The Cretan Mediterranean Diet”
The optimal diet for cardiobiadesity?

Professor Catherine Itsiopoulos
Head of School of Allied Health
Professor of Dietetics and Human Nutrition
La Trobe University
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Head of School of Allied Health
Professor of Dietetics and Human Nutrition,
La Trobe University

Catherine is a recognised leader in Dietetics and has international standing as a leader in Mediterranean diet research. She is an Accredited Practising Dietitian, the deputy chair of the Australian Dietetics Council, and is the founding head of the department of Dietetics and Human Nutrition at La Trobe University. Her current role is Head of School of Allied Health at La Trobe University. Catherine’s specific research area of interest is Mediterranean diet studies focusing both on migration impact on diet and lifestyle and chronic disease risk and dietary clinical intervention trials using the traditional Cretan Mediterranean diet (and elements of) as intervention models in the prevention and management of metabolic syndrome, Non-Alcoholic Fatty Liver Disease, type 2 diabetes, cardiovascular disease, and more recently mental health. Catherine has authored over 50 peer-reviewed publications with 720 citations, has co-edited a Nutrition textbook, and has published 2 Mediterranean Diet Cookbooks (The Mediterranean Diet 2013, The Mediterranean Diet Cookbook 2015).
Globally Obesity has reached crisis proportions!

- More than 2.1 billion – 30% of global population – are overweight or obese!

- By 2030 it is estimated that 50% of our population will be overweight or obese.

- Global economic impact of obesity is $2 trillion (2.8% GDP) via related diseases diabetes and CHD.

http://www.mckinsey.com/insights/mgi/in_the_news/the_obesity_crisis
Number of people with diabetes by IDF Region, 2013

~2 Million In Australia

63% of adult Australians and 25% of children are overweight/obese
We live in an Obesogenic Environment!

- **Urbanisation**
  - sedentary occupations
  - computerisation and mechanisation
  - improved transportation

- **Nutrition transitions**
  - exponential growth in fast food industry (highly processed, high fat, sugar, salt)
  - livestock revolution (intensively reared animals with a high n6/n3 fatty acid profile – 20:1 vs 2:1 – not enough omega 3!)
  - highly processed grains (poor in fibre, micronutrients, and phytochemicals)
Somewhere, something has gone terribly wrong!

Recent Australian Health Survey of 12,000 people shows that we are eating 30% less fruits and vegetables than 15 years ago.

25% of Adults eat NO vegetables on an average day and only 7% eating recommended 5 serves per day!

We eat 3kg of food and beverages each day and 35% of energy comes from high fat, high sugar foods such as cakes, biscuits, alcohol, soft drink and chips.
Could a Mediterranean-style Diet be the answer?
Historical Overview: Traditional Mediterranean diet studies

- 7 countries study (1950s)
- Paradox Intervention (late 1990s)
- AUSMED Heart Trial (2014-)
- Lyon Heart study (1990s)
- PREDIMED (2013)
- SMILE, MEDINA, MEDIBRAIN, AUSMED ASTHMA

LA TROBE UNIVERSITY
MEDLEY
University of South Australia

HELFIMED
Healthy Eating for Life with a Mediterranean Diet

THE UNIVERSITY OF MELBOURNE

AUSMED
Heart Trial
(2014-)
Ancient Mediterranean Diet: triad of “wheat, olive oil, and wine”

Considered as a ‘gift of the gods’ the olive tree was an important symbol for the ancient Greeks. It was connected to their diet and their religion and considered a symbol of peace, wisdom and victory.

Archaeological finds such as stone mortars and presses used for olive oil extraction date back to 5000 BC!

http://www.explocrete.com/nature/olive-oil-history.html
Ancel Keys 1904-2004

The 7 Countries Study

“The Archetypal Cretan Mediterranean Diet”

The Diet-Heart Hypothesis
Heart Disease is Complex!

