BMJ Open

# Quantifying the role of modifiable risk factors in the differences in cardiovascular disease mortality rates between metropolitan and rural populations in Australia: A macrosimulation modelling study.



| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2017-018307 |
| Article Type: | Research |
| Date Submitted by the Author: | 22-Jun-2017 |
| Complete List of Authors: | Alston, Laura; Deakin University, Waterfront Campus<br>Peterson, Karen; Deakin University - Geelong Waterfront Campus<br>Jacobs, Jane; Deakin University - Geelong Waterfront Campus<br>Allender, Steven; Deakin University, Faculty of Health<br>Nichols, Melanie; Deakin University, Faculty of Health; |
| Primary Subject Heading: | Public health |
| Secondary Subject Heading: | Epidemiology |
| Keywords: | Coronary heart disease < CARDIOLOGY, NUTRITION & DIETETICS, PREVENTIVE MEDICINE, PUBLIC HEALTH |
| | |

**TITLE**: Quantifying the role of modifiable risk factors in the differences in cardiovascular disease mortality rates between metropolitan and rural populations in Australia: A macrosimulation modelling study.

**Authors:** Laura Alston[a], Karen Louise Peterson[a], Jane P Jacobs[a], Steven Allender[a], Melanie Nichols[a].

**Author affiliations**: [a]WHO Collaborating Centre for Obesity Prevention, Faculty of Health, Deakin University, Geelong, Australia.

**Corresponding author**: Laura Alston. Address: WHO Collaborating Centre for Obesity Prevention, Faculty of Health, Deakin University, Locked Bag 20001, Geelong, VIC 3220 Australia. Telephone: +61 3 5247 9426. Email: laura.alston@deakin.edu.au.

**Previous presentations of this research**: none to declare.

**Funding acknowledgments:** MN, KP, LA and JJ are supported by funding from the National Heart Foundation of Australia and Deakin University. SA is supported by funding from an Australian National Health and Medical Research Council/ National Heart Foundation of Australia Career Development Fellowship (APP1045836). He is also a researcher on the US National Institutes of Health grant titled, "Systems Science to Guide Whole-of- Community Childhood Obesity Interventions" (1R01HL115485-01A1) and within a NHMRC Centre for Research Excellence in Obesity Policy and Food Systems (APP1041020).

**Keywords:** Rural, Risk factors, Cardiovascular disease, Ischaemic heart disease, Inequalities, Prevention

**Word count (excluding references and abstract): 3,115 words**

## ABSTRACT

**Objectives:** Aims: (1) to quantify differences in modifiable risk factors between urban and rural populations, and (2) to determine the number of rural CVD and IHD deaths that could be averted or delayed if risk factor levels in rural areas were equivalent to metropolitan areas.

**Setting:** National population estimates, risk factor prevalence, CVD and IHD deaths data were analysed by rurality using the Preventable Risk Integrated Model (PRIME) macro-simulation chronic disease risk model. Uncertainty analysis was conducted using a Monte Carlo simulation of 10,000 iterations to calculate 95% credible intervals (CI).

**Participants:** National datasets of males and females over the age of 18 years living in urban and rural Australia.

**Results:** If people living in rural Australia had the same levels of risk factors as those in metropolitan areas, approximately 1458 (95% credible interval (CI): 1088, 1803) deaths could be delayed from cardiovascular disease (CVD) annually. Of these CVD deaths, 793 (95%CI: 506, 1065) would be from IHD. The IHD mortality gap between metropolitan and rural populations would be reduced by 38.2% (95%CI: 24.4%, 50.6%).

**Conclusions:** A significant portion of deaths from CVD and IHD could be averted with improvements in risk factors; more than one third of the excess IHD deaths in rural Australia were attributed to differences in risk factors. As much as two thirds of the increased IHD mortality rate in rural areas could not be accounted for by modifiable risk factors, however, and this requires further investigation.

**ARTICLE SUMMARY:**

*Strengths:*

- This is the first study to attempt to quantify the role of modifiable factors in the increased burden of cardiovascular diseases in rural areas when compared to urban Australia.
- The PRIME model has been previously published and is internationally recognised.
- This study used three representative national datasets, including the Census, Australian Institute of Health and Welfare National Mortality Database and the Australian Health Survey, as inputs for the PRIME model.

*Limitations:*

- Data used in the model were self-reported, and could lead to underestimations of the level of behavioural risk factors and subsequently, mortality gap reductions, although it less likely that these biases would differentially affect rural vs metro populations.
- Very remote populations of Australia (0.9% of the total population) were excluded.

## INTRODUCTION

Despite high quality, universal health care systems and standards in Australia, there are still disparities in the burden of chronic disease experienced by people with lower socio-economic status, Aboriginal and Torres Strait Islanders and rural residents(1). Australians living outside major cities experience a substantially increased burden of cardiovascular diseases(2), which is consistent with findings for rural populations in other developed countries such as the United States, Canada, and the United Kingdom(3-5). Cardiovascular disease (CVD), in its most common form, Ischaemic heart disease (IHD) is the leading cause of death in Australia(6), and individuals residing in a regional or remote areas are estimated to be between 1.2 and 1.5 times more likely to die from IHD than those residing in metropolitan areas(1).

The reasons for observed health inequalities between metropolitan and rural populations appear to be multifactorial and highly complex(2, 7-9). It has been hypothesised that rural populations experience greater CVD and IHD burden due to variation in access to health services, individual socio-economic status, rates of modifiable risk factors, as well as reduced access to evidence-based treatments in rural hospitals(7, 10-13). The National Rural Health Alliance (NRHA) of Australia states that if rural Australians are to achieve the same health outcomes as their metropolitan counterparts by the year 2020, it is not just access to health services that need to be improved(14), but that more focus needs to be placed on improving the socio-economic determinants of health (such as lower education, incomes, and employment) for rural communities, and reducing risk factors for chronic diseases such as smoking and physical inactivity(14).

Cardiovascular diseases, particularly IHD, are largely preventable (12), and the modifiable risk factors are well known(13). Clinical risk factors such as high cholesterol, high blood pressure, and obesity interact with behavioural factors such as poor diet, smoking, risky alcohol consumption, and physical inactivity to increase the risk of IHD and CVD(13). Based on population health surveys, these risk factors differ by rurality, with higher smoking rates, increased high risk alcohol consumption and lower physical activity levels being reported by non-city dwelling Australians(2).

Currently, there is minimal evidence quantifying the extent to which modifiable risk factors contribute to the increased burden of CVD and IHD in rural areas, and how much of this burden could be reduced if behavioural risk factors were comparable among rural Australians as those among their counterparts in cities. Increased knowledge of how differential risk factor rates contribute to the increased rural CVD burden could support the identification of policy priorities and prevention programs for rural areas, as previous public health prevention efforts have been shown to be less effective for rural populations compared to those living in metropolitan areas(15).

**Aims:**

This study aimed to: (1) Quantify differences in prevalence of major CVD risk factors between rural and metropolitan populations, and (2) Determine the number and proportion of rural deaths from CVD, and specifically from IHD, that could be averted or delayed in rural areas if the levels of risk factors were equivalent to those in metropolitan Australia.

## METHODS

### The Preventable Risk Integrated Model (PRIME)

This study used a macrosimulation model, the Preventable Risk Integrated Model (PRIME)(16), to estimate age- and sex-specific changes in CVD and IHD mortality that would result from changes to the population prevalence of risk factors in Australia. PRIME has been used in the UK, New Zealand and Canada to model a range of risk factor scenarios(16-20). The model can be used to examine the likely changes in mortality rates of many chronic diseases, including IHD, under different counterfactual scenarios of population behavioural risk factors(16).

The PRIME model is built on a framework of linkage between, 1) modifiable behaviours; 2) clinical risk factors; and 3) mortality outcomes. This framework is parameterised using the best available evidence from meta-analyses of published studies, and is described in detail elsewhere(16). PRIME requires data on prevalence of modifiable risk factors, mortality rates and population estimates by 5 year age groups and sex, for both baseline and counterfactual scenarios. For this study, PRIME was used to estimate the number of CVD and IHD deaths that would be delayed or averted if those living in rural Australia had the same modifiable risk factor levels as those living in major cities. The baseline scenario used the current levels of modifiable risk factors in those living in rural areas, and the counterfactual scenario involved applying the level of behavioural risk factors currently observed among those living in metropolitan areas, to the rural population.

**Population data**

Population size estimates by age, sex and rurality were derived from the most recent (2011) Australian Census. The 'rural' population was defined as all residents not classified by the ABS as living in major cities(21).

**Risk factor data**

The risk factors included in the PRIME model were mean dietary intakes, alcohol consumption, prevalence of smoking, and physical activity levels. Mean body mass index (BMI) scores, based on measured height and weight data, from the rural population only, were also included in the baseline

model. All risk factor estimates were obtained from the 2011-12 Australian Health Survey (AHS), which surveyed people aged 2 years and over from all areas of Australia, excluding very remote areas(22). Results were generated for 9973 individuals aged 15 years and over.

Dietary intake data were collected using a 24-hour recall of all foods and fluids consumed in the day prior to the interview. Participants provided 24-hour recall data on two separate occasions, at least 8 days apart. Implausible intakes were excluded if the day of intake data had an energy intake (EI) to basal metabolic rate (BMR) ratio of less than 0.9, as per recommendation from the Australian Bureau of Statistics(23). Mean daily dietary intakes were calculated for each participant for: energy (kcal/day), fruit (g/day), vegetables (g/day), fibre (g/day), dietary cholesterol (mg/day), salt (g/day), total fat (% EI), saturated fat (% EI), monounsaturated fat (% EI), and polyunsaturated fat (% EI). The percentage of people who consumed less than one serve of fruit and less than one serve of vegetables was also calculated as required by the model. Mean BMI for the rural population, by 5 year age group and sex, was required by the model, and the effect of obesity on mortality rates was modelled using the differences in energy intake and physical activity levels between the two populations. AHS participants were also asked to report if they were current smokers, ex-smokers, or if they had never smoked, and the age- sex- and location-specific prevalence of each of these categories were derived.

The PRIME model requires the proportion of the population classified as 'sedentary', and physical activity levels in the form of mean Metabolic Equivalent of Task (MET) hours per week, in the remaining (active) population. The sedentary proportion of the population was calculated as the sum of those classified as insufficiently active or sedentary by the ABS. Participants were classified as insufficiently active or sedentary if they did not meet the physical activity recommendations of 150 minutes per week, over 5 separate sessions(24). Mean minutes of moderate and vigorous activity over the last week as reported by AHS participants were used to calculate average daily minutes of

activity. This duration was then multiplied by standard intensity factors (metabolic equivalents) to convert the estimates to MET-hours of activity per week.

The model requires the percentage of non-drinkers within each population by age and sex, which was calculated as those who reported either no alcohol consumption, or <1g per day, over the surveyed period. Mean daily intake of pure alcohol in millilitres (mL), by age group and sex, was calculated as the weighted daily mean (mL) within TableBuilder, then converted to grams of pure alcohol.

**Mortality data**

Deaths due to CVD (ICD-10 code 100-199 ) and IHD (ICD-10 code 120-125) by state or territory and remoteness area of usual residence, by sex and 5-year age group, among people aged 15 years and over was provided by the Australian Institute of Health and Welfare (AIHW) for the year 2011 from the AIHW National Mortality Database (unpublished).

**Mortality gap**

The mortality gap between rural and metropolitan areas was calculated by applying the metropolitan death rate for those aged 15 years and over, to the rural population, to determine the number of rural deaths that would be expected if cause-specific mortality rates were equal between metropolitan and rural areas. This figure was subtracted from the actual number of deaths in rural areas, to calculate the gap in mortality between the two populations.

**Uncertainty analysis**

Monte Carlo simulation of 10,000 iterations was used to generate 95% credible intervals for each of the estimates of deaths delayed or averted under the counterfactual scenario.

**RESULTS**

**Differences in risk factors between rural and metropolitan areas**

There were a mixture of differences in dietary intake, between rural and metropolitan (Table 1), that were statistically significant for many dietary components, although many were relatively small in absolute magnitude. Some of the differences in intakes were favourable in rural areas, and others, more favourable in metropolitan areas. Vegetable intakes were significantly higher for rural populations ($p < 0.001$), while intake of fruit was not significantly different between the two populations.

Energy intakes and the percentage of energy from saturated fat were significantly higher among rural populations ($p<0.05$). Rural females reported a significantly higher dietary cholesterol intake ($p<0.05$) and lower percentage energy from polyunsaturated fat ($p<0.01$) than their metropolitan counterparts. There were no other significant differences in intake across the other dietary components analysed.

Mean alcohol intake (g/day) in those who reported drinking alcohol was significantly higher in rural areas for females ($p<0.05$), however there was no differences for males. There were no significant differences in the proportion of low alcohol consumers between the two populations. There were significantly more current smokers in rural areas compared to major cities (females 19.5% vs 14.0%; males 24.2% vs 18.7%). The proportion of people who had never smoked was higher in metropolitan areas.

Mean BMI for females was significantly higher ($p<0.001$) in rural areas compared to major cities (females 26.8 vs 27.6 kg/m$^2$; males 27.3 vs 27.8 kg/m$^2$).

Fewer rural people were meeting recommendations for physical activity; 37.1% of males in rural areas were meeting recommendations compared to 44.0% in major cities. This was also true for females (36.5% in rural areas, 46.3% in cities). There were no significant differences between the two populations in the mean MET hours per week of moderate-vigorous activity performed by the active population.

