EFFECTS OF MEDITERRANEAN DIET ON CARDIOVASCULAR DISEASE: LESSONS FROM THE PREDIMED TRIAL

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Origin of the Mediterranean Diet
1) Prevalence of coronary heart disease:
   - United States: 4.6%
   - Finland: 3.4%
   - Italy: 1.1%
   - Greece: 0.5%

2) 10-year mortality due to coronary heart disease:
   - Finland: 45.5 / 10,000
   - United States: 42.4
   - Netherlands: 31.7
   - Italy: 20.3
   - Greece: 6.6
Hierarchy of Evidence-based Medicine

- Systematic Revisions - Meta-analyses
- Large Multicenter Clinical Trials
- Randomized Clinical Trials
- Non-Randomized Controlled Studies
- Cohort Studies
- Case – Control Studies
- Case Series
Effects of Mediterranean Diet on Primary Prevention of Cardiovascular Disease (PREDIMED Study)
Primary Aims

• To test the effect of a Mediterranean Diet enriched with extra virgin olive oil on the risk of cardiovascular diseases (a composite endpoint of cardiovascular death, myocardial infarction, and stroke)

• To test the effect of a Mediterranean diet enriched with supplementary nuts (walnuts, almonds, and hazelnuts) on the risk of cardiovascular diseases

• To test the effect of moderate wine and beer intake on the risk of cardiovascular diseases
Men: 55-80 yr
Women: 60-80 yr
High CV risk without CVD
Type 2 diabetics
3+ risk factors

PREDIMED TRIAL: DESIGN

Random

1. Smoking
2. Hypertension
3. ↑ LDL
4. ↓ HDL
5. Overweight/obese
6. Family history

All free of CVD at baseline

Mediet + Virgin Olive Oil
Mediet + Nuts
Control Low-fat
Sample Size and Randomization

7,447 participants

- Mediterranean Diet
  - Extra Virgin Olive Oil (1L/week)
  - Nuts (30g/day)
- Low-fat Diet
  - “American Heart Association guidelines”

n=2,543
n=2,454
n=2,450
## Participants

<table>
<thead>
<tr>
<th></th>
<th>DM + EVOO (n=2.543)</th>
<th>DM + Nuts (n=2.454)</th>
<th>Control (n=2.450)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD)</td>
<td>67 (6)</td>
<td>67 (6)</td>
<td>67 (6)</td>
</tr>
<tr>
<td>Women (%)</td>
<td>59</td>
<td>54</td>
<td>60</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>50</td>
<td>47</td>
<td>49</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>82</td>
<td>82</td>
<td>84</td>
</tr>
<tr>
<td>Current Smokers (%)</td>
<td>14</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Dyslipidemia (%)</td>
<td>72</td>
<td>73</td>
<td>72</td>
</tr>
<tr>
<td>BMI, kg/m² (SD)</td>
<td>30 (4)</td>
<td>30 (4)</td>
<td>30 (4)</td>
</tr>
<tr>
<td>Waist Perimeter (SE)</td>
<td>100  (10)</td>
<td>100 (11)</td>
<td>101 (11)</td>
</tr>
<tr>
<td>Med Diet score(DE)</td>
<td>8.7 (2)</td>
<td>8.7 (2)</td>
<td>8.4 (2)</td>
</tr>
</tbody>
</table>
Introduce changes in the overall food pattern

- **Mediterranean diet: 2 groups**
  - Total Fat: *ad libitum*
  - High in
    - MUFA (extra virgin olive oil)
    - Fish
    - Fruits, vegetables, legumes
  - Low in meats & dairy
  - Alcohol permitted: wine

- **Low-fat diet - Control**
  - Reduce every fat
  - Increase CHO

- **No Energy restriction**
- No specific recommendation on Physical Activity
## Strategies for behavior change

### ADDITIONAL STRATEGIES

- Seasonal buying lists
- Menus and recipes

### Intervention groups of Mediterranean Diet

- Provision of key foods

### Key Foods

- Olive oil: 1L/w – 50 ml/d
- Nuts: 30g/d
End-points

PRIMARY END-POINTS

Cardiovascular Death
No-fatal Acute Myocardial Infarction
No-fatal Stroke
3-MONTH CARDIOVASCULAR RISK FACTORS: CHANGES IN HOMA

