

# **Mediterranean Diet Deconstructed: Evidence-based Culinary Medicine and Practical Applications**

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### THE PROBLEM:

- ❖ In one year, a typical adult consumes<sup>1</sup>:
  - 40 lb white bread
  - 41 lb potatoes
  - 30 lb cheese
  - 75 lbs added fats
  - 32 gallons soda
- ❖ “Vegetable consumption” has increased 12 % (yay!), but 2/3 of this is potato chips, french fries, mashed potatoes and iceberg lettuce (ugh.)
- ❖ In the 1990’s food consumption rose by 8% and obesity increased 61%
- ❖ In 2000, Americans spent \$110 billion on fast food – 20 times more than 3 decades ago

We have a problem here and the short-term prognosis is not very promising. Is there a better place to look for hope?

Yes.



## WHAT IS A MEDITERRANEAN DIET?

- ❖ Based on traditional eating patterns of the Mediterranean region<sup>2</sup>
  - Olive oil as primary fat
  - High fruit and vegetable consumption
  - Whole grains
  - Moderate fish intake ~ about 2 servings per week
  - Moderate dairy – mostly yogurt and cheese
  - Moderate wine consumption (5 oz glass for women, two glasses for men)
  - Limited red meats and saturated fats
  - More favorable balance of n-6:n-3 fatty acids (~2:1) – typical US diet is 10-20:1 – fish, locally consumed wild greens, herbs, walnuts, and figs (all sources of n-3 fatty acids) help contribute to this balance.<sup>3</sup>

Excellent website is <http://www.oldwayspt.org/> - Offers great info on the Mediterranean food pyramid, educational events and other resources.

## **Deconstructed--**

### **Evidence for the healthful components of the Mediterranean diet**

#### OLIVE OIL

- ❖ High quantity – 77% – of monounsaturated fats MUFAs
  - Less prone to oxidization – only one susceptible double bond
- ❖ High in antioxidants<sup>4</sup> – tocopherol, hydroxytyrosol, and oleuropein
- ❖ High in sterols which help reduce LDL and increase HDL
- ❖ Omega-9 fatty acids do not upset n-6:n-3 balance – may modify production of inflammatory cytokines, decreasing severity of autoimmune disorders
- ❖ May also possess some NSAID-like activity<sup>5 6</sup>
- ❖ Enhances gallbladder emptying consequently reducing cholelithiasis risk
- ❖ Decreases gastric secretions in response to food and is associated with improved gastric ulcer healing.<sup>7</sup>
- ❖ Extra virgin (or “first-press”) olive oil has been shown to have more health benefits than refined olive oil<sup>8</sup>
- ❖ Can favorably affect gene expression related to atherosclerosis development.<sup>9</sup>

#### FISH

- ❖ High in omega-3 fatty acids, especially anti-inflammatory EPA and DHA, less prone to conversion to pro-inflammatory cytokines.
- ❖ Omega-3 fatty acids increase production of nitric oxide by 43% - promotes arterial relaxation<sup>10</sup>
- ❖ Regular consumption lowers risk of fatal MI<sup>11</sup>
- ❖ Very long chain n-3 fatty acids decrease risk of cardiac death by 30-45%<sup>12</sup> Fish consumption of about 150 g (5.3 ounces) per week was associated with 38% lower odds of developing ACS as compared to no consumption.<sup>13</sup>

- ❖ DART (the Diet and Reinfarction Trial) 2-y overall mortality was reduced by 29% in survivors of a first myocardial infarction after consumption of n-3 fatty acid-rich fatty fish at least twice a week had been advised.<sup>14</sup>
- ❖ A small, but important study shows that eating oily fish (salmon) WITH beans helps to overcome problems with iron absorption due to phytates.<sup>15</sup>
- ❖ Even taking consideration of trace heavy metal exposure, a recent review<sup>16</sup> reports that the benefits of fish intake exceed the potential risks. *Avoid those highest in methylmercury = shark, swordfish, golden bass (tilefish), king mackerel*

## NUTS

- ❖ High in unsaturated or monounsaturated fats/low in saturated fats
- ❖ One study showed that 5oz nuts per week conferred a RR of 0.65 for CAD<sup>17</sup>
- ❖ Walnuts particularly high in n-3 fatty acids – addition of walnuts to Mediterranean Diet lowered LDL another 6%<sup>18</sup>

