

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Epidemiology of overweight and obesity in early childhood in the Gulf Cooperation Council countries: a systematic review and meta-analysis protocol
AUTHORS	Nahhas, Mahmoud; Asamoah, Felix; Mullen, Stephen; Nwaru, Bright; Nurmatov, Ulugbek

VERSION 1 – REVIEW

REVIEWER	Leonie Elsenburg University Medical Center Groningen, the Netherlands
REVIEW RETURNED	25-Sep-2017

GENERAL COMMENTS	<p>The authors have written a protocol for a systematic review on the epidemiology of overweight and obesity in early childhood in Gulf Cooperation Council countries. A systematic review on the prevalence, incidence and time trends of overweight and obesity in children in Gulf Cooperation Council countries seems a nice addition to the literature.</p> <p>General comments</p> <p>The information provided in the protocol is, however, not sufficient to determine what contributions will be made by this systematic review and how these contributions will be made. In the protocol there is a lack of information regarding what studies are eligible for inclusion in the review and a lack of information about how information from different studies will be synthesized narratively and if possible, quantitatively (for guidance see the Cochrane Handbook). In addition, the scope of this review is very broad; it will involve both epidemiological parameters of as well as risk factors for overweight and obesity. If the authors want to assess both outcomes in this review, it should be made clear how this will be done and probably different in- and exclusion criteria, ways of rating the quality of both types of studies and ways of synthesizing the information on both types of studies should be specified.</p> <p>Introduction</p> <ol style="list-style-type: none">1. You mention the term 'early life years'. This term requires specification in the introduction.2. Elaborate on why you think risk factors for overweight and obesity in GCC countries are different from risk factors in other countries. This is important as otherwise there is no reason to specifically investigate the risk factors in GCC countries.
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3. You should elaborate on the rationale for combining the estimates of the prevalence of all GCC countries. Additionally, in the protocol you mention that you are also going to look at country-specific prevalence, if possible. This deserves more attention.

4. Elaborate on why the studies mentioned on p.3, line 51 provide unclear results regarding the epidemiological burden of overweight and obesity in the GCC countries and how this systematic review will provide improved estimates.

5. In the introduction you mention that you want to bring together all available evidence on epidemiological parameters including incidence, prevalence, risk factors and trends over time. This should be an exhaustive list of the measures you are going to investigate. Also change this in the abstract.

6. You mention that you want to provide contemporaneous estimates, yet in the protocol there is no publication date restriction or year of conduct restriction. If there indeed is no date restriction, how will data on different years be combined?

7. The cut-off used for early life is 8 years. Why specifically this age?

8. The objectives and/or research questions should be clearly specified.

Methods

9. How will you handle articles that include children around the age of 8? Does the mean age have to be below 8 years or is there a maximum percentage of children above the age of 8 years that may be included? This needs to be specified.

10. You mention that you are going to include randomized controlled trials and case-control studies. How will these types of studies provide estimates of prevalence and incidence? In addition, you also want to include estimates of unpublished and ongoing studies. What type of information will be considered appropriate? Please also include this in the abstract.

11. In the primary outcomes, you mention that the primary outcomes include objectively defined measures of the incidence and prevalence of obesity. Again, this should be an exhaustive list of measures. Further, it is not clear what objectively defined measures of incidence and prevalence of obesity are. This should be specified. Additionally, the outcomes are only about obesity. Is it only about obesity or also about overweight as the title and introduction suggest?

12. Secondary outcomes will include risk factors. This makes the scope of the review very broad. Will there be any restrictions with regard to the risk factors that will be examined? Additionally, studies assessing risk factors will probably be different from studies assessing prevalence and incidence. Why and how (practically) do you want to investigate both type of outcomes in one systematic review?

13. Why are the time trends specified as secondary outcome measures? I assume that time trends in prevalence and incidence are meant. In that case they seem part of the primary outcomes.

