Author’s response to reviews

Title: What has been the impact of the Traditional Herbal Registration (THR) Scheme in the UK on information provided with herbal products bought over the counter?

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Version: 1 Date: 01 Mar 2019

Author’s response to reviews:

Thank you for your comments, from both the reviewers and the editors. We have considered the responses and made the amendments as follows (See table below). The table is also included as a word document titled Reviewers Comment HERB-II 1.3.19.

Reviewer comment
   Response
   Page/ line number

Reviewer one
1. Abstract, results - the phrase "products containing frequency of risk of harm" is confusing; perhaps re-word to "products with frequency of risk of harm information".  
   Thank you for your comments - we have amended the sentence as recommended to say

   “Products with frequency of risk of harm information”
   Abstract

Page 2
Line 44

2. Methods, study design, first sentence - "...to undertake a content analysis of five herbal products" suggests you are analyzing the actual contents of the pills; to clarify you might re-phrase as "...to
undertake a content analysis of the information provided with five herbal products"

Thank you for this comment – we have amended as suggested as this is much clearer.

“content analysis of the information provided with five herbal products:”

Methods
Study design
Page 4
Line 119
3. Methods, study design - the inclusion criteria state "evidence of a drug interaction between the herb and a prescribed medication"; yet, I don't believe echinacea fits this criterion (and your Figure 1 appears to confirm this). Please explain why it was included in the study. This sentence has been amended as follows:

“The herbal products were chosen as they met one or more of the following criteria”

This is consistent with the methods of the previous study.

Methods
study design
Page 4
Line 122
4. Methods, study design - you do not use Latin binomials to refer to the herbs so could you clarify that you if are including all types of echinacea and ginseng (this is especially important for ginseng as there are multiple different plants with different safety profiles and your Figure 1 clarifies you are using the safety profile for Asian ginseng (Panax ginseng) which would not be accurate for a Siberian ginseng (Eleutherococcus senticosus) product). How did you account for the different types of ginseng?

Ginseng – We acknowledge your comments re: ginseng and have consequently excluded products containing Siberian ginseng from the analysis as we do not have an equivalent method for assessing their safety profile. Ginseng now reads as Asian ginseng.

The data has been adjusted accordingly – we eliminated 4 products which contained Siberian ginseng. None of these products were THR regulated. 1 contained a leaflet. We have highlighted in pink the data which have been amended as a consequence of this.

The Echinacea products that have been included include all types of Echinacea. Throughout document Please see pink highlighting

5. Results - the majority of the results are presented in the positive (i.e., the number of percentage of products reporting safety information); however, occasionally this is reversed and reported as the number of products NOT reporting safety information (e.g., p12 "11 out of 27 leaflets" did not present any information of frequency....") which is confusing. I recommend all results be reported in the positive for clarity.

We have addressed this confusion by amending the following:

• We found 21 garlic products, 4 of these communicated 1 out of 4 of the key points of safety information and 17 did not contain any of the key points of information.

• We identified more leaflets reporting frequency information, but this was not statistically
significant. In 2017, 15 out of 26 leaflets presented some information of the frequency associated with side effects. This compared to 2 out of 9 leaflets identified in the 2011 sample (Chi2 = 3.4; df = 1; p= 0.066).

Page 11
Line 236

Page 12
Line 263
6. Results, nature of products - how does the 67 products in this study compare with the number of products found last time? Was there a big difference in brands (i.e., did some leave the market place while new ones entered or are all the product brands the same?)

As a consequence of your recommendations above we excluded 4 products containing Siberian ginseng. The sample now contains 63 products. We reported on the number of products included in the 2011 sample and compared and contrasted the difference between 2011 and 2018.

We did not undertake any analysis on the brands - anecdotally the samples contained largely similar brands, but we did not analyze this due to limitations with word count. (Many were brands associated with the place of purchase)

7. Results, information provided, line 53-54, "The THR registration scheme was associated with an increased likelihood of the presence of a leaflet" - shouldn't this more correctly be phrased as "Registration with the THR registration scheme was associated with an increased likelihood of the presence of a leaflet"?

This has been amended as follows:

Registration with the THR registration scheme was associated with an increased likelihood of the presence of a leaflet

Page 6
Line 182
8. I noted a few typos and grammatical errors that I have listed here:
   a. garlic is generally lower case throughout, but Echinacea, Ginkgo and Ginseng are often capitalized….. since you are not using Latin binomials, I believe they should all be lower case.
   b. Discussion, page 12, line 43 - "..... consumers should be reassured that the THR registered products accompanied with improved and more complete information ....." Perhaps change to ""..... consumers should be reassured that the THR registered products are usually accompanied with improved and more complete information ....."
   c. Discussion, page 13, lines 6-7, phrase "regarded to be" is repeated twice; insert "be" before "available as food supplements."
      a. We have amended the spellings as recommended.

b. We have amended the sentence as recommended

“consumers should be reassured that the THR registered products are usually accompanied with improved and more complete information than those not registered.”
c. This has been amended to say:

There are a number of St John’s wort and Echinacea products which are registered as THRs, others, such as garlic, may be regarded to be within the definition of a medicine, but may also be available as food supplements Throughout manuscript

Page 12
Line 281

Page 13
Line 293
Reviewer two
1. In a cross-sectional study, the investigator measures the outcome and the exposures in the study participants at the same time and then study their association. In this manuscript, the outcome is information provided with herbal products while exposure is the THR scheme.
   a) Rather than comparing registered herbal products in 2011 with 2016, this study did not actually compare exposure with non-exposure or estimate the odds between these two groups. There are 37.3% (25) of the registered products in this study. If authors can compare these 25 registered products with 42 non-registered products, it will provide much more useful information on the impact of the THR on the information of herbal products.
   b) From the perspective of research methodology, this study is NOT a cross-sectional study. Thank you for your comments – For clarity, we have amended the terminology to exclude use of ‘cross-sectional’

On page 6 under 'information provided' we have added the following:

"Registered products were more likely to be provided with a leaflet (Chi2 = 51.4; df - 1; p<.0001)."

Page 6
Line 184
2. There were inclusion and exclusion criteria described in study design section. In the title and conclusion, authors tried to draw conclusion of herbal products. That would be acceptable If authors can explain in the introduction or discussion about why they only include single ingredient herbal products but they still conclude on overall herbal products which include cream, liquids, oils, etc.

We have added a sentence to the strengths and limitations section as follows:

We acknowledge our sample did not include products such as creams, liquids and tinctures and our findings may not be applicable to these products. Conclusion

Strengths and limitations
Page 14
Line 349
3. Even though authors said they want to include only single-ingredient herbal products, from those
tables, they looked like single herbs, rather than single-ingredient herbal products.

Thank you for this comment – we have changed the wording to products containing single herbs i.e. not combined products to clarify this point.

Page 5
Line 127
4. There is a typo on page 5 line 51 and 57: NCAMM should be NCCAM. This has been amended to NCCAM Page 5
Line 151
Editors comments
- Please ensure that capitalisation for herbal product names is correct, the is a mix in the manuscript and in most cases these should be lower case
  This has been amended
Throughout manuscript
- Check that all abbreviation are given in full the first time mentions and that abbreviations are given as notes in Tables
  The following key has been added to all tables:-

Ph = pharmacy, HF = Health food store, SM = Supermarket, THR = Traditional Herbal Registration, U = unregulated, O = other
  See tables on pages 7-10
- Check that all p values have a leading 0 before the decimal point This has been checked and amended.
  Throughout manuscript