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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.

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2
3 1 **TITLE:** Quantifying the role of modifiable risk factors in the differences in cardiovascular
4 2 disease mortality rates between metropolitan and rural populations in Australia: A
5 3 macrosimulation modelling study.

6
7 4 **Authors:** Laura Alston^a, Karen Louise Peterson^a, Jane P Jacobs^a, Steven Allender^a, Melanie
8 5 Nichols^a.

9
10 6 **Author affiliations:** ^aWHO Collaborating Centre for Obesity Prevention, Faculty of Health,
11 7 Deakin University, Geelong, Australia.

12
13 8 **Corresponding author:** Laura Alston. Address: WHO Collaborating Centre for Obesity
14 9 Prevention, Faculty of Health, Deakin University, Locked Bag 20001, Geelong, VIC 3220
15 10 Australia. Telephone: +61 3 5247 9426. Email: laura.alston@deakin.edu.au.

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28 20 Prevention

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2
3 24 **ABSTRACT**
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5 25 **Objectives:** Aims: (1) to quantify differences in modifiable risk factors between urban and rural
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7
8 26 populations, and (2) to determine the number of rural CVD and IHD deaths that could be averted or
9
10 27 delayed if risk factor levels in rural areas were equivalent to metropolitan areas.

11
12
13 28 **Setting:** National population estimates, risk factor prevalence, CVD and IHD deaths data were
14
15 29 analysed by rurality using the Preventable Risk Integrated Model (PRIME) macro-simulation chronic
16
17 30 disease risk model. Uncertainty analysis was conducted using a Monte Carlo simulation of 10,000
18
19 31 iterations to calculate 95% credible intervals (CI).

20
21
22 32 **Participants:** National datasets of males and females over the age of 18 years living in urban and
23
24 33 rural Australia.

25
26
27 34 **Results:** If people living in rural Australia had the same levels of risk factors as those in metropolitan
28
29 35 areas, approximately 1458 (95% credible interval (CI): 1088, 1803) deaths could be delayed from
30
31 36 cardiovascular disease (CVD) annually. Of these CVD deaths, 793 (95%CI: 506, 1065) would be from
32
33 37 IHD. The IHD mortality gap between metropolitan and rural populations would be reduced by 38.2%
34
35 38 (95%CI: 24.4%, 50.6%).

36
37
38 39 **Conclusions:** A significant portion of deaths from CVD and IHD could be averted with improvements
39
40 40 in risk factors; more than one third of the excess IHD deaths in rural Australia were attributed to
41
42 41 differences in risk factors. As much as two thirds of the increased IHD mortality rate in rural areas
43
44 42 could not be accounted for by modifiable risk factors, however, and this requires further
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46 43 investigation.

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47 **ARTICLE SUMMARY:**48 *Strengths:*

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

55 *Limitations:*

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

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3 69 **INTRODUCTION**
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6 70 Despite high quality, universal health care systems and standards in Australia, there are still
7
8 71 disparities in the burden of chronic disease experienced by people with lower socio-economic status,
9
10 72 Aboriginal and Torres Strait Islanders and rural residents(1). Australians living outside major cities
11
12 73 experience a substantially increased burden of cardiovascular diseases(2), which is consistent with
13
14 74 findings for rural populations in other developed countries such as the United States, Canada, and
15
16 75 the United Kingdom(3-5). Cardiovascular disease (CVD), in its most common form, Ischaemic heart
17
18 76 disease (IHD) is the leading cause of death in Australia(6), and individuals residing in a regional or
19
20 77 remote areas are estimated to be between 1.2 and 1.5 times more likely to die from IHD than those
21
22 78 residing in metropolitan areas(1).
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28
29 80 The reasons for observed health inequalities between metropolitan and rural populations appear to
30
31 81 be multifactorial and highly complex(2, 7-9). It has been hypothesised that rural populations
32
33 82 experience greater CVD and IHD burden due to variation in access to health services, individual
34
35 83 socio-economic status, rates of modifiable risk factors, as well as reduced access to evidence-based
36
37 84 treatments in rural hospitals(7, 10-13). The National Rural Health Alliance (NRHA) of Australia states
38
39 85 that if rural Australians are to achieve the same health outcomes as their metropolitan counterparts
40
41 86 by the year 2020, it is not just access to health services that need to be improved(14), but that more
42
43 87 focus needs to be placed on improving the socio-economic determinants of health (such as lower
44
45 88 education, incomes, and employment) for rural communities, and reducing risk factors for chronic
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47 89 diseases such as smoking and physical inactivity(14).
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3 92 Cardiovascular diseases, particularly IHD, are largely preventable (12), and the modifiable risk
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5 93 factors are well known(13). Clinical risk factors such as high cholesterol, high blood pressure, and
6
7 94 obesity interact with behavioural factors such as poor diet, smoking, risky alcohol consumption, and
8
9 95 physical inactivity to increase the risk of IHD and CVD(13). Based on population health surveys, these
10
11 96 risk factors differ by rurality, with higher smoking rates, increased high risk alcohol consumption and
12
13 97 lower physical activity levels being reported by non-city dwelling Australians(2).
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20 99 Currently, there is minimal evidence quantifying the extent to which modifiable risk factors
21
22 100 contribute to the increased burden of CVD and IHD in rural areas, and how much of this burden
23
24 101 could be reduced if behavioural risk factors were comparable among rural Australians as those
25
26 102 among their counterparts in cities. Increased knowledge of how differential risk factor rates
27
28 103 contribute to the increased rural CVD burden could support the identification of policy priorities and
29
30 104 prevention programs for rural areas, as previous public health prevention efforts have been shown
31
32 105 to be less effective for rural populations compared to those living in metropolitan areas(15).
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38 107 **Aims:**

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41 108 This study aimed to: (1) Quantify differences in prevalence of major CVD risk factors between rural
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43 109 and metropolitan populations, and (2) Determine the number and proportion of rural deaths from
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45 110 CVD, and specifically from IHD, that could be averted or delayed in rural areas if the levels of risk
46
47 111 factors were equivalent to those in metropolitan Australia.
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53 113 **METHODS**

56 114 **The Preventable Risk Integrated Model (PRIME)**

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2
3 115 This study used a macrosimulation model, the Preventable Risk Integrated Model (PRIME)(16), to
4
5 116 estimate age- and sex-specific changes in CVD and IHD mortality that would result from changes to
6
7 117 the population prevalence of risk factors in Australia. PRIME has been used in the UK, New Zealand
8
9 118 and Canada to model a range of risk factor scenarios(16-20). The model can be used to examine the
10
11 119 likely changes in mortality rates of many chronic diseases, including IHD, under different
12
13 120 counterfactual scenarios of population behavioural risk factors(16).

14
15
16 121 The PRIME model is built on a framework of linkage between, 1) modifiable behaviours; 2) clinical
17
18 122 risk factors; and 3) mortality outcomes. This framework is parameterised using the best available
19
20 123 evidence from meta-analyses of published studies, and is described in detail elsewhere(16). PRIME
21
22 124 requires data on prevalence of modifiable risk factors, mortality rates and population estimates by 5
23
24 125 year age groups and sex, for both baseline and counterfactual scenarios. For this study, PRIME was
25
26 126 used to estimate the number of CVD and IHD deaths that would be delayed or averted if those living
27
28 127 in rural Australia had the same modifiable risk factor levels as those living in major cities. The
29
30 128 baseline scenario used the current levels of modifiable risk factors in those living in rural areas, and
31
32 129 the counterfactual scenario involved applying the level of behavioural risk factors currently observed
33
34 130 among those living in metropolitan areas, to the rural population.

35 36 37 38 39 131 **Population data**

40
41 132 Population size estimates by age, sex and rurality were derived from the most recent (2011)
42
43 133 Australian Census. The 'rural' population was defined as all residents not classified by the ABS as
44
45 134 living in major cities(21).

