Reviewer's report

Title: A randomised controlled trial of eicosapentaenoic acid and/or aspirin for colorectal adenoma (or polyp) prevention during colonoscopic surveillance in the NHS Bowel Cancer Screening Programme: The seAFOod (Systematic Evaluation of Aspirin and Fish Oil) Polyp Prevention Trial

Version: 2 Date: 22 April 2013

Reviewer: Keith Wheatley

Reviewer's report:

This seems like a good trial, described in a mostly well written paper.

Major:
1. The trial has a 2x2 factorial design, so there is an evaluation of aspirin versus no aspirin, yet there is very little mention of this. This should be rectified.
2. The two primary hypotheses are stated (EPA alone more effective than placebo; EPA and ASP have additive effect) do not fit the standard analyses in a factorial design (i.e. evaluation of EPA; evaluation of ASP).
3. If 10-15% of patients are expected to drop out, how will missing data be dealt with, especially for the primary endpoint?

Minor:
1. I don’t see why there should be a “potential confounding effect” of missed adenomas; this will simply introduce “noise”, which I don’t think is the same as “confounding”.
2. What is the point of randomly varying block size (this doesn’t make prediction of the next allocation less likely), especially in a placebo-controlled trial where the treatment allocated won’t be known?

Discretionary:
1. The primary endpoint should be adenoma, not the number of participants with adenoma (applies to other endpoints also).
2. I found it confusing that the primary endpoint relates to the “number of ‘high risk’ participants”, suggesting that there are also non-high risk participants; but there aren’t, are there?
3. The sample size is too precise. I do find it quite amusing that people put in various assumptions (that won’t actually be observed exactly in reality – e.g. 10% drop out), along with other factors (such as decision to use continuity correct) that might be varied, but then come up with such a precise sample size as, e.g., 2757 people needing to be screened!
4. Value of per protocol analysis unclear, so rationale for it should be given.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.