Cardiovascular disease and cancer are the common causes of death worldwide, and worrisomely their incidence will continue to increase in the near future. Fortunately, both diseases can be largely preventable through a healthy lifestyle, particularly a healthy diet. To date, several studies have evaluated the potential beneficial effects of different dietary patterns, foods and nutrients on the prevention of cardiovascular disease and cancer as well as on increasing longevity. However, analysis of dietary patterns rather than single foods or nutrients may be a more useful option since it examines the effects of the overall diet with the synergistic interaction of its food and nutrient components. In this respect, a systematic review of the evidence supporting the causal link between dietary factors and cardiovascular disease ranked the Mediterranean diet as the most likely dietary model to provide protection against disease. Moreover, researchers have demonstrated increased interest in analysing the protective effects of key foods of healthy diets, such as nuts.

In this issue of the *International Journal of Epidemiology*, van den Brandt and Schouten make a relevant contribution to this field by analysing the relationship of tree nut and peanut intake with total and cause-specific mortality in 120 852 men and women included in the Netherlands Cohort Study. The authors used a nested case-cohort design in which a random subsample of the baseline study participants ($n = 5000$) was chosen. Random selection of a subcohort allows variables to be measured in a subsample rather than the entire study population, yet the findings are still generalizable to the full cohort. Noticeably, tree nut and peanut intakes were inversely related to all-cause mortality, whereas peanut butter was not. In addition, in those participants who reported an intake of 10 g/day or more of nuts, neurodegenerative disease, respiratory disease, cancer and cardiovascular mortalities were reduced by 46%, 39%, 21% and 17%, respectively, compared with non-consumers. They also observed an interesting interaction between nut and alcohol intakes.

Nuts are nutrient-dense fruits characterized by a hard shell and dry seed rich in unsaturated fatty acids, high-quality protein, fibre, vitamins (folate, niacin, vitamin E), minerals (potassium, calcium, magnesium), carotenoids, phytosterols and phenolic compounds such as ellagic acid and urolithins. The food matrix plays a crucial role in determining accessibility and extractability of these bioactive compounds and hence their absorption, metabolism and final biological action in the human body. In addition, some important compounds such as polyphenols and other antioxidants are mainly in the skin of nuts. All these facts may explain, at least in part, why peanut butter use does not confer protection, whereas peanuts and tree nuts do.

Two observational studies, the Doetinchem Cohort Study and the Nurses’ Health Study, found that long-term nut consumption was related to better overall cognition at older age, but not to cognitive decline during follow-up for 5 to 6 years. Likewise, in a long-term

### Commentary: Frequent nut consumption protects against cardiovascular and cancer mortality, but the effects may be even greater if nuts are included in a healthy diet

**Ramon Estruch**$^{1,2,\ast}$ and **Cristina Sierra**$^1$

$^1$Department of Internal Medicine, Hospital Clinic, Institut de Recerca Biomèdica August Pi i Sunyer, University of Barcelona, Barcelona, Spain and $^2$CIBER OBN, Instituto de Salud Carlos III, Madrid, Spain

$^\ast$Corresponding author. Department of Internal Medicine, Hospital Clinic, Villarroel, 170, 08036 Barcelona, Spain. E-mail: restruch@clinic.ub.es

Accepted 9 March 2015
randomized intervention trial, the PREDIMED study, participants allocated to the Mediterranean diet plus nuts group showed improvement in memory compared with those ascribed to the control group, after 5 years of intervention. The results of the study of van der Brandt and Schouten go in the same direction: nut intake protects against neurodegenerative diseases and ageing. The protective effect of nuts on respiratory mortality is impressive. Although other studies have observed that healthy diets were associated with a lower risk for developing chronic obstructive pulmonary disease, the evidence is still limited and new studies on this issue are warranted.

More interesting are the results on the protective effects of nut consumption on cancer mortality. A recent systematic review and meta-analysis has found that nut consumption was associated with decreased risk of cancer deaths, comparing the highest with the lowest categories of intake [risk ratio (RR) 0.86; 95% confidence interval (CI): 0.75, 0.98], an effect size similar to that observed in the study discussed. Possible mechanisms that may explain these effects include changes in specific processes related to cancer development such as DNA protection, regulation of cell differentiation and proliferation, reduction of tumour initiation or promotion, and regulation of immunological and inflammatory response.

The protective effects of nuts on cardiovascular morbidity and mortality and their intermediate biomarkers (e.g. blood pressure and lipid profile) are better known. However, the interaction observed between nuts and alcohol intake is more novel. There is ample scientific evidence that regular light-to-moderate consumption of alcohol is associated with a lower risk of fatal and non-fatal coronary heart disease, stroke and all-cause mortality, as opposed to binge drinking. Part of the beneficial effects of alcoholic beverages is due to the alcohol content (ethanol) and another part is attributed to its non-alcoholic components, mainly polyphenols. Since some evidence has suggested that ethanol may favour intestinal absorption of bioactive compounds of wine, it can be hypothesized that alcohol may also favour the absorption of polyphenols of other dietary foods such as nuts.

Interestingly, these protective effects of nut consumption over all and cause-specific mortality were observed in participants who reported intakes of 10 g a day or more compared with non-consumers. This amount is much lower than that recommended by the Food and Drug Administration that approved a health claim that eating 1.5 oz (43 g) of nuts daily reduces the risk of heart disease. Another important issue is how nuts are prepared (e.g. salted, spiced, roasted and raw). The influence of the nut preparation method on their effects on health and disease should be analysed in future long-term randomized trials.

Ideally, sound nutritional recommendations for health prevention should be based on the results of large randomized clinical trials with ‘hard’ end-points as main outcomes. Such evidence has been obtained for the Mediterranean diet plus mixed nuts in the results of the PREDIMED primary prevention trial. However, new randomized nutrition trials using an intervention including only nuts are warranted to help refine advice on the best dosage and the type of nuts most useful to prevent disease. In the meantime, there is compelling evidence to recommend the use of nuts (better raw nuts than salted or toasted) at least three times a week in order to live longer and healthier lives.

Conflict of interest: None declared.

References