46 47 48 49 135 **Risk factor data**

50
51 136 The risk factors included in the PRIME model were mean dietary intakes, alcohol consumption,
52
53 137 prevalence of smoking, and physical activity levels. Mean body mass index (BMI) scores, based on
54
55 138 measured height and weight data, from the rural population only, were also included in the baseline
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3 139 model. All risk factor estimates were obtained from the 2011-12 Australian Health Survey (AHS),
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5 140 which surveyed people aged 2 years and over from all areas of Australia, excluding very remote
6
7 141 areas(22). Results were generated for 9973 individuals aged 15 years and over.
8
9
10 142 Dietary intake data were collected using a 24-hour recall of all foods and fluids consumed in the day
11
12 143 prior to the interview. Participants provided 24-hour recall data on two separate occasions, at least 8
13
14 144 days apart. Implausible intakes were excluded if the day of intake data had an energy intake (EI) to
15
16 145 basal metabolic rate (BMR) ratio of less than 0.9, as per recommendation from the Australian
17
18 146 Bureau of Statistics(23). Mean daily dietary intakes were calculated for each participant for: energy
19
20 147 (kcal/day), fruit (g/day), vegetables (g/day), fibre (g/day), dietary cholesterol (mg/day), salt (g/day),
21
22 148 total fat (% EI), saturated fat (% EI), monounsaturated fat (% EI), and polyunsaturated fat (% EI). The
23
24 149 percentage of people who consumed less than one serve of fruit and less than one serve of
25
26 150 vegetables was also calculated as required by the model. Mean BMI for the rural population, by 5
27
28 151 year age group and sex, was required by the model, and the effect of obesity on mortality rates was
29
30 152 modelled using the differences in energy intake and physical activity levels between the two
31
32 153 populations. AHS participants were also asked to report if they were current smokers, ex-smokers,
33
34 154 or if they had never smoked, and the age- sex- and location-specific prevalence of each of these
35
36 155 categories were derived.
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41 156 The PRIME model requires the proportion of the population classified as 'sedentary', and physical
42
43 157 activity levels in the form of mean Metabolic Equivalent of Task (MET) hours per week, in the
44
45 158 remaining (active) population. The sedentary proportion of the population was calculated as the sum
46
47 159 of those classified as insufficiently active or sedentary by the ABS. Participants were classified as
48
49 160 insufficiently active or sedentary if they did not meet the physical activity recommendations of 150
50
51 161 minutes per week, over 5 separate sessions(24). Mean minutes of moderate and vigorous activity
52
53 162 over the last week as reported by AHS participants were used to calculate average daily minutes of
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3 163 activity. This duration was then multiplied by standard intensity factors (metabolic equivalents) to
4
5 164 convert the estimates to MET-hours of activity per week.
6
7

8 165 The model requires the percentage of non-drinkers within each population by age and sex, which
9
10 166 was calculated as those who reported either no alcohol consumption, or <1g per day, over the
11
12 167 surveyed period. Mean daily intake of pure alcohol in millilitres (mL), by age group and sex, was
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14 168 calculated as the weighted daily mean (mL) within TableBuilder, then converted to grams of pure
15
16 169 alcohol.
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18

19 170 **Mortality data**

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22 171 Deaths due to CVD (ICD-10 code 100-199) and IHD (ICD-10 code 120-125) by state or territory and
23
24 172 remoteness area of usual residence, by sex and 5-year age group, among people aged 15 years and
25
26 173 over was provided by the Australian Institute of Health and Welfare (AIHW) for the year 2011 from
27
28 174 the AIHW National Mortality Database (unpublished).
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30

31 175 **Mortality gap**

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33
34 176 The mortality gap between rural and metropolitan areas was calculated by applying the
35
36 177 metropolitan death rate for those aged 15 years and over, to the rural population, to determine the
37
38 178 number of rural deaths that would be expected if cause-specific mortality rates were equal between
39
40 179 metropolitan and rural areas. This figure was subtracted from the actual number of deaths in rural
41
42 180 areas, to calculate the gap in mortality between the two populations.
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45 181 **Uncertainty analysis**

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48 182 Monte Carlo simulation of 10,000 iterations was used to generate 95% credible intervals for each of
49
50 183 the estimates of deaths delayed or averted under the counterfactual scenario.
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52

53 184 **RESULTS**

54 55 56 185 **Differences in risk factors between rural and metropolitan areas** 57 58 59 60

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2
3 186 There were a mixture of differences in dietary intake, between rural and metropolitan (Table 1), that
4
5 187 were statistically significant for many dietary components, although many were relatively small in
6
7 188 absolute magnitude. Some of the differences in intakes were favourable in rural areas, and others,
8
9 189 more favourable in metropolitan areas. Vegetable intakes were significantly higher for rural
10
11 190 populations ($p < 0.001$), while intake of fruit was not significantly different between the two
12
13 191 populations.

14
15
16 192 Energy intakes and the percentage of energy from saturated fat were significantly higher among
17
18 193 rural populations ($p < 0.05$). Rural females reported a significantly higher dietary cholesterol intake
19
20 194 ($p < 0.05$) and lower percentage energy from polyunsaturated fat ($p < 0.01$) than their metropolitan
21
22 195 counterparts. There were no other significant differences in intake across the other dietary
23
24 196 components analysed.

25
26
27
28 197 Mean alcohol intake (g/day) in those who reported drinking alcohol was significantly higher in rural
29
30 198 areas for females ($p < 0.05$), however there was no differences for males. There were no significant
31
32 199 differences in the proportion of low alcohol consumers between the two populations. There were
33
34 200 significantly more current smokers in rural areas compared to major cities (females 19.5% vs 14.0%;
35
36 201 males 24.2% vs 18.7%). The proportion of people who had never smoked was higher in metropolitan
37
38 202 areas.

39
40
41 203 Mean BMI for females was significantly higher ($p < 0.001$) in rural areas compared to major cities
42
43 204 (females 26.8 vs 27.6 kg/m²; males 27.3 vs 27.8 kg/m²).

44
45
46 205 Fewer rural people were meeting recommendations for physical activity; 37.1% of males in rural
47
48 206 areas were meeting recommendations compared to 44.0% in major cities. This was also true for
49
50 207 females (36.5% in rural areas, 46.3% in cities). There were no significant differences between the
51
52 208 two populations in the mean MET hours per week of moderate-vigorous activity performed by the
53
54 209 active population.
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Table 1: Differences in dietary intakes, rural compared with metropolitan areas, females and males 2011-12, with 95% Confidence Intervals (CI).

| Dietary component | Females | | | | Males | | | |
|----------------------------|---|------------------------------------|-----------------|------------------|----------------------------|------------------------------------|-----------------|------------------|
| | 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

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

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

4 In total, 1461 (1107, 1791) or 11% of all rural CVD deaths would be delayed or averted, if rural
5 populations were to have the same levels of risk factors as their metropolitan counterparts (Table 2).

6 Of the deaths prevented from CVD, 793 (510, 1065) would be from IHD, slightly more of these
7 among males (418) than females (374), a 10.5% reduction in rural IHD deaths. Premature IHD deaths
8 (75 years and under), would account for 38.3% of the IHD deaths that would be delayed or averted,
9 or 4% of all rural IHD deaths. Most of these premature deaths would be averted for males, 266 (232,
10 301) compared to 37 (28, 46) in females.

11 *Table 2: Deaths averted or delayed from chronic diseases in rural Australia, under the*
12 *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% |

14 Deaths attributable to individual risk factors

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

18 areas, contributing 1,309 (1000, 1608), and 337 (290, 388) deaths delayed or averted respectively for
 19 CVD, and 740 (95% CI: 504, 955) and 225 (95% CI: 192, 260) for IHD. The adjustment of fruit and
 20 vegetable intakes showed that more people would die from CVD (-290 (-475, -103)) and IHD (-298
 21 (95% CI: -486, -111)) if intakes in rural areas were adjusted to match those of metropolitan areas,
 22 since in this case vegetable intakes would be worse under the counterfactual scenario. If the rural
 23 diet as an individual risk factor were to be adjusted to the counterfactual scenario, an additional 190
 24 (95% CI: 4, 380) IHD deaths would occur among rural Australians.

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

30 *Table 3: Preventable deaths from CVD and IHD attributable to individual risk factors if rural*
 31 *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) |
|----------------|------------------|----------------|

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

34

35 **DISCUSSION**

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

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

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

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3 56 outcomes for rural populations, as lower health literacy has been linked to poorer outcomes in
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5 57 patients with heart disease(27).
6
7
8 58 In terms of individual risk factors, differences in obesity and tobacco smoking appeared to have the
9
10 59 biggest impact on the increased burden of IHD in the rural population, when compared to
11
12 60 metropolitan areas. Obesity is a well-known risk factor for IHD(28), and has been consistently shown
13
14 61 to be higher in rural populations of Australia for the past few decades(29, 30). Differences in energy
15
16 62 intake and physical activity energy expenditure between rural and metropolitan populations led to
17
18 63 substantial reductions in obesity-mediated mortality in the counterfactual scenario. These
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20 64 reductions explained the largest proportion of the mortality gap between the two populations of any
21
22 65 of the behaviours studied. Higher energy intakes in the rural sample, which increase the likelihood
23
24 66 of a higher BMI(31), could be reflective of the consumption of more low cost, energy dense foods
25
26 67 possibly in part, due to reduced access to healthier foods, which has been well documented in rural
27
28 68 and regional areas(32).
29
30
31
32 69 Tobacco smoking is recognised as the largest single preventable cause of mortality and morbidity in
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34 70 Australia (33), and higher smoking rates in rural areas have been apparent since at least 1993(15,
35
36 71 25). Despite numerous public health initiatives and interventions over this period, the rural smoking
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38 72 rate has remained comparatively high whilst the metropolitan rate has continued to decline(15, 33),
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40 73 possibly indicating that such preventative efforts have not adequately reached rural Australians(15).
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44 74 The results of this study suggest that substantial gains could be made in reducing the CVD mortality
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46 75 gap between metropolitan and rural populations if modifiable risk behaviours could be improved in
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48 76 rural areas. Improving risk factor profiles in rural populations to at least match that of their
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50 77 metropolitan counterparts could be assumed to be a reasonable target, given that even
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52 78 metropolitan risk factor levels are far from ideal(34, 35). Importantly, even if this scenario were to
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54 79 be achieved, a significant proportion (almost two-thirds) of the excess deaths would remain, a
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3 80 finding which should prompt major reflection on the role of disadvantage, health care provision and
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5 81 other, less prominent risk factors in the perpetuation of rural health inequalities.
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22 83 **Strengths:**

