Reviewer's report

Title: Efficacy of Aerobic Exercise and a Prudent Diet for Improving Selected Lipids and Lipoproteins in Adults: A Meta-Analysis of Randomized Controlled Trials

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Reviewer: Robert G Staudte

Reviewer's report:

My overall impression is that this work is a thorough traditional meta-analysis that uses

1. the Der Simonian and Laird [32] random effects model to combine study results. (see 2nd par, page 8).

and

2. a 'simple, random effects meta-regression (method of moments approach)' to test for dependence of effects on covariates. see top of page 9).

No reference is given to this 'simple' approach, although the authors later state that they carried out all meta-analytic analyses using Comprehensive Meta-Analysis, version 2.2 [41].

When I searched the WEB for details, I found a package and a picture of experts who created the package, but no scholarly references or description of the methods used. I therefore assume they are using the traditional weighted regression with inverse variance weights. Since it is a random effects meta-regression I presume they are also estimating a variance component. If the authors know more about the methodology used in this package I would like to see it.

My concern is that these traditional meta-analytic methods have not really been subjected very much to rigorous statistical analysis or even simulations.
The fact that they are widely used is no reason to believe that they are reliable.

For example, see the Statistics in Medicine paper by Brockwell and Gordon (2001). They show that even for large sample sizes the DerSimonian and Laird methodology intervals do not achieve desired coverage for the odds-ratio.
The reason is the use of estimated inverse variance weights which include estimates of the variance component.
See also Hardy and Thompson (1996), Statistics in Medicine, for a critique of the traditional approach.

Also, Mallow, Prendergast and Staudte about to appear in the Electronic Journal of Statistics, an Institute of Mathematical Statistics journal, that shows large bias
when using the inverse variance weights approach in meta-regression.

Thus I was hoping to compare the presumably traditional approach results of this paper with those obtained by more modern methods involving stable weights (Kulinskaya, Morgenthaler and Staudte, Wiley 2008), to see if there is much difference. However, while the authors supply the differences in means in their forest plots, they do not supply the pooled estimates of the assumed common variance in control and treatment groups. On the second half of page 7, the authors do calculate these basic statistics, but for some reason do not make them available. Thus if someone, even a reviewer like myself, wants to replicate their results, he has to start from scratch. Why not make it easier for the reader?

I would like to see references to the literature where the methods of the package Comprehensive Meta-Analysis are described, since they do not seem to be described in the package or the website or this manuscript.

The authors might also be interested in the Multivariate Meta-regression methodology of Lidia J. Arends and her coauthors.

Sorry I cannot be more positive about the manuscript, which appears to have been a careful and substantial effort.

Best wishes,
Bob

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