PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Ethnicity and the association between anthropometric indices of obesity and cardiovascular risk in women: a cross-sectional study
AUTHORS	Goh, Louise; Dhaliwal, Satvinder; Welborn, Timothy; Lee, Andy; Della, Phillip

VERSION 1 - REVIEW

REVIEWER	Parvin Mirmiran Department of Clinical Nutrition and Dietetics, Faculty of Nutrition Sciences and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran
REVIEW RETURNED	11-Mar-2014

GENERAL COMMENTS	The section of "study participans" in Methods should be explain more. It should be mentioned in the methods that how components of Framingham risk score model such as ECG-Left ventricular hypertrophy were measured? The title is not correct and should be re-write.

REVIEWER	Stanley Ulijaszek University of Oxford
REVIEW RETURNED	12-Mar-2014

GENERAL COMMENTS	I have answered questions 1, 9 and 11 as N/A because there is no question that considers if the research question is appropriate. The issue for me hinges around the idea of ethnicity. It is a very loose category that can represent a number of things, and often does not map onto the group identities of the people that are studied. For example, Pacific Islanders might be a census category in Australia (useful for purposes of governance and planning) people assigned this category may not identify with it (thinking of themselves as Tongans, for example). Ethnicity can also be a proxy for structural inequality. For example, African Americans are likely to have poor outcomes on a range of social measures not because of their ethnicity but because of the difficult circumstances they may live under. Ethnicity is therefore a blend of the social, political and biological, and categorisations vary from country to country. These categorisations may be useful in social, forensic and health settings, as they can be used in typologies of risk (of deprivation, criminal behaviour and disease in these three domains).

	In the present investigation, health risk is examined in relation to anthropometric measures according to categories of ethnicity. The categories seen to differ at least in part from those of the Australian Bureau of Statistics (2008) publication cited as reference 4. Taking a quick look as this reference, I come up with the statement that 'Adults born in Southern and Eastern Europe and the Oceania region (excluding Australia) were the most likely to be overweight or obese (65% and 63% respectively). While those born in Australia were less likely to be overweight or obese (55%), adults born in South East Asia were least likely to be classified in this way (31%)'. The categories in the present analysis that map onto the ABS categories (as far as I can see) are 'Australian-born, and South European'. As census categories are not used, it would be useful to know what structural basis the categories of ethnicity were chosen and what work they are expected to do in the larger world (as an aside, I can see myself falling into two of the three categories, while my children could fall into three simultaneously, so the potential for misclassification of ethnicity must be thought about, even if not measured). I recommend a reanalysis using categories that are broadly used, or welcome a rebuttal, with evidence, that the categories used here are indeed broadly used. The ethnicity categories need to be justified: do epidemiologists and/or clinical practitioners use them to help in understanding disease patterns or clinical diagnosis? If not, why are they structured in this way (and who would use this knowledge in a practical sense)? Further comment is needed about what is common about: the UK and Ireland; Northern Europe (which countries); Southern Europe (again, which countries) and Asia (yet again, which countries). Note that each ethnicity classification used here is a group-nationality one, and that each has a great deal of political and social variation. There is more variation in the range of odds ratios for most if not all ethnicity categories relative to Australia, suggesting an expression of social and political premigration histories to their biological risk (Table 3a). This is worthy of comment. Another issue is the one of mechanism: why do the different ethnicities as presented here show different associations between anthropometric measures and measures of risk? I can only think that the major difference between most of the European groups represented in this article are in respect of exposure earlier environments. Discussion of potential mechanisms that might contribute to the difference reported (whether existing or new analysis) is needed.

REVIEWER	Simi Kohli Simon Fraser University, Burnaby, BC Florida Hospital, Orlando, FL
REVIEW RETURNED	18-Mar-2014

GENERAL COMMENTS	Overall, it was a good paper. I do have a few comments that I would like to see addressed prior to final submission. 1. The Framingham risk score, although widely used, was done on a