## VEGETABLES & FRUIT

- ❖ Many of the most nutritious vegetables originated in the Mediterranean area – e.g. members of the *brassica* family (cabbage, kale, broccoli, cauliflower), also mustards, watercress, and beets<sup>19</sup>
  - *Brassica* (aka “cruciferous” vegetables) contain isothiocyanates – help fight toxins, and beta-carotene, vitamin C and sulforaphanes.
- ❖ Tomatoes, brought to Mediterranean from New World in 16<sup>th</sup> century, are used extensively in Mediterranean cooking
  - Contain lycopene – potent antioxidant
  - 57 documented associations between high serum lycopene and decreased risk of cancer – especially prostate, lung, and stomach<sup>20</sup>
  - Serum lycopene increases 82% when tomatoes are cooked in olive oil<sup>21</sup>
- ❖ Vegetables contain highest concentrations of vitamins, minerals, and other protective phytochemicals with fewer calories
- ❖ Plant fiber is essential for good bowel health<sup>15a</sup>
- ❖ Fresh fruits supplant rich, sugary desserts in Mediterranean cuisine
  - Loaded with phytochemicals and fiber similar to vegetables
  - Review of 200 studies shows that low fruit intake (bottom quartile) is associated with doubled increase risk of cancer<sup>22</sup>
  - Fruit/vegetable consumption also associated with beneficial effect on blood pressure<sup>23</sup>

## CARBOHYDRATES AND GLYCEMIC INDEX

- ❖ Along with olive oil, complex carbohydrates make up the backbone of the Mediterranean diet
- ❖ Soluble fiber in whole grains delays gastric emptying and slows enzymatic breakdown of carbohydrates<sup>24</sup>
- ❖ Pasta commonly has lower glycemic index than other carbohydrates
- ❖ High dietary fiber may benefit diabetics by slowing increase in blood glucose<sup>25</sup>
- ❖ Two challenges with changing American diet
  - Changing from processed carbohydrates to whole grains – only 2% of wheat flour consumed in American diet is whole wheat<sup>26</sup>
  - Decreasing portion size – 1 serving = ½ cup COOKED pasta or grains

## LEGUMES

- ❖ Nutritional powerhouse – loaded with protein, fiber, iron, folic acid and B vitamins
- ❖ Powerful ancient Roman families were named after legumes: Fabius (fava), Lentulus (lentil), Piso (peas), and Cicero (chickpea)
- ❖ Most legumes deficient in essential amino acids methionine (Met) and tryptophan (Trp) but, luckily, these are found in sufficient amount in most grains.
- ❖ 80% of protein in legumes is digestible, compared to about 90% from animal proteins<sup>27</sup>
- ❖ Increased legume consumption associated with decreased coronary heart disease<sup>28</sup>
- ❖ Regular consumption of chickpeas can help lower LDL cholesterol and decrease fasting insulin.<sup>29</sup>

## WINE

- ❖ Recommended daily intake is 2 (5 ounce) glasses for men/1 for women
- ❖ Wine has similar protective phytochemical profile to olive oil and provides anti-atherogenic properties<sup>30</sup>
- ❖ A glass of red wine per day can lower plasma fibrinogen and factor VIIc and increase tissue plasminogen.<sup>31</sup>
- ❖ White wine does not seem to provide the same degree of protection against collagen-induced platelet aggregation as red wine<sup>32</sup>

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Despite “deconstructing” the Mediterranean diet, it is interesting to note that several studies suggest that there is no one factor to pinpoint its health benefits on and truly the whole diet is better than the sum of component parts.

IS THE MEDITERRANEAN DIET COST-EFFECTIVE? YES.

- ❖ WHO defines very cost-effective interventions as costing less than mean GDP per head, in US, this is \$31,000. In comparison, cost per life year saved:<sup>33</sup>
  - Mediterranean Diet \$703
  - Tob cessation coun. \$1300-3900
  - Beta-blocker \$ 3,600
  - Lovastatin \$20,200
  - CABG \$9200 – 1,142,000
  
- ❖ Another intervention showed that adherence to Mediterranean diet did not increased daily food costs.<sup>34</sup>

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LONGEVITY

Several large prospective observational studies overwhelmingly confirm the benefits of adopting a Mediterranean diet on longevity.

