

The PREDIMED¹ trial examined 7447 participants ranging from 55 to 80 years of age who were at high cardiovascular risk, but with no cardiovascular disease at enrollment, to one of three diets:

- a “Mediterranean Diet” supplemented with extra-virgin olive oil
- a “Mediterranean Diet” supplemented with mixed nut or
- a control diet with advice to reduce dietary fat.

The “Mediterranean Diet” was the participants normal diet. For all three groups, the mean BMI at the start of the trial was 30 – that is, obese. The majority of the participants were receiving medications that conflicts with the claim that there was “no cardiovascular disease at enrollment”. 50% were receiving ACE inhibitors, 20% diuretics, 29% other antihypertensive agents, 40% statins, 20% antiplatelet therapy. This is not a full list of medications.

- Angiotensin-converting enzyme (ACE) inhibitors are a group of medications that dilate blood vessels and consequently lowers blood pressure and increase the flow of blood. Nitric oxide is produced by the endothelial cells to produce the same effect.
- Diuretics increase the amount of water and salt expelled as urine. They are most commonly used to treat high blood pressure.
- Other anti-hypertensive agents are used to treat high blood pressure.
- Statins are used to reduce the levels of cholesterol in the blood.
- Antiplatelet therapy drugs are used to decrease platelets from clotting. Platelets are involved in forming blood clots to prevent bleeding and are used to prevent stroke and heart attacks.

All participants received educational sessions and free provision of extra-virgin olive oil, mixed nuts or non-food gifts depending on group assignment.

Despite the fact that obesity is a major risk factor for cardiac disease, the average BMI at the end of the five year trial was not published. The change to medication use after five years was also omitted. The use of medications confounds and invalidates any results that may be due to dietary intervention.

After five years, the average absolute risk for a major cardiovascular event (heart attack, stroke, or death from cardiovascular causes) was 5.7% for the control diet. For the Mediterranean Diet with Extra Virgin Olive Oil, the average risk was 3.6% and 4.0% for the Mediterranean Diet with Nuts.

The relative decrease in the primary outcome for the Olive Oil diet was 37% and 34% for the Nut diet which may seem reassuring, it only resulted an absolute decrease in risk of 2.1% and 1.7% respectively.

Over 4.8 years of follow-up, metabolic syndrome developed in 50.0% of the participants who did not have the condition at baseline. The risk of developing metabolic syndrome did not differ between participants assigned to the control diet or to either the two Mediterranean diets.²

Condition	Normal Diet		Med Diet + EVOO		Med Diet + Nuts	
	Baseline %	Final %	Baseline %	Final %	Baseline %	Final %
Metabolic syndrome	64.7	68.6	65.1	66.6	61.8	64.9
Central obesity	75.3	75.0	74.4	74.1	69.5	70.9
High triglycerides	32.5	33.4	34.3	32.6	32.5	30.6
High blood pressure	94.7	95.4	93.5	95.4	93.8	94.8
High fasting serum glucose	66.3	71.9	65.6	68.9	64.5	68.9

Prevalence (%) of participants with metabolic syndrome and component conditions

After nearly 5 years of follow-up, all diets increased the markers of metabolic syndrome with the exception of triglycerides which was marginally reduced.

The average fat consumed for all three groups at the start of the trial was 40%. Since the participants were given free olive oil or free nuts, it is unsurprising that the consumption of these items were increased, resulting in an increase of fat consumption at 12 months to 41% for the olive oil group and 43% for the nut group. The control group, the misnamed **Low-fat Diet**, reduced their fat consumption to 38%.

The average US fat consumption is 33%.

To summarise, 50% of the participants that did not have metabolic syndrome at the start of the trial, were afflicted at the end of the trial.

The only dietary change that the participants made was the addition of either olive oil or nuts to their normal diet - a diet that led them to be very overweight with the majority having metabolic syndrome and taking medications in the first place.

A lead researcher of the PREDIMED trial was emailed asking if the medication use at the end of the trial was published. A response was received on the 28th August 2019, stating, in bold lettering, that **"You are right. We have not published yet this information."** The same applies to the weight status. Given the large increase of consumption of both olive oil and nuts in the intervention diets,³ it is highly likely that both the extra olive oil and nuts groups increased their weight and medication use. This was the experience in the Lyon Diet-Heart Study.

The participants were very unhealthy at the start of trial and were worse at the end. The change in medication use is not recorded so this confounds the results - it is not possible to determine if the results are a reflection of medication use or dietary interventions.

This is not an endorsement of the Mediterranean Diet - or at least the Mediterranean Diet as defined by the PREDIMED study.

Footnotes

1. Estruch, R. et al. (2018) Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. *New England Journal of Medicine*. 378 (25), e34.
2. Babio, N. et al. (2014) Mediterranean diets and metabolic syndrome status in the PREDIMED randomized trial. *Canadian Medical Association Journal*. 186 (17), 9.
3. Salas-Salvadó, J. et al. (2008) Effect of a Mediterranean Diet Supplemented With Nuts on Metabolic Syndrome Status. *Archives of Internal Medicine*. 168 (22), 2449.