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Invited Commentary

Mediterranean diet: the whole is more than the sum of its parts

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The Mediterranean diet corresponds to the traditional dietary pattern found in Greece, Southern Italy, Spain and other olive-growing countries of the Mediterranean basin in the 1960s. It included the abundant use of olive oil as the major culinary fat, a high consumption of plant foods (nuts, fruits, vegetables, legumes and whole grains), moderate to high fish consumption and a moderate consumption of wine. In contrast, consumption of red meats, processed meats, meat products and butter was very low[1]. This pattern fits well with the current paradigm of assessing overall food patterns instead of isolated foods or nutrients[2]. The profile of nutrient intake of the Mediterranean diet includes a high monounsaturated: saturated fat ratio, a high intake of α-linolenic acid, moderate ethanol intake, high intakes of fibre, vitamins, folate and natural antioxidants, and a low intake of animal protein.

The pioneering Seven Countries study[3] followed an ecological design and suggested that the traditional Mediterranean diet could be the most plausible explanation for increased longevity and lower CHD rates observed in Mediterranean countries. Trichopoulou *et al.*[4,5] conducted two seminal studies and introduced on operational nine-point Mediterranean diet score, which has been subsequently used in many epidemiological investigations. One of these papers has made a profound contribution to knowledge of the place of nutrition in public health. It assessed the Greek EPIC cohort (*n* 22 043) and convincingly showed an inverse association between conformity to the Mediterranean diet and total mortality[5]. A two-point increment in this score corresponded to a 25 % reduction in total mortality. Other cohort studies confirmed these findings. Of these, nine were pooled in a quantitative meta-analysis[6]. For each two-point increment in the 0–9 Mediterranean diet score, the pooled relative risks were 0·92 (95 % CI 0·90, 0·94) for total mortality (nine studies) and 0·90 (95 % CI 0·87, 0·93) for CVD (eight studies). There was no evidence of between-study heterogeneity. Notably, six of the eight individual cardiovascular studies showed significant protection. In this issue of the *British Journal of Nutrition*, Dilis *et al.*[7] show, in the Greek EPIC cohort with a longer follow-up, that the Mediterranean diet specifically protects against CHD. Inverse associations of the Mediterranean diet with the incidence of or mortality from CHD have been reported by three previous cohorts (two in Spain and another in the USA) and a recent publication from the Northern Manhattan Study[8]. Moreover, some studies have identified the Mediterranean diet as a *post hoc* food pattern, using factor analysis, and have found that it was associated with a lower risk of CHD[9].

Beyond merely statistical associations, and beyond the 'myths' surrounding the concept of the Mediterranean diet, an interesting systematic review gave support to a truly causal protection (strength, consistency, temporality and coherence)[10]. That review assessed the effect of thirty-two potential candidate dietary factors on CHD, and ranked the Mediterranean diet in the first place as the dietary model with the strongest causal evidence of protection. An important advantage of the Mediterranean diet was the availability of a randomised trial (the Lyon Diet Heart Study) showing a protective effect[11]. Randomised trials of dietary intervention constitute hallmarks in the acquisition of knowledge in this field. The Lyon trial was prematurely stopped after 27 months because of a striking reduction in cardiovascular events in comparison with a prudent Western pattern (fourteen *v.* forty-four events). However, the Lyon trial only included survivors of a myocardial infarction, the number of observed events was small, and no special consideration was given to olive oil, which is the major source of fat in Mediterranean countries. The final results of the PREDIMED (Prevención con Dieta Mediterránea; Prevention with Mediterranean Diet) randomised trial[12], including 7447 high-risk subjects in primary cardiovascular prevention, are expected in 2012. They will shed further light on the potential role of a Mediterranean diet on CVD prevention.

Every individual component of the Mediterranean diet has been separately investigated in the paper by Dilis *et al.*[7]. Most of them individually showed no evidence whatsoever of an association with CHD. The exceptions were an inverse association with fruits and nuts and a direct association for red meats. The Spanish SUN (Seguimiento Universidad de Navarra; Follow-up University of Navarra Study) cohort also found for fruits and nuts a significant inverse association with respect to overall CVD and the strongest (albeit non-significant) inverse association with coronary disease[13]. Interestingly, the PREDIMED trial uses supplementation with nuts in one of the randomised arms[12]. Regarding red meats, a recent report from two large American cohorts is consistent with the present results in showing a direct association of red meats with mortality[14].

The biological plausibility to support a causal role of the Mediterranean diet in CHD prevention needs to take into account that the effect of an overall dietary pattern is likely

to be considerably greater than the effect of individual foods or nutrients. The belief that a single nutrient will lower disease risk implies a reductionist and overly optimistic view. The complexity of the pathophysiological processes involved in the genesis of coronary disease suggests that multiple, cumulative and synergistic mechanisms are involved. The Mediterranean dietary pattern supports the concept of an overall healthy eating pattern that also seems the best known model to fulfil nutrient requirements[15]; it is possible that a combination of nutrient-rich foods synergises to foster favourable changes in intermediate pathways of cardiometabolic risk, as supported by randomised trials[16]. The Mediterranean diet supplies abundant polyphenols from virgin olive oil, fresh fruits, vegetables, nuts and legumes, with important antioxidant and anti-inflammatory properties, and includes moderate intake of alcohol. A key feature of the typical frugality of the Mediterranean diet is the scarce consumption of processed meats, red meats and *trans*-fat. Each of these individual aspects of the diet is known to be associated with substantially lower cardiovascular risk. It is very likely that the joint effect of all of them together might be larger than the sum of their parts.

In light of the increasing global burden of CVD, cardiovascular prevention constitutes a major public health goal, and the Mediterranean diet is an achievable and sustainable objective that should be promoted.

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