- ❖ The HALE study, The Healthy Ageing: a Longitudinal study in Europe, followed healthy elderly men and women aged 70-90 and confirmed that adherence to a Mediterranean diet and healthful lifestyle is associated with a more than 50% lower rate of all-causes and cause-specific mortality.<sup>35</sup>
  
- ❖ Data from the US AARP Diet and Health study, followed 330,000 people for a decade. All cause mortality dropped 21%, and 17% due to cancer for men. For women, all-cause mortality dropped 20% and 12% due to cancer.<sup>36</sup>
  
- ❖ AND 9 other cohort studies have done variations of Mediterranean diet score and 10/10 show decreased mortality with adherence to Mediterranean diet !! (same as above)

CARDIOVASCULAR

Ever since Ancel Keys published his landmark Seven Countries study in the 1950's, attention has been paid to the remarkable reduction in total and cardiovascular mortality attributable to the Mediterranean diet.

- ❖ The Lyon Diet Heart study<sup>37</sup> – this was another landmark study conducted on patients with known CAD. The study diet was high in fat, 40% of calories from fat – from olive oil and special high monounsaturated spread. The Lyon Diet was also high in fruits, vegetables, whole grains, and emphasized legumes and fish. There was a **70% reduction in cardiac morbidity.**
  
- ❖ GIZZI-Prevenzione study<sup>38</sup> -- n= 11,323 men and women with myocardial infarction. There was a 50% reduction of death in participants with high dietary scores cp to lowest quarter. “Regardless of any drug treatment prescribed, clinicians should routinely advise patients with myocardial infarction to increase their frequency of consumption of Mediterranean foods.”

- ❖ EPIC (the European Prospective Investigation Into Cancer and Nutrition cohort)<sup>39</sup> trial -- Higher adherence to the Mediterranean diet by 2 units was associated with a 27% lower mortality rate among persons with prevalent coronary heart disease.
- ❖ A matched-control study<sup>40</sup> showed that the adoption of a Mediterranean diet was associated with a 35% reduction of coronary risk in 505 patients with metabolic syndrome.
- ❖ Women with CHD (coronary heart disease) may be more responsive to Mediterranean diet.<sup>41</sup> This year, a report from the Nurses' Health Study shows about 30% lower risk of CHD, 13% lower stroke, and reduced cardiovascular disease mortality by nearly 40%.<sup>42</sup>
- ❖ Some of the mechanisms to explain the greater cardiac protection conferred by the Mediterranean diet may be increased intake of anti-inflammatory omega 3 fats and olive oil, and reduced saturated fat intake. Some studies (ATTICA)<sup>43</sup> specifically show lower levels of C-reactive protein, interleukin-6, homocysteine, and fibrinogen, as well as increased total antioxidant capacity (TAC).<sup>44</sup>
- ❖ A final note, PIZZA may save your heart! <sup>45</sup> ☺ The multivariate odds ratios for acute MI were 0.78 for occasional, 0.62 for regular and 0.44 for frequent eaters. There is no single explanation for the present findings.

## CANCER

The overall cancer incidence in Mediterranean countries is lower than in Scandinavian countries, the UK and the United States and several studies show that much of this may be attributable to dietary factors.

- ❖ The Lyon Diet Heart study by DeLorgeril M et al was designed to look at the impact of a Mediterranean diet on cardiovascular disease, AND a subanalysis showed **61% less cancer incidence** as well.<sup>46</sup>
- ❖ A recent systematic analysis<sup>47</sup> of case-control studies reviewed 12,000 cases of 20 cancer sites and 10,000 controls.
  - Epithelial cancers, the risk decreased with increasing vegetable and fruit consumption, with relative risk (RR) between 0.3 and 0.7 for the highest versus the lowest tertile.
  - For digestive tract cancers, population-attributable risks for low intake of vegetables and fruit ranged between 15 and 40%.
  - A protective effect was observed also for breast, female genital tract, & urinary tract neoplasms.
  - Intake of whole-grain foods was related to a reduced risk of several types of cancer, particularly of the upper digestive tract