14. When is the search performed and will it be performed only once, or will the search be updated at some point?

15. In addition to referring to the search in the appendix, mention the search terms (e.g. search terms relate to obesity, epidemiological parameters, the GCC countries and the study type).

16. The selection criteria are not mentioned. These are very important and should be mentioned. You may not want to publish your selection criteria form at this stage, but you should at least mention what criteria will be used.

17. How will you handle duplicates?

18. How will you handle estimates from the same study sample published in different articles?

19. Elaborate on how the methodological quality will be assessed using the EPHPP or include the methodological quality assessment form.

20. Will you calculate a measure of the agreement between the reviewers regarding the quality of the studies?

21. Include the data extraction sheets or mention what kind of data will be extracted.

22. If you are going to synthesize the information quantitatively, how is this going to be done? What measures will be quantitatively summarized? Will measures be converted for the quantitative summary? How will the different types of outcomes be quantitatively synthesized? And will the risk factors be divided into categories? And if yes, into what categories will they be divided?

23. Regarding the subgroup analyses, you should clearly mention what subgroup analyses you are planning to do. Again, this should be an exhaustive list. In addition, you mention that you want to perform a subgroup analysis for body mass index. How will this be done for prevalence and incidence estimates of obesity (or probably overweight and obesity)?

24. Will authors of papers providing incomplete information (to determine eligibility or to synthesize data quantitatively) be contacted?

Contributions

25. Can you mention who will do what for the review?

Funding

26. There is no information on funding

Minor comments

27. p. 3, line 16: Why do you cite a German study regarding the cost of childhood overweight and obesity? Is there any reason to believe that the costs in Germany are comparable to the costs in the GCC countries?

28. p.3, line 22: Why do you specifically mention the number of

	<p>overweight/obese children in developing countries? In the abstract you specifically mention the increase in prevalence of overweight and obesity in industrialized countries (p.2, line 8-9).</p> <p>29. p. 5, line 39: Word missing.</p>
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REVIEWER	Milagros Ruiz University College London United Kingdom
REVIEW RETURNED	28-Sep-2017

GENERAL COMMENTS	<p>I commend the authors on their work to address the research gap and generate up-to-date evidence of early childhood adiposity in the GCC countries.</p> <p>I have the following comments to the study protocol:</p> <p>1) Page 4, line 21: If the SR aims to present up-to-date evidence of the burden of overweight/obesity, is it necessary to include all studies published since inception? Why not look at papers since 2000, for example?</p> <p>2) Page 5, line 13 contradicts other statements that unpublished and ongoing studies will be included</p> <p>3) The inclusion of risk factors as a secondary outcome makes the protocol very ambitious and wide in scope. Risk factors for obesity are complex and range from cultural, structural, behavioural, nutritional, physiological, etc. I would omit this as a secondary outcome or do a separate SR of risk factors in this region as a follow-up study.</p> <p>4) Page 7, line 8-9: 'Statistically homogeneous': I would rephrase this, as you plan on doing random-effects meta-analysis. Fixed-effects meta-analysis is performed for studies where the variation is entirely due to sampling variation. Homogeneous implies fixed effects.</p> <p>5) Page 7, line 11-13: What about subgroup analyses by study design (cohort, cross-sectional, case-control) which could vastly explain differences in the assessment of the burden? What about subgroup analyses by gender? There is a known gender difference in the burden of adiposity between males and females, some of which is related to lifestyle and cultural norms. Different gender roles from a young age could be relevant for these countries.</p> <p>6) Page 7, lines 32-37: Whether or not the the review will be the most unbiased depends on the state of the evidence, and largely on what has been/has not been published. I would remove this word as all SRs in theory address study bias. If this is the first SR on this topic, how can authors claim to 'present the most comprehensive ... synthesis'? This implies that there are other reviews which authors are addressing in this protocol. I would replace 'most' with 'first comprehensive synthesis of the evidence relating to...'</p> <p>Other minor comments:</p> <p>1) Page 4, lines 14-16: The impact on society is not only economic, but social as it can lead to great overweight/obesity inequalities between and within GCC countries. Is the economic burden largely due to health care costs? Why not focus on other costs such as obesity-related illnesses that prevent those from working and earning an income etc? The reference to the German study is odd. I would replace it with a similar study that is either global or from the region.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1

