

The Official Voice of the International Nut and Dried Fruit Council Foundation for the World Nut and Dried Fruit Trade

MELBOURNE WELCOMES 2014 INC CONGRESS

NEW! WORLD TRADE MAP DEBUTS 2014 INC RESEARCH FUNDING NOW AVAILABLE



NUTS REDUCE THE RISK OF MORTALITY IN INDIVIDUALS AT HIGH CARDIOVASCULAR RISK: LAST RESULTS OF THE PREDIMED STUDY

JORDI SALAS-SALVADÓ AND MARTA GUASCH-FERRÉ HUMAN NUTRITION UNIT, FACULTY OF MEDICINE AND HEALTH SCIENCES, ROVIRA I VIRGILI UNIVERSITY, REUS, SPAIN.



Nuts are an important component of the Mediterranean diet (MedDiet) and a good source of unsaturated fatty acids, fiber, minerals (potassium, calcium and magnesium), vitamins (folate and tocopherols) and other bioactive compounds, such as phytosterols and polyphenols $(^{1, 2})$. The healthy benefits of nuts have been attributed to their unique nutritional composition.

Previous studies have suggested that frequent nut consumption is associated with a reduced risk of several cardiovascular risk factors such as dyslipidemia, type 2 diabetes mellitus, metabolic syndrome and also cardiovascular disease (³). A small protective effect on all-cause and cancer mortality has been suggested, however the beneficial effect might be more robust in Mediterranean regions, where nut consumption per person is relatively high compared to other countries.

The main aim of the PREDIMED study, which included 7,447 elderly men and women at high cardiovascular risk, was to test the efficacy of two Mediterranean diets (one supplemented with extra-virgin olive oil and another with nuts: walnuts, almonds and hazelnuts), as compared to a control diet (advice on a low-fat diet), on primary cardiovascular prevention; the results have been published in the New England Journal of Medicine and have shown lower risk of stroke (in the nut supplemented group) and a 30% relative risk reduction in major cardiovascular events in those individuals following a Mediterranean Diet enriched with either olive oil or nuts compared to the control group (⁴). Furthermore, a recent study conducted by our Human Nutrition Research Unit in the framework of the PREDIMED Study has been published in BMC Medicine. In this manuscript our aims were only to assess the association between baseline consumption of nuts (that is, the consumption of nuts previous to starting the intervention) and total mortality, cardiovascular and cancer mortality (instead of cardiovascular events). We have additionally included the repeated measurements for the consumption of nuts during follow-up as another exposure, regardless of the allocated arm of the trial; this is in contrast with the original PREDIMED study, which used an intention-to-treat analysis. In our longitudinal cohort study of individuals at high cardiovascular risk from the PREDIMED Study, THE FREQUENCY OF NUT CONSUMPTION WAS INVERSELY RELATED TO

TOTAL MORTALITY (ALL-CAUSE MORTALITY) after 4.8 years of follow-up (⁵).

Although our findings are in agreement with previous epidemiologic studies relating nuts, cardiovascular and all-cause mortality and we have hypothesized that there will be a significant effect of nuts on mortality, we have been surprised that THE INVERSE ASSOCIATIONS BETWEEN NUTS, CARDIOVASCULAR, CANCER AND ALL-CAUSE MORTALITY WERE SO STRONG. The reduction in total mortality for those participants consuming more than 3 servings of nuts per week were of 39%, and also a 55% lower risk of cardiovascular mortality was shown compared to those who never consumed nuts. In our study, 28 grams of nuts were considered one serving. The results on cancer mortality (showing 40% reduction in cancer death for those who consume >3 servings per week) were relatively new as few studies have evaluated this associations before. We have also observed that relative risk reductions were similar for the upper baseline category of nonwalnut nuts (34%) or walnut consumption (45%), and when we evaluated the repeated measurements of total nut consumption and all-cause mortality over time (32%). Those subjects consuming more nuts at baseline and allocated to the intervention with a MedDiet supplemented with nuts showed a significantly reduced risk of total mortality of 63%. As we have observed that consuming more than 84 grams of nuts per week are beneficial in preventing mortality; it must be pointed that previous studies have also shown that consuming higher amounts of nuts do not lead to an increase in body weight, increased risk of diabetes, metabolic syndrome and other chronic diseases (6).