<table>
<thead>
<tr>
<th>1° &amp; Messenger Inflamm.</th>
<th>Cellular Adhesion Molecules</th>
<th>Plaque Destabilization</th>
<th>Plaque Rupture</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1</td>
<td>sICAM</td>
<td>IL-18*</td>
<td>MPO*</td>
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<tr>
<td>TNF-α</td>
<td>sVCAM</td>
<td>oxLDL*</td>
<td>MMPs*</td>
</tr>
<tr>
<td>MCP-1*</td>
<td>sSelectins</td>
<td>Lp-PLA₂*</td>
<td>MCP-1*</td>
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<td></td>
<td></td>
<td>GPₓ-1*</td>
<td>PIGF*</td>
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Acute Phase Reactants
CRP*, sPLA₂*, SAA, Fibrinogen, WBCC

http://atvb.ahajournals.org/content/27/1/15/F1.large.jpg
The multidisciplinary team of the PREDIMED study assembles outstanding research groups involved in nutrition and cardiovascular risk in Spain. Partners are 16 groups distributed in 7 autonomous communities in Spain, which are formed by university researchers, hospital clinicians, primary care physicians, nutritionists and epidemiologists working in various public institutions. The team takes advantage of modern communication technologies and performs as a research network.
Figure 1. Incidence of Primary End-Point (a combination of acute myocardial infarction, stroke and all-cause death) following use of the Mediterranean Diet for the primary prevention of cardiovascular disease.

EVOO = Extra Virgin Olive Oil

Med diet, EVOO: hazard ratio, 0.70 (95% CI, 0.53–0.91); P=0.009
Med diet, nuts: hazard ratio, 0.70 (95% CI, 0.53–0.94); P=0.02

30% Reduction in CVD Mortality/Morbidity

Effect independent of weight loss

(Estruch et al, 2013)
PREDIMED Cumulative diabetes free-survival: Med diets (a,b) vs control (c)

Salas-Salvadó J et al. Diab Care 2011;34:14-19

55% Risk Reduction Diabetes Incidence
Polyphenol intake and mortality risk: a re-analysis of the PREDIMED trial

Anna Tresserra-Rimbau1,2, Eric B Rimm3, Alexander Medina-Remón2,17, Miguel A Martínez-González2,4, M Carmen López-Sabater1,2, María I Covás2,9, Dolores Corella2,9, Jordi Salas-Salvadó2,7, Enrique Gómez-Gracia2,8, José Lapetra9, Fernando Arós2,10, Miquel Fiol1,11, Emili Ros1,12, Lluís Serra-Majem2,13, Xavier Pinto2,14, Miguel A Muñoz2,15, Alfredo Gea2,4, Valentina Ruiz-Gutiérrez2,16, Ramón Estruch2,17, Rosa M Lamuela-Raventós1,2*
and on behalf of the PREDIMED Study Investigators

Abstract

Background: Polyphenols may lower the risk of cardiovascular disease (CVD) and other chronic diseases due to their antioxidant and anti-inflammatory properties, as well as their beneficial effects on blood pressure, lipids and insulin resistance. However, no previous epidemiological studies have evaluated the relationship between the intake of total polyphenols intake and polyphenol subclasses with overall mortality. Our aim was to evaluate whether polyphenol intake is associated with all-cause mortality in subjects at high cardiovascular risk.

37% reduction in mortality in Q5 vs Q1 of polyphenol intake
PREDIMED: Mortality and Polyphenol Intake (by type)

Tresserra-Rimbau et al. BMC Medicine, 2014
Results suggest that a Mediterranean diet supplemented with 30g nuts/day (almonds, walnuts, hazelnuts) reduces the risk of depression in people with Diabetes.
An almond-enriched diet increases plasma α-tocopherol and improves vascular function but does not affect oxidative stress markers or lipid levels

K. Choudhury, J. Clark & H. R. Griffiths

Aston Research Centre for Healthy Ageing Life, and Health Sciences, Aston University, Birmingham, UK

Healthy middle aged men (n=20), healthy young men (n=20) and young men with CVD risk factors (n=20) consumed 50g almonds for 4 weeks, compared to controls (n=15) who consumed habitual diet.
Figure 2. Flow-mediated dilatation was measured in each subject at baseline, following 4 weeks 25 g almonds/day (d) and following 4 weeks of almond intervention (50 g/d). Data are expressed as box and whisker plots with the box showing median and 75% confidence intervals and data range shown as whiskers where * represents $p<0.05$ and represents $p<0.01$. 
A synthesis of all (304) pooled meta-analyses and systematic reviewed published 1950-2013
Mediterranean Diet Protective for Deaths from multiple conditions.