*Table 1: Differences in dietary intakes, rural compared with metropolitan areas, females and males 2011-12, with 95% Confidence Intervals (CI).*

| | **Females** | | | | **Males** | | | |
|---|---|---|---|---|---|---|---|---|
| **Dietary component** | **Mean intake (95%Confidence interval): Rural** | **Mean intake (95% CI): Metropolitan** | **Mean difference** | **p-value (t-test)** | **Mean intake (95%CI): Rural** | **Mean intake (95% CI): Metropolitan** | **Mean difference** | **p-value (t-test)** |
| **Fruit (g)** | 257 (250, 264) | 264 (258, 269) | 7 | p= NS | 222 (214, 231) | 231 (225, 237) | 9 | p=NS |
| **Serves*** | 1.7 serves | 1.9 serves | | | 1.5 serves | 1.5 serves | | |
| **Vegetables (g)** | 201 (196, 205) | 184 (180, 187) | 17 | p<0.0001 | 180 (176, 186) | 158 ( 155, 176) | 23 | p<0.0001 |
| **Serves*** | 2.7 serves | 2.45 serves* | | | 2.4 serves | 2.1 serves | | |
| **Energy intake (kJ)** | 8496 (8372, 8620) | 8332 (8241, 8424) | 164 | P=0.03 | 10,987 (10,818, 11,157) | 10,760 (10,634, 10,887) | 227 | p=0.03 |
| **Fibre (g)** | 23.10 (23, 24) | 23 (23, 24) | 0.4 | p=NS | 27.0 (26.3, 27.7) | 26.6 (26.1, 27.0) | 0.4 | p=NS |
| **Sodium (mg)** | 2339.25 (2282, 2396) | 2279 (2236, 2320) | 61 | p=NS | 3046 (2969, 3121) | 2973 (2914, 3032) | 72 | p=NS |
| **Dietary cholesterol** | 299 (289, 309) | 284 (277, 292) | 15 | p=0.02 | 380 (366, 393) | 375 (363, 385) | 5 | p=NS |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **(mg)** | | | | | | | | |
| **% energy from fat** | 32 (31.7, 32.5) | 32 (31.5, 32) | 0.3 | p=NS | 31.5 (31, 32) | 31 (30.5, 31.1) | 0.7 | p=0.01 |
| **% energy from saturated fat** | 13.1 (12.8, 13.3) | 12.4 (12.2, 12.5) | 0.7 | p<0.0001 | 12.9 (12.7, 13.2) | 12.1 (11.9, 12.3) | 0.8 | p<0.0001 |
| **% energy from monounsaturated fat** | 12 (11.8, 12.1) | 12.1 (11.9, 12.3) | 0.1 | p=NS | 12 (11.6, 12.0) | 12 (11.8, 12.1) | 0.1 | p=NS |
| **% energy from polyunsaturated fat** | 4.8 (4.7, 4.9) | 5 (5.0, 5.14) | 0.2 | p=0.0016 | 4.6 (4.5, 4.7) | 4.7 (4.6, 4.8) | 0.8 | p=NS |
| **Alcohol intake (g)** | 21.6 | 17.5 | 4.1 | p=0.02 | 23.0 | 19.5 | 3.5 | p=NS |
| **% Current smokers** | 17.4 | 12.5 | 4.9 | p=0.04 | 22.8 | 16 | 6.8 | p=0.002 |
| **Physical activity (MET hours)** | 13.3 | 14.2 | 0.9 | p=NS | 14.0 | 14.5 | 0.5 | p=NS |

*Notes: *One serve of fruit is 150g, 1 serve of vegetables is 75g according to Australian dietary guidelines*

**Deaths from CVD and IHD averted or delayed by risk factor changes**

In 2011, 13,600 people aged 15 years and over died from CVD outside of major cities. Of these deaths, 7560 of these deaths were caused by IHD.

In total, 1461 (1107, 1791) or 11% of all rural CVD deaths would be delayed or averted, if rural populations were to have the same levels of risk factors as their metropolitan counterparts (Table 2). Of the deaths prevented from CVD, 793 (510, 1065) would be from IHD, slightly more of these among males (418) than females (374), a 10.5% reduction in rural IHD deaths. Premature IHD deaths (75 years and under), would account for 38.3% of the IHD deaths that would be delayed or averted, or 4% of all rural IHD deaths. Most of these premature deaths would be averted for males, 266 (232, 301) compared to 37 (28, 46) in females.

*Table 2: Deaths averted or delayed from chronic diseases in rural Australia, under the counterfactual scenario, 95% Credible Intervals (CI), by sex.*

| Deaths | Females (95% CI) | Males (95% CI) | Total (95% CI) | % of total deaths from condition |
|---|---|---|---|---|
| **Overall CVD** | 828 (546, 1,092) | 629 (487, 768) | 1461 (1107, 1791) | 11% |
| **CVD (Under 75 years)** | 78 (66, 88) | 343 (305, 380) | 420 (375,465) | 3% |
| **IHD** | 375(147, 579) | 418 (280, 549) | 793 (506, 1,065) | 10.5% |
| **IHD (Under 75 years)** | 37 (29, 46) | 267 (231, 301) | 304 (263, 345) | 4% |

**Deaths attributable to individual risk factors**

Table 3 shows the number of deaths that would be delayed or averted under the counterfactual scenario for each individual risk factor for both CVD and IHD. Obesity and smoking, as individual risk factors, accounted for the largest numbers of CVD and IHD deaths that could be prevented in rural

areas, contributing 1,309 (1000, 1608), and 337 (290, 388) deaths delayed or averted respectively for CVD, and 740 (95% CI: 504, 955) and 225 (95% CI: 192, 260) for IHD. The adjustment of fruit and vegetable intakes showed that more people would die from CVD (-290 (-475, -103)) and IHD (-298 (95% CI: -486, -111)) if intakes in rural areas were adjusted to match those of metropolitan areas, since in this case vegetable intakes would be worse under the counterfactual scenario. If the rural diet as an individual risk factor were to be adjusted to the counterfactual scenario, an additional 190 (95% CI: 4, 380) IHD deaths would occur among rural Australians.

Table 3 shows the percentage of the mortality gap between major cities and rural areas that is attributable to the risk factors modelled. There were 2075 excess IHD deaths in the rural population in 2011. For the total rural population, risk factors accounted for 38.2% of the gap, leaving 61.8% due to other, unmeasured factors. There were substantial differences by sex, with 28.1% of the gap attributable to risk factor differences for males, compared to 66.7% for females.

*Table 3: Preventable deaths from CVD and IHD attributable to individual risk factors if rural populations had the same risk factor levels as populations in major cities.*

| Risk factor | Total CVD deaths averted/delayed under counterfactual scenario (95% CI) | Total IHD deaths averted/delayed under counterfactual scenario (95% CI) |
|---|---|---|
| **Overall diet** | -199 (-389, -10) | -190 (-380, -4) |
| **Fruit and vegetables** | -290 (-475,-103) | -298 (-486, -111) |
| **Fibre** | -70 (-103, -39) | - 47 ( -75, -19) |
| **Fats** | 121 (98-145) | 133 (113-155) |
| **Salt** | 40 (17-62) | 19 (8-31) |
| **Physical activity** | 84 (66-103) | 53 (38-69) |
| **Smoking** | 337 (290-388) | 225 (192-260) |
| **Alcohol** | -55 (-101, -18) | -28 (-52, -5) |

| | | |
|---|---|---|
| **Obesity** | 1309 (100, 1608) | 740 (50, -955) |

*Note: positive numbers represent deaths delayed or averted under the counterfactual scenario, negative numbers represent an increase in deaths.*

## DISCUSSION

This analysis showed that more than one third of the IHD mortality inequality between metro and rural areas can be attributed to differences in modifiable risk factors, an important consideration for health policy and intervention planning. Importantly, however, over 60% of the increased mortality burden in rural areas was unexplained by risk factor differences.

The majority of modifiable risk factors were found to differ between rural and metropolitan areas, with significantly higher BMI, energy intakes and proportion of energy intake from fats observed in rural populations, along with higher levels of high risk alcohol consumption and sedentary behaviour. Rural people did, however, report significantly higher vegetable intakes, which equated to consumption of approximately 10% more vegetables than their metropolitan counterparts, consistent with previous health survey data(2).

The origins of the differences in modifiable IHD risk factors between rural and metropolitan areas (2), are likely to be complex, arising from the interaction of a range of factors at the individual and community level, including socio-economic disadvantage, education levels, access to primary health services and health literacy(28). Living outside of metropolitan areas has been associated with more risk factors for chronic diseases in adults(25), with some evidence that geographic location should be assessed as a social determinant of health, above and beyond socio-economic status and area level disadvantage (26). There is evidence for this in that self-reported prevalence of IHD, diabetes and cerebrovascular disease were found to be similar in rural and metropolitan areas, despite much higher measured mortality rates from these diseases in rural areas, potentially revealing reduced health awareness in rural populations (22). This may be an important contributor to differences in

outcomes for rural populations, as lower health literacy has been linked to poorer outcomes in patients with heart disease(27).

In terms of individual risk factors, differences in obesity and tobacco smoking appeared to have the biggest impact on the increased burden of IHD in the rural population, when compared to metropolitan areas. Obesity is a well-known risk factor for IHD(28), and has been consistently shown to be higher in rural populations of Australia for the past few decades(29, 30). Differences in energy intake and physical activity energy expenditure between rural and metropolitan populations led to substantial reductions in obesity-mediated mortality in the counterfactual scenario. These reductions explained the largest proportion of the mortality gap between the two populations of any of the behaviours studied. Higher energy intakes in the rural sample, which increase the likelihood of a higher BMI(31), could be reflective of the consumption of more low cost, energy dense foods possibly in part, due to reduced access to healthier foods, which has been well documented in rural and regional areas(32).

Tobacco smoking is recognised as the largest single preventable cause of mortality and morbidity in Australia (33), and higher smoking rates in rural areas have been apparent since at least 1993(15, 25). Despite numerous public health initiatives and interventions over this period, the rural smoking rate has remained comparatively high whilst the metropolitan rate has continued to decline(15, 33), possibly indicating that such preventative efforts have not adequately reached rural Australians(15).

The results of this study suggest that substantial gains could be made in reducing the CVD mortality gap between metropolitan and rural populations if modifiable risk behaviours could be improved in rural areas. Improving risk factor profiles in rural populations to at least match that of their metropolitan counterparts could be assumed to be a reasonable target, given that even metropolitan risk factor levels are far from ideal(34, 35). Importantly, even if this scenario were to be achieved, a significant proportion (almost two-thirds) of the excess deaths would remain, a

finding which should prompt major reflection on the role of disadvantage, health care provision and other, less prominent risk factors in the perpetuation of rural health inequalities.

**Strengths:**

This study used three representative national datasets, including the Census, AIHW National Mortality Database and the Australian Health Survey, as inputs for the PRIME model. The PRIME model also has many strengths, including that it is able to model the effect of changes in multiple risk factors simultaneously on mortality rates from different chronic diseases, by age and sex. The model has been designed using the strongest available scientific evidence on the links between chronic disease mortality and dietary intake, alcohol consumption, smoking, physical activity and obesity levels(16).

**Limitations:**

Data used in the model were self-reported, which carries multiple limitations, and could lead to underestimations of the level of behavioural risk factors and subsequently, mortality gap reductions (23), although it less likely that these biases would differentially affect rural vs metro populations. Very remote areas of Australia were not sampled in AHS, therefore risk factor levels for these populations were not included in the analysis(22). This may lead to an underestimation of the prevalence of some risk factors, as residents of very remote areas are known to experience even higher burden from IHD than the broader rural population(2), however they also represent a very small percentage of the total Australian population (0.9%)(25). The uncertainty analysis conducted on the number of deaths averted, only accounts for uncertainty within the model parameters, but not the uncertainty of estimates from the Australian Heath Survey.

**CONCLUSIONS**

There is potential for improvements in the level of cardiovascular disease burden observed in rural Australians, if the prevalence of modifiable risk factors such as obesity and smoking were to be reduced to match those of metropolitan areas. If such a scenario was to be achieved, 38% of the mortality gap between rural and metropolitan areas could be reduced, however, investigations into factors responsible for the remaining 62% of this inequality are needed in order to work towards achieving health equality for rural populations.

**Author Contributions**

LA organised the collection and conversion of data, completed all data entry into the PRIME model, analysis of the results, and writing of the manuscript. MN contributed to defining the original research idea, data collection, use of the PRIME model and analysis. KP and JJ assisted with conversion of the data to be compatible with the PRIME model. SA contributed to defining the original research idea. All authors reviewed and contributed to the manuscript and all stages of compilation.

**Acknowledgements**

Dr Peter Scarborough and team, who developed and provided the PRIME model used in this study.

**Conflict of Interest declaration**

The authors declare there are no conflicts of interest

**Funding acknowledgments**

MN, KP, LA and JJ are supported by funding from the National Heart Foundation of Australia and Deakin University. SA is supported by funding from an Australian National Health and Medical Research Council/ National Heart Foundation of Australia Career Development Fellowship (APP1045836). He is also a researcher on the US National Institutes of Health grant titled, "Systems Science to Guide Whole-of- Community Childhood Obesity Interventions" (1R01HL115485-01A1) and within a NHMRC Centre for Research Excellence in Obesity Policy and Food Systems (APP1041020).

130

131

132

133

**REFERENCES:**


1. Australian Institute of Health and Welfare. Mortality inequalities in Australia: bulletin 124. Canberra: AIHW; 2014.
2. Australian Bureau of Statistics. HEALTH OUTSIDE MAJOR CITIES Australia: ABS; 2011 [cited 2015 10/06/2015]. Available from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/4102.0Main+Features30Mar+2011.
3. Levin KA, Leyland AH. Urban-rural inequalities in ischemic heart disease in Scotland, 1981-1999. Am J Public Health. 2006 Jan;96(1):145-51.
4. Kulshreshtha A, Goyal A, Dabhadkar K, Veledar E, Vaccarino V. Urban-rural differences in coronary heart disease mortality in the United States: 1999-2009. Public Health Rep. 2014 Jan-Feb;129(1):19-29.
5. Terashima M, Rainham DG, Levy AR. A small-area analysis of inequalities in chronic disease prevalence across urban and non-urban communities in the Province of Nova Scotia, Canada, 2007-2011. BMJ open. 2014;4(5)
6. ABS. 3303.0 - Causes of Death, Australia, 2013 Australia: ABS; 2015 [cited 2016 29/02/2016]. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/3303.0~2013~Main%20Features~Summary%20of%20findings~10000.
7. Dinh Vu H, Heller RF, Lim LLY, D'Este C, O'Connell RL. Mortality after acute myocardial infarction is lower in metropolitan regions than in non-metropolitan regions. Journal of Epidemiology and Community Health. 2000;54(8):590-5.
8. Waters AM, Trinh L, Chau T, Bourchier M, Moon L. Latest statistics on cardiovascular disease in Australia. Clinical and Experimental Pharmacology and Physiology. 2013;40(6):347-56.
9. Sexton PT, Sexton TLH. Excess coronary mortality among Australian men and women living outside the capital city statistical divisions. Medical Journal of Australia. 2000;172(8):370-4.
10. Beard JR, Earnest A, Morgan G, Chan H, Summerhayes R, Dunn TM, et al. Socioeconomic disadvantage and acute coronary events: A spatiotemporal analysis. Epidemiology. 2008;19(3):485-92.
11. Dobson A, McLaughlin D, Vagenas D, Wong KY. Why are death rates higher in rural areas? Evidence from the Australian Longitudinal Study on Women's Health. Australian And New Zealand Journal Of Public Health. 2010;34(6):624-8.
12. Gausia K, Katzenellenbogen JM, Sanfilippo FM, Knuiman MW, Thompson PL, Hobbs MST, et al. Evidence-based prescribing of drugs for secondary prevention of acute coronary syndrome in Aboriginal and non- Aboriginal patients admitted to Western Australian hospitals. Internal Medicine Journal. 2014;44(4):353-61.
13. Jordan S, Wilson A, Dobson A. Management of heart conditions in older rural and urban Australian women. Internal Medicine Journal. 2011;41(10):722-9.
14. National Rural Health Alliance of Australia. The determinants of health in rural and remote Australia: fact sheet 28. Australian Captial Territory: National Rural Health Alliance; 2011.
15. National Rural Health Alliance of Australia. Smoking and rural health. Australian Capital Territory: National Rural Health Alliance; 2014.
16. Scarborough P, Harrington RA, Mizdrak A, Zhou LM, Doherty A. The Preventable Risk Integrated ModEl and Its Use to Estimate the Health Impact of Public Health Policy Scenarios. Scientifica. 2014.
17. Scarborough P, Morgan RD, Webster P, Rayner M. Differences in coronary heart disease, stroke and cancer mortality rates between England, Wales, Scotland and Northern Ireland: the role of diet and nutrition. BMJ open. 2011 Jan 1;1(1):e000263.
18. Scarborough P, Allender S, Clarke D, Wickramasinghe K, Rayner M. Modelling the health impact of environmentally sustainable dietary scenarios in the UK. European journal of clinical nutrition. 2012 Jun;66(6):710-5.