i. Reviewer Name: Leonie Elsenburg

Institution and Country: University Medical Center Groningen, the Netherlands Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below the authors have written a protocol for a systematic review on the epidemiology of overweight and obesity in early childhood in Gulf Cooperation Council countries. A systematic review on the prevalence, incidence and time trends of overweight and obesity in children in Gulf Cooperation Council countries seems a nice addition to the literature.

General comments

The information provided in the protocol is, however, not sufficient to determine what contributions will be made by this systematic review and how these contributions will be made. In the protocol there is a lack of information regarding what studies are eligible for inclusion in the review and a lack of information about how information from different studies will be synthesized narratively and if possible, quantitatively (for guidance see the Cochrane Handbook). In addition, the scope of this review is very broad; it will involve both epidemiological parameters of as well as risk factors for overweight and obesity. If the authors want to assess both outcomes in this review, it should be made clear how this will be done and probably different in- and exclusion criteria, ways of rating the quality of both types of studies and ways of synthesizing the information on both types of studies should be specified.

R: In the Methods and Analysis section of the protocol (pages 4-6), we have followed the standard PICOS framework and provided detailed information on study design, type of participants, outcome measures, inclusion and exclusion criteria. In addition, in the protocol we have mentioned how we will handle the data. If there are homogenous studies, we will pool data statistically and conduct meta-analysis; otherwise, the synthesis will be done narratively if the studies are too heterogeneous to be combined. Our overarching goal is to produce a paper that provides a comprehensive picture of the epidemiology (estimates of prevalence, incidence, and risk factors) of obesity and overweight in the Gulf region. Having these different aspects in one paper will give the evidence emanating from the review better impact in the field and we believe should argue against splitting the topic into different papers that cover different aspects of the epidemiology of obesity. We have experience of undertaking similar reviews (please see Reference 1 below as an example),¹ thus we will capitalise on these previous experiences in undertaking this work. With regards to tools to be used for quality appraisal, we have indicated that we will utilise the Effective Public Health Practice tool, which has appraisal tools for each of these different study designs. The approach to data synthesis will remain the routine approach for systematic reviews/meta-analyses.

ii. Introduction

1. You mention the term 'early life years'. This term requires specification in the introduction.

R: We have now made provision for this in the introduction. In addition, we have now provided information on early childhood framework, early years concept with relevant references.^{2,3}

iii. Elaborate on why you think risk factors for overweight and obesity in GCC countries are different from risk factors in other countries. This is important as otherwise there is no reason to specifically investigate the risk factors in GCC countries.

R: Differences in populations' structure, culture, location and seasons in GCC greatly affect aspects of health, which we hope to understand through this study. We do not know yet country-specific risk factors for obesity in GCC countries, but believe this

will emanate from this synthesis. We have now added statement on this aspect in the manuscript with supporting reference (please page 3).

iv. You should elaborate on the rationale for combining the estimates of the prevalence of all GCC countries. Additionally, in the protocol you mention that you are also going to look at country-specific prevalence, if possible. This deserves more attention.

R: The GCC countries maintain essential similarities in their population structure, culture and various aspects of education for early years children, hence a good motivation to provide regional estimates of the study parameters. However, in deriving pooled regional estimates, we will employ random effects meta-analysis, which takes into account any differences that may exist between the different entities being combined. Moreover, in order to make cross-country comparisons, we will also provide country-specific estimates of the study parameters.

v. Elaborate on why the studies mentioned on p.3, line 51 provide unclear results regarding the epidemiological burden of overweight and obesity in the GCC countries and how this systematic review will provide improved estimates.

