterranean diet with lower amounts of carbohydrates are more likely to remain medication free for longer periods of time than those without said diet intervention.⁹ In a study whose primary outcome measure was initiation of medications to treat diabetes the data stated that 44% of patients on the Mediterranean diet eventually needed medication to regulate hyperglycemia while 70% of patients who were assigned a simple low-fat diet eventually required medication.⁹ With the entirety those in the low-fat diet group taking an average of 6 years to arrive and need for medication to reduce blood glucose levels and the

entirety of those in the Mediterranean diet group taking an average of 8 years to arrive at need for medication to reduce blood glucose levels.⁹ The incidence of return to a state of glucose homeostasis was more prevalent in the Med Diet group than in the low-fat diet group although it was minimal between both groups 0.9% in the low-fat group compared to 4.6% in the Med diet group.

Discussion

All this brings us back to the question at hand which is: What are the certain lifestyle interventions effective at preventing the onset or progression from a pre-diabetic or impaired glucose tolerance state to full blown diabetes. The most efficacious diet for promoting optimal health and inhibiting the onset of disease has extensively been documented to be Mediterranean diet.^{2,9} A meta-analysis suggests that adherence to the Mediterranean diet offers compellingly powerful protection from the genesis of various significant chronic degenerative diseases.² In somewhat more quantifiable terms a 2 point increase in fidelity to the Mediterranean diet lowered the frequency of neurodegenerative disease by 13%, lowered incidences of cerebrovascular disease by 10%, lowered occurrence of neoplastic disease by 6% with an overall decrease in mortality.²

A constant state of global inflammation appears to influence the pathophysiology of a suite of disease states including type 2 diabetes mellitus.¹⁰ In a study from 2005 the authors theorize that the therapeutic and preventative nature of the Mediterranean Diet might be

attributed to its capacity to regulate and reduce certain coagulation properties along with global inflammatory response.¹⁰

The most paramount modifiable risk factor that drives the development of diabetes is surplus body weight.⁸ The frequency of diabetes is directly related to the increase in obesity. Thus losing excess weight or not gaining weight to begin with can be a powerful panacea to prevent the onset of type 2 diabetes.⁸ In spite of their less than stellar results over the extended course of the disease, treatment with drugs that promote weight loss in addition to lowered blood sugar levels have been shown to have salubrious effects correlated to glycemic control, insulin sensitivity, and overall diabetes risk.⁸ Which begs the question why not just forgo gaining excess weight in the first place? The inverse relationship between weight gain and physical activity and thus development of diabetes mellitus is well documented and doesn't need to be expounded upon. However, it is my belief that with the increased sedentary lifestyle being led by not only Americans but industrialized countries the world over, weight control through diet does not receive the amount of attention warranted with respect to its ability to improve overall health and wellness.

In summation it has been demonstrated that a traditional Mediterranean diet that consists of low consumption of high fat dairy, meat, and sweets; moderate consumption of fish, red wine; and high consumption of fruits, vegetables, whole grains, nuts, and olive oil is optimum for maintenance of overall health and prevention of chronic disease.⁸ There are some distinct attributes of the to the Mediterranean diet: sauce derived from tomato, garlic, onion,

pepper etc. for preparation of meals, consumption of wine in modest amounts, and copious volumes of olive oil extra virgin or otherwise.⁸ This abundance of olive oil helps promote the consumption of more vegetables as it used to produce emulsions and other dressing to make them more palatable.⁸ New and forthcoming data support a diet such as the Mediterranean diet that derives a minimum of 1/3 of its total calories from good fat sources (nuts & olive oil) can assist in the prevention of type 2 diabetes mellitus in the general population as well as those who have been given a diagnosis of pre-diabetes.⁸

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