





## Abstract

# Combination of Adherence to a Traditional Mediterranean Diet and Ultra-Processed Food Consumption in Relation to All-Cause and Cardiovascular Mortality: Prospective Findings from the Moli-Sani Study <sup>†</sup>

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**Abstract:** Background and objectives: The Mediterranean Diet (MD) has been consistently associated with lower mortality in cohort studies worldwide. Ultra-processed foods (UPF) are increasingly displacing nutritious traditional diets, with alarming health results globally. We examined the combined association of an MD and UPF consumption in relation to all-cause and cardiovascular disease (CVD) mortality in a cohort of Italian adults. Methods: Longitudinal analyses on 22,895 participants of the Moli-sani Study (2005–2010) followed for 12.2 years (median). Food intake was assessed using a 188-item FFQ. UPF was defined following the NOVA classification and calculated as the ratio (weight ratio; %) between UPF (g/d) and total food (g/d). The Mediterranean Diet Score (MDS; range 0–9) was used to assess adherence to MD. Low/High MD adherence (i.e. MDS < 6 or ≥ 6, respectively) was combined with low/high UPF consumption (i.e. <9.4 or ≥9.4% corresponding to the population’s median intake of UPF) to obtain a 4-level dietary variable reflecting dietary combinations from ‘low MD and high UPF’ to ‘high MD and low UPF’. Results: In multivariable-adjusted analysis controlled for known risk factors, compared to the ‘low MD and high UPF’ combination, taken as reference, the ‘high MD and low UPF’ combination had a significant 24% lower rate of all-cause mortality (Hazard ratio = 0.76; 95% CI 0.67–0.86). Participants reporting both “low MD and low UPF” had a significant but only 15% lower death rate (Hazard ratio = 0.85; 0.77–0.95), while individuals consuming both “high MD and high UPF” had a 4% not significant lower death rate (Hazard ratio = 0.96; 0.80–1.14; *p*-value for difference across groups < 0.001; *p*-value for interaction between MD and UPF = 0.47). Similar results were found for CVD mortality, with highest protection observed in the ‘high MD and low UPF’ dietary combination group (Hazard ratio = 0.74; 0.60–0.92) as compared to the reference combination. Discussion and conclusions: The combination of both high adherence to an MD and low UPF intake was associated with lowest all-cause and CVD death rate; the effects of both dietary exposures were additive. Besides the adoption, or maintenance, of an MD, dietary guidelines should also recommend to contextually reduce the dietary share of UPF to maximize Mediterranean diet-related health benefits.

**Keywords:** Mediterranean Diet; ultra-processed food; survival; cardiovascular mortality



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