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24 84 This study used three representative national datasets, including the Census, AIHW National
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26 85 Mortality Database and the Australian Health Survey, as inputs for the PRIME model. The PRIME
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28 86 model also has many strengths, including that it is able to model the effect of changes in multiple
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30 87 risk factors simultaneously on mortality rates from different chronic diseases, by age and sex. The
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32 88 model has been designed using the strongest available scientific evidence on the links between
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34 89 chronic disease mortality and dietary intake, alcohol consumption, smoking, physical activity and
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36 90 obesity levels(16).
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49 91 **Limitations:**

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51 92 Data used in the model were self-reported, which carries multiple limitations, and could lead to
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53 93 underestimations of the level of behavioural risk factors and subsequently, mortality gap reductions
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55 94 (23), although it less likely that these biases would differentially affect rural vs metro populations.
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57 95 Very remote areas of Australia were not sampled in AHS, therefore risk factor levels for these
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59 96 populations were not included in the analysis(22). This may lead to an underestimation of the
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61 97 prevalence of some risk factors, as residents of very remote areas are known to experience even
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63 98 higher burden from IHD than the broader rural population(2), however they also represent a very
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65 99 small percentage of the total Australian population (0.9%)(25). The uncertainty analysis conducted
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67 100 on the number of deaths averted, only accounts for uncertainty within the model parameters, but
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69 101 not the uncertainty of estimates from the Australian Health Survey.
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102 **CONCLUSIONS**

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3 103 There is potential for improvements in the level of cardiovascular disease burden observed in rural
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5 104 Australians, if the prevalence of modifiable risk factors such as obesity and smoking were to be
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7 105 reduced to match those of metropolitan areas. If such a scenario was to be achieved, 38% of the
8
9 106 mortality gap between rural and metropolitan areas could be reduced, however, investigations into
10
11 107 factors responsible for the remaining 62% of this inequality are needed in order to work towards
12
13 108 achieving health equality for rural populations.

16 109 **Author Contributions**

17
18 110 LA organised the collection and conversion of data, completed all data entry into the PRIME model,
19
20 111 analysis of the results, and writing of the manuscript. MN contributed to defining the original
21
22 112 research idea, data collection, use of the PRIME model and analysis. KP and JJ assisted with
23
24 113 conversion of the data to be compatible with the PRIME model. SA contributed to defining the
25
26 114 original research idea. All authors reviewed and contributed to the manuscript and all stages of
27
28 115 compilation.

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38 120 **Conflict of Interest declaration**

39
40 121 The authors declare there are no conflicts of interest

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44
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48
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50
51 127 (APP1045836). He is also a researcher on the US National Institutes of Health grant titled, "Systems
52
53 128 Science to Guide Whole-of- Community Childhood Obesity Interventions" (1R01HL115485-01A1) and
54
55 129 within a NHMRC Centre for Research Excellence in Obesity Policy and Food Systems (APP1041020).

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

| Dietary component | Females | | | | Males | | | |
|----------------------------|---|------------------------------------|-----------------|------------------|----------------------------|------------------------------------|-----------------|------------------|
| | 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 |

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|-----------------------------------|-------------------|-------------------|-----|----------|-------------------|-------------------|-----|----------|
| (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

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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.

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

4 **Authors:** Laura Alston^a, Karen Louise Peterson^a, Jane P Jacobs^a, Steven Allender^a, Melanie
5 Nichols^a.

6 **Author affiliations:** ^aGlobal Obesity Centre, Faculty of Health, Deakin University, Geelong,
7 Australia.

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

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15 Australia Career Development Fellowship (APP1045836). He is also a researcher on the US
16 National Institutes of Health grant titled, "Systems Science to Guide Whole-of- Community
17 Childhood Obesity Interventions" (1R01HL115485-01A1) and within a NHMRC Centre for
18 Research Excellence in Obesity Policy and Food Systems (APP1041020).

19

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

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

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2
3 25 **ABSTRACT**
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5 26 **Objectives:** Aims: (1) to quantify differences in modifiable risk factors between urban and rural
6
7 27 populations, and (2) to determine the number of rural cardiovascular disease (CVD) and ischaemic
8
9 28 heart disease (IHD) deaths that could be averted or delayed if risk factor levels in rural areas were
10
11 29 equivalent to metropolitan areas.
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15 30 **Setting:** National population estimates, risk factor prevalence, CVD and IHD deaths data were
16
17 31 analysed by rurality using the Preventable Risk Integrated Model (PRIME) macro-simulation chronic
18
19 32 disease risk model. Uncertainty analysis was conducted using a Monte Carlo simulation of 10,000
20
21 33 iterations to calculate 95% credible intervals (CI).
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24 34 **Participants:** National datasets of males and females over the age of 18 years living in urban and
25
26 35 rural Australia.
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29 36 **Results:** If people living in rural Australia had the same levels of risk factors as those in metropolitan
30
31 37 areas, approximately 1461 (95% credible interval (CI): 1107, 1791) deaths could be delayed from
32
33 38 cardiovascular disease (CVD) annually. Of these CVD deaths, 793 (95%CI: 506, 1065) would be from
34
35 39 IHD. The IHD mortality gap between metropolitan and rural populations would be reduced by 38.2%
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37 40 (95%CI: 24.4%, 50.6%).
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39
40 41 **Conclusions:** A significant portion of deaths from CVD and IHD could be averted with improvements
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42 42 in risk factors; more than one third of the excess IHD deaths in rural Australia were attributed to
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44 43 differences in risk factors. As much as two thirds of the increased IHD mortality rate in rural areas
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46 44 could not be accounted for by modifiable risk factors, however, and this requires further
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48 45 investigation.
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49 **ARTICLE SUMMARY:**50 *Strengths:*

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

57 *Limitations:*

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

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3 71 **INTRODUCTION**
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6 72 Despite high quality, universal health care systems and standards in Australia, there are still
7
8 73 disparities in the burden of chronic disease experienced by people with lower socio-economic status,
9
10 74 Aboriginal and Torres Strait Islanders and rural residents(1). Australians living outside major cities
11
12 75 experience a substantially increased burden of cardiovascular diseases(2), which is consistent with
13
14 76 findings for rural populations in other developed countries such as the United States, Canada, and
15
16 77 the United Kingdom(3-5). Cardiovascular disease (CVD), in its most common form, Ischaemic heart
17
18 78 disease (IHD) is the leading cause of death in Australia(6), and individuals residing in a regional or
19
20 79 remote areas are estimated to be between 1.2 and 1.5 times more likely to die from IHD than those
21
22 80 residing in metropolitan areas(1).
23
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27
28 82 The reasons for observed health inequalities between metropolitan and rural populations appear to
29
30 83 be multifactorial and highly complex(2, 7-9). It has been hypothesised that rural populations
31
32 84 experience greater CVD and IHD burden due to variation in access to health services, individual
33
34 85 socio-economic status, rates of modifiable risk factors, as well as potentially reduced access to
35
36 86 specialised evidence-based treatments, such as prompt surgical intervention in rural hospitals(7, 10-
37
38 87 13). The National Rural Health Alliance (NRHA) of Australia states that if rural Australians are to
39
40 88 achieve the same health outcomes as their metropolitan counterparts by the year 2020, it is not just
41
42 89 access to health services that need to be improved(14), but that more focus needs to be placed on
43
44 90 improving the socio-economic determinants of health (such as lower education, incomes, and
45
46 91 employment) for rural communities, and reducing risk factors for chronic diseases such as smoking
47
48 92 and physical inactivity(14).
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1
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3 95 Cardiovascular diseases, particularly IHD, are largely preventable, and the modifiable, behavioural
4
5 96 risk factors are well known(15). Clinical risk factors such as high cholesterol, high blood pressure, and
6
7 97 obesity interact with behavioural factors such as poor diet, smoking, risky alcohol consumption, and
8
9 98 physical inactivity to increase the risk of IHD and CVD(13). Based on population health surveys, these
10
11 99 risk factors differ by rurality, with higher smoking rates, increased high risk alcohol consumption and
12
13
14 100 lower physical activity levels being reported by non-city dwelling Australians(2).
15
16
17 101
18
19
20 102 Currently, there is minimal evidence quantifying the extent to which modifiable individual risk
21
22 103 factors contribute to the increased burden of CVD and IHD in rural areas, and how much of this
23
24 104 burden could be reduced if behavioural risk factors were comparable among rural Australians as
25
26 105 those among their counterparts in cities. Increased knowledge of how differential risk factor rates
27
28 106 contribute to the increased rural CVD burden could support the identification of policy priorities and
29
30 107 prevention programs for rural areas, as previous public health prevention efforts have been shown
31
32 108 to be less effective for rural populations compared to those living in metropolitan areas(16).
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37

