PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A comparison of Australian rural and metropolitan cardiovascular risk and mortality: the Greater Green Triangle and North West Adelaide Population Surveys.
AUTHORS	Peach, Elizabeth; Tideman, Philip; Taylor, Anne; Janus, Edward; Philpot, Ben; Clark, Robyn; Laatikainen, Tiina; Vartiainen, Erkki; Tirimacco, Rosy; Montgomerie, Alicia; Grant, Janet; Versace, Vincent; Dunbar, James

VERSION 1 - REVIEW

REVIEWER	Allamanda Faatoese, PhD Assistant Research Fellow Christchurch Heart Institute University of Otago, Christchurch
REVIEW RETURNED	27-May-2013

THE STUDY	Is the overall study design appropriate and adequate to answer the research question? This paper addresses an important issue in identifying factors that contribute to CVD disparity between rural and urban communities by comparing cardiovascular risk factor levels, and CVD mortality rates within those regions by a measure of socioeconomic status (IRSD). This manuscript has several areas that need to be addressed: The two cohorts (regions) selected in this study are not dissimilar with regards to cardiovascular risk profiles, demographic profiles, CVD mortality and IRSD indices. Therefore, this restricts the identification of contributors to CVD disparity between these cohorts. If these localities are diverse (eg. health care services available to regional and urban localities) then this needs to be made clear in the manscript. To adequately address the objective of this manuscript, the inclusion of cardiovascular risk data for remote/very remote areas within South Australia would have been more informative addressing unmet needs. I would recommend a change in study objective because the selected cohorts were inadequate to address this. This jump from cohort study descriptives to CVD mortality and socioeconomic status is rather disjointed. It is stated in the manuscript that self-reported socioeconomic status for both regional and urban cohorts are representative of national data for respective localities. However, do the CVD mortality rates by age-groups also reflect the SES of regional and urban localities? Is the main outcome measure clear? The main outcome was that metropolitan areas are not necessarily

	better than regional profiles. These selected cohorts are not different (as indicated by socioeconomic status and CVD mortality rates), therefore recommendations for improving health systems are very limited in this study. Are the statistical methods appropriate? In the methods section it is unclear as to the proportion of regional participants with complete data (self-administered questionnaire and attended survey site for anthropometric and biomedical measures). How was missing data handled? Were levels for cardiovascular risk factors imputed? Absolute CVD-risk was calculated for participants aged from 35 - 74 years. In this paper, 42% and 49% of the participants (GGTRFS and NWAHS respectively) were aged 25 - 49 years that suggests a significant proportion of study participants were below the age threshold of 35 years for CVD risk calculation. Table 2 presents the means of comparisons of cardiovascular risk factors. It is stated that these have been weighted to the 2006 Australian population, yet it remains unclear as to whether the comparison of risk factor levels have been age-adjusted to account for the younger age profile of the urban cohort.
RESULTS & CONCLUSIONS	Do the results answer the research question? This stated objective for this study is inaccurate. The similarity of cohort profiles cannot identify contributors of CVD disparity. Socioeconomic status, independent of locality is identified as a CVD risk factor, yet this is not a novel finding. This manscript shows compelling evidence for higher CVD mortality rates in the NWA region compared to other urban Australian cities, yet there is a lack of addressing what factors contribute to this significant difference. Are they well presented? (see comments regarding cohort study to national statistics) Ammendments to Tables and Figures: Figure legends for Figures 1a and 1b are not well-labelled and similarly for Figure 2 (a - d). Table 2 is missing waist circumference data (total) and the layout of the Current smoking and Known diabetes/Impaired fasting glucose is difficult to read. I suggest that it be presented as %, 95% CI (N) Table 3 - title needs to show that it refers to ABS national statistics.

REVIEWER	Kerin O'Dea Professor of Population Health and Nutrition School of Population Health University of South Australia. I have no competing interests.
REVIEW RETURNED	04-Jun-2013

THE STUDY	I could not see any documents in supplemental documents file.
GENERAL COMMENTS	1. I thought the legends on the Table were repetitive. Clearly the data were from the North West Adelaide Health Study Stage 2 and the Greater Green Triangle. This was clearly explained in the methods.

