**Discussion S1**

The significant heterogeneity among the studies included in this meta-analysis may be related to potential limitations of the trials depending on their quality. Indeed, 11 studies [[1-11](#_ENREF_1)] did not report blinding process, 3 studies [[5](#_ENREF_5), [12](#_ENREF_12), [13](#_ENREF_13)] did not report nature of placebo and 3 [[3](#_ENREF_3), [14](#_ENREF_14), [15](#_ENREF_15)] did not report number dropouts. In 16 studies [[1](#_ENREF_1), [2](#_ENREF_2), [4](#_ENREF_4), [9](#_ENREF_9), [11](#_ENREF_11), [12](#_ENREF_12), [16-25](#_ENREF_16)] baseline characteristics were not clearly reported and in one study [[5](#_ENREF_5)] significantly differed between intervention and placebo groups. Thirty-one studies [[1](#_ENREF_1), [4-6](#_ENREF_4), [9](#_ENREF_9), [12](#_ENREF_12), [14-17](#_ENREF_14), [19](#_ENREF_19), [20](#_ENREF_20), [22-24](#_ENREF_22), [26-40](#_ENREF_26)] did not mention to have controlled for dietary intake of fish or omega-3 fatty acids and 18 [[1](#_ENREF_1), [4](#_ENREF_4), [6](#_ENREF_6), [8-10](#_ENREF_8), [12](#_ENREF_12), [21](#_ENREF_21), [26](#_ENREF_26), [27](#_ENREF_27), [29](#_ENREF_29), [30](#_ENREF_30), [32](#_ENREF_32), [34](#_ENREF_34), [35](#_ENREF_35), [37](#_ENREF_37), [41](#_ENREF_41), [42](#_ENREF_42)] did not assess for compliance using red blood cells membrane or plasma phospholipid analyses. The quality of some studies was affected by dropouts, ranging from 1% [[21](#_ENREF_21)] to 30% [[43](#_ENREF_43)] of the study participants, whereas nearly half of the studies did not use an intention-to-treat design. Another potential source of heterogeneity among trials was the lack of results by gender. Due to the different prevalence rates of depression between men and women and different metabolic pathways of omega-3 PUFA (such as higher levels of plasma DHA in women than in men despite identical diet) [[44](#_ENREF_44)], it would be highly desirable to stratify results by gender.

Among the studies excluded from the systematic review, studies reporting the depressive status as a categorical variable were conducted for the prevention of post-partum depression [[14](#_ENREF_14), [45](#_ENREF_45), [46](#_ENREF_46)] and on women with bipolar disorder who discontinued all conventional psychotropic medications while attempting to conceive [[26](#_ENREF_26)]. All of these studies showed comparable outcomes between intervention and control groups, similarly to the RCTs included in the meta-analysis conducted on analogous population. However, one study [[14](#_ENREF_14)] reported that women with BDI scores >10 showed a significant improvement in their mood scores after pregnancy, despite still having more depressive symptoms (higher mood scores) in the post-partum than the women with no depressive symptoms at 20 weeks. Another study conducted on CVD survivors categorizing the outcome (depression yes/not) reported no beneficial effects of a long-term, low-dose supplementation of omega-3 fatty acids on depressive symptoms [[1](#_ENREF_1)]. In two studies [[47](#_ENREF_47), [48](#_ENREF_48)] on men with angina and healthy subjects, respectively, participants were advised to eat fish (>3 servings per week) with no effects on mood and depression scores. One trial with poorly comparable placebo, used omega-3 18:12 fish oil (containing 18% EPA and 12% DHA) *vs.* commercial krill oil (containing itself unquantifiable omega-3 fatty acids) administered on women with premenstrual syndrome [[41](#_ENREF_41)], a study using Efamol in women with severe premenstrual syndrome [[49](#_ENREF_49)], and a trial not placebo-controlled conducted on adolescent with juvenile bipolar disorder [[50](#_ENREF_50)], reported all beneficial effect of omega-3 fatty acids on depressive symptoms. Among the studies that used poorly comparable scores to assess symptoms severity of depression, one conducted on women with premenstrual syndrome used a visual analogue score [[27](#_ENREF_27)] and one conducted on subjects with post viral fatigue measured depression on a scale of from 0-3 (0, absent; 1, mild; 2, moderate; 3, severe) [[16](#_ENREF_16)], both reporting a decrease of the mean severity of depressive symptoms in the intervention group supplemented with omega-3 fatty acids. In conclusion, despite a significant heterogeneity in study design and quality, the excluded trials reported comparable results to those trials included in the systematic review conducted in the analogue population.

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