PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

| TITLE (PROVISIONAL) | Effectiveness of strategies for nutritional therapy for patients with type 2 diabetes and/or hypertension in primary care: a protocol of a systematic review of randomized controlled trials |
|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| AUTHORS             | Galendi, Julia; Leite, Renata; Mendes, Adriana; Nunes-Nogueira, Vania                                                                                                                                   |

VERSION 1 – REVIEW

| REVIEWER           | Satoru Yamada
|--------------------| Kitsato Institute Hospital, Japan |
| REVIEW RETURNED    | 22-Mar-2019 |

GENERAL COMMENTS

This is a protocol paper of a systematic review and meta-analysis of nutrition therapy for patients with type 2 and/or hypertension. Although the topic is interesting and important, several points are difficult to understand. Authors should clarify these points.

Major points

1. In APPENDIX, authors described Medline search strategy which showed #1 (=diabetes) OR #2 (=hypertension). That is, this paper includes “individuals with T2DM or AH”, but not “patients with T2DM and hypertension” in the title. Title is not appropriate.
2. In APPENDIX, authors described Medline search strategy which showed #3 (=primary care) OR #4 (=community health planning). Why did authors avoid certified diabetologists and high-risk approach? I feel #3 and #4 are unnecessary for this study.
3. In page 13, author described that Interventions are nutrition strategies for T2DM and/or AH and Comparisons are conventional treatment of DM including drug treatment. I recognize the comparison between nutrition therapy and drug therapy as unfair. For example, nutrition strategy for lean type 2 diabetes without weight reduction and sodium restriction must be less effective to control blood pressure comparing with conventional thiazide.
4. I think “nutrition strategies” are too broad as a search term for appropriate number of papers. How about focusing on several specific dietary patterns such as Mediterranean, DASH, low-carbohydrate, and vegetarian? Of course, low-Glycemic Index diet is a candidate.
5. In the effect of sodium restriction, there is an ethnic difference (African origin > Mongoloid > Caucasian). Thus, authors should perform stratification analysis with ethnicity.
6. As primary outcomes, authors gave too many (about 10) endpoints. Please focus on one or two endpoint(s). If authors keep
10 or more endpoints, p-value <0.05 is too high to judge statistical significance.

Minor points
1. Page 5, lines 31; 2079 should be 20-79.
2. Page 5, lines 45; reference 2 should be updated to 2019.
3. Page 6, lines 3; dysglycemia should be dysglycaemia.
4. In INTRODUCTION section, authors often describe diabetes and hypertension status in Brazil. Please give us diabetes and hypertension status in the global (or Europe, UK).
5. Page 6, lines 19; reference 4 should be publication from WHO.
6. Page 6, lines 24; nephropathy should be kidney disease as well as lines 56.
7. Page 6, lines 37; Although authors described low-fat nutrition was recommended, ADA/EASD consensus report in 2018 recommended Mediterranean, DASH, low-carbohydrate, and vegetarian (Diabetes Care 2018, 41, 2669-2701). Please change this description.
8. Page 7, lines 3; reference 8 should be N Engl J Med 1993, 329, 977-986.
9. Page 7, lines 5; reference 9 should be Lancet 1998, 352, 837-853 and 854-865.
10. Page 8, lines 15; reference 18 is not a multicentric study conducted in nine Latin American countries, because the title describe “in a public hospital in Peru; a cross-sectional study in a low-middle income country”.
11. Page 8, lines 44; reference 20 should be updated to 2019.
12. Page 9, lines 23; reference 23 is guidelines of Canadian Diabetes Association. Here, author refer other guidelines from ADA, Australian College of General Practitioners.
13. Page 9, lines 31; reference 24 should be JAMA 2007, 297, 969-977.
14. Page 9, lines 38; Low-fat diet is not recognized as cardioprotective diet (JAMA 2015, 313, 2421-2422). Please change this description.
15. Page 15, lines 56; Authors should not search for unpublished studies.