	primarily Caucasian population (which was addressed) and the age ranged from 20-69 however the Framingham score does not apply to ages <30. The analysis includes this age group 20-30 which cannot be appropriately used for a risk assessment. It is important to remember that age is strong variant in the model such that a female with an age of 20 will still be at low risk according to the Framingham risk score despite very poor SBP and total cholesterol versus a woman in their 40s. 2. Please address and justify the choice of ethnic populations. Often most European populations are lumped together; however, it was not here, yet the Asian population was. The differences between to two races are vastly different however, I don't seem to quite understand the need to further subdivide the European populations - perhaps justify the choice and define what Northern vs. Southern European equates to. 3. The study only uses women; however, menopausal status was not clearly indicated in this population. This can affect CVD risk assessment not only from a metabolic standpoint and this risk score standpoint, but also in regards to anthropometry. Pre-menopausal women will have smaller WHR and have greater cardio-protective effects of adiposity in the hips; vs. post-menopausal women will have great WC's. Adjusting for these variables is necessary when dealing with studies involving women and CVD. Also if not able to provide it, listing in the limitations section would be of value. 4. The Pearson correlation - although does allow for visualization of the data, it cannot be concluded that one is greater than the other as they need to be statistically compared correlation co-efficient. Please clarify or address this. 5. Please list the inter- and intra-observation error as this is of value when doing anthropometric analyses. Also detail in methodology how hip circumference was conducted. 6. There are additional risk factor models used in European populations such as SCORE and QRISK2 that may of value to mention in the discussion.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Parvin Mirmiran
Institution and Country: Department of Clinical Nutrition and Dietetics, Faculty of Nutrition Sciences and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Please state any competing interests or state 'None declared': None declared

The section of "study participants" in Methods should be explain more.

Response: We thank the reviewer for the comment. We have expanded the section on "study participants" to include further details.

It should be mentioned in the methods that how components of Framingham risk score model such as ECG-Left ventricular hypertrophy were measured?

Response: We thank the reviewer for the comment. Participants were assumed not to have LVH as ECG was not undertaken in the National Heart Foundation third Risk Factor Prevalence Study. The absence of ECG-LVH was handled similarly in a number of studies, for example: Chen L, Tonkin AM, Moon L, et al. Recalibration and validation of the SCORE risk chart in the Australian population: The AusSCORE chart. Eur J Cardiovasc Prev Rehabil 2009;16(5):562-70.

The title is not correct and should be re-write.

Response: The authors believe that the title appropriately describes the results of the study. Being a cross-sectional study, the authors are reluctant to be more assertive in the title. Our publication is about the association between anthropometric indices of obesity and cardiovascular risk in women, within ethnic groups.

Reviewer: 2
Reviewer Name: Stanley Ulijaszek
Institution and Country: University of Oxford
Please state any competing interests or state 'None declared': None declared

Queries related to the use of term ethnicity and its determination.

Response: The authors thank the reviewer for his comments on ethnicity. Country of birth was used as a surrogate for ethnicity and was grouped into regions as described by the Australian Risk Factor Prevalence Study Management Committee (1990). The authors agree with the reviewer that there are limitations with the use of country of birth as a proxy for ethnicity. The limitations section has been expanded to discuss issues related to this, with appropriate references.

The United Kingdom and Ireland region consisted of participants who were born in England, Wales, Scotland, Northern Ireland or Republic of Ireland.

The Northern Europe region consisted of participants who were born in Austria, Belgium, Czechoslovakia, Denmark, Estonia, Finland, France, East or West Germany, Greenland, Hungary, Iceland, Latvia, Liechtenstein, Lithuania, Luxemburg, Netherlands, Norway, Poland, Sweden, Switzerland or USSR.

The Southern Europe region consisted of participants who were born in Albania, Andorra, Bulgaria, Gibralta, Greece, Italy, Malta, Monaco, Portugal, Rumania, San Marino, Spain, Ukraine, Vatican City or Yugoslavia.

The Asia region consisted of participants who were born in Afghanistan, Bahrain, Bangladesh, Bhutan, Brunei, Burma, China, Cyprus, Gaza Strip, Hong Kong, India, Indonesia, Iran, Iraq, Israel, Japan, Jordan, Kampuchea, Korea, Kuwait, Laos, Lebanon, Macao, Malaysia, Maldive Islands, Mongolia, Muscat, Nepal, Oman, Pakistan, Philippines, Qatar, Saudi Arabia, Sikkim, Singapore, Sri Lanka, Syria, Taiwan, Thailand, Tibet, Timor, Trucial States, Turkey, United Arab Emirates, Vietnam or Yemen.

These groupings were also used in another publication by some of the authors: Dhaliwal SS, Welborn TA. Measurement error and ethnic comparisons of measures of abdominal obesity. Prev Med 2009;49(2–3):148-52.

Reviewer: 3
Reviewer Name: Simi Kohli

Institution and Country: Simon Fraser University, Burnaby, BC
Florida Hospital, Orlando, FL
Please state any competing interests or state 'None declared': None

Overall, it was a good paper. I do have a few comments that I would like to see addressed prior to final submission.

1. The Framingham risk score, although widely used, was done on a primarily Caucasian population (which was addressed) and the age ranged from 20-69 however the Framingham score does not apply to ages <30. The analysis includes this age group 20-30 which cannot be appropriately used for a risk assessment. It is important to remember that age is strong variant in the model such that a female with an age of 20 will still be at low risk according to the Framingham risk score despite very poor SBP and total cholesterol versus a woman in their 40s.