Systematic review and meta-analysis of international studies between 1966-2010 involving over 4 Million people, demonstrated that a 2-point increase in adherence to a Mediterranean diet was associated with:

- 10% reduction overall mortality
- 10% reduction in CVD deaths
- 6% reduction in Cancer deaths
- 13% reduction in Alzheimer’s and Parkinson’s

REVIEW

Adherence to a Mediterranean-style diet can slow the rate of cognitive decline and decrease the risk of dementia: a systematic review

Rachelle Sara OPIE, Robin A. RALSTON and Karen Z. WALKER
Department of Nutrition and Dietetics, Monash University, Clayton, Victoria, Australia

Abstract
Aim: The aim of the present study was to explore the association between a Mediterranean-style diet and cognitive performance, dementia, Alzheimer's disease and associated mortality in ageing populations.
Methods: A systematic search of Ovid Medline, Embase and Cinahl plus databases for papers published from September 1970.
Results: Ten prospective cohort studies and one cross-sectional study were included in this review. Higher adherence to a Mediterranean-style diet was associated with significantly decreased risks for all-cause dementia, Alzheimer's disease, Alzheimer's disease mortality and infarcts detected by magnetic resonance imaging. Adherence to a Mediterranean-style diet was not, however, consistently associated with tests of cognitive performance and was not associated with the presence of white matter hyper-intensities in the brain. In four of six studies, subjects in the highest tertile for Mediterranean diet adherence had a 25-48% lower risk for development of dementia or Alzheimer's disease than subjects in the lowest tertile. For subjects with Alzheimer's disease, those in the highest tertile of adherence to a Mediterranean-style diet had a 73% lower mortality risk than those in the lowest tertile (fully adjusted hazard ratio 0.27, 95% CIs: 0.10-0.69, P for trend = 0.003).
Conclusions: There is strong evidence for the protective role of a Mediterranean-style diet against cognitive decline and development of Alzheimer's disease. Strategies should now be sought to promote this eating pattern in older Australians. Support for dietitians in implementing this change has potential to reduce the high health-care costs associated with cognitive decline on ageing.
Western diet is associated with a smaller hippocampus: a longitudinal investigation

Felice N. Jacka, Nicolas Cherbuin, Kaarin J. Anstey, Perminder Sachdev and Peter Butterworth

N = 255, 46% Female, mean age 63 yrs, ACT

Healthy Diet
- Fresh vegetables
- Salads
- Fresh Fruit
- Grilled Fish

Unhealthy Diet
- Roast meat
- Sausages
- Hamburgers
- Steak
- Chips
- Crisps and Soft drinks

Greater retention of brain volume over 4 yrs with healthy diet!
Is a Mediterranean Diet Feasible in a non-Mediterranean Multi-Ethnic Society like Australia?
First RCT using a reconstructed Cretan Mediterranean diet in a clinical trial in Diabetes in Australia.

Can the Mediterranean diet lower HbA1c in type 2 diabetes? Results from a randomized cross-over study.

C. Itsiopoulos a, b, L. Brazionis a, M. Kaimakamis c, M. Cameron c, J.D. Best a, b, K. O’Dea c, K. Rowley f

➢ 12 week RCT of Greek-style Med diet “ad libitum” vs Usual Diet in T2DM

➢ Clinically significant change in HbA1c (of the order found in many OH drug trials)

➢ Change of - 0.3 HbA1c% = 10% reduction in CHD Mortality in T2 diabetes

➢ Health benefits independent of weight loss!

Cooked meals and staples (olive oil, dried fruit, nuts, sourdough bread) provided for duration of study.
After 6 weeks on a Mediterranean Diet there was an almost 40% drop in liver fat compared with only 7% drop on the low fat diet.

Insulin resistance improved on the Mediterranean Diet but no change on the low fat diet.

Aims
Examine the potential of a Mediterranean diet vs low fat diet in, reducing risk of secondary events at 12 months in patients surviving a cardiac event mediating cardiometabolic markers at 6 months

Design

Intervention:
Tailored menus, cookbook and hamper of key staple foods (Med diet) vs control std diet for CVD risk reduction (NHF guidelines). Intensive dietetic counselling in both arms.

Recruitment to date: 49 - Med diet intervention arm (n=27) vs. low fat diet control arm (n=22)

Most common cultural backgrounds: Australian, European, and South Asian.

Feasibility: Med diet adherence score using 14-item PREDIMED tool shows intervention arm (n=16): baseline score 5.4 vs 6 month score 10.9

CIs: Itsiopoulos, Wilson, van Gaal, Tierney, Thomas, Kingsley, Brazionis, Vally, Salim, Segal.

PhD students: Teagan Kucianski, Hannah Mayr
### Our Mediterranean trials experience: Challenges and Solutions!