	2. There were so few Aboriginal and Torres Strait Islander participants in either group, I did not think the 'slightly lower proportion' in NWAHS was worth commenting on. 3. Any thoughts on why the NWAHS subjects had lower mean systolic BP, but higher mean diastolic BP? Could it have been related to different methodologies?

VERSION 1 – AUTHOR RESPONSE

Reviewer 1
Reviewer: Allamanda Faatoese, PhD
Assistant Research Fellow
Christchurch Heart Institute
University of Otago, Christchurch

Reviewer comment 1: Is the overall study design appropriate and adequate to answer the research question?
This paper addresses an important issue in identifying factors that contribute to CVD disparity between rural and urban communities by comparing cardiovascular risk factor levels, and CVD mortality rates within those regions by a measure of socioeconomic status (IRSD).
The two cohorts (regions) selected in this study are not dissimilar with regards to cardiovascular risk profiles, demographic profiles, CVD mortality and IRSD indices. Therefore, this restricts the identification of contributors to CVD disparity between these cohorts. If these localities are diverse (eg. health care services available to regional and urban localities) then this needs to be made clear in the manscript. To adequately address the objective of this manuscript, the inclusion of cardiovascular risk data for remote/very remote areas within South Australia would have been more informative addressing unmet needs. I would recommend a change in study objective because the selected cohorts were inadequate to address this.

Our response 1: We believe that our stated objectives are sound. The outcome that metropolitan NWA and rural GGT were similar was contrary to our expectations at the beginning of the study. This led us to look at the national context. Exploration of additional factors to explain rural-urban CVD disparities were beyond the scope of this study. Therefore we have not modified the objectives of the study.

To our knowledge, there are no existing datasets incorporating CVD risk factors that are available in remote areas of South Australia that would be appropriate for a comparison study with the GGT RFS.

We have not made any changes to the manuscript on these points.

Reviewer comment 2: This jump from cohort study descriptives to CVD mortality and socioeconomic status is rather disjointed. It is stated in the manuscript that self-reported socioeconomic status for both regional and urban cohorts are representative of national data for respective localities. However, do the CVD mortality rates by age-groups also reflect the SES of regional and urban localities?

Our response 2: We don't believe that these two sections are disjointed. The study aim in the introduction states:

The study aim was to more objectively understand causes of geographical CVD mortality disparities by; (a) comparing measures of CVD risk (objective and self-reported data) between GGT and NWA; (b) comparing CVD mortality rates between GGT and NWA and other areas Australia-wide and (c) describing the relationship between socioeconomic status (SES) and CVD mortality rates.

The subsections in the Results are as follows:
• Comparing measures of CVD risk
• Comparing CVD mortality outcomes
• Relationship between SES and CVD mortality rates

We assume that CVD mortality rates across all age groups are influenced by SES in both regional and urban localities. However, quantifying this influence beyond what we have presented is a much more complex task and is beyond the scope of this article. Accordingly, we have not made any changes to the text of the manuscript.

Reviewer comment 3: Is the main outcome measure clear?
The main outcome was that metropolitan areas are not necessarily better than regional profiles. These selected cohorts are not different (as indicated by socioeconomic status and CVD mortality rates), therefore recommendations for improving health systems are very limited in this study.

Our response 3: In this study there was the possibility of making a comparison of mortality, risk factors (including biomedical data and absolute CVD risk) and SES at the same time from very different areas which is quite unique. In these analyses, surprisingly the differences in mortality were minor as were the differences in risk factors and absolute CVD risk. This result itself is an important finding.

We believe that health outcomes should be similar between all regions of Australia. For this reason we believe that the findings in our paper support the claim that improvements to health systems in rural and remote and some metropolitan areas need to be improved, particularly in areas of low SES. Accordingly, we have not made any modifications to the text.

Reviewer comment 4: Are the statistical methods appropriate?
In the methods section it is unclear as to the proportion of regional participants with complete data (self-administered questionnaire and attended survey site for anthropometric and biomedical measures). How was missing data handled? Were levels for cardiovascular risk factors imputed?

Our response 4: There was no imputation of missing data. With reference to the Framingham risk calculations, only participants with data for age, gender, SBP, cholesterol (total and HDL), smoking and diabetes status were used.