19. Nichols M, Scarborough P, Allender S, Rayner M. What is the optimal level of population alcohol consumption for chronic disease prevention in England? Modelling the impact of changes in average consumption levels. BMJ open. 2012;2(3).
20. Belanger M, Poirier M, Jbilou J, Scarborough P. Modelling the impact of compliance with dietary recommendations on cancer and cardiovascular disease mortality in Canada. Public health. 2014 Mar;128(3):222-30.
21. Australian Bureau of Statistics. Australian Statistical Geography Standard Canberra, Australia: ABS; 2014 [cited 2016 04/07/2016]. Available from: http://www.abs.gov.au/websitedbs/D3310114.nsf/home/Australian+Statistical+Geography+Standard+(ASGS).
22. Australian Bureau of Statistics. 4363.0.55.001 - Australian Health Survey: Users' Guide, 2011-13: Sample design and selection Canberra: Australian Bureau of Statistics; 2015 [cited 2016 20/06/2016]. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4363.0.55.001Chapter2102011-13.
23. Australian Bureau of Statistics. 4363.0.55.001 - Australian Health Survey: Users' Guide, 2011-13: UNDER-REPORTING IN NUTRITION SURVEYS Canberra: Australian Bureau of statistics; 2015 [cited 2016 20/06/2016]. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4363.0.55.001Chapter651512011-13.
24. Australian Bureau of Statistics. 4363.0.55.001 - Australian Health Survey: Users' Guide, 2011-13 : Adult Physical Activity: Australian Bureau of Statistics 2015 [cited 2016 27/06/2016]. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/59FF6FE5D62BABE1CA257BAC00225A07?opendocument.
25. 2014. Australian Institute of Health and Welfare. Australia's health 2014: Australia's health series no. 14. Cat. no. AUS 178: Health in regional and remote areas. . Canberra, Australia: AIHW; 2014.
26. Patterson KA, Cleland V, Venn A, Blizzard L, Gall S. A cross-sectional study of geographic differences in health risk factors among young Australian adults: the role of socioeconomic position. BMC public health. 2014;14:1278.
27. Wu JR, Moser DK, DeWalt DA, Rayens MK, Dracup K. Health Literacy Mediates the Relationship Between Age and Health Outcomes in Patients With Heart Failure. Circulation Heart failure. 2016 Jan;9(1):e002250.
28. World Heart Federation. World Heart Federation: 25 by 2025 Targets. Melbourne: World Heart Federation, 2014.
29. National Rural Health Alliance of Australia. Obesity in rural Australia. Australian Capital Territory: National Rural Health Alliance; 2013.
30. Australian Institute of Health and Welafre. Rural, regional and remote health: Indicators of health status and determinants of health. Canberra, Australia: Australian Institute of Health and Welfare; 2008.
31. French SA, Story M, Jeffery RW. Environmental influences on eating and physical activity. Annual review of public health. 2001;22:309-35.
32. Queensland health. 2014 Healthy food access basket survey, Queensland Queensland, Australia: Queensland Government; 2015 [cited 2016 22/06/2016]. Available from: https://www.health.qld.gov.au/research-reports/reports/food/access/guidelines/default.asp.
33. Australian Institute of Health and Welfare. Australia's health 2014: Leading types of ill health: AIHW; 2014 [cited 2016 22/06/2016]. Available from: http://www.aihw.gov.au/australias-health/2014/ill-health/#t.
34. Ball K, Mishra GD, Thane CW, A H. How well do Australian women comply with dietary guidelines?.Public Health Nutrition 2004;4;7(3):443–52.
35. Australian Bureau of Statistics. 4364.0.55.012 - Australian Health Survey: Consumption of Food Groups from the Australian Dietary Guidelines, 2011-12 Canberra,: Australian Bureau of

Statistics 2016 [cited 2016 04/07/2016]. Available from: http://www.abs.gov.au/websitedbs/D3310114.nsf/home/Australian+Statistical+Geography+Standard+(ASGS).

*Table 1: Differences in dietary intakes, rural compared with metropolitan areas, females and males 2011-12, with 95% Confidence Intervals (CI).*

| | Females | | | | Males | | | |
|---|---|---|---|---|---|---|---|---|
| **Dietary component** | **Mean intake (95%Confidence interval): Rural** | **Mean intake (95% CI): Metropolitan** | **Mean difference** | **p-value (t-test)** | **Mean intake (95%CI): Rural** | **Mean intake (95% CI): Metropolitan** | **Mean difference** | **p-value (t-test)** |
| **Fruit (g)** **Serves*** | 257 (250, 264) 1.7 serves | 264 (258, 269) 1.9 serves | 7 | p= NS | 222 (214, 231) 1.5 serves | 231 (225, 237) 1.5 serves | 9 | p=NS |
| **Vegetables (g)** **Serves*** | 201 (196, 205) 2.7 serves | 184 (180, 187) 2.45 serves* | 17 | p<0.0001 | 180 (176, 186) 2.4 serves | 158 ( 155, 176) 2.1 serves | 23 | p<0.0001 |
| **Energy intake (kJ)** | 8496 (8372, 8620) | 8332 (8241, 8424) | 164 | P=0.03 | 10,987 (10,818, 11,157) | 10,760 (10,634, 10,887) | 227 | p=0.03 |
| **Fibre (g)** | 23.10 (23, 24) | 23 (23, 24) | 0.4 | p=NS | 27.0 (26.3, 27.7) | 26.6 (26.1, 27.0) | 0.4 | p=NS |
| **Sodium (mg)** | 2339.25 (2282, 2396) | 2279 (2236, 2320) | 61 | p=NS | 3046 (2969, 3121) | 2973 (2914, 3032) | 72 | p=NS |
| **Dietary cholesterol** | 299 (289, 309) | 284 (277, 292) | 15 | p=0.02 | 380 (366, 393) | 375 (363, 385) | 5 | p=NS |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **(mg)** | | | | | | | | |
| **% energy from fat** | 32 (31.7, 32.5) | 32 (31.5, 32) | 0.3 | p=NS | 31.5 (31, 32) | 31 (30.5, 31.1) | 0.7 | p=0.01 |
| **% energy from saturated fat** | 13.1 (12.8, 13.3) | 12.4 (12.2, 12.5) | 0.7 | p<0.0001 | 12.9 (12.7, 13.2) | 12.1 (11.9, 12.3) | 0.8 | p<0.0001 |
| **% energy from monounsaturated fat** | 12 (11.8, 12.1) | 12.1 (11.9, 12.3) | 0.1 | p=NS | 12 (11.6, 12.0) | 12 (11.8, 12.1) | 0.1 | p=NS |
| **% energy from polyunsaturated fat** | 4.8 (4.7, 4.9) | 5 (5.0, 5.14) | 0.2 | p=0.0016 | 4.6 (4.5, 4.7) | 4.7 (4.6, 4.8) | 0.8 | p=NS |
| **Alcohol intake (g)** | 21.6 | 17.5 | 4.1 | p=0.02 | 23.0 | 19.5 | 3.5 | p=NS |
| **% Current smokers** | 17.4 | 12.5 | 4.9 | p=0.04 | 22.8 | 16 | 6.8 | p=0.002 |
| **Physical activity (MET hours)** | 13.3 | 14.2 | 0.9 | p=NS | 14.0 | 14.5 | 0.5 | p=NS |

*Notes: *One serve of fruit is 150g, 1 serve of vegetables is 75g according to Australian dietary guidelines*

*Table 2: Deaths averted or delayed from chronic diseases in rural Australia, under the counterfactual scenario, 95% Credible Intervals (CI), by sex.*

| Deaths | Females (95% CI) | Males (95% CI) | Total (95% CI) | % of total deaths from condition |
|---|---|---|---|---|
| **Overall CVD** | 828 (546, 1,092) | 629 (487, 768) | 1461 (1107, 1791) | 11% |
| **CVD (Under 75 years)** | 78 (66, 88) | 343 (305, 380) | 420 (375,465) | 3% |
| **IHD** | 375(147, 579) | 418 (280, 549) | 793 (506, 1,065) | 10.5% |
| **IHD (Under 75 years)** | 37 (29, 46) | 267 (231, 301) | 304 (263, 345) | 4% |

*Table 3: Preventable deaths from CVD and IHD attributable to individual risk factors if rural populations had the same risk factor levels as populations in major cities.*

| Risk factor | Total CVD deaths averted/delayed under counterfactual scenario (95% CI) | Total IHD deaths averted/delayed under counterfactual scenario (95% CI) |
|---|---|---|
| **Overall diet** | -199 (-389, -10) | -190 (-380, -4) |
| **Fruit and vegetables** | -290 (-475,-103) | -298 (-486, -111) |
| **Fibre** | -70 (-103, -39) | - 47 ( -75, -19) |
| **Fats** | 121 (98-145) | 133 (113-155) |
| **Salt** | 40 (17-62) | 19 (8-31) |
| **Physical activity** | 84 (66-103) | 53 (38-69) |
| **Smoking** | 337 (290-388) | 225 (192-260) |
| **Alcohol** | -55 (-101, -18) | -28 (-52, -5) |
| **Obesity** | 1309 (100, 1608) | 740 (50, -955) |

Note: positive numbers represent deaths delayed or averted under the counterfactual scenario, negative numbers represent an increase in deaths.

BMJ Open

# Quantifying the role of modifiable risk factors in the differences in cardiovascular disease mortality rates between metropolitan and rural populations in Australia: A macrosimulation modelling study.



| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2017-018307.R1 |
| Article Type: | Research |
| Date Submitted by the Author: | 09-Aug-2017 |
| Complete List of Authors: | Alston, Laura; Deakin University, Waterfront Campus<br>Peterson, Karen; Deakin University - Geelong Waterfront Campus<br>Jacobs, Jane; Deakin University - Geelong Waterfront Campus<br>Allender, Steven; Deakin University, Faculty of Health<br>Nichols, Melanie; Deakin University, Faculty of Health; |
| Primary Subject Heading: | Public health |
| Secondary Subject Heading: | Epidemiology |
| Keywords: | Coronary heart disease < CARDIOLOGY, NUTRITION & DIETETICS, PREVENTIVE MEDICINE, PUBLIC HEALTH |
| | |

**TITLE**: Quantifying the role of modifiable risk factors in the differences in cardiovascular disease mortality rates between metropolitan and rural populations in Australia: A macrosimulation modelling study.

**Authors:** Laura Alston[a], Karen Louise Peterson[a], Jane P Jacobs[a], Steven Allender[a], Melanie Nichols[a].

**Author affiliations**: [a]Global Obesity Centre, Faculty of Health, Deakin University, Geelong, Australia.

**Corresponding author**: Laura Alston. Address: WHO Collaborating Centre for Obesity Prevention, Faculty of Health, Deakin University, Locked Bag 20001, Geelong, VIC 3220 Australia. Telephone: +61 3 5247 9426. Email: laura.alston@deakin.edu.au.

**Previous presentations of this research**: none to declare.

**Funding acknowledgments:** MN, KP, LA and JJ are supported by funding from the National Heart Foundation of Australia and Deakin University. SA is supported by funding from an Australian National Health and Medical Research Council/ National Heart Foundation of Australia Career Development Fellowship (APP1045836). He is also a researcher on the US National Institutes of Health grant titled, "Systems Science to Guide Whole-of- Community Childhood Obesity Interventions" (1R01HL115485-01A1) and within a NHMRC Centre for Research Excellence in Obesity Policy and Food Systems (APP1041020).

**Keywords:** Rural, Risk factors, Cardiovascular disease, Ischaemic heart disease, Inequalities, Prevention

**Word count (excluding references and abstract): 3,115 words**

## ABSTRACT

**Objectives:** Aims: (1) to quantify differences in modifiable risk factors between urban and rural populations, and (2) to determine the number of rural cardiovascular disease (CVD) and ischaemic heart disease (IHD) deaths that could be averted or delayed if risk factor levels in rural areas were equivalent to metropolitan areas.

**Setting:** National population estimates, risk factor prevalence, CVD and IHD deaths data were analysed by rurality using the Preventable Risk Integrated Model (PRIME) macro-simulation chronic disease risk model. Uncertainty analysis was conducted using a Monte Carlo simulation of 10,000 iterations to calculate 95% credible intervals (CI).

**Participants:** National datasets of males and females over the age of 18 years living in urban and rural Australia.

**Results:** If people living in rural Australia had the same levels of risk factors as those in metropolitan areas, approximately 1461 (95% credible interval (CI): 1107, 1791) deaths could be delayed from cardiovascular disease (CVD) annually. Of these CVD deaths, 793 (95%CI: 506, 1065) would be from IHD. The IHD mortality gap between metropolitan and rural populations would be reduced by 38.2% (95%CI: 24.4%, 50.6%).

**Conclusions:** A significant portion of deaths from CVD and IHD could be averted with improvements in risk factors; more than one third of the excess IHD deaths in rural Australia were attributed to differences in risk factors. As much as two thirds of the increased IHD mortality rate in rural areas could not be accounted for by modifiable risk factors, however, and this requires further investigation.

**ARTICLE SUMMARY:**

*Strengths:*

- This is the first study to attempt to quantify the role of modifiable factors in the increased burden of cardiovascular diseases in rural areas when compared to urban Australia.
- The PRIME model has been previously published and is internationally recognised.
- This study used three representative national datasets, including the Census, Australian Institute of Health and Welfare National Mortality Database and the Australian Health Survey, as inputs for the PRIME model.

*Limitations:*

- Data used in the model were self-reported, and could lead to underestimations of the level of behavioural risk factors and subsequently, mortality gap reductions, although it is unlikely that these biases would differentially affect rural vs metro populations.
- Very remote populations of Australia (0.9% of the total population) were excluded.

## INTRODUCTION

Despite high quality, universal health care systems and standards in Australia, there are still disparities in the burden of chronic disease experienced by people with lower socio-economic status, Aboriginal and Torres Strait Islanders and rural residents(1). Australians living outside major cities experience a substantially increased burden of cardiovascular diseases(2), which is consistent with findings for rural populations in other developed countries such as the United States, Canada, and the United Kingdom(3-5). Cardiovascular disease (CVD), in its most common form, Ischaemic heart disease (IHD) is the leading cause of death in Australia(6), and individuals residing in a regional or remote areas are estimated to be between 1.2 and 1.5 times more likely to die from IHD than those residing in metropolitan areas(1).

