

CORRESPONDENCE



Retraction and Republication: Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. N Engl J Med 2013;368:1279-90.

TO THE EDITOR: Because of irregularities in the randomization procedures, we wish to retract the following article: Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. N Engl J Med 2013;368:1279-90. DOI: 10.1056/NEJMoa1200303.¹ We have reanalyzed the data and have published a new report: Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. N Engl J Med. DOI: 10.1056/NEJMoa1800389.²

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Editor's note: An analysis of reports of randomized trials for improbable distributions of baseline data included 934 reports published in the *Journal* and identified 11 with distributions of baseline variables that did not appear consistent with randomization (Carlisle JB. *Anaesthesia* 2017;72:944-52. DOI: 10.1111/anae.13938. Epub 2017 June 4). We reviewed these 11 trial reports and replicated the Carlisle analysis. In 5 reports, standard errors were inadvertently reported as standard deviations, or vice versa. These errors explained the findings and have been corrected; the 5 reports are as follows: High-Dose Atorvastatin after Stroke or Transient Ischemic Attack (N Engl J Med 2006; 355:549-59), Treatment of Periodontitis and Endothelial Function (N Engl J Med 2007;356:911-20), Extended Antiretroviral Prophylaxis to Reduce Breast-Milk HIV-1 Transmission (N Engl J Med 2008;359:119-29), Effect of Bronchoconstriction on Airway Remodeling in Asthma (N Engl J Med 2011;364:2006-15), and Horse versus Rabbit Antithymocyte Globulin in Acquired Aplastic Anemia (N Engl J Med 2011;365:430-8). For 5 other reports,

limitations in the Carlisle analysis, such as lack of accounting for correlation among baseline variables, most likely explained the findings.

For the remaining report, Primary Prevention of Cardiovascular Disease with a Mediterranean Diet (N Engl J Med 2013;368:1279-90), the authors' subsequent review of their data and randomization procedures identified protocol deviations, including the enrollment of participants who were not randomized. The authors have therefore withdrawn their original report (Retraction and Republication: Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. N Engl J Med 2013;368:1279-90. N Engl J Med. DOI: 10.1056/NEJMc1806491). The *Journal* has now published their new report of the study, which describes the protocol deviations and reports reanalyses of the data (Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. N Engl J Med. DOI: 10.1056/NEJMoa1800389).

This letter was published on June 13, 2018, at NEJM.org.

1. Estruch R, Ros E, Salas-Salvadó J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med 2013;368:1279-90.

2. Estruch R, Ros E, Salas-Salvadó J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet supplemented with extra-virgin olive oil or nuts. N Engl J Med 2018;378:e34(1)-e34(14).

DOI: 10.1056/NEJMc1806491

Molecular Minimal Residual Disease in Acute Myeloid Leukemia

TO THE EDITOR: Jongen-Lavrencic and colleagues (March 29 issue)¹ highlight the clinical usefulness of a next-generation sequencing panel to identify minimal residual disease in patients with acute myeloid leukemia (AML) during complete remission. The authors found that the detection of nonclonal hematopoiesis-associated mutations (non-*DTA* mutations, or those not involving *DNMT3A*, *TET2*, or *ASXL1*) during complete remission predicted a poor prognosis; however, these findings are called into question by the considerable rate of false negative results of next-generation sequencing.

In Figure 3 of the article, available at NEJM.org, the rate of false negative results with next-generation sequencing (i.e., a negative result on next-generation sequencing and a positive result on multiparameter flow cytometry) was 12.1% (among 41 of 340 patients). Thus, next-generation sequencing had a disconcertingly high false negative rate of detection of non-*DTA* mutations during complete remission. Given that patients with negative results on next-generation sequencing and positive results on multiparameter flow cytometry have a worse prognosis than those with negative results on both tests, the data

shown in Figure 2 of the article are called into question by the false negative results with next-generation sequencing. In that figure, next-generation sequencing was used to stratify patients according to detection or no detection of non-*DTA* mutations during complete remission.

Thus, it is likely that a considerable number of patients in the “no detection of non-*DTA* mutation” category were mistakenly classified because of a false negative result on next-generation sequencing. Do the authors have a sense of how many patients in this group had minimal residual disease that was detected by means of multiparameter flow cytometry?

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No potential conflict of interest relevant to this letter was reported.

1. Jongen-Lavrencic M, Grob T, Hanekamp D, et al. Molecular minimal residual disease in acute myeloid leukemia. N Engl J Med 2018;378:1189-99.

DOI: 10.1056/NEJMc1805501

TO THE EDITOR: Jongen-Lavrencic et al. report that the detection of mutations unrelated to clonal