38 110 **Aims:**

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40
41 111 This study aimed to: (1) Quantify differences in prevalence of major CVD risk factors between rural
42
43 112 and metropolitan populations, and (2) Determine the number and proportion of rural deaths from
44
45 113 CVD, and specifically from IHD, that could be averted or delayed in rural areas if the levels of risk
46
47 114 factors were equivalent to those in metropolitan Australia.
48
49
50 115

51 52 53 116 **METHODS**

54 55 56 117 **The Preventable Risk Integrated Model (PRIME)** 57 58 59 60

1
2
3 118 This study used a macrosimulation model, the Preventable Risk Integrated Model (PRIME)(17), to
4
5 119 estimate age- and sex-specific changes in CVD and IHD mortality that would result from changes to
6
7 120 the population prevalence of risk factors in Australia. An exemption from ethics review was obtained
8
9 121 from Deakin University's Human Research Ethics Unit. PRIME has been used in the UK, New Zealand
10
11 122 and Canada to model a range of risk factor scenarios(17-20). The model can be used to examine the
12
13 123 likely changes in mortality rates of many chronic diseases, including IHD, under different
14
15 124 counterfactual scenarios of population behavioural risk factors(17).

16
17
18
19 125 The PRIME model is built on a framework of linkage between, 1) modifiable behaviours; 2) clinical
20
21 126 risk factors; and 3) mortality outcomes. This framework is parameterised using the best available
22
23 127 evidence from meta-analyses of published studies, and is described in detail elsewhere(17). PRIME
24
25 128 requires data on prevalence of modifiable risk factors, mortality rates and population estimates by 5
26
27 129 year age groups and sex, for both baseline and counterfactual scenarios. For this study, PRIME was
28
29 130 used to estimate the number of CVD and IHD deaths that would be delayed or averted if those living
30
31 131 in rural Australia had the same modifiable risk factor levels as those living in major cities. The
32
33 132 baseline scenario used the current levels of modifiable risk factors in those living in rural areas, and
34
35 133 the counterfactual scenario involved applying the level of risk factors currently observed in the
36
37 134 metropolitan population. An additional 'best case' scenario was also modelled, by only changing risk
38
39 135 factor levels that were more favourable among those living in metropolitan areas, when compared
40
41 136 to the rural population.

42 43 44 45 137 **Population data**

46
47
48 138 Population size estimates by age, sex and rurality were derived from the 2011 Australian Census.
49
50 139 The 'rural' population was defined as all residents not classified by the ABS as living in major
51
52 140 cities(21). These data were accessed through subscription to the online ABS data program
53
54 141 TableBuilder(22).

55 56 57 142 **Risk factor data**

1
2
3 143 The individual modifiable risk factors included in the PRIME model (table 1) were; mean dietary
4
5 144 intakes, alcohol consumption, prevalence of smoking, physical activity levels and mean body mass
6
7 145 index (BMI) scores. All risk factor estimates were obtained from 9973 individuals aged 15 years and
8
9
10 146 over surveyed for the 2011-12 Australian Health Survey (AHS), which surveyed people from all areas
11
12 147 of Australia, excluding very remote areas(23). Mean values were calculated by age, sex and
13
14 148 remoteness for each risk factor parameter, through the ABS program TableBuilder(22).

15
16
17 149 *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 |

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

151

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

1
2
3 155 basal metabolic rate (BMR) ratio of less than 0.9, as per recommendation from the Australian
4
5 156 Bureau of Statistics(23). Mean daily dietary intakes from the two days of data collection were
6
7 157 calculated for each participant for: energy (kcal/day), fruit (g/day), vegetables (g/day), fibre (g/day),
8
9 158 dietary cholesterol (mg/day), salt (g/day), total fat (% EI), saturated fat (% EI), monounsaturated fat
10
11 159 (% EI), and polyunsaturated fat (% EI). The percentage of people who consumed less than one serve
12
13
14 160 of fruit and less than one serve of vegetables was also calculated as required by the model. Mean
15
16 161 BMI for the rural population, by 5 year age group and sex, was required by the model, and the effect
17
18 162 of obesity on mortality rates was modelled using the differences in energy intake and physical
19
20 163 activity levels between the two populations. Participants reported if they were current smokers, ex-
21
22 164 smokers, or if they had never smoked, and the age- sex- and location-specific prevalence of each of
23
24 165 these categories were derived.

26
27 166 The PRIME model requires the proportion of the population classified as 'sedentary', and physical
28
29 167 activity levels in the form of mean Metabolic Equivalent of Task (MET) hours per week, in the
30
31 168 remaining (active) population. The sedentary proportion of the population was calculated as the sum
32
33 169 of those classified as insufficiently active or sedentary by the ABS. Participants were classified as
34
35 170 insufficiently active or sedentary if they did not meet the physical activity recommendations of 150
36
37 171 minutes per week, over 5 separate sessions(24). Mean minutes of moderate and vigorous activity
38
39 172 over the last week were used to calculate average daily minutes of activity. This duration was then
40
41 173 multiplied by metabolic equivalents as provided by the ABS, to convert the estimates to MET-hours
42
43 174 of activity per week.

46
47 175 The model requires the percentage of non-drinkers within each population by age and sex, which
48
49 176 was calculated as those who reported either no alcohol consumption, or <1g per day on average,
50
51 177 over the surveyed period. Mean daily intake of pure alcohol in millilitres (mL), by age group and sex,
52
53 178 was calculated as the weighted daily mean (mL) within TableBuilder, then converted to grams of
54
55 179 pure alcohol.
56
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180 Mortality data

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

186 Mortality gap

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

192 Uncertainty analysis

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

201 RESULTS**202 Differences in individual risk factors between rural and metropolitan areas**

1
2
3 203 There were a mixture of differences in dietary intake, between rural and metropolitan (Table 2), that
4
5 204 were statistically significant for many dietary components, although many were relatively small in
6
7 205 absolute magnitude. Two of the dietary intake levels were more favourable in rural areas, and the
8
9 206 rest were more favourable in metropolitan areas. Vegetable intakes were significantly higher for
10
11 207 rural populations ($p < 0.001$), also resulting in a slightly higher fibre intake, while intake of fruit was
12
13 208 not significantly different between the two populations.

14
15
16 209 Energy intakes and the percentage of energy from saturated fat were significantly higher among
17
18 210 rural populations ($p < 0.05$). Rural females reported a significantly higher dietary cholesterol intake
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20 211 ($p < 0.05$) and lower percentage energy from polyunsaturated fat ($p < 0.01$) than their metropolitan
21
22 212 counterparts. There were no other significant differences in intake across the other dietary
23
24 213 components analysed.

25
26
27
28 214 Mean alcohol intake (g/day) in those who reported drinking alcohol was significantly higher in rural
29
30 215 areas for females ($p < 0.05$), however there was no differences for males. There were significantly
31
32 216 more current smokers in rural areas compared to major cities (females 19.5% vs 14.0%; males 24.2%
33
34 217 vs 18.7%). The proportion of people who had never smoked was higher in metropolitan areas.

35
36
37 218 Fewer rural people were meeting recommendations for physical activity; 37.1% of males in rural
38
39 219 areas were meeting recommendations compared to 44.0% in major cities. This was also true for
40
41 220 females (36.5% in rural areas, 46.3% in cities). There were no significant differences between the
42
43 221 two populations in the mean MET hours per week of moderate-vigorous activity performed by the
44
45 222 active population.