Response: The authors agree with the reviewer that the risk in young adults is very rarely elevated, even in the presence of significant risk factors (Greenland et al. 2010). In the 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults, published in Circulation in 2010, this recommendation went even further to calculate the life-time risk for young adults and consider "a global risk score possibly worthwhile even in persons as young as age 20". Hence, the authors believe that the use of the Framingham risk score model to predict the 10 year risk in young adults is appropriate. The authors have addressed the reviewer comment by including this as a limitation of the use of 10-year CVD risk score models in the clinical assessment of young adults.

The Framingham equations have also been used in young adults less than 30 years in Scheltens et al. (2008). Other publications that use the Framingham risk score model for those less than 30 years old include Zomer et al. (2014), Esteghamati et al. (2013), Pandya, Weinstein and Gaziano (2011), and Raiko et al. (2010).

References:

Greenland P, Alpert JS, Beller GA, Benjamin EJ, Budoff MJ, et al. (2010) 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults. Circulation 122: e584-e636

Scheltens T, Verschuren WMM, Boshuizen HC, Hoes AW, Zuithoff NP, et al. (2008) Estimation of cardiovascular risk: a comparison between the Framingham and the SCORE model in people under 60 years of age. Eur J Cardiovasc Prev Rehabil 15: 562-566.

Zomer E, Liew D, Owen A, Magliano DJ, Ademi Z, et al. (2014) Cardiovascular risk prediction in a population with the metabolic syndrome: Framingham vs. UKPDS algorithms. Eur J Prev Cardiol 21: 384-390.

Esteghamati A, Mousavizadeh M, Noshad S, Shoar S, Khalilzadeh O, et al. (2013) Accuracy of Anthropometric Parameters in Identification of High-risk Patients Predicted With Cardiovascular Risk Models. Am J Med Sci 346: 26-31.

Pandya A, Weinstein MC, Gaziano TA (2011) A Comparative Assessment of Non-Laboratory-Based versus Commonly Used Laboratory-Based Cardiovascular Disease Risk Scores in the NHANES III Population. PLoS One 6: e20416.

Raiko JR, Magnussen CG, Kivimäki M, Taittonen L, Laitinen T, et al. (2010) Cardiovascular risk scores in the prediction of subclinical atherosclerosis in young adults: evidence from the cardiovascular risk in a young Finns study. Eur J Cardiovasc Prev Rehabil 17: 549-555.

2. Please address and justify the choice of ethnic populations. Often most European populations are lumped together; however, it was not here, yet the Asian population was. The differences between to two races are vastly different however, I don't seem to quite understand the need to further subdivide the European populations - perhaps justify the choice and define what Northern vs. Southern European equates to.

Response: To improve clarity in relation to ethnicity, the methods section has been expanded to include further details on the country of birth and their groupings into regions for the determination of ethnicity. Please also refer to our response to Reviewer 2. Thank you.

3. The study only uses women; however, menopausal status was not clearly indicated in this population. This can affect CVD risk assessment not only from a metabolic standpoint and this risk score standpoint, but also in regards to anthropometry. Pre-menopausal women will have smaller WHR and have greater cardio-protective effects of adiposity in the hips; vs. post-menopausal women will have great WC's. Adjusting for these variables is necessary when dealing with studies involving women and CVD. Also if not able to provide it, listing in the limitations section would be of value.

Response: Menopause is currently not a variable in all the risk score models discussed in this publication. The authors have addressed the reviewer comment by including the effect of menopause on cardiovascular risk in the limitations section.

4. The Pearson correlation - although does allow for visualization of the data, it cannot be concluded that one is greater than the other as they need to be statistically compared correlation co-efficient. Please clarify or address this.

Response: The authors agree with the reviewer, the manuscript has been edited to reflect this concern, and the authors have toned-down the statements.

5. Please list the inter- and intra-observation error as this is of value when doing anthropometric analyses. Also detail in methodology how hip circumference was conducted.

Response: The details about measurement error are described in a previous publication by some of the authors: Dhaliwal SS, Welborn TA. Measurement error and ethnic comparisons of measures of abdominal obesity. Prev Med 2009;49(2–3):148-52. The manuscript has been edited to further describe how hip circumference was measured and to discuss the measurement error encountered when performing anthropometric measurements.

6. There are additional risk factor models used in European populations such as SCORE and QRISK2 that may of value to mention in the discussion.

Response: We thank the reviewer for the comment. We have now discussed the SCORE risk chart and QRISK model in the limitations section.

VERSION 2 – REVIEW

REVIEWER	Stanley Ulijaszek University of Oxford, UK
REVIEW RETURNED	15-Apr-2014

- The reviewer completed the checklist but made no further comments.