REVIEWER
Shahrad Taheri
Weill Cornell Medicine

REVIEW RETURNED
04-Apr-2019

GENERAL COMMENTS
This is an interesting systematic review protocol. It is generally well presented. Apart from the primary care aspect, the authors need to add work from previous systematic reviews on the topic; as it is, this is not discussed sufficiently. Furthermore, the authors need to define what they mean by the interventions; will they for example include micronutrients? For the review, it is essential to know whether publications in all languages will be used. On a minor note, there is a need to give units e.g. hba1c %. Also hba1c should be given in mmol.
| REVIEWER                  | Shahrad Taheri          | Weill Cornell Medicine |
|--------------------------|-------------------------|------------------------|
| REVIEW RETURNED          | 04-Apr-2019             |
| GENARAL COMMENTS         | This is an interesting systematic review protocol. It is generally well presented. Apart from the primary care aspect, the authors need to add work from previous systematic reviews on the topic; as it is, this is not discussed sufficiently. Furthermore, the authors need to define what they mean by the interventions; will they for example include micronutrients? For the review, it is essential to know whether publications in all languages will be used. On a minor note, there is a need to give units e.g. hba1c %. Also hba1c should be given in mmol. |

| REVIEWER                  | Antonio Facciorusso     | University of Foggia, Italy |
|--------------------------|-------------------------|---------------------------|
| REVIEW RETURNED          | 10-May-2019             |
| GENERAL COMMENTS         | The protocol is well written and explicative. I just suggest to consider performing meta-regression in the case of high heterogeneity. |

**VERSION 1 – AUTHOR RESPONSE**

Reviewer 1
Thank you very much for your comments and suggestions that absolutely improved the quality of our review protocol. All your suggestions were included in the revised manuscript, as you can see below:

**Major points**

1. In APPENDIX, authors described Medline search strategy which showed #1 (=diabetes) OR #2 (=hypertension). That is, this paper includes “individuals with T2DM or AH”, but not “patients with T2DM and hypertension” in the title. Title is not appropriate.
   **Answer:** We apologize for this miscomprehension; this review includes individuals with T2DM and/or hypertension. We have rewritten the title and eligibility criteria to make this more understandable (participants). Page 8, line 36

2. In APPENDIX, authors described Medline search strategy which showed #3 (=primary care) OR #4 (=community health planning). Why did authors avoid certified diabetologists and high-risk approach? I feel #3 and #4 are unnecessary for this study.
   **Answer:** Thank you for excellent observation, however our objective is to evaluate the effectiveness of nutritional therapy in primary care. As the incidence of diabetes has increased specially in low- and middle-income countries, we hope that our findings can help health managers to implement nutritional strategies in diabetes and hypertension in primary care. In addition, we have had a public involvement in this protocol, which pointed primary care management as priority (page 8, line 11)

3. In page 13, author described that Interventions are nutrition strategies for T2DM and/or AH and Comparisons are conventional treatment of DM including drug treatment. I recognize the comparison between nutrition therapy and drug therapy as unfair. For example, nutrition strategy for lean type 2 diabetes without weight reduction and sodium restriction must be less effective to control blood pressure comparing with conventional thiazide.
Answer: Again, we apologize for this miscomprehension, both intervention and control group will receive the drug treatment, the difference will be only the nutrition therapy. We have rewritten the type of interventions section (page 9, line 3).

4. I think “nutrition strategies” are too broad as a search term for appropriate number of papers. How about focusing on several specific dietary patterns such as Mediterranean, DASH, low-carbohydrate, and vegetarian? Of course, low-Glycemic Index diet is a candidate.
Answer: We have rewritten the types of interventions section, and we have focused on specific dietary patterns, as well as in energy restriction (page 9, line 11).