<table>
<thead>
<tr>
<th>Challenges</th>
<th>Solutions</th>
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<tbody>
<tr>
<td>Cultural diversity/ interest in Med diet</td>
<td>Adjust current foods embedding key Med diet ingredients</td>
</tr>
<tr>
<td>Fear of eating too much fat – 4 tbs EVOO/day</td>
<td>Focus on heart health benefits of EVOO, polyphenols, taste</td>
</tr>
<tr>
<td>Dislike of some food staples (yoghurt)</td>
<td>Try plain Greek-style with fresh fruit, walnuts, honey</td>
</tr>
<tr>
<td>Concern over eating “carbs” e.g. bread/ pasta</td>
<td>Approach is moderate carbs, focus on sourdough/grain, and high plant:animal food ratio</td>
</tr>
<tr>
<td>Poor cooking skills/ no time to cook</td>
<td>Focus on ‘no cooking req’ options, cook in bulk and freeze</td>
</tr>
<tr>
<td>Ingredient challenges (garlic, EVOO, leafy greens, legumes)</td>
<td>Add spinach and lentils to lasagne. Bake veggies with garlic and EVOO. Simple lunches – leafy salad, tinned salmon/tuna, 4 bean mix, EVOO.</td>
</tr>
</tbody>
</table>
AUSMED Heart Trial: Adherence to Mediterranean Diet at 3 months

Mayr et al, ICD Conference 2016

Almonds
Walnuts
(Hazelnuts)
Why is the Mediterranean Diet beneficial in cardiometabolic conditions?
Anti-inflammatory/ Palatable/
Sustainable/ Ecological

4:1 Plant to Animal Food Ratio

• Vit C
• Vit E
• Carotenoids
• Phytoestrogens
• Phenolics
• Allylthiosulfinates
• Flavonoids
• Selenium
• N3 fatty acids:
  ◆ ALA and EPA DHA

Ref: Simopoulos and Sidosis. What is so special about the Greek diet? World Rev Nutr Diet 2000
A predominantly plant-based diet with fish and seafood!
Balanced Plate – Mediterranean Style

4:1 ratio of Plant: Animal Foods
The Mediterranean Diet is High in Omega-3 fats from a range of sources.

- Wild edible leafy greens
- Nuts
- Pumpkin seeds ‘πασατέμπο’
- Greek village eggs “free range”
- Snails (Crete)
- Free range goat - milk and cheese
- Offal – κοκορέτσι!
Protective Metabolic Pathways


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Translating the Mediterranean Diet Principles: The Toolkit
### 14-item food diet quality guide: PREDIMED Study (Martinez-Gonzalez et al, 2013).

**Foods Positively Associated with Mediterranean Diet**

- **Olive oil as main fat**
  - ≥ 4 tbsp olive oil/day
- ≥ 2 serves vegetables (2x200g cooked, 100g raw)/day
- ≥ 3 serves of fruit/day
- ≥ 7 glasses wine/week (If a consumer of alcohol)
- ≥ 3 serves (3x150g) legumes/week
- ≥ 3 serves fish (100-150g) or shellfish (200g)/week
- ≥ 3 serves (3x30g) nuts/week
- Chicken, turkey, wild meats as main meats
- ≥ 2/week dishes cooked in tomato, onion, garlic, olive oil (sofrito or salsa)

**Foods Negatively Associated with the Mediterranean Diet**

- < 1 serve red meat/meat products (100-150g)/day
- < 1 serve butter, margarine or cream/day
- < 1 sweet/carbonated beverage/day
- < 3/week commercial sweets, cakes, biscuits.
Translating the traditional Mediterranean Diet: 10 Commandments

1. Extra Virgin Olive oil as the main added fat!
2. Vegetables /salads with every main meal
   - Use herbs and spices to flavour foods
3. Legumes twice per week
4. Fish/seafood twice a week
5. Meat/Chicken less often, small portions
6. Wholegrain sourdough breads
7. Fresh fruit everyday
8. Fermented dairy every day “yoghurt”
9. Nuts everyday
10. Wine in moderation, always with meals.
   - Sweets on special occasions

© Itsiopoulos, C
New Nutrition Australia pyramid has a strong Mediterranean Diet focus!

- Predominance of fruits and vegetables supporting and 4:1 plant to animal food ratio.
- Olive oil included in pyramid.
- Moderate in carbohydrates.
- Legumes in eat most section.
- Herbs and spices included.
Typical Australian-born Anglo-Celtic Plate 2:1 Plant to Animal Food ratio

Traditional Mediterranean plate 4:1 Plant to Animal Food ratio
Putting the Mediterranean Diet into Practice!