Reviewer comment 5: Absolute CVD-risk was calculated for participants aged from 35 - 74 years. In this paper, 42% and 49% of the participants (GGTRFS and NWAHS respectively) were aged 25 - 49 years that suggests a significant proportion of study participants were below the age threshold of 35 years for CVD risk calculation.

Our response 5: The weighted results presented in Table 1 indicate there was a large proportion of individuals in the 25-44 year band. The majority of these participants within this band for both GGTRFS and NWAHS were in fact 35-44 year olds, which were ultimately included in the Framingham calculations. The reason the actual numbers aren't reported in the manuscript is because an ANOVA looking at the survey area (GGT vs NWAHS), age (35-39; 40-44; 45-49….70-74), and the interaction between survey area*age indicated there was no significant difference between survey area and the interaction term was also non-significant. There was a difference between the age classes, which was expected. These results are presented under the heading 'Comparing measures of CVD risk': Framingham 5-year absolute CVD risk scores were not

significantly different between GGT RFS and NWAHS participants (age-specific groups and overall, Figure 1(a)). The inclusion of Figure 1a allows the reader to visualise the non-significant interaction.

Reviewer comment 6: Table 2 presents the means of comparisons of cardiovascular risk factors. It is stated that these have been weighted to the 2006 Australian population, yet it remains unclear as to whether the comparison of risk factor levels have been age-adjusted to account for the younger age profile of the urban cohort.

Our response 6: The results presented in Table 2 reflect the age structure of the 2006 population. This table is intended as an overview of the individual risk factors. Figure 1a reflects the Framingham risk scores. As well as the Framingham calculation which accounts for age, they are presented stratified by 5-year age classes.

Reviewer comment 7: Do the results answer the research question?
This stated objective for this study is inaccurate. The similarity of cohort profiles cannot identify contributors of CVD disparity. Socioeconomic status, independent of locality is identified as a CVD risk factor, yet this is not a novel finding.

Our response 7: As noted above, we believe that our stated objectives are sound.

Our study is novel in the respect that there have been few biomedical studies investigating cardiovascular risk, particularly combinations of risk factors, mortality and SES in rural areas of Australia. Accordingly, we have not modified the manuscript on this point.

Reviewer comment 8: This manuscript shows compelling evidence for higher CVD mortality rates in the NWA region compared to other urban Australian cities, yet there is a lack of addressing what factors contribute to this significant difference.

Our response 8: Our research indicates that differences in SES are a significant contributing factor to the differential mortality rates between NWA and other major Australian cities. This is demonstrated in Figure 2b.

Additional factors that could be contributing to differential CVD mortality rates between rural, remote and metropolitan regions of Australia were beyond the stated objectives of this paper. Accordingly, we have not modified the manuscript on this point.

Reviewer comment 9: Are they well presented?
(see comments regarding cohort study to national statistics)

Our response 9: Please see our response to the corresponding reviewer comment above.

Reviewer comment 10: Ammendments to Tables and Figures:
• Figure legends for Figures 1a and 1b are not well-labelled and similarly for Figure 2 (a - d).
• Table 2 is missing waist circumference data (total)
• The layout of the Current smoking and Known diabetes/Impaired fasting glucose is difficult to read. I suggest that it be presented as %, 95% CI (N)
• Table 3 - title needs to show that it refers to ABS national statistics.

Our response 10:
• We believe Figure 1a and 1b have appropriate legends. Figure 1a illustrates the change in mean risk score for participants in the Greater Green Triangle Risk Factor Survey (GGTRFS), while Figure 1b illustrates mortality in the Greater Green Triangle (GGT) region. Figure 1a illustrates the change in mean risk score for the North West Adelaide Health Study (NWAHS), while Figure 1b illustrates mortality for the North West Adelaide (NWA) region. We have provided this extra detail to try and clarify any misunderstanding if it arose from the slightly different names in the legend. We believe Figure 2 (a-d) do not require legends and have adequately labelled axis titles, which are complemented by the caption and the main body of the manuscript. Accordingly, we have not made any changes to the Figure legends.
• We do not believe that it is appropriate to combine waist circumference data for men and women, as these measures are not comparable between the sexes. Accordingly, we have not incorporated a combined measure Table 2.
• The layout of Current Smoking and Known Diabetes/Impaired fasting glucose has been amended to reflect the reviewer's suggestion.
• The title of Table 3 has been amended to:Table 3: Comparison of ischaemic heart disease (IHD) and stroke mortality rates by age group (Source: 2003-2007 Australian Bureau of Statistics).