The reasons for observed health inequalities between metropolitan and rural populations appear to be multifactorial and highly complex(2, 7-9). It has been hypothesised that rural populations experience greater CVD and IHD burden due to variation in access to health services, individual socio-economic status, rates of modifiable risk factors, as well as potentially reduced access to specialised evidence-based treatments, such as prompt surgical intervention in rural hospitals(7, 10-13). The National Rural Health Alliance (NRHA) of Australia states that if rural Australians are to achieve the same health outcomes as their metropolitan counterparts by the year 2020, it is not just access to health services that need to be improved(14), but that more focus needs to be placed on improving the socio-economic determinants of health (such as lower education, incomes, and employment) for rural communities, and reducing risk factors for chronic diseases such as smoking and physical inactivity(14).

Cardiovascular diseases, particularly IHD, are largely preventable, and the modifiable, behavioural risk factors are well known(15). Clinical risk factors such as high cholesterol, high blood pressure, and obesity interact with behavioural factors such as poor diet, smoking, risky alcohol consumption, and physical inactivity to increase the risk of IHD and CVD(13). Based on population health surveys, these risk factors differ by rurality, with higher smoking rates, increased high risk alcohol consumption and lower physical activity levels being reported by non-city dwelling Australians(2).

Currently, there is minimal evidence quantifying the extent to which modifiable individual risk factors contribute to the increased burden of CVD and IHD in rural areas, and how much of this burden could be reduced if behavioural risk factors were comparable among rural Australians as those among their counterparts in cities. Increased knowledge of how differential risk factor rates contribute to the increased rural CVD burden could support the identification of policy priorities and prevention programs for rural areas, as previous public health prevention efforts have been shown to be less effective for rural populations compared to those living in metropolitan areas(16).

**Aims:**

This study aimed to: (1) Quantify differences in prevalence of major CVD risk factors between rural and metropolitan populations, and (2) Determine the number and proportion of rural deaths from CVD, and specifically from IHD, that could be averted or delayed in rural areas if the levels of risk factors were equivalent to those in metropolitan Australia.

## METHODS

### The Preventable Risk Integrated Model (PRIME)

This study used a macrosimulation model, the Preventable Risk Integrated Model (PRIME)(17), to estimate age- and sex-specific changes in CVD and IHD mortality that would result from changes to the population prevalence of risk factors in Australia. An exemption from ethics review was obtained from Deakin University's Human Research Ethics Unit. PRIME has been used in the UK, New Zealand and Canada to model a range of risk factor scenarios(17-20). The model can be used to examine the likely changes in mortality rates of many chronic diseases, including IHD, under different counterfactual scenarios of population behavioural risk factors(17).

The PRIME model is built on a framework of linkage between, 1) modifiable behaviours; 2) clinical risk factors; and 3) mortality outcomes. This framework is parameterised using the best available evidence from meta-analyses of published studies, and is described in detail elsewhere(17). PRIME requires data on prevalence of modifiable risk factors, mortality rates and population estimates by 5 year age groups and sex, for both baseline and counterfactual scenarios. For this study, PRIME was used to estimate the number of CVD and IHD deaths that would be delayed or averted if those living in rural Australia had the same modifiable risk factor levels as those living in major cities. The baseline scenario used the current levels of modifiable risk factors in those living in rural areas, and the counterfactual scenario involved applying the level of risk factors currently observed in the metropolitan population. An additional 'best case' scenario was also modelled, by only changing risk factor levels that were more favourable among those living in metropolitan areas, when compared to the rural population.

**Population data**

Population size estimates by age, sex and rurality were derived from the 2011 Australian Census. The 'rural' population was defined as all residents not classified by the ABS as living in major cities(21). These data were accessed through subscription to the online ABS data program TableBuilder(22).

**Risk factor data**

The individual modifiable risk factors included in the PRIME model (table 1) were; mean dietary intakes, alcohol consumption, prevalence of smoking, physical activity levels and mean body mass index (BMI) scores. All risk factor estimates were obtained from 9973 individuals aged 15 years and over surveyed for the 2011-12 Australian Health Survey (AHS), which surveyed people from all areas of Australia, excluding very remote areas(23). Mean values were calculated by age, sex and remoteness for each risk factor parameter, through the ABS program TableBuilder(22).

*Table 1: Summary of risk factor data entered into the PRIME model.*

| Risk factor | Parameter | Unit |
|---|---|---|
| Diet | Total energy intake | Kcal/day |
| | Proportion of low/non-consumers of fruit (<1 serve/day) | % of population |
| | Proportion of low/non-consumers of vegetables (<1 serve/day) | % of population |
| | Mean vegetable consumption remaining population | g/day |
| | Mean fruit consumption remaining population | g/day |
| | Fibre consumption | g/day |
| | Dietary cholesterol consumption | mg/day |
| | Salt consumption | g/day |
| | Total fat intake | % of total energy intake |
| | Saturated fat intake | % of total energy intake |
| | Mono-unsaturated fat intake | % of total energy intake |
| | Poly-unsaturated fat intake | % of total energy intake |
| Alcohol | Proportion of low consumers (<1g/day) | % of population |
| | Mean consumption among remaining population | g/day of pure alcohol |
| Smoking | Current smokers | % of population |
| | Ex-smokers | % of population |
| | Never smokers | % of population |
| Physical activity | Proportion of population who are sedentary | % of population |
| | Amount of moderate-vigorous activity among remaining population | MET-hours per week |
| Anthropometry | BMI | $kg/m^2$ |
| | Height | metres |

*Abbreviations: BMI= Body Mass Index, g=grams, MET= metabolic equivalent task.*

Dietary intake data were collected using a 24-hour recall of all foods and fluids consumed in the day prior to the interview. Participants provided 24-hour recall data on two separate occasions, at least 8 days apart. Implausible intakes were excluded if the day of intake data had an energy intake (EI) to

basal metabolic rate (BMR) ratio of less than 0.9, as per recommendation from the Australian Bureau of Statistics(23). Mean daily dietary intakes from the two days of data collection were calculated for each participant for: energy (kcal/day), fruit (g/day), vegetables (g/day), fibre (g/day), dietary cholesterol (mg/day), salt (g/day), total fat (% EI), saturated fat (% EI), monounsaturated fat (% EI), and polyunsaturated fat (% EI). The percentage of people who consumed less than one serve of fruit and less than one serve of vegetables was also calculated as required by the model. Mean BMI for the rural population, by 5 year age group and sex, was required by the model, and the effect of obesity on mortality rates was modelled using the differences in energy intake and physical activity levels between the two populations. Participants reported if they were current smokers, ex-smokers, or if they had never smoked, and the age- sex- and location-specific prevalence of each of these categories were derived.

The PRIME model requires the proportion of the population classified as 'sedentary', and physical activity levels in the form of mean Metabolic Equivalent of Task (MET) hours per week, in the remaining (active) population. The sedentary proportion of the population was calculated as the sum of those classified as insufficiently active or sedentary by the ABS. Participants were classified as insufficiently active or sedentary if they did not meet the physical activity recommendations of 150 minutes per week, over 5 separate sessions(24). Mean minutes of moderate and vigorous activity over the last week were used to calculate average daily minutes of activity. This duration was then multiplied by metabolic equivalents as provided by the ABS, to convert the estimates to MET-hours of activity per week.

The model requires the percentage of non-drinkers within each population by age and sex, which was calculated as those who reported either no alcohol consumption, or <1g per day on average, over the surveyed period. Mean daily intake of pure alcohol in millilitres (mL), by age group and sex, was calculated as the weighted daily mean (mL) within TableBuilder, then converted to grams of pure alcohol.

**Mortality data**

Deaths due to CVD (ICD-10 codes I00-I99 ) and IHD (ICD-10 code I20-I25) by state or territory and remoteness area of usual residence, by sex and 5-year age group, among people aged 15 years and over was provided by the Australian Institute of Health and Welfare (AIHW) for the year 2011 from the AIHW National Mortality Database (unpublished). These data were provided after an application for a specific request to the AIHW, and are not publicly available.

**Mortality gap**

The mortality gap between rural and metropolitan areas was calculated by applying the metropolitan death rate for those aged 15 years and over, to the rural population, to determine the number of rural deaths that would be expected if cause-specific mortality rates were equal between metropolitan and rural areas. This figure was subtracted from the actual number of deaths in rural areas, to calculate the gap in mortality between the two populations.

**Uncertainty analysis**

The PRIME model has a built in Monte Carlo analysis function to generate 95% credible intervals around the outputs, which allows for the different distribution of epidemiological parameters (for example the level of relative risk for a disease outcome for a particular risk factor level) within the model that have been derived from the literature(17).The intervals produced are based only on the uncertainty in the model parameters, and not on the variability of the original data used in the baseline and counterfactual scenarios. Monte Carlo simulation of 10,000 iterations was used to generate 95% credible intervals for each of the estimates of deaths delayed or averted under the counterfactual scenario.

## RESULTS

**Differences in individual risk factors between rural and metropolitan areas**

There were a mixture of differences in dietary intake, between rural and metropolitan (Table 2), that were statistically significant for many dietary components, although many were relatively small in absolute magnitude. Two of the dietary intake levels were more favourable in rural areas, and the rest were more favourable in metropolitan areas. Vegetable intakes were significantly higher for rural populations ($p < 0.001$), also resulting in a slightly higher fibre intake, while intake of fruit was not significantly different between the two populations.

Energy intakes and the percentage of energy from saturated fat were significantly higher among rural populations ($p<0.05$). Rural females reported a significantly higher dietary cholesterol intake ($p<0.05$) and lower percentage energy from polyunsaturated fat ($p<0.01$) than their metropolitan counterparts. There were no other significant differences in intake across the other dietary components analysed.

Mean alcohol intake (g/day) in those who reported drinking alcohol was significantly higher in rural areas for females ($p<0.05$), however there was no differences for males. There were significantly more current smokers in rural areas compared to major cities (females 19.5% vs 14.0%; males 24.2% vs 18.7%). The proportion of people who had never smoked was higher in metropolitan areas.

Fewer rural people were meeting recommendations for physical activity; 37.1% of males in rural areas were meeting recommendations compared to 44.0% in major cities. This was also true for females (36.5% in rural areas, 46.3% in cities). There were no significant differences between the two populations in the mean MET hours per week of moderate-vigorous activity performed by the active population.

Smoking rates were significantly higher in rural areas for both females and males. Mean BMI for females was significantly higher ($p<0.001$) in rural areas compared to major cities (females 26.8 vs 27.6 $kg/m^2$; males 27.3 vs 27.8 $kg/m^2$).

*Table 2: Differences in individual risk factors, rural compared with metropolitan areas, females and males 2011-12, with 95% Confidence Intervals (CI).*

| | Females | | | | Males | | | |
|---|---|---|---|---|---|---|---|---|
| **Dietary component** | **Mean intake (95%Confidence interval): Rural** | **Mean intake (95% CI): Metropolitan** | **Mean difference** | **p-value (t-test)** | **Mean intake (95%CI): Rural** | **Mean intake (95% CI): Metropolitan** | **Mean difference** | **p-value (t-test)** |
| **Fruit (g)** **Serves*** | 257 (250, 264) 1.7 serves | 264 (258, 269) 1.9 serves | 7 | p= NS | 222 (214, 231) 1.5 serves | 231 (225, 237) 1.5 serves | 9 | p=NS |
| **Vegetables (g)** **Serves*** | 201 (196, 205) 2.7 serves | 184 (180, 187) 2.45 serves* | 17 | p<0.0001 | 180 (176, 186) 2.4 serves | 158 ( 155, 176) 2.1 serves | 23 | p<0.0001 |
| **Energy intake (kJ)** | 8496 (8372, 8620) | 8332 (8241, 8424) | 164 | P=0.03 | 10,987 (10,818, 11,157) | 10,760 (10,634, 10,887) | 227 | p=0.03 |
| **Fibre (g)** | 23.10 (23, 24) | 23 (23, 24) | 0.1 | p=NS | 27.0 (26.3, 27.7) | 26.6 (26.1, 27.0) | 0.4 | p=NS |
| **Sodium (mg)** | 2339 (2282, 2396) | 2279 (2236, 2320) | 61 | p=NS | 3046 (2969, 3121) | 2973 (2914, 3032) | 72 | p=NS |
| **Dietary cholesterol** | 299 (289, 309) | 284 (277, 292) | 15 | p=0.02 | 380 (366, 393) | 375 (363, 385) | 5 | p=NS |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **(mg)** | | | | | | | | |
| **% energy from fat** | 32 (31.7, 32.5) | 32 (31.5, 32) | 0.3 | p=NS | 31.5 (31, 32) | 31 (30.5, 31.1) | 0.5 | p=0.01 |
| **% energy from saturated fat** | 13.1 (12.8, 13.3) | 12.4 (12.2, 12.5) | 0.7 | p<0.0001 | 12.9 (12.7, 13.2) | 12.1 (11.9, 12.3) | 0.8 | p<0.0001 |
| **% energy from monounsaturated fat** | 12.0 (11.8, 12.1) | 12.1 (11.9, 12.3) | 0.1 | p=NS | 12.0 (11.6, 12.0) | 12.0 (11.8, 12.1) | 0.1 | p=NS |
| **% energy from polyunsaturated fat** | 4.8 (4.7, 4.9) | 5.0 (5.0, 5.14) | 0.2 | p=0.0016 | 4.6 (4.5, 4.7) | 4.7 (4.6, 4.8) | 0.1 | p=NS |
| **Alcohol intake (g)** | 21.6 | 17.5 | 4.1 | p=0.02 | 23.0 | 19.5 | 3.5 | p=NS |
| **% Current smokers** | 17.4 | 12.5 | 4.9 | p=0.04 | 22.8 | 16 | 6.8 | p=0.002 |
| **Physical activity (MET hours)** | 13.3 | 14.2 | 0.9 | p=NS | 14.0 | 14.5 | 0.5 | p=NS |

*Notes: *One serve of fruit is 150g, 1 serve of vegetables is 75g according to Australian dietary guidelines*

**Deaths from CVD and IHD averted or delayed by risk factor changes**

In 2011, 13600 people aged 15 years and over died from CVD in rural areas, with 6846 and 6754 deaths occurring in males and females respectively. In terms of premature deaths, 3137 of these deaths occurred in those aged under 75 years, 2200 in males, and 915 in females. IHD was the cause of 7560 deaths, with 2089 deaths occurring in those under 75 years (1636 Males, and 452 females).