R: The studies that we mentioned on p.3, line 51 are literature reviews, individual papers, with single assessment of burden of overweight and obesity in the GCC countries. In order to gain strong evidence in this field a systematic approach, a systematic review is required.

vi. In the introduction you mention that you want to bring together all available evidence on epidemiological parameters including incidence, prevalence, risk factors and trends over time. This should be an exhaustive list of the measures you are going to investigate. Also change this in the abstract.

R: We have now incorporated the suggestion into the abstract.

vii. You mention that you want to provide contemporaneous estimates, yet in the protocol there is no publication date restriction or year of conduct restriction. If there indeed is no date restriction, how will data on different years be combined?

R: We have redefined the period of studies to from 2000 to capture current and strong evidence in this systematic review.

viii. The cut-off used for early life is 8 years. Why specifically this age?

R: As we have provided information on early years framework (pre-birth to 8 years old), early years concept from different countries, this definition of early years is a recognition of the importance of a child's early development milestones (physical, cognitive, psychological and behavioural) and includes from pre-birth to the transition into primary school. This is a very crucial window for all population-based research, preventative strategies in children.

ix. The objectives and/or research questions should be clearly specified.

R: In the introduction section, we have clarified our objectives. We said that we will undertake a systematic review to identify, appraise and synthesise all available evidence on the epidemiology, including the incidence, prevalence, time trends, risk factors of overweight and obesity in children during the early years of life in GCC countries.

x. Methods

How will you handle articles that include children around the age of 8? Does the mean age have to be below 8 years or is there a maximum percentage of children above the age of 8 years that may be included? This needs to be specified.

R: We will include and extract data only for children aged under 8 years old not average age. If there are aggregated data and no sub-group analysis for children aged up to 8 years old we will exclude those papers.

xi. You mention that you are going to include randomized controlled trials and case-control studies. How will these types of studies provide estimates of prevalence and incidence? In addition, you also want to include estimates of unpublished and ongoing studies. What type of information will be considered appropriate? Please also include this in the abstract.

R: The main source of data on the incidence and prevalence of obesity will come from cohort and cross-sectional studies, respectively. We are including clinical trials and case-control studies as these will additionally provide data on risk factors for obesity.

xii. In the primary outcomes, you mention that the primary outcomes include objectively defined measures of the incidence and prevalence of obesity. Again, this should be an exhaustive list of measures. Further, it is not clear what objectively defined measures of incidence and prevalence of obesity are. This should be specified. Additionally, the outcomes are only about obesity. Is it only about obesity or also about overweight as the title and introduction suggest?

R: For consistency, we will use the standard, validated WHO definition of overweight and obesity in children based on body mass index (BMI) measurements.

xii. Secondary outcomes will include risk factors. This makes the scope of the review very broad. Will there be any restrictions with regard to the risk factors that will be examined? Additionally, studies assessing risk factors will probably be different from studies assessing prevalence and incidence. Why and how (practically) do you want to investigate both type of outcomes in one systematic review?

R: We will have no restrictions on the risk factors to study. We aim to synthesise the evidence on all risk factors that have so far been studied. As already mentioned above, our aim is to produce a paper that provides a comprehensive synthesis of the epidemiology of obesity in the GCC countries. This has been our approach in previous works¹ and we will capitalise on the experiences gained from the previous works in undertaking this synthesis.

xiii. Why are the time trends specified as secondary outcome measures? I assume that time trends in prevalence and incidence are meant. In that case they seem part of the primary outcomes.

R: Indeed, these are part of the primary outcomes and we have now included this part of the primary outcomes to study.

xiv. When is the search performed and will it be performed only once, or will the search be updated at some point?

R: At the moment, we have now searched the relevant databases to be included in the review and these searches were performed on the 19th of August 2017. We plan to perform updated searches at the end of this year to assess whether additional papers have been published between August 2017 and end of December 2017.

xv. In addition to referring to the search in the appendix, mention the search terms (e.g. search terms relate to obesity, epidemiological parameters, the GCC countries and the study type).