46
47
48 223 Smoking rates were significantly higher in rural areas for both females and males. Mean BMI for
49
50 224 females was significantly higher ($p < 0.001$) in rural areas compared to major cities (females 26.8 vs
51
52 225 27.6 kg/m²; males 27.3 vs 27.8 kg/m²).

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

| Dietary component | Females | | | | Males | | | |
|----------------------------|---|------------------------------------|-----------------|------------------|----------------------------|------------------------------------|-----------------|------------------|
| | 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) | 0.1 | 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

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

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

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

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

17
18 *Table 3: Deaths averted or delayed from chronic diseases in rural Australia, under the*
19 *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% |

20

21 **Deaths attributable to individual risk factors**

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

30

31 *Table 4: Preventable deaths from CVD and IHD attributable to individual risk factors if*
 32 *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) |

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

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

42 *Table 5: Deaths averted or delayed from chronic diseases in rural Australia, under the 'best case'*
 43 *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% |

44

45

46 **DISCUSSION**

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

1
2
3 49 health policy and intervention planning. Importantly, however, over 60% of the increased mortality
4
5 50 burden in rural areas was unexplained by risk factor differences.
6
7

8 51 The majority of individual risk factors were found to differ between rural and metropolitan areas,
9
10 52 with significantly higher BMI, energy intakes and proportion of energy intake from fats observed in
11
12 53 rural populations, along with higher levels of high risk alcohol consumption and sedentary
13
14 54 behaviour. Rural people did, however, report significantly higher vegetable intakes, which equated
15
16 55 to consumption of approximately 10% more vegetables than their metropolitan counterparts,
17
18 56 consistent with previous health survey data(2).
19

20
21 57 The origins of the differences in individual modifiable IHD risk factors between rural and
22
23 58 metropolitan areas(2), are likely to be complex, arising from the interaction of a range of factors at
24
25 59 the individual and community level, including socio-economic disadvantage, education levels, access
26
27 60 to primary health services and health literacy(28). Living outside of metropolitan areas has been
28
29 61 associated with more risk factors for chronic diseases in adults(25), with some evidence that
30
31 62 geographic location should be assessed as a social determinant of health, above and beyond socio-
32
33 63 economic status and area level disadvantage(26). There is evidence for this in that self-reported
34
35 64 prevalence of IHD, diabetes and cerebrovascular disease were found to be similar in rural and
36
37 65 metropolitan areas, despite much higher measured mortality rates from these diseases in rural
38
39 66 areas, potentially revealing reduced health awareness in rural populations(27). This may be an
40
41 67 important contributor to differences in outcomes for rural populations, as lower health literacy has
42
43 68 been linked to poorer outcomes in patients with heart disease(28).
44
45
46
47

48 69 In terms of individual risk factors, differences in obesity and tobacco smoking appeared to have the
49
50 70 biggest impact on the increased burden of IHD in the rural population, when compared to
51
52 71 metropolitan areas. Obesity is a well-known risk factor for IHD(15), and has been consistently shown
53
54 72 to be higher in rural populations of Australia for the past few decades(27, 29). Differences in energy
55
56 73 intake and physical activity energy expenditure between rural and metropolitan populations led to
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2
3 74 substantial reductions in obesity-mediated mortality in the counterfactual scenario. These
4
5 75 reductions explained the largest proportion of the mortality gap between the two populations of any
6
7 76 of the behaviours studied. Higher energy intakes in the rural sample, which increase the likelihood
8
9 77 of a higher BMI(30), could be reflective of the consumption of more low cost, energy dense foods
10
11 78 possibly in part, due to reduced access to healthier foods, which has been well documented in rural
12
13 79 and regional areas(31).

14
15
16
17 80 The cardio-protective effects of alcohol consumption are often debated(32). Our results showed that
18
19 81 current levels of alcohol intake do not appear to contribute to increased cardiovascular risk for rural
20
21 82 populations, with 55 fewer CVD deaths averted (an increase in deaths overall) as a result of the
22
23 83 difference in consumption between the two populations. This was mainly due to the fact that
24
25 84 although overall intakes were higher in rural areas, intakes among males over 75 years of age were
26
27 85 lower in rural areas than in metro areas, therefore leading to a modelled increase in consumption
28
29 86 and therefore associated deaths in this group under the counterfactual scenario.

30
31
32 87 Tobacco smoking is recognised as the largest single preventable cause of mortality and morbidity in
33
34 88 Australia(33), and higher smoking rates in rural areas have been apparent since at least 1993(16, 25).
35
36 89 Despite numerous public health initiatives and interventions over this period, the rural smoking rate
37
38 90 has remained comparatively high whilst the metropolitan rate has continued to decline(16, 33),
39
40 91 possibly indicating that such preventative efforts have not adequately reached rural Australians(16).

41
42
43 92 The results of this study suggest that substantial gains could be made in reducing the CVD mortality
44
45 93 gap between metropolitan and rural populations if modifiable risk factors could be improved in rural
46
47 94 areas. Improving risk factor profiles in rural populations to at least match that of their metropolitan
48
49 95 counterparts could be assumed to be a reasonable target, and is certainly a relatively modest goal,
50
51 96 given that even metropolitan risk factor levels are far from ideal(34, 35). Importantly, even if this risk
52
53 97 factor reduction scenario were to be achieved, a significant proportion (almost two-thirds) of the
54
55 98 excess deaths would remain, a finding which should prompt major reflection on the role of
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3 99 disadvantage, health care provision and other, less prominent risk factors in the perpetuation of
4
5 100 rural health inequalities.
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10
11 102 **Strengths:**

12
13 103 This study used three routinely collected, representative national datasets, including the Census,
14
15 104 AIHW National Mortality Database and the Australian Health Survey, as inputs for the PRIME model.
16
17 105 These datasets represent the highest quality, and comprehensive population data available currently
18
19 106 for Australia. The use of three robust datasets is required for PRIME to provide accurate disease
20
21 107 outputs. The PRIME model also has many strengths, including that it is able to model the effect of
22
23 108 changes in multiple risk factors simultaneously on mortality rates from different chronic diseases, by
24
25 109 age and sex. The model has been designed using the strongest available scientific evidence on the
26
27 110 links between chronic disease mortality and dietary intake, alcohol consumption, smoking, physical
28
29 111 activity and obesity levels(16).
30
31
32

33 112 **Limitations:**

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36 113 Data used in the model were self-reported, which carries multiple limitations, and could lead to
37
38 114 underestimations of the level of behavioural risk factors and subsequently, mortality gap reductions
39
40 115 (36), although it less likely that these biases would differentially affect rural vs metro populations.
41
42 116 Very remote areas of Australia were not sampled in AHS, therefore risk factor levels for these
43
44 117 populations were not included in the analysis(23). This may lead to an underestimation of the
45
46 118 prevalence of some risk factors, as residents of very remote areas are known to experience even
47
48 119 higher burden from IHD than the broader rural population(2), however they also represent a very
49
50 120 small percentage of the total Australian population (0.9%)(25). The uncertainty analysis conducted
51
52 121 on the number of deaths averted, only accounts for uncertainty within the model parameters, but
53
54 122 not the uncertainty of estimates from the Australian Health Survey. Lastly, we were unable to
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3 123 account for the diversity in characteristics between differing levels of remoteness (e.g. inner regional
4
5 124 areas compared to outer regional or remote areas) due to small population numbers. Instead, it was
6
7 125 necessary to make a single comparison between those living within and outside major cities.
8
9 126 Differences in population characteristics, access to health services and environmental factors can
10
11 127 vary significantly by differing levels of remoteness, and this is an important consideration for policy
12
13 128 and planning when trying to improve health in non-metropolitan areas.

16 129 **CONCLUSIONS**

19 130 There is potential for improvements in the level of cardiovascular disease burden observed in rural
20
21 131 Australians, if the prevalence of modifiable risk factors such as obesity and smoking were to be
22
23 132 reduced to match those of metropolitan areas. If such a scenario was to be achieved, 38% of the
24
25 133 mortality gap between rural and metropolitan areas could be reduced, however, investigations into
26
27 134 factors responsible for the remaining 62% of this inequality are needed in order to work towards
28
29 135 achieving health equality for rural populations.

32 136 **Author Contributions**

33 137 LA organised access to and analysis of the raw data, completed all data entry into the PRIME model,
34
35 138 analysis of the results, and writing of the manuscript. MN contributed to defining the original
36
37 139 research idea, data collection, use of the PRIME model and analysis. KP and JJ assisted with data
38
39 140 analysis. SA contributed to defining the original research idea. All authors reviewed and contributed
40
41 141 to the manuscript and all stages of compilation.

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46 142

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49 144 Dr Peter Scarborough and team, who developed and provided the PRIME model used in this study.