In total, 1461 (1107, 1791) or 11% of all rural CVD deaths would be delayed or averted, if rural populations were to have the same levels of individual risk factors as their metropolitan counterparts (Table 3). Of the deaths prevented from CVD, 793 (510, 1065) would be from IHD, slightly more of these among males (418) than females (374), a 10.5% reduction in rural IHD deaths. Premature IHD deaths (75 years and under), would account for 38.3% of the IHD deaths that would be delayed or averted, or 4% of all rural IHD deaths. Most of these premature deaths would be averted for males, 266 (232, 301) compared to 37 (28, 46) in females.

There were 2075 excess IHD deaths in the rural population in 2011. In the counterfactual scenario, risk factors differences accounted for 38.2% of the gap, leaving 61.8% due to other, unmeasured factors. There were substantial differences by sex, with 28.1% of the gap attributable to risk factor differences for males, compared to 66.7% for females.

*Table 3: Deaths averted or delayed from chronic diseases in rural Australia, under the counterfactual scenario, 95% credible intervals (CI), by sex.*

| Deaths | Females (95% CI) | Males (95% CI) | Total (95% CI) | % of total deaths from condition (based on 2011 death rate) |
|---|---|---|---|---|
| **Overall CVD** | 828 (546, 1,092) | 629 (487, 768) | 1461 (1107, 1791) | 11% |
| **CVD (Under 75** | 78 (66, 88) | 343 (305, 380) | 420 (375,465) | 3% |

| | | | | |
|---|---|---|---|---|
| **years)** | | | | |
| **IHD** | 375(147, 579) | 418 (280, 549) | 793 (506, 1065) | 10.5% |
| **IHD (Under 75 years)** | 37 (29, 46) | 267 (231, 301) | 304 (263, 345) | 4% |

**Deaths attributable to individual risk factors**

Table 4 shows the number of deaths that would be delayed or averted under the counterfactual scenario for each individual risk factor for both CVD and IHD. Obesity and smoking, as individual risk factors, accounted for the largest numbers of CVD and IHD deaths that could be prevented in rural areas, contributing 1,309 (1000, 1608), and 337 (290, 388) deaths delayed or averted respectively for CVD, and 740 (504, 955) and 225 (192, 260) for IHD. The adjustment of fruit and vegetable intakes showed that more people would die from CVD (-290 (-475, -103)) and IHD (-298 (95% CI: -486, -111)) if intakes in rural areas were to match those of metropolitan areas, since in this case vegetable intakes would be worse under the counterfactual scenario.

*Table 4: Preventable deaths from CVD and IHD attributable to individual risk factors if rural populations had the same risk factor levels as populations in major cities.*

| **Risk factor** | **Total CVD deaths averted/delayed under counterfactual scenario (95% CI)** | **Total IHD deaths averted/delayed under counterfactual scenario (95% CI)** |
|---|---|---|
| **Overall diet** | -199 (-389, -10) | -190 (-380, -4) |
| **Fruit and vegetables** | -290 (-475,-103) | -298 (-486, -111) |
| **Fibre** | -70 (-103, -39) | - 47 ( -75, -19) |
| **Fats** | 121 (98-145) | 133 (113-155) |
| **Salt** | 40 (17-62) | 19 (8-31) |

| | | |
|---|---|---|
| **Physical activity** | 84 (66-103) | 53 (38-69) |
| **Smoking** | 337 (290-388) | 225 (192-260) |
| **Alcohol** | -55 (-101, -18) | -28 (-52, -5) |
| **Obesity** | 1309 (100, 1608) | 740 (50, 955) |

*Note: positive numbers represent deaths delayed or averted under the counterfactual scenario, negative numbers represent an increase in deaths under the counterfactual scenario.*

An additional 'best case' scenario was explored in which only risk factor changes that resulted in improvements in cardiovascular mortality were modelled. As shown in table 4, changes to rural vegetable, fibre and alcohol intakes to match those in major cities resulted in an increase in deaths from CVD, therefore these three risk factors were held unchanged in the 'best case' scenario. Table 5 shows that in this scenario, a total of 1669 (1380, 1950) deaths could be delayed or averted in rural areas. Of this total, 1161 (943, 1365) deaths would be averted from IHD, which would lead to a mortality gap reduction of 56% (45.4%, 65.7 %) in rural Australia.

*Table 5: Deaths averted or delayed from chronic diseases in rural Australia, under the 'best case' scenario, 95% credible intervals (CI), by sex.*

| **Deaths** | **Females (95% CI)** | **Males (95% CI)** | **Total (95% CI)** | **% of total deaths from condition** |
|---|---|---|---|---|
| **Overall CVD** | 898 (628, 1154) | 771 (702, 838) | 1669 (1380, 1950) | 12.2% |
| **CVD (Under 75 years)** | 74 (69, 78) | 371 (343, 397) | 445 (415,472) | 3.4% |
| **IHD** | 456 (245,644) | 707(643,769) | 1161 (943, 1365) | 15.3% |
| **IHD (Under 75 years)** | 44 (40, 47) | 309 (283, 333) | 352 ( 327,377) | 4.6% |

## DISCUSSION

This analysis showed that more than one third of the IHD mortality inequality between metro and rural areas can be attributed to differences in individual risk factors, an important consideration for

health policy and intervention planning. Importantly, however, over 60% of the increased mortality burden in rural areas was unexplained by risk factor differences.

The majority of individual risk factors were found to differ between rural and metropolitan areas, with significantly higher BMI, energy intakes and proportion of energy intake from fats observed in rural populations, along with higher levels of high risk alcohol consumption and sedentary behaviour. Rural people did, however, report significantly higher vegetable intakes, which equated to consumption of approximately 10% more vegetables than their metropolitan counterparts, consistent with previous health survey data(2).

The origins of the differences in individual modifiable IHD risk factors between rural and metropolitan areas(2), are likely to be complex, arising from the interaction of a range of factors at the individual and community level, including socio-economic disadvantage, education levels, access to primary health services and health literacy(28). Living outside of metropolitan areas has been associated with more risk factors for chronic diseases in adults(25), with some evidence that geographic location should be assessed as a social determinant of health, above and beyond socio-economic status and area level disadvantage(26). There is evidence for this in that self-reported prevalence of IHD, diabetes and cerebrovascular disease were found to be similar in rural and metropolitan areas, despite much higher measured mortality rates from these diseases in rural areas, potentially revealing reduced health awareness in rural populations(27). This may be an important contributor to differences in outcomes for rural populations, as lower health literacy has been linked to poorer outcomes in patients with heart disease(28).

In terms of individual risk factors, differences in obesity and tobacco smoking appeared to have the biggest impact on the increased burden of IHD in the rural population, when compared to metropolitan areas. Obesity is a well-known risk factor for IHD(15), and has been consistently shown to be higher in rural populations of Australia for the past few decades(27, 29). Differences in energy intake and physical activity energy expenditure between rural and metropolitan populations led to

substantial reductions in obesity-mediated mortality in the counterfactual scenario. These reductions explained the largest proportion of the mortality gap between the two populations of any of the behaviours studied. Higher energy intakes in the rural sample, which increase the likelihood of a higher BMI(30), could be reflective of the consumption of more low cost, energy dense foods possibly in part, due to reduced access to healthier foods, which has been well documented in rural and regional areas(31).

The cardio-protective effects of alcohol consumption are often debated(32). Our results showed that current levels of alcohol intake do not appear to contribute to increased cardiovascular risk for rural populations, with 55 fewer CVD deaths averted (an increase in deaths overall) as a result of the difference in consumption between the two populations. This was mainly due to the fact that although overall intakes were higher in rural areas, intakes among males over 75 years of age were lower in rural areas than in metro areas, therefore leading to a modelled increase in consumption and therefore associated deaths in this group under the counterfactual scenario.

Tobacco smoking is recognised as the largest single preventable cause of mortality and morbidity in Australia(33), and higher smoking rates in rural areas have been apparent since at least 1993(16, 25). Despite numerous public health initiatives and interventions over this period, the rural smoking rate has remained comparatively high whilst the metropolitan rate has continued to decline(16, 33), possibly indicating that such preventative efforts have not adequately reached rural Australians(16).

The results of this study suggest that substantial gains could be made in reducing the CVD mortality gap between metropolitan and rural populations if modifiable risk factors could be improved in rural areas. Improving risk factor profiles in rural populations to at least match that of their metropolitan counterparts could be assumed to be a reasonable target, and is certainly a relatively modest goal, given that even metropolitan risk factor levels are far from ideal(34, 35). Importantly, even if this risk factor reduction scenario were to be achieved, a significant proportion (almost two-thirds) of the excess deaths would remain, a finding which should prompt major reflection on the role of

disadvantage, health care provision and other, less prominent risk factors in the perpetuation of rural health inequalities.

**Strengths:**

This study used three routinely collected, representative national datasets, including the Census, AIHW National Mortality Database and the Australian Health Survey, as inputs for the PRIME model. These datasets represent the highest quality, and comprehensive population data available currently for Australia. The use of three robust datasets is required for PRIME to provide accurate disease outputs. The PRIME model also has many strengths, including that it is able to model the effect of changes in multiple risk factors simultaneously on mortality rates from different chronic diseases, by age and sex. The model has been designed using the strongest available scientific evidence on the links between chronic disease mortality and dietary intake, alcohol consumption, smoking, physical activity and obesity levels(16).

**Limitations:**

Data used in the model were self-reported, which carries multiple limitations, and could lead to underestimations of the level of behavioural risk factors and subsequently, mortality gap reductions (36), although it less likely that these biases would differentially affect rural vs metro populations. Very remote areas of Australia were not sampled in AHS, therefore risk factor levels for these populations were not included in the analysis(23). This may lead to an underestimation of the prevalence of some risk factors, as residents of very remote areas are known to experience even higher burden from IHD than the broader rural population(2), however they also represent a very small percentage of the total Australian population (0.9%)(25). The uncertainty analysis conducted on the number of deaths averted, only accounts for uncertainty within the model parameters, but not the uncertainty of estimates from the Australian Heath Survey. Lastly, we were unable to

account for the diversity in characteristics between differing levels of remoteness (e.g. inner regional areas compared to outer regional or remote areas) due to small population numbers. Instead, it was necessary to make a single comparison between those living within and outside major cities. Differences in population characteristics, access to health services and environmental factors can vary significantly by differing levels of remoteness, and this is an important consideration for policy and planning when trying to improve health in non-metropolitan areas.

**CONCLUSIONS**

There is potential for improvements in the level of cardiovascular disease burden observed in rural Australians, if the prevalence of modifiable risk factors such as obesity and smoking were to be reduced to match those of metropolitan areas. If such a scenario was to be achieved, 38% of the mortality gap between rural and metropolitan areas could be reduced, however, investigations into factors responsible for the remaining 62% of this inequality are needed in order to work towards achieving health equality for rural populations.

**Author Contributions**

LA organised access to and analysis of the raw data, completed all data entry into the PRIME model, analysis of the results, and writing of the manuscript. MN contributed to defining the original research idea, data collection, use of the PRIME model and analysis. KP and JJ assisted with data analysis. SA contributed to defining the original research idea. All authors reviewed and contributed to the manuscript and all stages of compilation.

**Acknowledgements**

Dr Peter Scarborough and team, who developed and provided the PRIME model used in this study.

**Data Sharing Statement**

The PRIME model is available upon request from Dr Peter Scarborough contactable at: peter.scarborough@dph.ox.ac.uk.

Population and health survey data were accessed through the Australian Bureau of Statistics TableBuilder. The mortality data (ICD deaths by remoteness) were provided by the AIHW under a specific data request.

**Conflict of Interest declaration**

The authors declare there are no conflicts of interest

**Funding acknowledgments**

MN, KP, LA and JJ are supported by funding from the National Heart Foundation of Australia and Deakin University. SA is supported by funding from an Australian National Health and Medical Research Council/ National Heart Foundation of Australia Career Development Fellowship (APP1045836). He is also a researcher on the US National Institutes of Health grant titled, "Systems Science to Guide Whole-of- Community Childhood Obesity Interventions" (1R01HL115485-01A1) and within a NHMRC Centre for Research Excellence in Obesity Policy and Food Systems (APP1041020).

**REFERENCES:**


1. AIHW. Mortality inequalities in Australia: bulletin 124. Canberra: AIHW; 2014.
2. ABS. Health Outside Major Cities Australia: ABS; 2011 [cited 2015 10/06/2015]. Available from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/4102.0Main+Features30Mar+2011.
3. Levin KA, Leyland AH. Urban-rural inequalities in ischemic heart disease in Scotland, 1981-1999. Am J Public Health. 2006 Jan;96(1):145-51.
4. Kulshreshtha A, Goyal A, Dabhadkar K, Veledar E, Vaccarino V. Urban-rural differences in coronary heart disease mortality in the United States: 1999-2009. Public Health Rep. 2014 Jan-Feb;129(1):19-29.
5. Terashima M, Rainham DG, Levy AR. A small-area analysis of inequalities in chronic disease prevalence across urban and non-urban communities in the Province of Nova Scotia, Canada, 2007-2011. BMJ open. 2014;4(5).
6. ABS. 3303.0 - Causes of Death, Australia, 2013 Australia: ABS; 2015 [cited 2016 29/02/2016]. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/3303.0~2013~Main%20Features~Summary%20of%20findings~10000.
7. Dinh Vu H, Heller RF, Lim LLY, D'Este C, O'Connell RL. Mortality after acute myocardial infarction is lower in metropolitan regions than in non-metropolitan regions. Journal of Epidemiology and Community Health. 2000;54(8):590-5.
8. Waters AM, Trinh L, Chau T, Bourchier M, Moon L. Latest statistics on cardiovascular disease in Australia. Clinical and Experimental Pharmacology and Physiology. 2013;40(6):347-56.
9. Sexton PT, Sexton TLH. Excess coronary mortality among Australian men and women living outside the capital city statistical divisions. Medical Journal of Australia. 2000;172(8):370-4.
10. Beard JR, Earnest A, Morgan G, Chan H, Summerhayes R, Dunn TM, et al. Socioeconomic disadvantage and acute coronary events: A spatiotemporal analysis. Epidemiology. 2008;19(3):485-92.
11. Dobson A, McLaughlin D, Vagenas D, Wong KY. Why are death rates higher in rural areas? Evidence from the Australian Longitudinal Study on Women's Health. Australian And New Zealand Journal Of Public Health. 2010;34(6):624-8.
12. Gausia K, Katzenellenbogen JM, Sanfilippo FM, Knuiman MW, Thompson PL, Hobbs MST, et al. Evidence-based prescribing of drugs for secondary prevention of acute coronary syndrome in Aboriginal and non- Aboriginal patients admitted to Western Australian hospitals. Internal Medicine Journal. 2014;44(4):353-61.
13. Jordan S, Wilson A, Dobson A. Management of heart conditions in older rural and urban Australian women. Internal Medicine Journal. 2011;41(10):722-9.
14. NHRHA. The determinants of health in rural and remote Australia: fact sheet 28. Australian Captial Territory: National Rural Health Alliance; 2011.
15. WHF. World Heart Federation: 25 by 2025 Targets. Melbourne: World Heart Federation, 2014.
16. NRHA. Smoking and rural health. Australian Capital Territory: National Rural Health Alliance; 2014.
17. Scarborough P, Harrington RA, Mizdrak A, Zhou LM, Doherty A. The Preventable Risk Integrated ModEl and Its Use to Estimate the Health Impact of Public Health Policy Scenarios. Scientifica. 2014;2014:748750.
18. Scarborough P, Morgan RD, Webster P, Rayner M. Differences in coronary heart disease, stroke and cancer mortality rates between England, Wales, Scotland and Northern Ireland: the role of diet and nutrition. BMJ open. 2011 Jan 1;1(1):e000263.
19. Scarborough P, Allender S, Clarke D, Wickramasinghe K, Rayner M. Modelling the health impact of environmentally sustainable dietary scenarios in the UK. European journal of clinical nutrition. 2012 Jun;66(6):710-5.