### Cumulative incidence of diabetes

**Online Appendix Table 2.** Cumulative incidence of diabetes by intervention group

<table>
<thead>
<tr>
<th></th>
<th>MedDiet with VOO group (n=139)</th>
<th>MedDiet with nuts group (n=145)</th>
<th>Control diet group (n=134)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person-years, No.</td>
<td>570</td>
<td>598</td>
<td>515</td>
</tr>
<tr>
<td>New cases of diabetes, No.</td>
<td>14</td>
<td>16</td>
<td>24</td>
</tr>
<tr>
<td>Rate per 1000 person-years (95% CI)</td>
<td>24.6 (13.5-40.8)</td>
<td>26.8 (15.3-43.0)</td>
<td>46.6 (30.1-68.5)</td>
</tr>
<tr>
<td>Cumulative incidence (95% CI)</td>
<td>10.1 (5.1-15.1)</td>
<td>11.0 (5.9-16.1)</td>
<td>17.9 (11.4-24.4)</td>
</tr>
</tbody>
</table>

Abbreviations: MedDiet, Mediterranean diet; VOO, virgin olive oil.
CUMULATIVE INCIDENCE OF DIABETES IN THE CONTROL GROUP AND THE INTERVENTION GROUPS DURING 4.5 YEARS

The Predimed Trial

52% Reduction in incidence

No differences on weight loss

Diabetes Care 2011
Incidence of diabetes by intervention group during the follow-up.

<table>
<thead>
<tr>
<th></th>
<th>MedDiet+EVOO (n=1154)</th>
<th>MedDiet+nuts (n=1240)</th>
<th>Control group (n=1147)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person-years, No.</td>
<td>4990</td>
<td>4876</td>
<td>4271</td>
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<tr>
<td>New cases of diabetes, No.</td>
<td>80</td>
<td>92</td>
<td>101</td>
</tr>
<tr>
<td>Rate per 1000 person-years (95% CI)</td>
<td>16.0 (12.7-19.9)</td>
<td>18.7 (15.1-22.9)</td>
<td>23.6 (19.3-28.7)</td>
</tr>
<tr>
<td>Cumulative incidence (95% CI)</td>
<td>6.93 (5.53-8.55)</td>
<td>7.42 (6.02-9.02)</td>
<td><strong>8.81 (7.23-10.60)</strong></td>
</tr>
</tbody>
</table>
PREVENTION OF DIABETES WITH MEDITERRANEAN DIETS:
A RANDOMIZED, CONTROLLED TRIAL

Cumulative diabetes incidence by intervention group: Outcome of diabetes onset and exposure to MedDiet intervention group vs. control group.
End-points

PRIMARY END-POINTS

Cardiovascular Death
No-fatal Acute Myocardial Infarction
No-fatal Stroke
Hazard Ratios (95% CI)*

EVOO: 0.70 (0.53-0.91), P=0.009
Nuts: 0.70 (0.53-0.94), P=0.016

Control diet
Med diet, nuts
Med diet, EVOO

<table>
<thead>
<tr>
<th>Years</th>
<th>Number at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2450</td>
</tr>
<tr>
<td>1</td>
<td>2268</td>
</tr>
<tr>
<td>2</td>
<td>2020</td>
</tr>
<tr>
<td>3</td>
<td>1583</td>
</tr>
<tr>
<td>4</td>
<td>1268</td>
</tr>
<tr>
<td>5</td>
<td>946</td>
</tr>
<tr>
<td>0</td>
<td>2543</td>
</tr>
<tr>
<td>1</td>
<td>2486</td>
</tr>
<tr>
<td>2</td>
<td>2320</td>
</tr>
<tr>
<td>3</td>
<td>1987</td>
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<tr>
<td>4</td>
<td>1687</td>
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<tr>
<td>5</td>
<td>1310</td>
</tr>
<tr>
<td>0</td>
<td>2454</td>
</tr>
<tr>
<td>1</td>
<td>2343</td>
</tr>
<tr>
<td>2</td>
<td>2093</td>
</tr>
<tr>
<td>3</td>
<td>1657</td>
</tr>
<tr>
<td>4</td>
<td>1389</td>
</tr>
<tr>
<td>5</td>
<td>1031</td>
</tr>
</tbody>
</table>
Results: Mortality