5. In the effect of sodium restriction, there is an ethnic difference (African origin > Mongoloid > Caucasian). Thus, authors should perform stratification analysis with ethnicity.
Answer: On subgroup analysis we have included stratification analysis according to ethnic difference (page 13, line 50)

6. As primary outcomes, authors gave too many (about 10) endpoints. Please focus on one or two endpoint(s). If authors keep 10 or more endpoints, p-value <0.05 is too high to judge statistical significance.
Answer: We revised all manuscript and decreased the number of outcomes for four (page 10, line 6)

Minor points
1. Page 5, lines 31; 2079 should be 20-79.
   Ok, we have corrected (page 5, line 18)
2. Page 5, lines 45; reference 2 should be updated to 2019
   Ok, we have updated (page 5, line 33)
3. Page 6, lines 3; dysglycemia should be dysglycaemia.
   In order to reduce the introduction, we have removed this phrase
4. In INTRODUCTION section, authors often describe diabetes and hypertension status in Brazil. Please give us diabetes and hypertension status in the global (or Europe, UK).
   Ok, we have included global information, second and fifth paragraph of introduction (page 5)
5. Page 6, lines 19; reference 4 should be publication from WHO.
   In order to reduce the introduction, we have removed this phrase
6. Page 6, lines 24; nephropathy should be kidney disease as well as lines 56.
   In order to reduce the introduction, we have removed this phrase
7. Page 6, lines 37; Although authors described low-fat nutrition was recommended, ADA/EASD consensus report in 2018 recommended Mediterranean, DASH, low-carbohydrate, and vegetarian (Diabetes Care 2018, 41, 2669-2701). Please change this description.
   Ok, we have corrected this information (page 6 and 7) and removed this sentence.
8. Page 7, lines 3; reference 8 should be N Engl J Med 1993, 329, 977-986.
   Ok, we have corrected
9. Page 7, lines 5; reference 9 should be Lancet 1998, 352, 837-853 and 854-865.
   In order to reduce the introduction, we have removed this phrase
10. Page 8, lines 15; reference 18 is not a multicentric study conducted in nine Latin American countries, because the title describe “in a public hospital in Peru; a cross-sectional study in a low-middle income country”.
    Ok, we have corrected this reference (page 6, line 18)
11. Page 8, lines 44; reference 20 should be updated to 2019.
    In order to reduce the introduction, we have removed this phrase
12. Page 9, lines 23; reference 23 is guidelines of Canadian Diabetes Association. Here, author refer other guidelines from ADA, Australian College of General Practitioners.
    In order to reduce the introduction, we have removed this phrase
13. Page 9, lines 31; reference 24 should be JAMA 2007, 297, 969-977.
In order to reduce the introduction, we have removed this phrase
14. Page 9, lines 38; Low-fat diet is not recognized as cardioprotective diet (JAMA 2015, 313, 2421-2422). Please change this description.
Ok, we have removed this phrase.
15. Page 15, lines 56; Authors should not search for unpublished studies.
We have removed the term “unpublished studies”, and maintained “We will also search for studies on ClinicalTrials.gov, the Brazilian Registry of Clinical Trials (Rebec), and the gray literature, through abstracts published in annals and lectures” (page 10, line)

Referee 2
Thank you very much for your comments and suggestions that absolutely improved the quality of our review. All your suggestions were included in the revised manuscript, as you can see below:
Apart from the primary care aspect, the authors need to add work from previous systematic reviews on the topic; as it is, this is not discussed sufficiently. Furthermore, the authors need to define what they mean by the interventions; will they for example include micronutrients? For the review, it is essential to know whether publications in all languages will be used. On a minor note, there is a need to give units e.g. hba1c %. Also hba1c should be given in mmol.
Answer: We have added work from one recent systematic review on this topic (page 7, line 13). We have defined the interventions (page 10, line 6). We have highlighted that there is no year and language restriction (page 10, line 44). We have given the unit for HbA1c and blood pressure (page 10, line 6)

Referee 3
Thank you very much for your comments and suggestions that absolutely improved the quality of our review. All your suggestions were included in the revised manuscript, as you can see below:
We have included a section regarding meta-regression (page 14, line 13)

We hope you will find our revised version suitable for publication in the prestigious BMJ Open.

VERSION 2 – REVIEW

| REVIEWER        | Satoru Yamada                        |
|-----------------|--------------------------------------|
| Kitasato Institute Hospital, Japan |
| REVIEW RETURNED | 05-Jul-2019                          |
| GENERAL COMMENTS| This manuscript is well-revised.      |