The healthy nutritional profile and the unique composition of nuts may account for the inverse associations observed between nuts, chronic disease and mortality. Nuts are high in monounsaturated fatty acids, fiber, minerals, vitamins and many bioactive compounds

(1,2); all these nutrients are beneficial for health and may partly explain its effects on cardiovascular disease and mortality. The frequency of nut consumption has been inversely related to several chronic prevalent conditions, such as diabetes, hyperlipidemia, hypertension, obesity, metabolic syndrome, cancer, and CHD, among others (^{3,7}). These inverse associations can be influenced by various mechanisms; nuts improve the blood lipid profile and appear to decrease insulin resistance, and there is also evidence suggesting that they can modulate inflammation, oxidative stress, and endothelial function (8). As a large body of evidence supports the beneficial effects of frequent nut consumption on many health outcomes, it is plausible that nuts protect as well against all-cause mortality. A possible explanation that may account for the inverse relationship between walnuts and cancer mortality could be that walnuts were richer in free and total polyphenols than all the other nuts. As walnuts are usually consumed raw, and roasting can cause a decline in the efficacy in the antioxidant capacity, it has been shown that raw walnuts, as consumed in the PREDIMED study, had the highest antioxidant efficacy among all the nuts (⁹); this could play a beneficial role in the prevention of cancer.

Our study provides further evidence of the inverse relationship between the frequency of nut consumption and the risk of mortality in a Mediterranean population at high cardiovascular risk with relatively high nut intake. The message that could be given based on our findings is mainly that the consumption of more than 3 servings per week (1 serving = 28 grams of nuts) is associated with lower risk of cardiovascular and cancer mortality and also all-cause mortality in a Mediterranean population at high cardiovascular risk. Even though the scientific evidence regarding this issue is consistent, further research would be helpful for understanding better the mechanisms by which nuts exert protective effects.

^{9.} Vinson JA, Cai Y: Nuts, especially walnuts, have both antioxidant quantity and efficacy and exhibit significant potential health benefits. *Food Funct* 2012, 3:134-140.



^{1.} Salas-Salvado J, Bullo M, Perez-Heras A, Ros E: Dietary fibre, nuts and cardiovascular diseases. Br J Nutr 2006, 96:S46-S51.

^{2.} Ros E, Tapsell LC, Sabate J: Nuts and berries for heart health. *Curr Atheroscler Rep* 2010, 12:397-406.

^{3.} Ros E: Health benefits of nut consumption. Nutrients 2010, 2:652-682.

^{4.} Estruch R, Ros E, Salas-Salvado J, et al.: **PREDIMED Study Investigators: primary prevention of cardiovascular disease with a** Mediterranean diet. *N Engl J Med* 2013, 368:1279-1290.

^{5.} Guasch-Ferre M, Bullo M, Martinez-Gonzalez MA, et al.: Frequency of nut consumption and mortality risk in the PREDIMED nutrition intervention trial. *BMC Med*. 2013 Jul 16;11:164.

^{6.} Sabate J, Ang Y: Nuts and health outcomes: new epidemiologic evidence. Am J Clin Nutr 2009, 89:1643S-1648S.

^{7.} Salas-Salvado J, Fernandez-Ballart J, Ros E, et al.: **PREDIMED Study Investigators: effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status: one-year results of the PREDIMED randomized trial.** *Arch Intern Med* 2008, 168:2449-2458.

^{8.} Sabate J, Oda K, Ros E: Nut consumption and blood lipid levels: a pooled analysis of 25 intervention trials. Arch Intern Med 2010, 170:821-827.