50
51 145

53 146 **Data Sharing Statement**

54
55 147 The PRIME model is available upon request from Dr Peter Scarborough contactable at:
56
57 148 peter.scarsborough@dph.ox.ac.uk.

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3 149 Population and health survey data were accessed through the Australian Bureau of Statistics
4
5 150 TableBuilder. The mortality data (ICD deaths by remoteness) were provided by the AIHW under a
6
7 151 specific data request.
8
9 152

10 153 **Conflict of Interest declaration**

11
12 154 The authors declare there are no conflicts of interest
13
14 155

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24
25 161 Science to Guide Whole-of- Community Childhood Obesity Interventions" (1R01HL115485-01A1) and
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27 162 within a NHMRC Centre for Research Excellence in Obesity Policy and Food Systems (APP1041020).
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For peer review only

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.

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

4 **Authors:** Laura Alston^a, Karen Louise Peterson^a, Jane P Jacobs^a, Steven Allender^a, Melanie
5 Nichols^a.

6 **Author affiliations:** ^aGlobal Obesity Centre, Faculty of Health, Deakin University, Geelong,
7 Australia.

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

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15 Australia Career Development Fellowship (APP1045836). He is also a researcher on the US
16 National Institutes of Health grant titled, "Systems Science to Guide Whole-of- Community
17 Childhood Obesity Interventions" (1R01HL115485-01A1) and within a NHMRC Centre for
18 Research Excellence in Obesity Policy and Food Systems (APP1041020).

19

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

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

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2
3 25 **ABSTRACT**
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5 26 **Objectives:** Aims: (1) to quantify differences in modifiable risk factors between urban and rural
6
7
8 27 populations, and (2) to determine the number of rural cardiovascular disease (CVD) and ischaemic
9
10 28 heart disease (IHD) deaths that could be averted or delayed if risk factor levels in rural areas were
11
12 29 equivalent to metropolitan areas.

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14
15 30 **Setting:** National population estimates, risk factor prevalence, CVD and IHD deaths data were
16
17 31 analysed by rurality using the Preventable Risk Integrated Model (PRIME) macro-simulation chronic
18
19 32 disease risk model. Uncertainty analysis was conducted using a Monte Carlo simulation of 10,000
20
21 33 iterations to calculate 95% credible intervals (CI).
22
23

24 34 **Participants:** National datasets of males and females over the age of 18 years living in urban and
25
26 35 rural Australia.
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29 36 **Results:** If people living in rural Australia had the same levels of risk factors as those in metropolitan
30
31 37 areas, approximately 1461 (95% credible interval (CI): 1107, 1791) deaths could be delayed from
32
33 38 cardiovascular disease (CVD) annually. Of these CVD deaths, 793 (95%CI: 506, 1065) would be from
34
35 39 IHD. The IHD mortality gap between metropolitan and rural populations would be reduced by 38.2%
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37 40 (95%CI: 24.4%, 50.6%).
38
39

40 41 **Conclusions:** A significant portion of deaths from CVD and IHD could be averted with improvements
41
42 42 in risk factors; more than one third of the excess IHD deaths in rural Australia were attributed to
43
44 43 differences in risk factors. As much as two thirds of the increased IHD mortality rate in rural areas
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46 44 could not be accounted for by modifiable risk factors, however, and this requires further
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48 45 investigation.
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49 **ARTICLE SUMMARY:**50 *Strengths:*

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

57 *Limitations:*

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

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3 71 **INTRODUCTION**
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6 72 Despite high quality, universal health care systems and standards in Australia, there are still
7
8 73 disparities in the burden of chronic disease experienced by people with lower socio-economic status,
9
10 74 Aboriginal and Torres Strait Islanders and rural residents(1). Australians living outside major cities
11
12 75 experience a substantially increased burden of cardiovascular diseases(2), which is consistent with
13
14 76 findings for rural populations in other developed countries such as the United States, Canada, and
15
16 77 the United Kingdom(3-5). Cardiovascular disease (CVD), in its most common form, Ischaemic heart
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18 78 disease (IHD) is the leading cause of death in Australia(6), and individuals residing in a regional or
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20 79 remote areas are estimated to be between 1.2 and 1.5 times more likely to die from IHD than those
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22 80 residing in metropolitan areas(1).
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28 82 The reasons for observed health inequalities between metropolitan and rural populations appear to
29
30 83 be multifactorial and highly complex(2, 7-9). It has been hypothesised that rural populations
31
32 84 experience greater CVD and IHD burden due to variation in access to health services, individual
33
34 85 socio-economic status, rates of modifiable risk factors, as well as potentially reduced access to
35
36 86 specialised evidence-based treatments, such as prompt surgical intervention in rural hospitals(7, 10-
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38 87 13). The National Rural Health Alliance (NRHA) of Australia states that if rural Australians are to
39
40 88 achieve the same health outcomes as their metropolitan counterparts by the year 2020, it is not just
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42 89 access to health services that need to be improved(14), but that more focus needs to be placed on
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44 90 improving the socio-economic determinants of health (such as lower education, incomes, and
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46 91 employment) for rural communities, and reducing risk factors for chronic diseases such as smoking
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48 92 and physical inactivity(14).
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3 95 Cardiovascular diseases, particularly IHD, are largely preventable, and the modifiable, behavioural
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5 96 risk factors are well known(15). Clinical risk factors such as high cholesterol, high blood pressure, and
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7 97 obesity interact with behavioural factors such as poor diet, smoking, risky alcohol consumption, and
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9 98 physical inactivity to increase the risk of IHD and CVD(13). Based on population health surveys, these
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11 99 risk factors differ by rurality, with higher smoking rates, increased high risk alcohol consumption and
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14 100 lower physical activity levels being reported by non-city dwelling Australians(2).
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20 102 Currently, there is minimal evidence quantifying the extent to which modifiable individual risk
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22 103 factors contribute to the increased burden of CVD and IHD in rural areas, and how much of this
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24 104 burden could be reduced if behavioural risk factors were comparable among rural Australians as
25
26 105 those among their counterparts in cities. Increased knowledge of how differential risk factor rates
27
28 106 contribute to the increased rural CVD burden could support the identification of policy priorities and
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30 107 prevention programs for rural areas, as previous public health prevention efforts have been shown
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32 108 to be less effective for rural populations compared to those living in metropolitan areas(16).
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38 110 **Aims:**

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41 111 This study aimed to: (1) Quantify differences in prevalence of major CVD risk factors between rural
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43 112 and metropolitan populations, and (2) Determine the number and proportion of rural deaths from
44
45 113 CVD, and specifically from IHD, that could be averted or delayed in rural areas if the levels of risk
46
47 114 factors were equivalent to those in metropolitan Australia.
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51 52 53 116 **METHODS**

54 55 56 117 **The Preventable Risk Integrated Model (PRIME)** 57 58 59 60

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3 118 This study used a macrosimulation model, the Preventable Risk Integrated Model (PRIME)(17), to
4
5 119 estimate age- and sex-specific changes in CVD and IHD mortality that would result from changes to
6
7 120 the population prevalence of risk factors in Australia. An exemption from ethics review was obtained
8
9 121 from Deakin University's Human Research Ethics Unit. PRIME has been used in the UK, New Zealand
10
11 122 and Canada to model a range of risk factor scenarios(17-20). The model can be used to examine the
12
13 123 likely changes in mortality rates of many chronic diseases, including IHD, under different
14
15 124 counterfactual scenarios of population behavioural risk factors(17).

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19 125 The PRIME model is built on a framework of linkage between, 1) modifiable behaviours; 2) clinical
20
21 126 risk factors; and 3) mortality outcomes. This framework is parameterised using the best available
22
23 127 evidence from meta-analyses of published studies, and is described in detail elsewhere(17). PRIME
24
25 128 requires data on prevalence of modifiable risk factors, mortality rates and population estimates by 5
26
27 129 year age groups and sex, for both baseline and counterfactual scenarios. For this study, PRIME was
28
29 130 used to estimate the number of CVD and IHD deaths that would be delayed or averted if those living
30
31 131 in rural Australia had the same modifiable risk factor levels as those living in major cities. The
32
33 132 baseline scenario used the current levels of modifiable risk factors in those living in rural areas, and
34
35 133 the counterfactual scenario involved applying the level of risk factors currently observed in the
36
37 134 metropolitan population. An additional 'best case' scenario was also modelled, by only changing risk
38
39 135 factor levels that were more favourable among those living in metropolitan areas, when compared
40
41 136 to the rural population.

42 43 44 45 137 **Population data**

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48 138 Population size estimates by age, sex and rurality were derived from the 2011 Australian Census.
49
50 139 The 'rural' population was defined as all residents not classified by the ABS as living in major
51
52 140 cities(21). These data were accessed through subscription to the online ABS data program
53
54 141 TableBuilder(22).

