Reviewer's report

Title: Use of Alternative Pharmacotherapy in Patients with Cardiovascular Diseases

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Reviewer: Glen Pearson

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General

The pattern increasing prevalence in the utilization of complementary and alternative therapies in chronic diseases is an interesting and important topic for health professionals. In this study by Chagan et al, the use of complementary and alternative therapies is explored in a population with a variety of cardiovascular diseases and/or cardiovascular risk factors. The major problem with this study is that the terminology does not seem to comply with contemporary standard definitions for complementary and alternative therapy. The authors utilize what appears to be an unvalidated survey tool to evaluate the utilization of "alternative" pharmacotherapy in a hospitalized population from a single-centre in New York City. The authors' ambitiously and naively identify that their study had 5 primary objectives! However, there sample size calculation was based on only one outcome, specifically difference between users and non-users of AP in terms factors which determine (the more appropriate term to use would have been "contribute to") the use of AP products (such as education level). Consequently, most of the data analysed and presented in the manuscript addressed what should be referred to as secondary objectives.

Overall, the manuscript is reasonably well-written; however, there are an unacceptable number of grammatical errors, run-on sentences, and incorrect tenses used throughout the manuscript. In addition, it was very difficult to read the paper, determine the results and extrapolate an overall conclusion. There is a lot of data present in the manuscript (6 tables, comprising 8 pages in the manuscript) and try to present the results in a more organized and focused (concise) manner.

Specific suggestions for revisions to this manuscript are detailed in the section below.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The introduction is excessively long and reviews previously published studies in this area in far too much detail. The authors should provide an overview of what is known about the use of complementary and alternative therapies in patients with cardiovascular diseases and detail the rationale for their study in the introduction. The major discussion of the results of other studies should be left to the Discussion Section where the results of the current study should be compared to what was found in previous research.

2. The authors start out the introduction with a number of terms (complementary and alternative medicine [CAM], alternative intervention therapies, and alternative pharmacotherapy) which have varying interpretations and recognized definitions. It would be appropriate that the authors identify and stick to terms with well accepted definitions -- it would be advisable that they consider using a consistent terminology that has accepted definitions. They should refer to the National Center for
Complementary and Alternative Medicine at the NIH. In following the definitions of CAM set forth by this group, the authors will note that their study appears to have focused solely upon the use of biologically based therapies -- dietary supplements, vitamins and herbal products. Clarification and consistent use of terminology is required. The authors frequently use the term “alternative pharmacotherapy” -- this implies that these pharmacotherapeutic agents were used by patients in place of (alternative) conventional therapies -- please clarify whether or not the survey was addressing alternative or complementary (agents used together with conventional medicine) pharmacotherapy use?

3. The authors state that they extensively reviewed the literature at two different points in time, finding only four studies in this area. However, they missed one significant study of this topic among patients with Cardiovascular Disease published over one year ago (Pharand C, Ackman ML, Jackevicius C, Paradiso-Hardy FL, Pearson GJ, for the Canadian Cardiovascular Pharmacists Network [CCPN/RCPC]. Use of OTC and Herbal Products in Patients with Cardiovascular Disease. Ann Pharmacother 2003;37(6):899-904). While this paper was published in the same month as the authors last reviewed the literature (June 2003), it was available on-line ahead of print in early May 2003. In any event, it is recommended that the authors perform a more recent review of the literature and include all current research in their manuscript.

4. The authors report that the data was collected utilizing a structured interview and a detailed survey. Please clarify whether or not the survey tool was validated prior to the study? Secondly, there were eight different investigators involved in this study, all of whom appear to have been involved in conducting the structured interviews of patients -- how did the investigators control for surveyor bias or influence? Was the survey itself "scripted" in detail?

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. The authors state that patients were included if they had documented a selected CV risk factor (HTN or dyslipidemia) and/or a specific CVD diagnosis. They provide the details regarding the distribution of CV and non-CV diseases in table 1, but nowhere do they ever describe the number of patients who qualified for the study and were included based on the presence of a CV risk factor alone! This data should be identified, since clearly there may be major differences in patients with a diagnosis of a chronic CVD and those with only CV risk factors. Just as importantly, the mean duration of the CVD diagnosis for this population should be clarified, as it is may impact upon the patient's desire to seek out alternative pharmacotherapy options -- this information appears to have collected in the survey, but is never reported in the paper.

2. In the manuscript, the tables are presented and discussed out of order (1, 2, 5, 3, 4 is the order in the text)-- tables should be relabelled as they must appear in order, from 1 through 5.

3. Page 13, Paragraph 2: The authors indicate that the survey revealed that patients cite that they most frequently purchase the alternative products that they use from pharmacies (33.9%) -- however, they also report purchase these products from health food stores (32.1%) and foreign sources (31.3%) with great frequency. This should be highlighted in the text. Did they authors perform any statistical analysis of this data (Table 5 results)?

4. Page 14, Paragraph 2, Knowledge Scores of Users of Alternative Pharmacotherapy: This data seems to offer very limited insight and not all that valuable without some context in which to evaluate it? For example, these findings would interesting and useful if the authors had evaluated the knowledge of prescription drugs for these patients. Does this population know as little about the potential side-effects and potential interacting foods for the prescription products that they take? It is highly likely that this is the case. Given that this data misleadingly infers that there is some degree of greater risk to patients who take alternative products because of a lack of knowledge about their
potential side-effects or food interactions, compared to conventional prescription products, needs to be clarified in the discussion. In addition, the fact that 33.6% of these patients report health providers as a source of information about alternative pharmacotherapy products warrants comment as it relates to this observed lack of knowledge/understanding of these products by patients who use them.

5. The authors devote a significant amount of attention in their study and the manuscript to the topic of potential conventional drug and alternative pharmacotherapeutic agent interactions. They identify 42 potential "drug-AP interctions" in their population and summary these in Table 6. This data needs to be qualified by the clinical significance of the drug interaction in order for the reader to be able to interpret anything valuable. It would be advisable for the authors to include some measure or qualifier of the clinical significance of each of the identified drug interactions. Just as importantly, the authors need to clarify whether or not each of the "drug-AP interctions" can occur with intermitent use of the AP or whether some continuous exposure to both drugs is required before the adverse outcome is likely to occur -- so could the adverse event result from a single occurrence of the coadministration of the drug and AP, or do the drug and AP need to be coadministered for a period of time (single dose or multiple dose AP effect).

6. Study Limitations -- the authors appropriate identify a number of important limitations with there study. The authors identify that there was a predominance of males in this study and suggest that extrapolation of the results to females with CVD may not be appropriate. I would strongly disagree with this conclusion -- the study included 36% female patients and adequately represents the population of patients with CVD!

In addition, there would appear to be a few additional important limitations which warrant some brief discussion in the manuscript which the authors have failed to identify and not included:
- Survey Tool: if it was not previously validated, this would constitute a major limitation.
- Similar to above, if the structured interviews were conducted by all eight investigators without a detailed script, the potential for introducing interviewer bias would be a major weakness.
- Single, large urban, inner city hospital was the source of the population included in this study -- external validity and generalizability of these results is very limited.

Discretionary Revisions (which the author can choose to ignore)


What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

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

Statistical review: No
Declaration of competing interests:
None!