## Omega-3 polyunsaturated fatty acids for the management of exercise-induced bronchoconstriction: insights from a meta-analysis

Christopher Thompson, Joe Sails, Rebecca Birch, Julie Stang, John Brannan, James H. Hull,
Oliver J. Price

Background: Omega-3 polyunsaturated fatty acids (PUFAs) are often cited as a non-pharmacological approach to the management of exercise-induced bronchoconstriction (EIB), however prior studies evaluating treatment efficacy have included modest sample sizes and yielded inconsistent results. Aim: To conduct a systematic appraisal of studies investigating omega-3 PUFA in adults with EIB. Method: Electronic databases were searched for original research up to May 2024. Inclusion criteria: adults ≥18 years with EIB comparing omega-3 PUFA (≥3 weeks EPA + DHA) vs. placebo. End-points: (1) pre-post fall in FEV<sub>1</sub> post indirect bronchial provocation ( $\Delta$ FEV<sub>1</sub>); (2) baseline fractional exhaled nitric oxide (FeNO). A random-effects model was used to determine the overall effect size using pre-to-post-intervention values to calculate the standard mean difference (SMD) and 95% confidence intervals (CIs). Results: Eight studies (n = 141) met the inclusion criteria. Five reported an improvement in  $\Delta FEV_1$  (P<0.05). Six studies (n = 106) were included in the meta-analysis (with three studies including FeNO (n = 60). Omega-3 PUFA attenuated  $\Delta FEV_1$  in response bronchial provocation (SMD = -0.96, [95% CI: -1.84 to -0.08], P=0.03), however substantial heterogeneity was observed between studies (I<sup>2</sup>=87%). No significant difference in FeNO was observed (SMD = -0.62, [95% CI -2.45 to 1.22], (P=0.52). Conclusion: While the mechanism of action is biologically plausible, further large-scale prospective trials, with

consideration for disease severity and sub-type (i.e., T2-high vs. T2-low endotypes) are required to fully determine the effectiveness of omega-3 PUFA for the management of EIB.