Hazard Ratios (95% CI)*

EVOO: 0.81 (0.63-1.05), P=0.109
Nuts: 0.95 (0.73-1.23), P=0.680

Number at risk

<table>
<thead>
<tr>
<th>Group</th>
<th>0 Years</th>
<th>1 Year</th>
<th>2 Years</th>
<th>3 Years</th>
<th>4 Years</th>
<th>5 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>2450</td>
<td>2268</td>
<td>2026</td>
<td>1585</td>
<td>1272</td>
<td>948</td>
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<tr>
<td>MeDiet+EVOO</td>
<td>2543</td>
<td>2485</td>
<td>2322</td>
<td>1988</td>
<td>1690</td>
<td>1308</td>
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<tr>
<td>MeDiet+Nuts</td>
<td>2454</td>
<td>2345</td>
<td>2097</td>
<td>1662</td>
<td>1395</td>
<td>1037</td>
</tr>
</tbody>
</table>
1. Among persons at high cardiovascular risk, a Mediterranean Diet supplemented with extra-virgin olive oil or nuts reduce the incidence of major cardiovascular events (cardiovascular death, acute myocardial infraction and stroke) by 30%, compared to a control low-fat diet.

2. The results of this study support the benefits of the Mediterranean diet for the primary prevention of cardiovascular disease with the highest level of scientific evidence.
3. It appears that it is never too late to change dietary habits with an ensuing measurable benefit on surrogate markers of cardiovascular risk.

4. A Mediterranean diet enhanced with high-fat, high-unsaturated fat foods (EVOO and nuts):
   a) Does not lead to weight gain and may even help lose weight and reduce waist circumference.
   b) May help reduce diabetes risk.
   c) Is associated with lower clinical blood pressure and lower blood pressure by ambulatory monitoring (an objective marker)
Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

Ramón Estruch, M.D., Ph.D., Emilio Ros, M.D., Ph.D., Jordi Salas-Salvadó, M.D., Ph.D., Maria-Isabel Covas, D.Pharm., Ph.D., Dolores Corella, D.Pharm., Ph.D., Fernando Arós, M.D., Ph.D., Enrique Gómez-Gracia, M.D., Ph.D., Valentina Ruiz-Gutiérrez, Ph.D., Miquel Fiol, M.D., Ph.D., José Lapetra, M.D., Ph.D., Rosa Maria Lamuela-Raventós, D.Pharm., Ph.D., Lluís Serra-Majem, M.D., Ph.D., Xavier Pintó, M.D., Ph.D., Josep Basora, M.D., Ph.D., Miguel Angel Muñoz, M.D., Ph.D., José V. Sorlí, M.D., Ph.D., José Alfredo Martínez, D.Pharm, M.D., Ph.D., and Miguel Angel Martínez-González, M.D., Ph.D., for the PREDIMED Study Investigators*
Press Impact

More than 150 sources of information only in USA

Timeline of articles

- A: It's the Olive Oil: Mediterranean Diet Lowers Risk of Heart Attack and Stroke
  TIME - Feb 25, 2013
- B: Mediterranean diet cuts risk of stroke
  USA TODAY - Feb 25, 2013
- C: Mediterranean diet ‘as good as statins’
  Telegraph.co.uk - Feb 26, 2013
- D: If You Eat the Mediterranean Way, Can You Drop Your Heart Meds?
  Forbes - Feb 26, 2013
- E: Can Olive Oil and Nuts Prevent Heart Attacks?
  Huffington Post - Feb 27, 2013

Sources:
- New York Times
- Huffington Post
- NBCNews.com
- San Francisco Chronicle
- Philadelphia Inquirer
- NPR (blog)
- CBS News
- Newsday
- TIME
TOWARDS AN EVEN HEALTHIER MEDITERRANEAN DIET

• TO CHANGE COMMON OLIVE OIL BY EXTRA VIRGIN OLIVE OIL.
• TO INCREASE INTAKE OF NUTS AND FATTY FISH.
• TO SUBSTITUTE REFINED CEREALS BY WHOLE GRAIN CEREALS; TO INCREASE CONSUMPTION OF DIETETIC FIBER.
• TO REDUCE SALT INTAKE (SODIUM).
• TO MANTAIN A MODERATE INTAKE OF RED WINE.
• TO REDUCE INTAKE OF RED MEAT AND PROCESSED MEATS.
• TO AVOID CONSUMPTION OF SODA DRINKS AND COMMERCIAL BAKERY, SWEETS AND PASTRIES.
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Thank you for your attention