Reviewer 2:
Kerin O'Dea Professor of Population Health and Nutrition
School of Population Health
University of South Australia.

Reviewer comment 1: I thought the legends on the Table were repetitive. Clearly the data were from the North West Adelaide Health Study Stage 2 and the Greater Green Triangle. This was clearly explained in the methods.

Our response 1: We have deleted this repetitive information from Tables 1 and 2 in the manuscript.

Reviewer comment 2: There were so few Aboriginal and Torres Strait Islander participants in either group, I did not think the 'slightly lower proportion' in NWAHS was worth commenting on.

Our response 2: This information has been removed from the text of the manuscript.

Reviewer comment 3: Any thoughts on why the NWAHS subjects had lower mean systolic BP, but higher mean diastolic BP? Could it have been related to different methodologies?

Our response 3: The same methodology was used in the NWAHS and GGT RFS for taking BP. We think that inter-observer variation is probably the main explanation for the observed differences. Measurement error due to the use of different mercury sphygmomanometers could also be a contributing factor as well as confounding from differences in the treatment of hypertension between the two populations, or seasonal variation. We have added a sentence in the limitations section of the manuscript to acknowledge this.

We know of other population-level factors, such as prevalence of vascular disease and salt intake, that may differentially affect systolic and diastolic blood pressure. For simplicity, we haven't included a more detailed discussion of these factors in the manuscript.

VERSION 2 – REVIEW

REVIEWER	Allamanda Faatoese, Phd Assistant Research Fellow University of Otago, Christchurch New Zealand The Reviewer declares that these is no conflict of interest.
REVIEW RETURNED	16-Jul-2013

GENERAL COMMENTS	I accept the comments and minor changes mady by the authors in response to my initial comments on the manuscript.

Correction

Tideman P, Taylor A, Janus E, *et al*. A comparison of Australian rural and metropolitan cardiovascular risk and mortality: the Greater Green Triangle and North West Adelaide Population Surveys. *BMJ Open* 2013;3:e003203. An error in the coding of one of the categorical variables used to calculate the Framingham five-year risk was detected following publication. The error does not affect the overall conclusions drawn in this paper but has changed figure 1A. The corrected figure 1A is below.

In addition, the first sentence of the Results section of the Abstract should now read: 'Few significant differences in CVD risk between the study regions, with mean absolute CVD risk ranging from approximately 1% in the age group 35–39 years to 14% in the age group 70–74 years.'

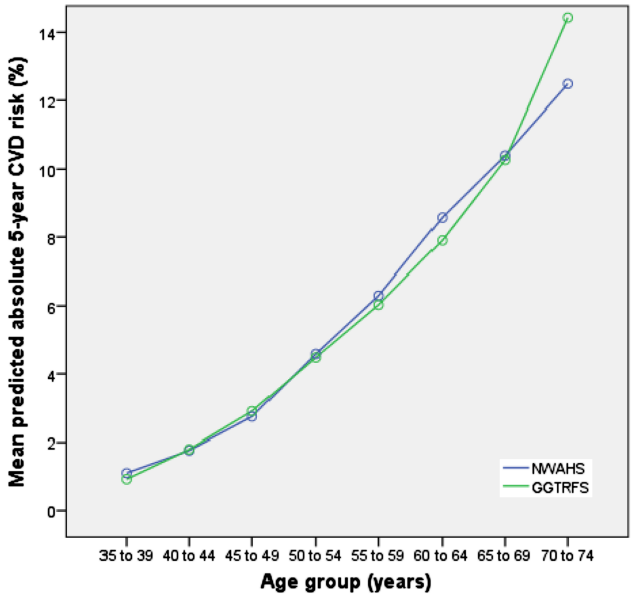

Figure 1A Framingham absolute cardiovascular disease risk by age.

BMJ Open 2014;**4**:e003203corr1. doi:10.1136/bmjopen-2013-003203corr1