R: In Appendix 1, we have provided a search strategy. Steps 1-10 include condition/disease related terms, 12-36 epidemiological parameters, including study designs and 38-46 include the GCC countries.

xvi. The selection criteria are not mentioned. These are very important and should be mentioned. You may not want to publish your selection criteria form at this stage, but you should at least mention what criteria will be used.

R: In the methods and analysis section, we have mentioned the whole selection process based on PICOS framework, screening of studies etc.

xvii. How will you handle duplicates?

R: We will handle duplication by maintaining only one study electronically. EndNote Library has this function and we will apply this.

xviii. How will you handle estimates from the same study sample published in different articles?

R: If there are multiple publications from the same population, we will use the main comprehensive paper that incorporates all relevant outcomes that meet our inclusion criteria.

xviii. Elaborate on how the methodological quality will be assessed using the EPHP or include the methodological quality assessment form.

R: We will use the standard critical appraisal of observational research using the Effective Public Health Practice tool.

xix. Will you calculate a measure of the agreement between the reviewers regarding the quality of the studies?

R: In this instance we would use the kappa test of agreements.

xx. Include the data extraction sheets or mention what kind of data will be extracted.

R: In the Appendix 2, we have now included data collection tools.

xxi. If you are going to synthesize the information quantitatively, how is this going to be done? What measures will be quantitatively summarized? Will measures be converted for the quantitative summary? How will the different types of outcomes be quantitatively synthesized? And will the risk factors be divided into categories? And if yes, into what categories will they be divided?

R: If studies deem to be reasonably clinically, methodologically and statistically homogenous, we will pool data statistically and conduct meta-analyses. Quantitative combination of the estimates will be done separately for the review outcomes: i.e. separately for prevalence, incidence, risk factors, and trend. Where applicable and feasible, we will convert between estimates in order to derive common estimates that will allow implementation of the meta-analysis. If the data is heterogeneous we will undertake a narrative synthesis of the data.

xxii. Regarding the subgroup analyses, you should clearly mention what subgroup analyses you are planning to do. Again, this should be an exhaustive list. In addition, you mention that you want to perform a subgroup analysis for body mass index. How will this be done for prevalence and incidence estimates of obesity (or probably overweight and obesity)?

R: We will conduct a subgroup analysis for overweight and obesity outcomes based on sex, age group, study design, and country.

xxiii. Will authors of papers providing incomplete information (to determine eligibility or to synthesize data quantitatively) be contacted?

R: Yes, we will contact the authors for additional information if needed.

xxiv. Contributions

Can you mention who will do what for the review?

R: Please see "contributors" section of the protocol. We have changed into: UBN and MN conceived the idea for this study. UBN, BIN and FA developed the methods and together with SM and MN drafted this protocol. MN, UN, FA, SM will extract data, appraisal of papers, UN will conduct meta-analyses, draft a manuscript and all authors will contribute to the final synthesis of evidence.

xxv. Funding

There is no information on funding

R: We have now provided information on funding in the protocol.

xxvii. p.3, line 22: Why do you specifically mention the number of overweight/obese children in developing countries? In the abstract you specifically mention the increase in prevalence of overweight and obesity in industrialized countries (p.2, line 8-9).

R: The WHO data on the burden of overweight and obesity in children from both, developing and developed countries is an overall estimation. In the abstract, we have mentioned that the prevalence has increased in industrialised countries; however, the true prevalence of overweight and obesity in children is unclear in GCC countries.

xxviii. p. 5, line 39: Word missing.

R: We have now added the missing word on p 5. Line 39

Reviewer: 2

Reviewer Name: Milagros Ruiz

Institution and Country: University College London, United Kingdom Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below I commend the authors on their work to address the research gap and generate up-to-date evidence of early childhood adiposity in the GCC countries.

i. Page 4, line 21: If the SR aims to present up-to-date evidence of the burden of overweight/obesity, is it necessary to include all studies published since inception? Why not look at papers since 2000, for example?