20. Belanger M, Poirier M, Jbilou J, Scarborough P. Modelling the impact of compliance with dietary recommendations on cancer and cardiovascular disease mortality in Canada. Public health. 2014 Mar;128(3):222-30.
21. ABS. Australian Statistical Geography Standard Canberra, Australia: ABS; 2014 [cited 2016 04/07/2016]. Available from: http://www.abs.gov.au/websitedbs/D3310114.nsf/home/Australian+Statistical+Geography+Standard+(ASGS).
22. ABS. TableBuilder:How to apply for access to microdata Australia: Australian Bureau of Statistics; 2011 [updated 30 June 2017; cited 2017 17/07/2017]. Available from: http://www.abs.gov.au/websitedbs/D3310114.nsf/home/About+TableBuilder.
23. ABS. 4363.0.55.001 - Australian Health Survey: Users' Guide, 2011-13: Sample design and selection Canberra: Australian Bureau of Statistics; 2015 [cited 2016 20/06/2016]. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4363.0.55.001Chapter2102011-13.
24. ABS. 4363.0.55.001 - Australian Health Survey: Users' Guide, 2011-13 : Adult Physical Activity: Australian Bureau of Statistics 2015 [cited 2016 27/06/2016]. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/59FF6FE5D62BABE1CA257BAC00225A07?opendocument.
25. 2014. AIoHaW. Australia's health 2014: Australia's health series no. 14. Cat. no. AUS 178: Health in regional and remote areas. . Canberra, Australia: AIHW; 2014.
26. Patterson KA, Cleland V, Venn A, Blizzard L, Gall S. A cross-sectional study of geographic differences in health risk factors among young Australian adults: the role of socioeconomic position. BMC public health. 2014;14:1278.
27. AIHW. Rural, regional and remote health: Indicators of health status and determinants of health. Canberra, Australia: Australian Institute of Health and Welfare; 2008.
28. Wu JR, Moser DK, DeWalt DA, Rayens MK, Dracup K. Health Literacy Mediates the Relationship Between Age and Health Outcomes in Patients With Heart Failure. Circulation Heart failure. 2016 Jan;9(1):e002250.
29. NHRA. Obesity in rural Australia. Australian Capital Territory: National Rural Health Alliance; 2013.
30. French SA, Story M, Jeffery RW. Environmental influences on eating and physical activity. Annual review of public health. 2001;22:309-35. PubMed PMID: 11274524.
31. health Q. 2014 Healthy food access basket survey, Queensland Queensland, Australia: Queensland Government; 2015 [cited 2016 22/06/2016]. Available from: https://www.health.qld.gov.au/research-reports/reports/food/access/guidelines/default.asp.
32. Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. Bmj. 2011 Feb 22;342:d671.
33. AIHW. Australia's health 2014: Leading types of ill health: AIHW; 2014 [cited 2016 22/06/2016]. Available from: http://www.aihw.gov.au/australias-health/2014/ill-health/#t.
34. Ball K, Mishra GD, Thane CW, A H. How well do Australian women comply with dietary guidelines? Public Health Nutrition 2004;4;7(3):443–52.
35. ABS. 4364.0.55.012 - Australian Health Survey: Consumption of Food Groups from the Australian Dietary Guidelines, 2011-12 Canberra, Asutra;oa: Australian Bureau of Statistics 2016 [cited 2016 04/07/2016]. Available from: http://www.abs.gov.au/websitedbs/D3310114.nsf/home/Australian+Statistical+Geography+Standard+(ASGS).
36. ABS. 4363.0.55.001 - Australian Health Survey: Users' Guide, 2011-13: UNDER-REPORTING IN NUTRITION SURVEYS Canberra: Australian Bureau of statistics; 2015 [cited 2016 20/06/2016]. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4363.0.55.001Chapter651512011-13.

267

268

BMJ Open

# Quantifying the role of modifiable risk factors in the differences in cardiovascular disease mortality rates between metropolitan and rural populations in Australia: A macrosimulation modelling study.



| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2017-018307.R2 |
| Article Type: | Research |
| Date Submitted by the Author: | 19-Sep-2017 |
| Complete List of Authors: | Alston, Laura; Deakin University, Waterfront Campus<br>Peterson, Karen; Deakin University - Geelong Waterfront Campus<br>Jacobs, Jane; Deakin University - Geelong Waterfront Campus<br>Allender, Steven; Deakin University, Faculty of Health<br>Nichols, Melanie; Deakin University, Faculty of Health; |
| Primary Subject Heading: | Public health |
| Secondary Subject Heading: | Epidemiology |
| Keywords: | Coronary heart disease < CARDIOLOGY, NUTRITION & DIETETICS, PREVENTIVE MEDICINE, PUBLIC HEALTH |
| | |

**TITLE**: Quantifying the role of modifiable risk factors in the differences in cardiovascular disease mortality rates between metropolitan and rural populations in Australia: A macrosimulation modelling study.

**Authors:** Laura Alston[a], Karen Louise Peterson[a], Jane P Jacobs[a], Steven Allender[a], Melanie Nichols[a].

**Author affiliations**: [a]Global Obesity Centre, Faculty of Health, Deakin University, Geelong, Australia.

**Corresponding author**: Laura Alston. Address: WHO Collaborating Centre for Obesity Prevention, Faculty of Health, Deakin University, Locked Bag 20001, Geelong, VIC 3220 Australia. Telephone: +61 3 5247 9426. Email: laura.alston@deakin.edu.au.

**Previous presentations of this research**: none to declare.

**Funding acknowledgments:** MN, KP, LA and JJ are supported by funding from the National Heart Foundation of Australia and Deakin University. SA is supported by funding from an Australian National Health and Medical Research Council/ National Heart Foundation of Australia Career Development Fellowship (APP1045836). He is also a researcher on the US National Institutes of Health grant titled, "Systems Science to Guide Whole-of- Community Childhood Obesity Interventions" (1R01HL115485-01A1) and within a NHMRC Centre for Research Excellence in Obesity Policy and Food Systems (APP1041020).

**Keywords:** Rural, Risk factors, Cardiovascular disease, Ischaemic heart disease, Inequalities, Prevention

**Word count (excluding references and abstract): 3,115 words**

## ABSTRACT

**Objectives:** Aims: (1) to quantify differences in modifiable risk factors between urban and rural populations, and (2) to determine the number of rural cardiovascular disease (CVD) and ischaemic heart disease (IHD) deaths that could be averted or delayed if risk factor levels in rural areas were equivalent to metropolitan areas.

**Setting:** National population estimates, risk factor prevalence, CVD and IHD deaths data were analysed by rurality using the Preventable Risk Integrated Model (PRIME) macro-simulation chronic disease risk model. Uncertainty analysis was conducted using a Monte Carlo simulation of 10,000 iterations to calculate 95% credible intervals (CI).

**Participants:** National datasets of males and females over the age of 18 years living in urban and rural Australia.

**Results:** If people living in rural Australia had the same levels of risk factors as those in metropolitan areas, approximately 1461 (95% credible interval (CI): 1107, 1791) deaths could be delayed from cardiovascular disease (CVD) annually. Of these CVD deaths, 793 (95%CI: 506, 1065) would be from IHD. The IHD mortality gap between metropolitan and rural populations would be reduced by 38.2% (95%CI: 24.4%, 50.6%).

**Conclusions:** A significant portion of deaths from CVD and IHD could be averted with improvements in risk factors; more than one third of the excess IHD deaths in rural Australia were attributed to differences in risk factors. As much as two thirds of the increased IHD mortality rate in rural areas could not be accounted for by modifiable risk factors, however, and this requires further investigation.

**ARTICLE SUMMARY:**

*Strengths:*

- This is the first study to attempt to quantify the role of modifiable factors in the increased burden of cardiovascular diseases in rural areas when compared to urban Australia.
- The PRIME model has been previously published and is internationally recognised.
- This study used three representative national datasets, including the Census, Australian Institute of Health and Welfare National Mortality Database and the Australian Health Survey, as inputs for the PRIME model.

*Limitations:*

- Data used in the model were self-reported, and could lead to underestimations of the level of behavioural risk factors and subsequently, mortality gap reductions, although it is unlikely that these biases would differentially affect rural vs metro populations.
- Very remote populations of Australia (0.9% of the total population) were excluded.

## INTRODUCTION

Despite high quality, universal health care systems and standards in Australia, there are still disparities in the burden of chronic disease experienced by people with lower socio-economic status, Aboriginal and Torres Strait Islanders and rural residents(1). Australians living outside major cities experience a substantially increased burden of cardiovascular diseases(2), which is consistent with findings for rural populations in other developed countries such as the United States, Canada, and the United Kingdom(3-5). Cardiovascular disease (CVD), in its most common form, Ischaemic heart disease (IHD) is the leading cause of death in Australia(6), and individuals residing in a regional or remote areas are estimated to be between 1.2 and 1.5 times more likely to die from IHD than those residing in metropolitan areas(1).

The reasons for observed health inequalities between metropolitan and rural populations appear to be multifactorial and highly complex(2, 7-9). It has been hypothesised that rural populations experience greater CVD and IHD burden due to variation in access to health services, individual socio-economic status, rates of modifiable risk factors, as well as potentially reduced access to specialised evidence-based treatments, such as prompt surgical intervention in rural hospitals(7, 10-13). The National Rural Health Alliance (NRHA) of Australia states that if rural Australians are to achieve the same health outcomes as their metropolitan counterparts by the year 2020, it is not just access to health services that need to be improved(14), but that more focus needs to be placed on improving the socio-economic determinants of health (such as lower education, incomes, and employment) for rural communities, and reducing risk factors for chronic diseases such as smoking and physical inactivity(14).

Cardiovascular diseases, particularly IHD, are largely preventable, and the modifiable, behavioural risk factors are well known(15). Clinical risk factors such as high cholesterol, high blood pressure, and obesity interact with behavioural factors such as poor diet, smoking, risky alcohol consumption, and physical inactivity to increase the risk of IHD and CVD(13). Based on population health surveys, these risk factors differ by rurality, with higher smoking rates, increased high risk alcohol consumption and lower physical activity levels being reported by non-city dwelling Australians(2).

Currently, there is minimal evidence quantifying the extent to which modifiable individual risk factors contribute to the increased burden of CVD and IHD in rural areas, and how much of this burden could be reduced if behavioural risk factors were comparable among rural Australians as those among their counterparts in cities. Increased knowledge of how differential risk factor rates contribute to the increased rural CVD burden could support the identification of policy priorities and prevention programs for rural areas, as previous public health prevention efforts have been shown to be less effective for rural populations compared to those living in metropolitan areas(16).

**Aims:**

This study aimed to: (1) Quantify differences in prevalence of major CVD risk factors between rural and metropolitan populations, and (2) Determine the number and proportion of rural deaths from CVD, and specifically from IHD, that could be averted or delayed in rural areas if the levels of risk factors were equivalent to those in metropolitan Australia.

## METHODS

### The Preventable Risk Integrated Model (PRIME)

This study used a macrosimulation model, the Preventable Risk Integrated Model (PRIME)(17), to estimate age- and sex-specific changes in CVD and IHD mortality that would result from changes to the population prevalence of risk factors in Australia. An exemption from ethics review was obtained from Deakin University's Human Research Ethics Unit. PRIME has been used in the UK, New Zealand and Canada to model a range of risk factor scenarios(17-20). The model can be used to examine the likely changes in mortality rates of many chronic diseases, including IHD, under different counterfactual scenarios of population behavioural risk factors(17).

The PRIME model is built on a framework of linkage between, 1) modifiable behaviours; 2) clinical risk factors; and 3) mortality outcomes. This framework is parameterised using the best available evidence from meta-analyses of published studies, and is described in detail elsewhere(17). PRIME requires data on prevalence of modifiable risk factors, mortality rates and population estimates by 5 year age groups and sex, for both baseline and counterfactual scenarios. For this study, PRIME was used to estimate the number of CVD and IHD deaths that would be delayed or averted if those living in rural Australia had the same modifiable risk factor levels as those living in major cities. The baseline scenario used the current levels of modifiable risk factors in those living in rural areas, and the counterfactual scenario involved applying the level of risk factors currently observed in the metropolitan population. An additional 'best case' scenario was also modelled, by only changing risk factor levels that were more favourable among those living in metropolitan areas, when compared to the rural population.

**Population data**

Population size estimates by age, sex and rurality were derived from the 2011 Australian Census. The 'rural' population was defined as all residents not classified by the ABS as living in major cities(21). These data were accessed through subscription to the online ABS data program TableBuilder(22).

**Risk factor data**

The individual modifiable risk factors included in the PRIME model (table 1) were; mean dietary intakes, alcohol consumption, prevalence of smoking, physical activity levels and mean body mass index (BMI) scores. All risk factor estimates were obtained from 9973 individuals aged 15 years and over surveyed for the 2011-12 Australian Health Survey (AHS), which surveyed people from all areas of Australia, excluding very remote areas(23). Mean values were calculated by age, sex and remoteness for each risk factor parameter, through the ABS program TableBuilder(22).

