Reviewer's report

Title: Interactions of commonly used dietary supplements with cardiovascular drugs: A systematic review

Version: 2 Date: 28 December 2011

Reviewer: Sydne Newberry

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Review of Kanji et al.

First, thank you for allowing me to review this fascinating systematic review, as it’s an incredibly important topic both from the efficacy and safety points of view. It is truly disappointing, but I guess not surprising, that the literature permits almost no useful conclusions to be drawn. With the exception of my relatively minor comments below (many of which pertain to editorial issues, and all of which are either minor essential revisions or discretionary revisions), I believe the paper is acceptable for publication as is. I find no major compulsory revisions.

Minor Essential Revisions (please note: The review was drafted in Word, and comments 3-5 originally contained revision marks; if the suggested revisions are unclear, please let me know, and I'll submit a Word file):

Abstract:
1. Line 52: Space-permitting, it would be helpful to specify what pharmaceutical(s) the omega-3 fatty acids and garlic were combined with, or at least to say, e.g., “with use of X and omega-3 fatty acids…” Otherwise, it appears some of the findings pertain to supplements themselves, rather than combinations of a supplement with a pharmaceutical. It’s a bit confusing, as reams of studies exist on the efficacy and safety of omega-3s alone.

Background:
2. It would be helpful to define or specify the classes of CV drugs. The clarity of the text could be improved with some editing, for example:
3. Line 62: “front line therapies treatment for prevention and tx of CVD are primarily pharmaceutical…”
4. Line 63: Start new paragraph with: “However billions of dollars are spent annually…”
5. Line 65: “…this expenditure is spent directly on …” Also, run line 66 back into line 65 to combine with that sentence.
6. Line 70: “have”# “has”
7. Line 76: “and” before “pharmacokinetic”

[I won’t continue listing suggested edits but if you would like, I can provide a marked up version of the draft, if you’d like. I consider these minor but necessary]
revisions.]

8. Line 88: Why only English and German? You address this point in the Discussion but it would make more sense to address here, I believe.

9. Line 92: I suggest citing the source of the definition of dietary supplement, which is probably something like the US DSHEA definition. http://www.fda.gov/food/dietarysupplements/consumerinformation/ucm110417.htm

10. Line 104: and Canada?

Results:

11. In the subsection entitled, “Clinical Outcomes of Effectiveness,” it would be extremely helpful to use leading sentences to distinguish paragraphs discussing studies with no evidence of an effect, studies of adherence, and studies with some evidence of an effect.

12. Also, I’d discuss adherence at the end of the subsection or in a separate subsection.

13. Line 167: are you referring to the strict inclusion criteria of your review or the studies themselves?


15. Line 247: please specify that nifedipine is a Ca-channel blocker.

16. Lines 264 and 265: please use “participants” or “subjects” consistently. I think “participants” is more appropriate for human studies.

17. Line 290: Please specify what a clinically significant change in warfarin pharmacokinetics would be, since the findings are apparently at least statistically significant.

18. Line 333: I would conjecture that another factor introducing error to study findings is the almost certain failure to assess baseline use of supplements, dietary intake (of dark fish and vitamin K, for example), and nutrient status. I suggest mentioning, space-permitting.

List of References:

19. Reference 17 seems to have an odd phrase added at the end

Discretionary Revisions:

Conclusion:

20. Line 427: I’m really not sure that seeking even well-conducted prospective observational studies, however tempting, is likely to be terribly productive, given the differences in supplement content from brand to brand and even batch to batch.

21. Line 430: Would it be possible to identify some combinations of supplements and pharmaceutical that, based on known mechanisms of action, might have the strongest potential for interactions? Doing so might help spur researchers to focus on the studies most likely to produce worthwhile results.
Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.