**[N Engl J Med](https://www.ncbi.nlm.nih.gov/pubmed/30281995" \o "The New England journal of medicine.)**[.](https://www.ncbi.nlm.nih.gov/pubmed/30281995" \o "The New England journal of medicine.) 2018 Oct 4;379(14):1388-1389. doi: 10.1056/NEJMc1809971.

**Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts.**

The authors reply:

Correia correctly affirms that the results of the PREDIMED trial remained basically unchanged after departures from individual randomization in a subgroup of participants were addressed. This observed effect of the Mediterranean diet on prevention of cardiovascular disease was expected, consistent with many previous observational studies[1,2](https://www.nejm.org/doi/10.1056/NEJMc1809971?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dwww.ncbi.nlm.nih.gov) and another randomized trial.[3](https://www.nejm.org/doi/10.1056/NEJMc1809971?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dwww.ncbi.nlm.nih.gov) In the PREDIMED trial, as reported, more frequent contacts with the intervention groups before October 2006 did not modify the effect of the intervention. Actually, the effect was not weaker, but stronger (hazard ratio, 0.49), after October 2006. Therefore, we do not agree that an alternative explanation for the observed effect is that “imbalances in medical care may have taken place after randomization.” There was no ascertainment bias because independent committee members who were completely unaware of the intervention assignment adjudicated the end points. The trial was discontinued early after intervention for 4.8 years, instead of the planned 6 years, as recommended by the data and safety monitoring board after stopping rules established *a priori* in the protocol.

We agree with Jenkins and colleagues that, when appropriate, honest errors can be corrected by simultaneous retraction and republication, which could desirably become standard practice by the ICMJE. We appreciate the opportunity to work with the *Journal*editors during this process.

Stewart’s assumption that “both participants and the nutritionists had reasons to prefer one diet over another” is unfounded. When the PREDIMED trial started in 2003, the low-fat American Heart Association Step I diet used for the control group was accepted as the standard of care for prevention of cardiovascular disease.[4](https://www.nejm.org/doi/10.1056/NEJMc1809971?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dwww.ncbi.nlm.nih.gov) The departures from randomization in the PREDIMED trial did not consist of individual “preference and negotiation,” but of assignments according to clusters (household members or small clinics) in a subsample. We did audit the sites, although we assume some limitations. Stewart’s conjecture that “differences in outcomes reported in the PREDIMED trial could therefore be explained by patient selection rather than diet” is also unfounded, because patient selection would have led to a largely imbalanced distribution of baseline covariates across intervention groups. However, the imbalance (in only a few of the many measured variables) did not account for the observed effect. In addition, Table S25 in the Supplementary Appendix (available with the full text of our article at NEJM.org) shows that unmeasured confounders were unlikely to explain the observed effect. Our thorough reanalyses of the data support robust and consistent beneficial effects of the Mediterranean diet on prevention of cardiovascular disease.

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*Since publication of their article, the authors report no further potential conflict of interest.*

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