Author's response to reviews

Title: Use of Biological Based Therapy in Patients with Cardiovascular Diseases in University-hospital Setting in New York City

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Letter to Reviewers

I. Sinikka Sihvo

Major Compulsory Revisions

1. Regarding Vitamin C and E and OTC or alternative therapies and pharmacy being the most common place to purchase these products

There are differences in definitions of alternative products or biologically based therapies among different authors in their studies and the official federal definition. Since the study was conducted in the US, we adapted the definition from the National Center of Complementary and Alternative Medicine. In summary, in the US, vitamins are not considered drugs, even though they are sold in pharmacies and are available OTC. I had addressed that the pharmacies are the most common place to purchase these products because they are easily accessible and available on the shelves of the drug stores and many patients have easy access to them.

2. Regarding "Lifetime users of these products"

We have discussed that there could be a recall bias associated with remembering the fact that some patients may have used some alternative products and forgot to mention it to the interviewer or it could truly be that they have not tried vitamins. We also clarified that most of our lifetime users were in fact current users at the time they were interviewed. Therefore, it is safe to conclude that they were probably using their BBT for cardiovascular diseases, this was further supported by the information we collected regarding use why they used their products. Please, see blue print in first paragraph under the "Results" section.

3. Information added to tables as suggested

Table 3 and 4 changed.

4. Regarding total number of eligible patients

We remember that no physicians have rejected us in including their patients in our study (the sentences is added to first paragraph in the results section). Therefore, how many patients we invited, that's how many patients agreed to participate.

Minor Essential Revisions

1. Prospective study corrected in the methods section
2. Regarding piloting ther survey

We did not pilot the survey, but we adapted a format from a similar study in Reference 6.

3. Regarding "total score of knowledge and what drug/food we considered may potentially interact with BBT:
we had added in the methods section (under BBT survey section) what we considered as an important food/drug interactions. We also searched the literature for adverse effects or reported interactions.

4. Regarding whether patients taking Vitamin C and E are recommended by physicians?
We counted the information and its been added to the result section.

II. Reviewer: Glen Pearson

General Comments:

Based on the suggestion, we now applied the definition of Biologically Based Therapy (BBT) instead of alternative pharmacotherapy, from the National Center for Complementary and Alternative Medicine (this definition applies to our study, because it includes everything that our study intended to include)
We also added secondary objective (see paragraph before Method section). It is correct, we calculated our sample size based on how many patients we needed to find out what factors may be important in leading patients to use BBT, but we never listed that as an objective. Its now listed as secondary objective.

We reviewed the manuscript for grammar again. In particularly, we have moved the literature review to the Discussion section.

Major Compulsory Revisions
1. Regarding suggestion for the introduction, see comments above
2. Definition of CAM, we changed it as per NIH.
3. Reference 26 added
4. Regarding our interviews being scripted, and survey validated
Our interviews were not scripted and the survey, although not validated, was adapted from a previous survey (ref. 6).
We had a script to invite patients to participate, we had a cover letter with primary investigators signature and explanation of the study.
When the interviewers interviewed patients, we had them read it word for word, we specifically instructed them to read verbatim from the cover letter and the survey questions, and document the responses as such.

Minor Essential Revisions:

1. Analyzing risk factors
Information regarding risk factors is presented in Table 2. However, we do not have the data regarding how long these patients have been having these diseases or risk factors. Since there we no statistically significant differences in risk factor distribution among the two groups, we do not believe it would have affected our results.
2. Regarding the order of the tables, it has been rearranged.
3. Site of purchase
The site of purchase of BBT is now highlighted in the text and emphasized the significance of this observation in the discussion section.
Regarding statistical analysis of the data, we only had the data for users, so we do not really have the groups to compare. There is no comparative analysis we would have performed.
4. Evaluation of knowledge scores.
We did not compare the knowledge between prescription medications and BBT. So, we do not have these data for the analysis. But we added the limitation in discussion section regarding the knowledge score.
In addition, we went back and reanalysed the data to include correlation between knowledge scores and where patients obtained this information regarding BBT. We also indicated that healthcare professionals are not doing a better job than a family or friends and other resources in educating patients about these products.
5. Regarding drug-drug/drug-food interactions.
The degree of severity of side effects are classified by the MicroMedex HealthCare Series Integrated Index. We have added that in the article and its also in the results section.
6. Limitation regarding male and females.
Deleted from the limitation section
7. Survey tool validity,
We did not pilot the survey, we adopted it from a similar tool used in Ref. 6. But to avoid bias, we have the script to help enroll patients (cover letter). We had it also added to our limitation section. We had also added a limitation of our results being applicable only to inner city hospital patients.
8. Checked for most updated prevalence of BBT use, please see reference 2 added.
Thank you for reviewing our study