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## Mediterranean Diet Can Lower All-Cause Mortality by 23%



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Nutrition and prevention guidelines emphasise dietary patterns over individual foods for health outcomes. A recent umbrella review of 495 meta-analyses on dietary patterns and cardiometabolic and anthropometric risk factors identified the Mediterranean diet as the most beneficial. This diet is endorsed by the US dietary guidelines, the American Heart Association, the European Society of Cardiology, and the Australian National Heart Foundation for improving cardiometabolic health and reducing cardiovascular disease (CVD) outcomes. Observational studies have shown that higher adherence to the Mediterranean diet correlates with reduced all-cause mortality, with a meta-analysis indicating a 10% reduction for every 2-point increase in Mediterranean diet adherence.

Despite this, long-term data on asymptomatic women is limited, warranting further investigation into the Mediterranean diet's impact on mortality in this group. The exact mechanisms linking the diet to lower mortality, particularly involving traditional and new cardiometabolic biomarkers (e.g., inflammation, lipids, glucose metabolism), are not fully understood. Improved inflammatory biomarkers, reduced oxidised LDL cholesterol, and lower blood pressure are associated with Mediterranean diet adherence, but their exact contributions to mortality reduction are unclear.

[A large-scale study](#) of 25,315 healthy US women over 25 years aims to explore this further, using mediation approaches to assess the contribution of both traditional and novel biomarkers to the mortality reduction associated with the Mediterranean diet.

### Evaluating the Impact of Mediterranean Diet Adherence on Mortality

The Women's Health Study (WHS) involved 39,876 female health professionals aged 45 and older, starting between April 30, 1993, and January 24, 1996, to assess the effects of low-dose aspirin, vitamin E, or placebos on cardiovascular and cancer outcomes. The trial ended in 2004 with no significant reduction in primary endpoints, and participants have since been followed observationally. For the current analysis, 25,315 women who provided baseline blood samples and dietary information were included.

Participants' adherence to the Mediterranean diet was assessed using a validated food-frequency questionnaire, with scores ranging from 0 to 9 based on intake of key components such as fruits, vegetables, nuts, and olive oil. They were categorised into three adherence levels: low (0–3), intermediate (4–5), and high (6–9).

Mortality was tracked through health questionnaires, family reports, and the National Death Index, with over 99% follow-up completeness. Blood samples collected at baseline were analysed for traditional biomarkers (e.g., cholesterol, CRP) and NMR spectroscopy was used for advanced cardiometabolic markers (e.g., lipoprotein subfractions, insulin resistance scores).

Statistical analysis involved Cox proportional hazards regression models to calculate hazard ratios (HRs) for mortality, adjusting for factors like age, smoking, physical activity, and menopausal status. Mediation analysis assessed whether biomarkers could explain the diet-mortality relationship, using both standard and counterfactual approaches.

Results indicated that higher adherence to the Mediterranean diet was associated with lower all-cause mortality. Biomarkers related to inflammation, lipid profiles, and glucose metabolism contributed to this association, but the specific mediating effects of these biomarkers on mortality reduction require further investigation.

### Mortality Reduction in Female Health Professionals: A 24.7-Year Cohort Study

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In the current analysis of 25,315 female healthcare professionals with a mean age of 54.6 years, participants with higher adherence to the Mediterranean diet generally led healthier lifestyles, with lower BMI and higher intake of beneficial foods. Differences were observed in most biomarker and risk factor profiles, with healthier biomarker profiles associated with higher diet adherence. However, some biomarkers like systolic blood pressure and LDL-C levels did not meet criteria for mediation but were included in subsequent analyses due to their previously reported associations with diet adherence.

During a 24.7-year follow-up, 3,879 all-cause deaths occurred, including 935 from cardiovascular disease (CVD) and 1,531 from cancer. Higher Mediterranean diet adherence was linked to decreased all-cause, CVD, and cancer mortality. Women with high diet scores ( $\geq 6$ ) had lower all-cause mortality (HR 0.77) compared to those with scores  $\leq 3$ . The diet's impact on cancer mortality was more pronounced than on CVD mortality.

After adjusting for confounders (smoking, physical activity, alcohol intake, menopausal factors), the mortality reduction remained significant for all-cause mortality but was attenuated for cancer and CVD mortality. In regression models, individual adjustments for risk factors mostly preserved the significance of all-cause mortality reductions.

Further analysis identified that small-molecule metabolites (homocysteine and alanine) and inflammation contributed the most to the diet's mortality benefits (14.8% and 13.0%, respectively), followed by TRLs (10.2%), BMI (10.2%), and insulin resistance (7.4%). HDL or LDL measures, hypertension, BCAAs, and haemoglobin A1c levels contributed less (<3%). Combined, these factors mediated 21.3% of the total diet-mortality association.

Sensitivity analyses confirmed the mediation results using both a counterfactual framework and standard mediation approaches.

### **Insights into Cardio-Metabolic Factors**

In this large-scale cohort study of 25,315 initially healthy US women followed for 25 years, higher adherence to the Mediterranean diet was associated with a 23% reduction in all-cause mortality. This reduction was partly mediated by small molecule metabolites (e.g., alanine), inflammatory biomarkers, TRL measures, insulin resistance, and BMI, but less so by blood pressure, HDL, LDL, apo B100, Lp(a), or glycemic measures.

These findings align with previous US and international studies reporting significant mortality reductions linked to higher Mediterranean diet adherence. While Mediterranean diet adherence was associated with lower cancer mortality more strongly than CVD mortality, consistent with findings from the UK Biobank study, prior shorter-term studies also demonstrated the diet's beneficial effects on cardiometabolic, inflammatory, and lipid biomarkers.

The study's strengths include its large cohort, validated dietary measures, comprehensive biomarker analysis, and high follow-up completeness. However, limitations include the predominantly non-Hispanic White, well-educated female participant base, potential exposure misclassification from dietary self-reports, and the lack of follow-up blood samples.

Adherence to the Mediterranean diet was associated with a 23% lower risk of all-cause mortality among US women, primarily through cardiometabolic risk factors. However, much of the diet's potential benefit remains unexplained, suggesting the need for future research on additional mediating pathways and cause-specific mortality.

**Source:** [JAMA Network Open](#)

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