*Table 1: Summary of risk factor data entered into the PRIME model.*

| Risk factor | Parameter | Unit |
|---|---|---|
| **Diet** | Total energy intake | Kcal/day |
| | Proportion of low/non-consumers of fruit (<1 serve/day) | % of population |
| | Proportion of low/non-consumers of vegetables (<1 serve/day) | % of population |
| | Mean vegetable consumption remaining population | g/day |
| | Mean fruit consumption remaining population | g/day |
| | Fibre consumption | g/day |
| | Dietary cholesterol consumption | mg/day |
| | Salt consumption | g/day |
| | Total fat intake | % of total energy intake |
| | Saturated fat intake | % of total energy intake |
| | Mono-unsaturated fat intake | % of total energy intake |
| | Poly-unsaturated fat intake | % of total energy intake |
| **Alcohol** | Proportion of low consumers (<1g/day) | % of population |
| | Mean consumption among remaining population | g/day of pure alcohol |
| **Smoking** | Current smokers | % of population |
| | Ex-smokers | % of population |
| | Never smokers | % of population |
| **Physical activity** | Proportion of population who are sedentary | % of population |
| | Amount of moderate-vigorous activity among remaining population | MET-hours per week |
| **Anthropometry** | BMI | $kg/m^2$ |
| | Height | metres |

*Abbreviations: BMI= Body Mass Index, g=grams, MET= metabolic equivalent task.*

Dietary intake data were collected using a 24-hour recall of all foods and fluids consumed in the day prior to the interview. Participants provided 24-hour recall data on two separate occasions, at least 8 days apart. Implausible intakes were excluded if the day of intake data had an energy intake (EI) to

basal metabolic rate (BMR) ratio of less than 0.9, as per recommendation from the Australian Bureau of Statistics(23). Mean daily dietary intakes from the two days of data collection were calculated for each participant for: energy (kcal/day), fruit (g/day), vegetables (g/day), fibre (g/day), dietary cholesterol (mg/day), salt (g/day), total fat (% EI), saturated fat (% EI), monounsaturated fat (% EI), and polyunsaturated fat (% EI). The percentage of people who consumed less than one serve of fruit and less than one serve of vegetables was also calculated as required by the model. Mean BMI for the rural population, by 5 year age group and sex, was required by the model, and the effect of obesity on mortality rates was modelled using the differences in energy intake and physical activity levels between the two populations. Participants reported if they were current smokers, ex-smokers, or if they had never smoked, and the age- sex- and location-specific prevalence of each of these categories were derived.

The PRIME model requires the proportion of the population classified as 'sedentary', and physical activity levels in the form of mean Metabolic Equivalent of Task (MET) hours per week, in the remaining (active) population. The sedentary proportion of the population was calculated as the sum of those classified as insufficiently active or sedentary by the ABS. Participants were classified as insufficiently active or sedentary if they did not meet the physical activity recommendations of 150 minutes per week, over 5 separate sessions(24). Mean minutes of moderate and vigorous activity over the last week were used to calculate average daily minutes of activity. This duration was then multiplied by metabolic equivalents as provided by the ABS, to convert the estimates to MET-hours of activity per week.

The model requires the percentage of non-drinkers within each population by age and sex, which was calculated as those who reported either no alcohol consumption, or <1g per day on average, over the surveyed period. Mean daily intake of pure alcohol in millilitres (mL), by age group and sex, was calculated as the weighted daily mean (mL) within TableBuilder, then converted to grams of pure alcohol.

**Mortality data**

Deaths due to CVD (ICD-10 codes I00-I99 ) and IHD (ICD-10 code I20-I25) by state or territory and remoteness area of usual residence, by sex and 5-year age group, among people aged 15 years and over was provided by the Australian Institute of Health and Welfare (AIHW) for the year 2011 from the AIHW National Mortality Database (unpublished). These data were provided after an application for a specific request to the AIHW, and are not publicly available.

**Mortality gap**

The mortality gap between rural and metropolitan areas was calculated by applying the metropolitan death rate for those aged 15 years and over, to the rural population, to determine the number of rural deaths that would be expected if cause-specific mortality rates were equal between metropolitan and rural areas. This figure was subtracted from the actual number of deaths in rural areas, to calculate the gap in mortality between the two populations.

**Uncertainty analysis**

The PRIME model has a built in Monte Carlo analysis function to generate 95% credible intervals around the outputs, which allows for the different distribution of epidemiological parameters (for example the level of relative risk for a disease outcome for a particular risk factor level) within the model that have been derived from the literature(17).The intervals produced are based only on the uncertainty in the model parameters, and not on the variability of the original data used in the baseline and counterfactual scenarios. Monte Carlo simulation of 10,000 iterations was used to generate 95% credible intervals for each of the estimates of deaths delayed or averted under the counterfactual scenario.

**RESULTS**

**Differences in individual risk factors between rural and metropolitan areas**

There were a mixture of differences in dietary intake, between rural and metropolitan (Table 2), that were statistically significant for many dietary components, although many were relatively small in absolute magnitude. Two of the dietary intake levels were more favourable in rural areas, and the rest were more favourable in metropolitan areas. Vegetable intakes were significantly higher for rural populations ($p < 0.001$), also resulting in a slightly higher fibre intake, while intake of fruit was not significantly different between the two populations.

Energy intakes and the percentage of energy from saturated fat were significantly higher among rural populations ($p<0.05$). Rural females reported a significantly higher dietary cholesterol intake ($p<0.05$) and lower percentage energy from polyunsaturated fat ($p<0.01$) than their metropolitan counterparts. There were no other significant differences in intake across the other dietary components analysed.

Mean alcohol intake (g/day) in those who reported drinking alcohol was significantly higher in rural areas for females ($p<0.05$), however there was no differences for males. There were significantly more current smokers in rural areas compared to major cities (females 19.5% vs 14.0%; males 24.2% vs 18.7%). The proportion of people who had never smoked was higher in metropolitan areas.

Fewer rural people were meeting recommendations for physical activity; 37.1% of males in rural areas were meeting recommendations compared to 44.0% in major cities. This was also true for females (36.5% in rural areas, 46.3% in cities). There were no significant differences between the two populations in the mean MET hours per week of moderate-vigorous activity performed by the active population.

Smoking rates were significantly higher in rural areas for both females and males. Mean BMI for females was significantly higher ($p<0.001$) in rural areas compared to major cities (females 26.8 vs 27.6 $kg/m^2$; males 27.3 vs 27.8 $kg/m^2$).

*Table 2: Differences in individual risk factors, rural compared with metropolitan areas, females and males 2011-12, with 95% Confidence Intervals (CI).*

| | Females | | | | Males | | | |
|---|---|---|---|---|---|---|---|---|
| **Dietary component** | **Mean intake (95%Confidence interval): Rural** | **Mean intake (95% CI): Metropolitan** | **Mean difference** | **p-value (t-test)** | **Mean intake (95%CI): Rural** | **Mean intake (95% CI): Metropolitan** | **Mean difference** | **p-value (t-test)** |
| **Fruit (g)** **Serves*** | 257 (250, 264) 1.7 serves | 264 (258, 269) 1.9 serves | 7 | p= NS | 222 (214, 231) 1.5 serves | 231 (225, 237) 1.5 serves | 9 | p=NS |
| **Vegetables (g)** **Serves*** | 201 (196, 205) 2.7 serves | 184 (180, 187) 2.45 serves* | 17 | p<0.0001 | 180 (176, 186) 2.4 serves | 158 ( 155, 176) 2.1 serves | 23 | p<0.0001 |
| **Energy intake (kJ)** | 8496 (8372, 8620) | 8332 (8241, 8424) | 164 | P=0.03 | 10,987 (10,818, 11,157) | 10,760 (10,634, 10,887) | 227 | p=0.03 |
| **Fibre (g)** | 23.10 (23, 24) | 23 (23, 24) | 0.1 | p=NS | 27.0 (26.3, 27.7) | 26.6 (26.1, 27.0) | 0.4 | p=NS |
| **Sodium (mg)** | 2339 (2282, 2396) | 2279 (2236, 2320) | 61 | p=NS | 3046 (2969, 3121) | 2973 (2914, 3032) | 72 | p=NS |
| **Dietary cholesterol** | 299 (289, 309) | 284 (277, 292) | 15 | p=0.02 | 380 (366, 393) | 375 (363, 385) | 5 | p=NS |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **(mg)** | | | | | | | | |
| **% energy from fat** | 32 (31.7, 32.5) | 32 (31.5, 32) | 0.3 | p=NS | 31.5 (31, 32) | 31 (30.5, 31.1) | 0.5 | p=0.01 |
| **% energy from saturated fat** | 13.1 (12.8, 13.3) | 12.4 (12.2, 12.5) | 0.7 | p<0.0001 | 12.9 (12.7, 13.2) | 12.1 (11.9, 12.3) | 0.8 | p<0.0001 |
| **% energy from monounsaturated fat** | 12.0 (11.8, 12.1) | 12.1 (11.9, 12.3) | 0.1 | p=NS | 12.0 (11.6, 12.0) | 12.0 (11.8, 12.1) | 0.1 | p=NS |
| **% energy from polyunsaturated fat** | 4.8 (4.7, 4.9) | 5.0 (5.0, 5.14) | 0.2 | p=0.0016 | 4.6 (4.5, 4.7) | 4.7 (4.6, 4.8) | 0.1 | p=NS |
| **Alcohol intake (g)** | 21.6 | 17.5 | 4.1 | p=0.02 | 23.0 | 19.5 | 3.5 | p=NS |
| **% Current smokers** | 17.4 | 12.5 | 4.9 | p=0.04 | 22.8 | 16 | 6.8 | p=0.002 |
| **Physical activity (MET hours)** | 13.3 | 14.2 | 0.9 | p=NS | 14.0 | 14.5 | 0.5 | p=NS |

*Notes: *One serve of fruit is 150g, 1 serve of vegetables is 75g according to Australian dietary guidelines*

**Deaths from CVD and IHD averted or delayed by risk factor changes**

In 2011, 13600 people aged 15 years and over died from CVD in rural areas, with 6846 and 6754 deaths occurring in males and females respectively. In terms of premature deaths, 3137 of these deaths occurred in those aged under 75 years, 2200 in males, and 915 in females. IHD was the cause of 7560 deaths, with 2089 deaths occurring in those under 75 years (1636 Males, and 452 females).

In total, 1461 (1107, 1791) or 11% of all rural CVD deaths would be delayed or averted, if rural populations were to have the same levels of individual risk factors as their metropolitan counterparts (Table 3). Of the deaths prevented from CVD, 793 (510, 1065) would be from IHD, slightly more of these among males (418) than females (374), a 10.5% reduction in rural IHD deaths. Premature IHD deaths (75 years and under), would account for 38.3% of the IHD deaths that would be delayed or averted, or 4% of all rural IHD deaths. Most of these premature deaths would be averted for males, 266 (232, 301) compared to 37 (28, 46) in females.

*Table 3: Deaths averted or delayed from chronic diseases in rural Australia, under the counterfactual scenario, 95% credible intervals (CI), by sex.*

| | Deaths | Averted or delayed deaths (% of total deaths in the category) |
|---|---|---|
| **CVD all ages** | | |
| **All** | 13,600 | 1,461 (10.7) |
| **Male** | 6,846 | 629 (9.2) |
| **Female** | 6754 | 828 (12.3) |
| **CVD < 75 years** | | |
| **All** | 3,137 | 420 (13.4) |
| **Male** | 2,200 | 343 (15.6) |
| **Female** | 915 | 78 (8.5) |
| **IHD all ages** | | |
| **All** | 7,560 | 793 (10.5) |
| **Male** | 4,367 | 418 (9.6) |
| **Female** | 3,193 | 374 (11.7) |
| **IHD < 75 years** | | |
| **All** | 2,089 | 304 (14.6) |
| **Male** | 1,636 | 267(16.3) |
| **Female** | 452 | 37 (8.2) |

*Notes: < 75 years: under 75 years of age.*

There were the equivalent of 2075 more IHD deaths in the rural population when compared to the metropolitan population in 2011 (data not shown). In the counterfactual scenario, risk factor differences accounted for 38.2% of the gap, leaving 61.8% due to other, unmeasured factors. There were substantial differences by sex, with 28.1% of the gap attributable to risk factor differences for males, compared to 66.7% for females.

**Deaths attributable to individual risk factors**

Table 4 shows the number of deaths that would be delayed or averted under the counterfactual scenario for each individual risk factor for both CVD and IHD. Obesity and smoking, as individual risk factors, accounted for the largest numbers of CVD and IHD deaths that could be prevented in rural areas, contributing 1,309 (1000, 1608), and 337 (290, 388) deaths delayed or averted respectively for CVD, and 740 (504, 955) and 225 (192, 260) for IHD. The adjustment of fruit and vegetable intakes showed that more people would die from CVD (-290 (-475, -103)) and IHD (-298 (95% CI: -486, -111)) if intakes in rural areas were to match those of metropolitan areas, since in this case vegetable intakes would be worse under the counterfactual scenario.

*Table 4: Preventable deaths from CVD and IHD attributable to individual risk factors if rural populations had the same risk factor levels as populations in major cities.*

| Risk factor | Total CVD deaths averted/delayed under counterfactual scenario (95% CI) | Total IHD deaths averted/delayed under counterfactual scenario (95% CI) |
|---|---|---|
| **Overall diet** | -199 (-389, -10) | -190 (-380, -4) |
| **Fruit and vegetables** | -290 (-475,-103) | -298 (-486, -111) |
| **Fibre** | -70 (-103, -39) | - 47 ( -75, -19) |
| **Fats** | 121 (98-145) | 133 (113-155) |
| **Salt** | 40 (17-62) | 19 (8-31) |

| | | |
|---|---|---|
| **Physical activity** | 84 (66-103) | 53 (38-69) |
| **Smoking** | 337 (290-388) | 225 (192-260) |
| **Alcohol** | -55 (-101, -18) | -28 (-52, -5) |
| **Obesity** | 1309 (100, 1608) | 740 (50, 955) |

*Note: positive numbers represent deaths delayed or averted under the counterfactual scenario, negative numbers represent an increase in deaths under the counterfactual scenario.*

An additional 'best case' scenario was explored in which only risk factor changes that resulted in improvements in cardiovascular mortality were modelled. As shown in table 4, changes to rural vegetable, fibre and alcohol intakes to match those in major cities resulted in an increase in deaths from CVD, therefore these three risk factors were held unchanged in the 'best case' scenario. Table 5 shows that in this scenario, a total of 1669 (1380, 1950) deaths could be delayed or averted in rural areas. Of this total, 1161 (943, 1365) deaths would be averted from IHD, which would lead to a mortality gap reduction of 56% (45.4%, 65.7 %) in rural Australia.

*Table 5: Deaths averted or delayed from chronic diseases in rural Australia, under the 'best case' scenario, 95% credible intervals (CI), by sex.*

| | **Averted or delayed deaths (% of total deaths in the category) best case** |
|---|---|
| **CVD all ages** | |
| **All** | 1,669 (12.2) |
| **Male** | 771 (11.2) |
| **Female** | 898 (13.3) |
| **CVD <75 years** | |
| **All** | 445 (14.2) |
| **Male** | 371 (16.8) |
| **Female** | 74 (8.0) |
| **IHD all ages** | |
| **All** | 1161 (15.3) |
| **Male** | 707 (16.2) |
| **Female** | 456 (14.2) |
| **IHD< 75 years** | |
| **All** | 352(16.9) |
| **Male** | 309 (18.9) |
| **Female** | 44(9.7) |

*Notes: < 75 years: under 75 years of age.*

## DISCUSSION

This analysis showed that more than one third of the IHD mortality inequality between metro and rural areas can be attributed to differences in individual risk factors, an important consideration for health policy and intervention planning. Importantly, however, over 60% of the increased mortality burden in rural areas was unexplained by risk factor differences.