Healthy Menu for Chronic Disease Prevention:
Diabetes, Heart Disease, Stroke, Dementia

<table>
<thead>
<tr>
<th></th>
<th>BREAKFAST</th>
<th>LUNCH</th>
<th>DINNER</th>
<th>SNACK</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUNDAY</td>
<td>Dukas (Buckwheat) Greek yogurt with lemon, mint, and walnuts.</td>
<td>Mani salad in white wine. Salad of chickpeas. Greek bread.</td>
<td>Eggplant moussaka with lamb, mint, and olives.</td>
<td>Low-fat Greek yogurt with honey and walnuts.</td>
</tr>
<tr>
<td>MONDAY</td>
<td>Whole wheat bread with poached eggs and sliced avocado sprinkled with lemon juice and black pepper.</td>
<td>Baked red potato, fresh mushrooms, and tomato salad in olive oil.</td>
<td>Baked chicken breast, salad, and tomato salad.</td>
<td>Low-fat Greek yogurt with walnuts and honey.</td>
</tr>
<tr>
<td>TUESDAY</td>
<td>Porridge (coconut milk with stevia) topped with fresh blueberries.</td>
<td>Skewers of marinated vegetables in olive oil.</td>
<td>Baked cod fillet, salad, and tomato salad.</td>
<td>Roast potato salad with whole-grain mustard.</td>
</tr>
<tr>
<td>WEDNESDAY</td>
<td>Apple (Pink Lady), milk, and Greek yogurt.</td>
<td>Sesame and walnut tree salad with cherry tomatoes and feta.</td>
<td>Vegetable soup, Greek salad, and lemon juice.</td>
<td>Oatmeal (1/2 cup) Greek yogurt with almonds (8-10)</td>
</tr>
<tr>
<td>THURSDAY</td>
<td>Porridge (coconut milk with stevia) topped with fresh blueberries.</td>
<td>Cannellini bean soup, Greek salad, and mixed greens.</td>
<td>Rabbit stew with red wine (can use chicken or pork)</td>
<td>Low-fat Greek yogurt with walnuts.</td>
</tr>
<tr>
<td>FRIDAY</td>
<td>Whole wheat bread with poached eggs and sliced avocado sprinkled with lemon juice and black pepper.</td>
<td>Baked vegetable spiced sandwich, Greek cheese, and mixed greens.</td>
<td>Baked cod fillet, salad, and tomato salad.</td>
<td>Olive oil cake.</td>
</tr>
<tr>
<td>SATURDAY</td>
<td>Poached eggs in steamed tomatoes, Greek bread, and whole orange.</td>
<td>Baked cod fillet in tomato sauce with rice, black bean salad, and tomato salad.</td>
<td>Stuffed tomatoes with rice, stuffed tomato with rice.</td>
<td>Rakia (or wine), Greek yogurt with honey.</td>
</tr>
</tbody>
</table>

Nutritional Information:
- 8000kcal: 25 g protein (100% energy), 190 g carbohydrate (80% energy), 150 g fat (40% energy), 6 g fiber (7.6% energy)
The solution is not just about changing our diets!
Try to emulate the Long Living “Blue Zones” Populations?

• Populations around the world living beyond 100 yrs:
  – Okinawa (Japan)
  – Sardinia (Italy)
  – Nicoya (Costa Rica)
  – Lima Loma (California)
  – Ikaria (Greece)

• Key lifestyle features of Ikarians (Itsiopoulos et al, 2016):
  – Very low levels of stress, happiness, and positivity
  – no smoking (in women)
  – active social life and being productive
  – Family coherence, eating together
  – physically active, walking everywhere, keeping home garden
  – a high plant-food diet focussed on fresh local foods and free range produce.
“Make Food Thy Medicine”

Hippocrates
Circ 400 BC
Thank you to the Researchers and industries providing foods for our studies.

- Professor Kerin O’Dea
- Prof Peter Brooks
- Dr Laima Brazionis
- Dr Andrew Wilson
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- A/Prof Bill van Gaal
- Dr Hassan Vally
- Dr Colleen Thomas
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- A/Prof Michael Kingsley
- Natalie Simmance
- Tanya Gilliver
- Dr Jessica Radcliffe
- A/Prof Catherine Itsiopoulos

PhD Students
- Tania Thodis
- Spero Tsindos
- Rachelle Opie
- Teagan Kucianski
- Elena Papamiltiadous
- Serpil Kucuktepe
- Hannah Mayr
- Oana Tatucu