55 56 57 142 **Risk factor data**

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2
3 143 The individual modifiable risk factors included in the PRIME model (table 1) were; mean dietary
4
5 144 intakes, alcohol consumption, prevalence of smoking, physical activity levels and mean body mass
6
7 145 index (BMI) scores. All risk factor estimates were obtained from 9973 individuals aged 15 years and
8
9 146 over surveyed for the 2011-12 Australian Health Survey (AHS), which surveyed people from all areas
10
11 147 of Australia, excluding very remote areas(23). Mean values were calculated by age, sex and
12
13 148 remoteness for each risk factor parameter, through the ABS program TableBuilder(22).

149 *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 |

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

151

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

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3 155 basal metabolic rate (BMR) ratio of less than 0.9, as per recommendation from the Australian
4
5 156 Bureau of Statistics(23). Mean daily dietary intakes from the two days of data collection were
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7 157 calculated for each participant for: energy (kcal/day), fruit (g/day), vegetables (g/day), fibre (g/day),
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9 158 dietary cholesterol (mg/day), salt (g/day), total fat (% EI), saturated fat (% EI), monounsaturated fat
10
11 159 (% EI), and polyunsaturated fat (% EI). The percentage of people who consumed less than one serve
12
13
14 160 of fruit and less than one serve of vegetables was also calculated as required by the model. Mean
15
16 161 BMI for the rural population, by 5 year age group and sex, was required by the model, and the effect
17
18 162 of obesity on mortality rates was modelled using the differences in energy intake and physical
19
20 163 activity levels between the two populations. Participants reported if they were current smokers, ex-
21
22 164 smokers, or if they had never smoked, and the age- sex- and location-specific prevalence of each of
23
24 165 these categories were derived.

26
27 166 The PRIME model requires the proportion of the population classified as 'sedentary', and physical
28
29 167 activity levels in the form of mean Metabolic Equivalent of Task (MET) hours per week, in the
30
31 168 remaining (active) population. The sedentary proportion of the population was calculated as the sum
32
33 169 of those classified as insufficiently active or sedentary by the ABS. Participants were classified as
34
35 170 insufficiently active or sedentary if they did not meet the physical activity recommendations of 150
36
37 171 minutes per week, over 5 separate sessions(24). Mean minutes of moderate and vigorous activity
38
39 172 over the last week were used to calculate average daily minutes of activity. This duration was then
40
41 173 multiplied by metabolic equivalents as provided by the ABS, to convert the estimates to MET-hours
42
43 174 of activity per week.

46
47 175 The model requires the percentage of non-drinkers within each population by age and sex, which
48
49 176 was calculated as those who reported either no alcohol consumption, or <1g per day on average,
50
51 177 over the surveyed period. Mean daily intake of pure alcohol in millilitres (mL), by age group and sex,
52
53 178 was calculated as the weighted daily mean (mL) within TableBuilder, then converted to grams of
54
55 179 pure alcohol.
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3 180 **Mortality data**
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5 181 Deaths due to CVD (ICD-10 codes I00-I99) and IHD (ICD-10 code I20-I25) by state or territory and
6
7 182 remoteness area of usual residence, by sex and 5-year age group, among people aged 15 years and
8
9 183 over was provided by the Australian Institute of Health and Welfare (AIHW) for the year 2011 from
10
11 184 the AIHW National Mortality Database (unpublished). These data were provided after an application
12
13 185 for a specific request to the AIHW, and are not publicly available.
14
15

16
17 186 **Mortality gap**
18

19
20 187 The mortality gap between rural and metropolitan areas was calculated by applying the
21
22 188 metropolitan death rate for those aged 15 years and over, to the rural population, to determine the
23
24 189 number of rural deaths that would be expected if cause-specific mortality rates were equal between
25
26 190 metropolitan and rural areas. This figure was subtracted from the actual number of deaths in rural
27
28 191 areas, to calculate the gap in mortality between the two populations.
29
30

31 192 **Uncertainty analysis**
32

33
34 193 The PRIME model has a built in Monte Carlo analysis function to generate 95% credible intervals
35
36 194 around the outputs, which allows for the different distribution of epidemiological parameters (for
37
38 195 example the level of relative risk for a disease outcome for a particular risk factor level) within the
39
40 196 model that have been derived from the literature(17).The intervals produced are based only on the
41
42 197 uncertainty in the model parameters, and not on the variability of the original data used in the
43
44 198 baseline and counterfactual scenarios. Monte Carlo simulation of 10,000 iterations was used to
45
46 199 generate 95% credible intervals for each of the estimates of deaths delayed or averted under the
47
48 200 counterfactual scenario.
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51
52 201 **RESULTS**
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54
55 202 **Differences in individual risk factors between rural and metropolitan areas**
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3 203 There were a mixture of differences in dietary intake, between rural and metropolitan (Table 2), that
4
5 204 were statistically significant for many dietary components, although many were relatively small in
6
7 205 absolute magnitude. Two of the dietary intake levels were more favourable in rural areas, and the
8
9 206 rest were more favourable in metropolitan areas. Vegetable intakes were significantly higher for
10
11 207 rural populations ($p < 0.001$), also resulting in a slightly higher fibre intake, while intake of fruit was
12
13 208 not significantly different between the two populations.

14
15
16 209 Energy intakes and the percentage of energy from saturated fat were significantly higher among
17
18 210 rural populations ($p < 0.05$). Rural females reported a significantly higher dietary cholesterol intake
19
20 211 ($p < 0.05$) and lower percentage energy from polyunsaturated fat ($p < 0.01$) than their metropolitan
21
22 212 counterparts. There were no other significant differences in intake across the other dietary
23
24 213 components analysed.

25
26
27
28 214 Mean alcohol intake (g/day) in those who reported drinking alcohol was significantly higher in rural
29
30 215 areas for females ($p < 0.05$), however there was no differences for males. There were significantly
31
32 216 more current smokers in rural areas compared to major cities (females 19.5% vs 14.0%; males 24.2%
33
34 217 vs 18.7%). The proportion of people who had never smoked was higher in metropolitan areas.

35
36
37 218 Fewer rural people were meeting recommendations for physical activity; 37.1% of males in rural
38
39 219 areas were meeting recommendations compared to 44.0% in major cities. This was also true for
40
41 220 females (36.5% in rural areas, 46.3% in cities). There were no significant differences between the
42
43 221 two populations in the mean MET hours per week of moderate-vigorous activity performed by the
44
45 222 active population.

46
47
48 223 Smoking rates were significantly higher in rural areas for both females and males. Mean BMI for
49
50 224 females was significantly higher ($p < 0.001$) in rural areas compared to major cities (females 26.8 vs
51
52 225 27.6 kg/m²; males 27.3 vs 27.8 kg/m²).

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

| Dietary component | Females | | | | Males | | | |
|----------------------------|---|------------------------------------|-----------------|------------------|----------------------------|------------------------------------|-----------------|------------------|
| | 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) | 0.1 | 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 |

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

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

230 In 2011, 13600 people aged 15 years and over died from CVD in rural areas, with 6846 and 6754
 231 deaths occurring in males and females respectively. In terms of premature deaths, 3137 of these
 232 deaths occurred in those aged under 75 years, 2200 in males, and 915 in females. IHD was the cause
 233 of 7560 deaths, with 2089 deaths occurring in those under 75 years (1636 Males, and 452 females).
 234 In total, 1461 (1107, 1791) or 11% of all rural CVD deaths would be delayed or averted, if rural
 235 populations were to have the same levels of individual risk factors as their metropolitan
 236 counterparts (Table 3). Of the deaths prevented from CVD, 793 (510, 1065) would be from IHD,
 237 slightly more of these among males (418) than females (374), a 10.5% reduction in rural IHD deaths.
 238 Premature IHD deaths (75 years and under), would account for 38.3% of the IHD deaths that would
 239 be delayed or averted, or 4% of all rural IHD deaths. Most of these premature deaths would be
 240 averted for males, 266 (232, 301) compared to 37 (28, 46) in females.