- In contrast, subjects reporting frequent red meat intake (7x per week cp to less than 3x per week) showed increased RR 1.3 – 2.0 for several common neoplasms.
- ❖ In the Greek EPIC (European Prospective Investigation into Cancer and nutrition) cohort with over 25,000 participants, a 12% reduction in cancer incidence was seen in those adhering to a traditional Mediterranean diet to a greater degree.<sup>48</sup>
- ❖ For lung cancer, a study<sup>49</sup> showed a protective effect for high consumption of carrots, tomatoes, white meat, exclusive use of olive oil, and regular consumption of sage.
- ❖ For breast cancer,<sup>50</sup> High intake of polyunsaturated fatty acids (chiefly derived from olive oil and seed oils) were found to be protective, and conversely, high intake of starch and saturated fat seemed to lead to an increase of cancer risk. “An excess of energy intake, particularly from refined bread and pasta, can be an unfavourable feature of the Mediterranean diet, in the presence of a sedentary lifestyle.”
- ❖ An interesting synergism between olive oil and breast cancer treatment seems to exist -- An up to 50-fold increase in the efficacy of trastuzumab (Herceptin) occurred in the presence of oleuropein aglycone, the major brittle principle in extra virgin olive oil.<sup>51</sup>

#### DIABETES

- ❖ In a prospective study of more than 13, 000 people, those with greater adherence to a traditional Mediterranean diet were 83% less likely to develop type 2 diabetes!<sup>52</sup>

#### OBESITY & METABOLIC SYNDROME

Despite having a higher percentage of calories as fat, typically 35-40% compared to the US Food Pyramid recommendation of no more than 30%, the Mediterranean diet has been associated with REDUCED obesity and subsequent risk of metabolic syndrome.

- ❖ More closely following a Mediterranean diet (i.e., highest tertile) was associated with a 51% lower odds of being obese and 59% lower odds of having central obesity compared with a non-Mediterranean diet.<sup>53</sup>
- ❖ In this prospective follow-up study (the SUN Project, Seguimiento Universidad de Navarra),<sup>54</sup> a high amount of olive oil consumption was not associated with higher weight gain or a significantly higher risk of developing overweight or obesity.
- ❖ In a small, but interesting study,<sup>55</sup> a carbohydrate rich diet was fed to insulin-resistant people. In comparison, an isocaloric monounsaturated-rich diet prevents central fat redistribution and the postprandial decrease in peripheral adiponectin gene expression and insulin resistance.

- ❖ In one study with over 800 high risk patients, those adhering to a Mediterranean diet had lower odds ratio (0.44) for having metabolic syndrome.<sup>56</sup>
- ❖ This was a weight loss randomized, controlled trial; despite a higher fat content (35% cp to 20%), participants eating a Mediterranean-based diet lost 4.1 kg compared to control who gained 2.9 kg over 18 months. *Caveat: both groups were counseled on reducing total caloric intake to 1500 kcal/day.*<sup>57</sup>
- ❖ This review<sup>58</sup> explored the relationship of metabolic syndrome (central/abdominal obesity, insulin resistance, hypertension, and dyslipidemia) and the Mediterranean diet. Some recent interventional studies have demonstrated a 25% net reduction in the prevalence of the syndrome following lifestyle changes mainly based on nutritional recommendations. Similar rates of resolution have been obtained with drugs, such as rosiglitazone.
- ❖ Diabetic women following a Mediterranean dietary pattern had 23% higher levels of adiponectin, a hormone secreted by fat cells that is inversely correlated with body fat percentage.<sup>59</sup>

#### COGNITIVE FUNCTION

- ❖ High intake of monounsaturated fats, wine and grains were associated with less cognitive decline.<sup>60 61</sup>
- ❖ Higher adherence to a Mediterranean diet was associated with 28% less risk of developing mild cognitive impairment in older Americans, and 40% less risk for developing Alzheimers.<sup>62</sup>
- ❖ A meta-analysis comprising of 1.5 million subjects from 3 continents concluded that greater adherence to Mediterranean diet determines at 13% reductions in incidence of Parkinson's and Alzheimer's disease.<sup>63</sup>

#### OTHER

- Rheumatoid Arthritis --- The Mediterranean diet has also been studied and shown to positively benefit patients with rheumatoid arthritis to reduce inflammatory activity, swollen joint counts and C-reactive protein levels, and improved function.<sup>64 65 66</sup>
- Sexual Function – Female sexual function index improved after 2 years on a Mediterranean diet compared to a control group<sup>67</sup>, and significantly more men on a Mediterranean diet had improved erectile function.<sup>68</sup>

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