The majority of individual risk factors were found to differ between rural and metropolitan areas, with significantly higher BMI, energy intakes and proportion of energy intake from fats observed in rural populations, along with higher levels of high risk alcohol consumption and sedentary behaviour. Rural people did, however, report significantly higher vegetable intakes, which equated to consumption of approximately 10% more vegetables than their metropolitan counterparts, consistent with previous health survey data(2).

The origins of the differences in individual modifiable IHD risk factors between rural and metropolitan areas(2), are likely to be complex, arising from the interaction of a range of factors at the individual and community level, including socio-economic disadvantage, education levels, access to primary health services and health literacy(28). Living outside of metropolitan areas has been associated with more risk factors for chronic diseases in adults(25), with some evidence that geographic location should be assessed as a social determinant of health, above and beyond socio-economic status and area level disadvantage(26). There is evidence for this in that self-reported prevalence of IHD, diabetes and cerebrovascular disease were found to be similar in rural and metropolitan areas, despite much higher measured mortality rates from these diseases in rural areas, potentially revealing reduced health awareness in rural populations(27). This may be an important contributor to differences in outcomes for rural populations, as lower health literacy has been linked to poorer outcomes in patients with heart disease(28).

In terms of individual risk factors, differences in obesity and tobacco smoking appeared to have the biggest impact on the increased burden of IHD in the rural population, when compared to metropolitan areas. Obesity is a well-known risk factor for IHD(15), and has been consistently shown

to be higher in rural populations of Australia for the past few decades(27, 29). Differences in energy intake and physical activity energy expenditure between rural and metropolitan populations led to substantial reductions in obesity-mediated mortality in the counterfactual scenario. These reductions explained the largest proportion of the mortality gap between the two populations of any of the behaviours studied. Higher energy intakes in the rural sample, which increase the likelihood of a higher BMI(30), could be reflective of the consumption of more low cost, energy dense foods possibly in part, due to reduced access to healthier foods, which has been well documented in rural and regional areas(31).

The cardio-protective effects of alcohol consumption are often debated(32). Our results showed that current levels of alcohol intake do not appear to contribute to increased cardiovascular risk for rural populations, with 55 fewer CVD deaths averted (an increase in deaths overall) as a result of the difference in consumption between the two populations. This was mainly due to the fact that although overall intakes were higher in rural areas, intakes among males over 75 years of age were lower in rural areas than in metro areas, therefore leading to a modelled increase in consumption and therefore associated deaths in this group under the counterfactual scenario.

Tobacco smoking is recognised as the largest single preventable cause of mortality and morbidity in Australia(33), and higher smoking rates in rural areas have been apparent since at least 1993(16, 25). Despite numerous public health initiatives and interventions over this period, the rural smoking rate has remained comparatively high whilst the metropolitan rate has continued to decline(16, 33), possibly indicating that such preventative efforts have not adequately reached rural Australians(16).

The results of this study suggest that substantial gains could be made in reducing the CVD mortality gap between metropolitan and rural populations if modifiable risk factors could be improved in rural areas. Improving risk factor profiles in rural populations to at least match that of their metropolitan counterparts could be assumed to be a reasonable target, and is certainly a relatively modest goal, given that even metropolitan risk factor levels are far from ideal(34, 35). Under the 'best case

scenario', if only unfavourable risk factors in rural areas were changed, (for example, vegetable intakes left the same), approximately 200 additional CVD deaths to the counterfactual scenario could be prevented every year. Targeting the unfavourable risk factors, such as smoking and obesity in rural people, could be modest and achievable targets for health policy and/or community interventions in order to reduce the rural death rate to be closer to the levels observed in metropolitan areas. Importantly, even if the counterfactual risk factor reduction scenario were to be achieved, a significant proportion (almost two-thirds) of the excess deaths would remain, a finding which should prompt major reflection on the role of disadvantage, health care provision and other, less prominent risk factors in the perpetuation of rural health inequalities.

**Strengths:**

This study used three routinely collected, representative national datasets, including the Census, AIHW National Mortality Database and the Australian Health Survey, as inputs for the PRIME model. These datasets represent the highest quality, and comprehensive population data available currently for Australia. The use of three robust datasets is required for PRIME to provide accurate disease outputs. The PRIME model also has many strengths, including that it is able to model the effect of changes in multiple risk factors simultaneously on mortality rates from different chronic diseases, by age and sex. The model has been designed using the strongest available scientific evidence on the links between chronic disease mortality and dietary intake, alcohol consumption, smoking, physical activity and obesity levels(16).

**Limitations:**

Data used in the model were self-reported, which carries multiple limitations, and could lead to underestimations of the level of behavioural risk factors and subsequently, mortality gap reductions (36), although it less likely that these biases would differentially affect rural vs metro populations.

Very remote areas of Australia were not sampled in AHS, therefore risk factor levels for these populations were not included in the analysis(23). This may lead to an underestimation of the prevalence of some risk factors, as residents of very remote areas are known to experience even higher burden from IHD than the broader rural population(2), however they also represent a very small percentage of the total Australian population (0.9%)(25). The uncertainty analysis conducted on the number of deaths averted, only accounts for uncertainty within the model parameters, but not the uncertainty of estimates from the Australian Heath Survey. Lastly, we were unable to account for the diversity in characteristics between differing levels of remoteness (e.g. inner regional areas compared to outer regional or remote areas) due to small population numbers. Instead, it was necessary to make a single comparison between those living within and outside major cities. Differences in population characteristics, access to health services and environmental factors can vary significantly by differing levels of remoteness, and this is an important consideration for policy and planning when trying to improve health in non-metropolitan areas.

## CONCLUSIONS

There is potential for improvements in the level of cardiovascular disease burden observed in rural Australians, if the prevalence of modifiable risk factors such as obesity and smoking were to be reduced to match those of metropolitan areas. If such a scenario was to be achieved, 38% of the mortality gap between rural and metropolitan areas could be reduced, however, investigations into factors responsible for the remaining 62% of this inequality are needed in order to work towards achieving health equality for rural populations.

## Author Contributions

LA organised access to and analysis of the raw data, completed all data entry into the PRIME model, analysis of the results, and writing of the manuscript. MN contributed to defining the original research idea, data collection, use of the PRIME model and analysis. KP and JJ assisted with data

analysis. SA contributed to defining the original research idea. All authors reviewed and contributed to the manuscript and all stages of compilation.

**Acknowledgements**

Dr Peter Scarborough and team, who developed and provided the PRIME model used in this study.

**Data Sharing Statement**

The PRIME model is available upon request from Dr Peter Scarborough contactable at: peter.scarborough@dph.ox.ac.uk.

Population and health survey data were accessed through the Australian Bureau of Statistics TableBuilder. The mortality data (ICD deaths by remoteness) were provided by the AIHW under a specific data request.

**Conflict of Interest declaration**

The authors declare there are no conflicts of interest

**Funding acknowledgments**

MN, KP, LA and JJ are supported by funding from the National Heart Foundation of Australia and Deakin University. SA is supported by funding from an Australian National Health and Medical Research Council/ National Heart Foundation of Australia Career Development Fellowship (APP1045836). He is also a researcher on the US National Institutes of Health grant titled, "Systems Science to Guide Whole-of- Community Childhood Obesity Interventions" (1R01HL115485-01A1) and within a NHMRC Centre for Research Excellence in Obesity Policy and Food Systems (APP1041020).

**REFERENCES:**


1. AIHW. Mortality inequalities in Australia: bulletin 124. Canberra: AIHW; 2014.
2. ABS. Health Outside Major Cities Australia: ABS; 2011 [cited 2015 10/06/2015]. Available from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/4102.0Main+Features30Mar+2011.
3. Levin KA, Leyland AH. Urban-rural inequalities in ischemic heart disease in Scotland, 1981-1999. Am J Public Health. 2006 Jan;96(1):145-51.
4. Kulshreshtha A, Goyal A, Dabhadkar K, Veledar E, Vaccarino V. Urban-rural differences in coronary heart disease mortality in the United States: 1999-2009. Public Health Rep. 2014 Jan-Feb;129(1):19-29.
5. Terashima M, Rainham DG, Levy AR. A small-area analysis of inequalities in chronic disease prevalence across urban and non-urban communities in the Province of Nova Scotia, Canada, 2007-2011. BMJ open. 2014;4(5).
6. ABS. 3303.0 - Causes of Death, Australia, 2013 Australia: ABS; 2015 [cited 2016 29/02/2016]. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/3303.0~2013~Main%20Features~Summary%20of%20findings~10000.
7. Dinh Vu H, Heller RF, Lim LLY, D'Este C, O'Connell RL. Mortality after acute myocardial infarction is lower in metropolitan regions than in non-metropolitan regions. Journal of Epidemiology and Community Health. 2000;54(8):590-5.
8. Waters AM, Trinh L, Chau T, Bourchier M, Moon L. Latest statistics on cardiovascular disease in Australia. Clinical and Experimental Pharmacology and Physiology. 2013;40(6):347-56.
9. Sexton PT, Sexton TLH. Excess coronary mortality among Australian men and women living outside the capital city statistical divisions. Medical Journal of Australia. 2000;172(8):370-4.
10. Beard JR, Earnest A, Morgan G, Chan H, Summerhayes R, Dunn TM, et al. Socioeconomic disadvantage and acute coronary events: A spatiotemporal analysis. Epidemiology. 2008;19(3):485-92.
11. Dobson A, McLaughlin D, Vagenas D, Wong KY. Why are death rates higher in rural areas? Evidence from the Australian Longitudinal Study on Women's Health. Australian And New Zealand Journal Of Public Health. 2010;34(6):624-8.
12. Gausia K, Katzenellenbogen JM, Sanfilippo FM, Knuiman MW, Thompson PL, Hobbs MST, et al. Evidence-based prescribing of drugs for secondary prevention of acute coronary syndrome in Aboriginal and non- Aboriginal patients admitted to Western Australian hospitals. Internal Medicine Journal. 2014;44(4):353-61.
13. Jordan S, Wilson A, Dobson A. Management of heart conditions in older rural and urban Australian women. Internal Medicine Journal. 2011;41(10):722-9.
14. NHRHA. The determinants of health in rural and remote Australia: fact sheet 28. Australian Captial Territory: National Rural Health Alliance; 2011.
15. WHF. World Heart Federation: 25 by 2025 Targets. Melbourne: World Heart Federation, 2014.
16. NRHA. Smoking and rural health. Australian Capital Territory: National Rural Health Alliance; 2014.
17. Scarborough P, Harrington RA, Mizdrak A, Zhou LM, Doherty A. The Preventable Risk Integrated ModEl and Its Use to Estimate the Health Impact of Public Health Policy Scenarios. Scientifica. 2014;2014:748750.
18. Scarborough P, Morgan RD, Webster P, Rayner M. Differences in coronary heart disease, stroke and cancer mortality rates between England, Wales, Scotland and Northern Ireland: the role of diet and nutrition. BMJ open. 2011 Jan 1;1(1):e000263.
19. Scarborough P, Allender S, Clarke D, Wickramasinghe K, Rayner M. Modelling the health impact of environmentally sustainable dietary scenarios in the UK. European journal of clinical nutrition. 2012 Jun;66(6):710-5.

20. Belanger M, Poirier M, Jbilou J, Scarborough P. Modelling the impact of compliance with dietary recommendations on cancer and cardiovascular disease mortality in Canada. Public health. 2014 Mar;128(3):222-30.
21. ABS. Australian Statistical Geography Standard Canberra, Australia: ABS; 2014 [cited 2016 04/07/2016]. Available from: http://www.abs.gov.au/websitedbs/D3310114.nsf/home/Australian+Statistical+Geography+Standard+(ASGS).
22. ABS. TableBuilder:How to apply for access to microdata Australia: Australian Bureau of Statistics; 2011 [updated 30 June 2017; cited 2017 17/07/2017]. Available from: http://www.abs.gov.au/websitedbs/D3310114.nsf/home/About+TableBuilder.
23. ABS. 4363.0.55.001 - Australian Health Survey: Users' Guide, 2011-13: Sample design and selection Canberra: Australian Bureau of Statistics; 2015 [cited 2016 20/06/2016]. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4363.0.55.001Chapter2102011-13.
24. ABS. 4363.0.55.001 - Australian Health Survey: Users' Guide, 2011-13 : Adult Physical Activity: Australian Bureau of Statistics 2015 [cited 2016 27/06/2016]. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/59FF6FE5D62BABE1CA257BAC00225A07?opendocument.
25. 2014. AIoHaW. Australia's health 2014: Australia's health series no. 14. Cat. no. AUS 178: Health in regional and remote areas. . Canberra, Australia: AIHW; 2014.
26. Patterson KA, Cleland V, Venn A, Blizzard L, Gall S. A cross-sectional study of geographic differences in health risk factors among young Australian adults: the role of socioeconomic position. BMC public health. 2014;14:1278.
27. AIHW. Rural, regional and remote health: Indicators of health status and determinants of health. Canberra, Australia: Australian Institute of Health and Welfare; 2008.
28. Wu JR, Moser DK, DeWalt DA, Rayens MK, Dracup K. Health Literacy Mediates the Relationship Between Age and Health Outcomes in Patients With Heart Failure. Circulation Heart failure. 2016 Jan;9(1):e002250.
29. NHRA. Obesity in rural Australia. Australian Capital Territory: National Rural Health Alliance; 2013.
30. French SA, Story M, Jeffery RW. Environmental influences on eating and physical activity. Annual review of public health. 2001;22:309-35. PubMed PMID: 11274524.
31. health Q. 2014 Healthy food access basket survey, Queensland Queensland, Australia: Queensland Government; 2015 [cited 2016 22/06/2016]. Available from: https://www.health.qld.gov.au/research-reports/reports/food/access/guidelines/default.asp.
32. Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. Bmj. 2011 Feb 22;342:d671.
33. AIHW. Australia's health 2014: Leading types of ill health: AIHW; 2014 [cited 2016 22/06/2016]. Available from: http://www.aihw.gov.au/australias-health/2014/ill-health/#t.
34. Ball K, Mishra GD, Thane CW, A H. How well do Australian women comply with dietary guidelines? Public Health Nutrition 2004;4;7(3):443–52.
35. ABS. 4364.0.55.012 - Australian Health Survey: Consumption of Food Groups from the Australian Dietary Guidelines, 2011-12 Canberra, Asutra;oa: Australian Bureau of Statistics 2016 [cited 2016 04/07/2016]. Available from: http://www.abs.gov.au/websitedbs/D3310114.nsf/home/Australian+Statistical+Geography+Standard+(ASGS).
36. ABS. 4363.0.55.001 - Australian Health Survey: Users' Guide, 2011-13: UNDER-REPORTING IN NUTRITION SURVEYS Canberra: Australian Bureau of statistics; 2015 [cited 2016 20/06/2016]. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4363.0.55.001Chapter651512011-13.

501

502