241

242 *Table 3: Deaths averted or delayed from chronic diseases in rural Australia, under the*
 243 *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) |

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

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

250 **Deaths attributable to individual risk factors**

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

259

260 *Table 4: Preventable deaths from CVD and IHD attributable to individual risk factors if*
 261 *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) |

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

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

271 *Table 5: Deaths averted or delayed from chronic diseases in rural Australia, under the 'best case'*
 272 *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) |

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

274

275 **DISCUSSION**

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2
3 276 This analysis showed that more than one third of the IHD mortality inequality between metro and
4
5 277 rural areas can be attributed to differences in individual risk factors, an important consideration for
6
7 278 health policy and intervention planning. Importantly, however, over 60% of the increased mortality
8
9 279 burden in rural areas was unexplained by risk factor differences.
10

11
12 280 The majority of individual risk factors were found to differ between rural and metropolitan areas,
13
14 281 with significantly higher BMI, energy intakes and proportion of energy intake from fats observed in
15
16 282 rural populations, along with higher levels of high risk alcohol consumption and sedentary
17
18 283 behaviour. Rural people did, however, report significantly higher vegetable intakes, which equated
19
20 284 to consumption of approximately 10% more vegetables than their metropolitan counterparts,
21
22 285 consistent with previous health survey data(2).
23

24
25
26 286 The origins of the differences in individual modifiable IHD risk factors between rural and
27
28 287 metropolitan areas(2), are likely to be complex, arising from the interaction of a range of factors at
29
30 288 the individual and community level, including socio-economic disadvantage, education levels, access
31
32 289 to primary health services and health literacy(28). Living outside of metropolitan areas has been
33
34 290 associated with more risk factors for chronic diseases in adults(25), with some evidence that
35
36 291 geographic location should be assessed as a social determinant of health, above and beyond socio-
37
38 292 economic status and area level disadvantage(26). There is evidence for this in that self-reported
39
40 293 prevalence of IHD, diabetes and cerebrovascular disease were found to be similar in rural and
41
42 294 metropolitan areas, despite much higher measured mortality rates from these diseases in rural
43
44 295 areas, potentially revealing reduced health awareness in rural populations(27). This may be an
45
46 296 important contributor to differences in outcomes for rural populations, as lower health literacy has
47
48 297 been linked to poorer outcomes in patients with heart disease(28).
49

50
51
52 298 In terms of individual risk factors, differences in obesity and tobacco smoking appeared to have the
53
54 299 biggest impact on the increased burden of IHD in the rural population, when compared to
55
56 300 metropolitan areas. Obesity is a well-known risk factor for IHD(15), and has been consistently shown
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3 301 to be higher in rural populations of Australia for the past few decades(27, 29). Differences in energy
4
5 302 intake and physical activity energy expenditure between rural and metropolitan populations led to
6
7 303 substantial reductions in obesity-mediated mortality in the counterfactual scenario. These
8
9 304 reductions explained the largest proportion of the mortality gap between the two populations of any
10
11 305 of the behaviours studied. Higher energy intakes in the rural sample, which increase the likelihood
12
13 306 of a higher BMI(30), could be reflective of the consumption of more low cost, energy dense foods
14
15 307 possibly in part, due to reduced access to healthier foods, which has been well documented in rural
16
17 308 and regional areas(31).

20
21 309 The cardio-protective effects of alcohol consumption are often debated(32). Our results showed that
22
23 310 current levels of alcohol intake do not appear to contribute to increased cardiovascular risk for rural
24
25 311 populations, with 55 fewer CVD deaths averted (an increase in deaths overall) as a result of the
26
27 312 difference in consumption between the two populations. This was mainly due to the fact that
28
29 313 although overall intakes were higher in rural areas, intakes among males over 75 years of age were
30
31 314 lower in rural areas than in metro areas, therefore leading to a modelled increase in consumption
32
33 315 and therefore associated deaths in this group under the counterfactual scenario.

36
37 316 Tobacco smoking is recognised as the largest single preventable cause of mortality and morbidity in
38
39 317 Australia(33), and higher smoking rates in rural areas have been apparent since at least 1993(16, 25).
40
41 318 Despite numerous public health initiatives and interventions over this period, the rural smoking rate
42
43 319 has remained comparatively high whilst the metropolitan rate has continued to decline(16, 33),
44
45 320 possibly indicating that such preventative efforts have not adequately reached rural Australians(16).

48
49 321 The results of this study suggest that substantial gains could be made in reducing the CVD mortality
50
51 322 gap between metropolitan and rural populations if modifiable risk factors could be improved in rural
52
53 323 areas. Improving risk factor profiles in rural populations to at least match that of their metropolitan
54
55 324 counterparts could be assumed to be a reasonable target, and is certainly a relatively modest goal,
56
57 325 given that even metropolitan risk factor levels are far from ideal(34, 35). Under the 'best case

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2
3 326 scenario', if only unfavourable risk factors in rural areas were changed, (for example, vegetable
4
5 327 intakes left the same), approximately 200 additional CVD deaths to the counterfactual scenario
6
7 328 could be prevented every year. Targeting the unfavourable risk factors, such as smoking and obesity
8
9 329 in rural people, could be modest and achievable targets for health policy and/or community
10
11 330 interventions in order to reduce the rural death rate to be closer to the levels observed in
12
13 331 metropolitan areas. Importantly, even if the counterfactual risk factor reduction scenario were to be
14
15 332 achieved, a significant proportion (almost two-thirds) of the excess deaths would remain, a finding
16
17 333 which should prompt major reflection on the role of disadvantage, health care provision and other,
18
19 334 less prominent risk factors in the perpetuation of rural health inequalities.
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335

336 Strengths:

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28 337 This study used three routinely collected, representative national datasets, including the Census,
29
30 338 AIHW National Mortality Database and the Australian Health Survey, as inputs for the PRIME model.
31
32 339 These datasets represent the highest quality, and comprehensive population data available currently
33
34 340 for Australia. The use of three robust datasets is required for PRIME to provide accurate disease
35
36 341 outputs. The PRIME model also has many strengths, including that it is able to model the effect of
37
38 342 changes in multiple risk factors simultaneously on mortality rates from different chronic diseases, by
39
40 343 age and sex. The model has been designed using the strongest available scientific evidence on the
41
42 344 links between chronic disease mortality and dietary intake, alcohol consumption, smoking, physical
43
44 345 activity and obesity levels(16).
45
46
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346 Limitations:

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49 347 Data used in the model were self-reported, which carries multiple limitations, and could lead to
50
51 348 underestimations of the level of behavioural risk factors and subsequently, mortality gap reductions
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53 349 (36), although it less likely that these biases would differentially affect rural vs metro populations.
54
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1
2
3 350 Very remote areas of Australia were not sampled in AHS, therefore risk factor levels for these
4
5 351 populations were not included in the analysis(23). This may lead to an underestimation of the
6
7 352 prevalence of some risk factors, as residents of very remote areas are known to experience even
8
9 353 higher burden from IHD than the broader rural population(2), however they also represent a very
10
11 354 small percentage of the total Australian population (0.9%)(25). The uncertainty analysis conducted
12
13 355 on the number of deaths averted, only accounts for uncertainty within the model parameters, but
14
15 356 not the uncertainty of estimates from the Australian Health Survey. Lastly, we were unable to
16
17 357 account for the diversity in characteristics between differing levels of remoteness (e.g. inner regional
18
19 358 areas compared to outer regional or remote areas) due to small population numbers. Instead, it was
20
21 359 necessary to make a single comparison between those living within and outside major cities.
22
23 360 Differences in population characteristics, access to health services and environmental factors can
24
25 361 vary significantly by differing levels of remoteness, and this is an important consideration for policy
26
27 362 and planning when trying to improve health in non-metropolitan areas.
28
29
30

31 **CONCLUSIONS**

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33
34 364 There is potential for improvements in the level of cardiovascular disease burden observed in rural
35
36 365 Australians, if the prevalence of modifiable risk factors such as obesity and smoking were to be
37
38 366 reduced to match those of metropolitan areas. If such a scenario was to be achieved, 38% of the
39
40 367 mortality gap between rural and metropolitan areas could be reduced, however, investigations into
41
42 368 factors responsible for the remaining 62% of this inequality are needed in order to work towards
43
44 369 achieving health equality for rural populations.
45
46
47

48 **Author Contributions**

49
50 371 LA organised access to and analysis of the raw data, completed all data entry into the PRIME model,
51
52 372 analysis of the results, and writing of the manuscript. MN contributed to defining the original
53
54 373 research idea, data collection, use of the PRIME model and analysis. KP and JJ assisted with data
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2
3 374 analysis. SA contributed to defining the original research idea. All authors reviewed and contributed
4
5 375 to the manuscript and all stages of compilation.
6
7

8 376

9
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12
13 379

14
15 380 **Data Sharing Statement**

16
17 381 The PRIME model is available upon request from Dr Peter Scarborough contactable at:

18 382 peter.scarsborough@dph.ox.ac.uk.
19
20

21 383 Population and health survey data were accessed through the Australian Bureau of Statistics

22 384 TableBuilder. The mortality data (ICD deaths by remoteness) were provided by the AIHW under a

23
24 385 specific data request.
25
26 386

27
28 387 **Conflict of Interest declaration**

29 388 The authors declare there are no conflicts of interest
30
31 389

32
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