R: We agree with the reviewer's comment and will include the studies between 2000 and 2017.

ii. Page 5, line 13 contradicts other statements that unpublished and ongoing studies will be included

R: Unpublished and ongoing studies refer to trials. We will search international trials repositories for unpublished or ongoing trials on obesity in children. The following databases will be searched: WHO International Clinical Trials Registry platform; Clinical trials.gov; Controlled-trials.com; Australian New Zealand Clinical Trials Registry.

iii. The inclusion of risk factors as a secondary outcome makes the protocol very ambitious and wide in scope. Risk factors for obesity are complex and range from cultural, structural, behavioural, nutritional, physiological, etc. I would omit this as a secondary outcome or do a separate SR of risk factors in this region as a follow-up study.

R: We agree with the reviewer's comment that risk factors for obesity are complex. However, as we mentioned to similar comment by reviewer 1 above, we have used this approach in similar reviews (e.g. see Reference 1 below) and believe that including synthesis of the incidence, prevalence, and risk factors of obesity in one paper will provide a comprehensive picture of the epidemiology of obesity in the GCC region. We will use our experiences of previous reviews in implementing the current study.

iv. Page 7, line 8-9: 'Statistically homogeneous': I would rephrase this, as you plan on doing random-effects meta-analysis. Fixed-effects meta-analysis is performed for studies where the variation is entirely due to sampling variation. Homogeneous implies fixed effects.

R: We agree with the assumption of the reviewer and have edited this section of the paper.

Page 7, line 11-13: What about subgroup analyses by study design (cohort, cross-sectional, case-control) which could vastly explain differences in the assessment of the burden? What about subgroup analyses by gender? There is a known gender difference in the burden of adiposity

between males and females, some of which is related to lifestyle and cultural norms. Different gender roles from a young age could be relevant for these countries.

R: We agree with the reviewer's comment. We will conduct subgroup analyses based on sex, age group, study design and country.

v. Page 7, lines 32-37: Whether or not the review will be the most unbiased depends on the state of the evidence, and largely on what has been/has not been published. I would remove this word as all SRs in theory address study bias. If this is the first SR on this topic, how can authors claim to 'present the most comprehensive ... synthesis'? This implies that there are other reviews which authors are addressing in this protocol. I would replace 'most' with 'first comprehensive synthesis of the evidence relating to...'

R: We appreciate the reviewer's comment and have now replaced the suggested wording.

vi. Other minor comments:

vii. Page 4, lines 14-16: The impact on society is not only economic, but social as it can lead to great overweight/obesity inequalities between and within GCC countries. Is the economic burden largely due to health care costs? Why not focus on other costs such as obesity-related illnesses that prevent those from working and earning an income etc? The reference to the German study is odd. I would replace it with a similar study that is either global or from the region.

R: We have now removed the German Study. Unfortunately, there are no formal assessments of cost of obesity from the GCC countries and to date we have a comprehensive systematic review on economic burden of obesity, which was published in 2017 and we have included this study in our protocol (reference 8).

We look forward to the Editorial Office's response in due course.

With kind regards,

Dr. Mahmoud Nahhas

Ministry of Health, Kingdom of Saudi Arabia, Riyadh, 11176

On behalf of the co-applicants

References:

1. Nwaru BI, Hickstein L, Panesar SS, Muraro A, Werfel T, Cardona V, et al. The epidemiology of food allergy in Europe: a systematic review and meta-analysis. *Allergy*. 2014;69(1):62-75.
2. Available at: <http://gov.wales/topics/people-and-communities/people/children-and-young-people/early-years/?lang=en>
3. Available at: <http://www.gov.scot/Resource/Doc/257007/0076309.pdf>
4. Available at: <http://www.ephpp.ca/tools.html>