Clinical Nutrition 38 (2019) 2462

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Letter to the Editor

Reply-letter to the editor-effects of omega-3 polyunsaturated fatty acid intake in patients with chronic kidney disease: Systematic review and meta-analysis of randomized controlled trials

We thank *Kumar A. and Shariff M* et al. for conducting a trial sequential analysis (TSA) on our meta-analysis of omega 3 fatty acid supplementation in chronic kidney disease. The authors estimated the required information size and trial sequential boundary to determine if the observed beneficial effect of omega 3 supplementation on cardiovascular mortality is conclusive or whether further evidence is needed. They found that an information size of 1314 is needed to detect a risk reduction of 56% in cardiovascular mortality with omega 3 supplementation. They assumed a power of 80%, an alpha of 5%, cardiovascular mortality rate of 5.26% in the control arm, and a diversity (D^2) of 0%. While the required information size was not achieved (1314 versus a pooled information size of 1104 in our meta-analysis), the authors reported the z curve crossed the estimated trial sequential boundary after study 8. Therefore, they concluded that there is sufficient evidence to confirm the benefits of omega-3 supplementation on cardiovascular mortality and no further trials are needed. Of note, the estimates of effects and study heterogeneity were sourced from our meta-analyses.

In our meta-analysis, we included only eight studies and the majority involved less than 100 patients. In presence of small number of trials and limited sample size, the I^2 test has low power to detect the heterogeneity between studies. Therefore, deriving the D^2 values from the available I^2 is not recommended (http://www.ctu.dk/tsa/files/tsa_manual.pdf). We suggest that estimations of the required information size and trial sequential boundary in this TSA are too optimistic as these were based on a D^2 of 0%. Notably, the trial sequential boundary is very sensitive to the D^2, and even under the most optimistic scenario, the z curve crossed the trial sequential boundary only marginally.

More importantly, certainty of the evidence is not only determined by the precision of the observed effect and the achievement of the required information size, but also other study design issues such as risk of bias leading to reduced confidence in the observed estimate of effect, equally applicable in our meta analysis. Given the uncertainties and ambiguities raised, future well-powered and quality trials are needed to define the direction and magnitude of the benefits of omega-3 supplementation on patient-relevant outcomes such as mortality in patients with chronic kidney disease.

Valeria M. Saglimbene*
Sydney School of Public Health, Faculty of Medicine and Health, University of Sydney, Edward Ford Building A27, NSW, 2006, Australia

Diaverum Medical-Scientific Office, Trollebergsvagen 2-4, 222 29, Lund, Sweden

Germaine Wong
Sydney School of Public Health, Faculty of Medicine and Health, University of Sydney, Edward Ford Building A27, NSW, 2006, Australia

Centre for Kidney Research, Children's Hospital at Westmead, 170 Hawkesbury Rd, Westmead, NSW, 2145, Australia

Department of Renal Medicine, Westmead Hospital, Hawkesbury Rd & Darcy Road, Westmead, NSW, 2145, Australia
E-mail address: germaine.wong@health.nsw.gov.au.

Armando Teixeira-Pinto
Sydney School of Public Health, Faculty of Medicine and Health, University of Sydney, Edward Ford Building A27, NSW, 2006, Australia

Centre for Kidney Research, Children's Hospital at Westmead, 170 Hawkesbury Rd, Westmead, NSW, 2145, Australia
E-mail address: armando.teixeira-pinto@sydney.edu.au.

Jonathan C. Craig
College of Medicine and Public Health, Flinders University, Bedford Park, SA, 5042, Adelaide, Australia
E-mail address: jonathan.craig@flinders.edu.au.

Giovanni F.M. Strippoli
Sydney School of Public Health, Faculty of Medicine and Health, University of Sydney, Edward Ford Building A27, NSW, 2006, Australia

Diaverum Medical-Scientific Office, Trollebergsvagen 2-4, 222 29, Lund, Sweden

Department of Emergency and Organ Transplantation, University of Bari, Piazza Giulio Cesare, 70124, Bari, Italy

Diaverum Academy, Via Solarino 5, Bari, 70124, Italy
E-mail address: gfmstrippoli@gmail.com.

* Corresponding author. Sydney School of Public Health, Faculty of Medicine and Health, University of Sydney, Edward Ford Building A27, NSW, 2006 Australia.
E-mail address: vsag1982@gmail.com (V.M. Saglimbene).

DOI of original article: https://doi.org/10.1016/j.clnu.2019.07.009.

1 July 2019

https://doi.org/10.1016/j.clnu.2019.07.005