To The Editor: Eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids, the 2 main omega-3 long-chain polyunsaturated fatty acids of marine origin, have shown promise for the prevention of cardiovascular disease (CVD) outcomes in animal studies and epidemiologic studies. Although several recent trials have shown benefits, as summarized in Mayo Clinic Proceedings in 2019, 2 randomized control trials published in late 2020 showed neutral results. The situation is summarized thoughtfully in a recent editorial by Farukhi et al, published in Mayo Clinic Proceedings, which cited our recent meta-analysis on myocardial infarction (MI) relative risk (RR), 0.87; 95% confidence interval (CI), 0.80 to 0.96, high GRADE certainty, fatal MI RR, 0.65; 95% CI, 0.46 to 0.91, moderate certainty and CHD mortality RR, 0.91; 95% CI, 0.85 to 0.98, low certainty remain unchanged.

The newly published results change slightly the meta-analysis estimates, but not the conclusions, for CVD events and CHD events. For CVD events, the pooled estimate is now RR, 0.96; 95% CI, 0.91 to 1.00 (changed from RR, 0.95; 95% CI, 0.90 to 1.00). For CHD events: RR, 0.91; 95% CI, 0.85 to 0.97 (changed from RR, 0.90; 95% CI, 0.84 to 0.97). These results are summarized in the Figure.

The effect remains dose dependent for MI; an additional 1 g/d in
EPA and DHA is associated with a 9% reduction in MI but no longer for CVD events. None of the other conclusions is changed; the effect remains independent of the year of publication, the population baseline risk, or whether the long-chain polyunsaturated fatty acids agent consisted of only EPA or a combination of EPA and DHA.

Although we believe that understanding why a high-dosage trial, such as STRENGTH, failed to find an effect will require more research, the totality of the evidence, including now 42 studies involving almost 150,000 participants, shows statistically significant reductions in fatal MI (−35%), MI (−13%), CHD events, and CHD mortality (both −9%). This is still consistent with the conclusion that EPA and DHA intake is an effective lifestyle intervention for protection against CVD.

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Potential Competing Interests: Dr Bernasconi is an employee of the Global Organization for EPA and DHA Omega-3s (GOED), a 501(c)6 not-for-profit trade association. Dr Lavie has served as speaker for Amarin Corporation, has consulted for DSM Nutritional Products, and has presented an educational video at the American Heart Association meeting for GOED. The other authors report no competing interests.

Does the Common Type 2 Diabetes-Susceptibility Variant in the MTNR1B Gene Matter for Glycemic Control Among Patients on Antidiabetic Pharmacotherapy?

To The Editor: The variant rs10830963 (G risk allele) in the melatonin receptor 1B (MTNR1B) gene increases the risk of type 2 diabetes.1 Here, we investigated whether the G risk allele is associated with poorer glycemic control among patients with type 2 diabetes on antidiabetic pharmacotherapy.

Type 2 diabetes was confirmed either by a validated algorithm based on self-reported disease, medication, and diagnosis of diabetes in medical history® or hemoglobin (HbA1c level ≥6.5%).3 Following exclusion (missing data on HbA1c and covariates, HbA1c z-values > 3 and < −3, and genetically related participants), 8979 White patients with type 2 diabetes were available for analysis. Data on subjects’ antidiabetic pharmacotherapy was taken from the UK Biobank verbal interview.

The MTNR1B rs10830963 genotype (chromosome 11, intron variant) was directly genotyped by the Affymetrix UK Biobank Lung Exome Evaluation Axiom array (Thermo Fisher Scientific, Santa Clara, California) or the Applied Biosystems UK Biobank Axiom array (Thermo Scientific). Quality control and imputation using the Haplotype Reference Consortium, UK10K, and 1000 Genomes phase 3 reference panels were conducted centrally. Testing for Hardy-Weinberg equilibrium revealed that the single nucleotide polymorphism did not deviate from the expected genotype proportion.

HbA1C values, measured by Bio-Rad VARIANT II TURBO HbA1c analyzer (Bio-Rad, Hercules, California), were naturally log transformed before analysis. We assumed additive genetic effects for all analyses. All analyses were performed with SPSS 24.0 (SPSS Statistics, IBM, Chicago, Illinois) and, if not otherwise specified, adjusted for participants’ age at UK Biobank investigation, sex, Townsend index reflecting socioeconomic status, body mass index, hypertension status, smoking status, level of physical activity, sleep duration, age at diagnosis of type 2 diabetes, number of prescribed antidiabetic drugs, the region of the